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Tobacco Free * Japan: Recommendations for Tobacco Control Policy

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Recommendations for Tobacco Control Policy

TOBACCO FREE*JAPAN

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Foreword

Message for “Tobacco Free＊Japan”

SHIGERU OMI

Regional Director
WHO Western Pacific Regional Office

Worldwide, every eight seconds, someone dies from tobacco use. Tobacco use is now responsible for a global total of about 5 million deaths a year, mostly in poor countries and poor populations. The impact of tobacco use in Western Pacific Region countries, including Japan, is particularly disturbing. Every day in the Region almost 3000 people die from tobacco use. Compared to other WHO regions, ours has the most smokers, the highest rates of male smoking, and the fastest increase of smoking uptake among youth and women. In both developed and developing countries within the Region tobacco consumption causes or aggravates chronic diseases that together comprise up to 18% of the total disability-adjusted life years (DALYs) lost, not including the years of healthy life lost by nonsmokers whose health is compromised by exposure to second-hand smoke.

The facts are equally alarming in Japan, home to over 31 million smokers, extremely high rates of male smoking, and where smoking was the leading cause of death for 114 000 people as recently as the year 2000. The percentage of adult male smokers has decreased over the past few years, but young women appear

to be taking up smoking in alarming numbers. Unfortunately, damage from the tobacco epidemic is just starting to be seen in Japan. It has been estimated that lung cancer deaths from smoking in Japan will double or triple by the year 2015. A recent Health, Labour and Welfare Ministry study concluded that smoking causes an estimated 80 000 Japanese men and 8000 Japanese women each year to develop cancer, and that 20% of cancers in Japan are due to smoking. In Japan, as in other countries, tobacco is a major factor increasing the incidence of numerous other cancers, coronary heart disease and cardiovascular disease, emphysema, diabetes, osteoporosis, infertility, miscarriages, low birth weight, sudden infant death syndrome, and impotence, which result in enormous medical care and lost productivity costs to the country.

But we have fixed our sights on a better future. The WHO Framework Convention on Tobacco Control, the world's first tobacco control treaty, was adopted by the World Health Assembly in May 2003, and is now the driving force for the global response to the pandemic of tobacco-induced death and disease. The Convention encourages and requires countries to implement cost-effective tobacco control strategies, such as bans on direct and indirect tobacco advertising, tobacco taxes and price increases, smoke-free environments in public and workplaces, and unmistakable, clear-cut health messages on tobacco packaging.

The World Health Report 2003 emphasized that the Convention provides an unprecedented opportunity for countries to strengthen national tobacco control capacity. But the success of the Convention requires continued political commitment, and the sustained efforts of government agencies, organizations, communities and individuals. As of this writing, Japan and over 100 countries have signed the Convention, signifying their political approval and their intent to become a contracting party. Eleven others have taken the next step and ratified the Convention, establishing their consent to be bound by it. For the Convention to enter into force, it needs to be signed and ratified by at least 40 WHO Member States.

Countries are at a critical point in addressing the tobacco epidemic, and must now make a decision to fight or ignore this global threat. Japan's decision to sign the Convention is a significant step towards controlling the tobacco epidemic, and is a commendable achievement for the officials, organizations and individuals who have dedicated themselves to this very difficult task. There are other encouraging signs of progress—smoke-free policies are now being increasingly implemented, and restrictions on tobacco advertising and promotion have been strengthened.

As in all countries, tobacco control in Japan is an ongoing process. “Tobacco Free ＊ Japan: Recommendations for Tobacco Control Policy” takes the process a large step forward and addresses every major aspect of evidence-based tobacco control: infrastructure, price and tax policy, smoke-free policies, product regulation including packaging and labeling, restrictions on advertising and promotion, support for cessation, youth access to tobacco products, and liability. The Tobacco Free ＊ Japan project has been a unique and innovative approach to establishing evidence-based tobacco control policy in Japan. The report provides a blueprint for action on the WHO Framework Convention on Tobacco Control recommendations, and with the wealth of data provided, should be a critical reference document for policy-makers and researchers.

Japan now has an opportunity to strengthen its national programmes and interregional collaboration to effectively address what is fast becoming the single most preventable cause of early death and chronic disability. This opportunity should not be wasted because too many lives have already been lost, and too many impoverished families have been prevented from improving their lives.

I congratulate the National Institute of Public Health and the many contributors and participants in the Tobacco Free ＊ Japan project. I urge the readers of this report to be inspired and act on the recommendations. I sincerely hope that this report will foster continued progress in Japan, and stimulate further action in the Region and the world in reducing death and disease caused by tobacco use.

May, 2004

Shigeru Omi, M.D., Ph. D.
Regional Director
WHO Regional Office for the Western Pacific

[Note: The Japanese government ratified the Framework Convention on Tobacco Control on June 8, 2004.]

Preface

This report, Tobacco Free ＊ Japan: Recommendations for Tobacco Control Policy, was written to provide a perspective on the state of the tobacco epidemic in Japan, including the burden of disease caused by smoking in Japan, efforts to control the epidemic to date, and a listing of steps that might be taken in the future to control the epidemic. The report places the tobacco epidemic in Japan within the broader context of experience in many other countries that have faced and responded to this same threat to public health. The report comes at a particularly critical time for Japan, in advance of its anticipated signing and ratification of the Framework Convention for Tobacco Control (FCTC). As Japan moves forward to act on the FCTC's tobacco control and research provisions, the recommendations made in Tobacco Free ＊ Japan should prove useful as a starting point for innovative policy development.

Recognizing the importance of tobacco control for Japan's public health, a team of public health researchers, coming from varied institutions, joined together in preparing this report. The report was planned and developed by an editorial team from Japan and the United States with guidance throughout by a distinguished Advisory Panel, that included representatives of medical organizations along with some of Japan's leading experts on tobacco and disease (see Table i for a listing of the Advisory Panel's members). These Advisory Panel's members and their organizations were not asked to formally approve the report and do not necessarily endorse each recommendation that is made, although they are fully supportive of the overall purpose of this report, advancing tobacco control in Japan.

The preparation of the report was led by three editors who coordinated a multidisciplinary team of authors from Japan and the United States (Table ii). The report was prepared by multiple authors, including some of Japan's leading researchers on tobacco and health. The authors prepared initial drafts that were subsequently reviewed and edited by the editorial team.

This report is accompanied by a database that includes findings of major studies on tobacco and health in Japan. The database includes not only bibliographic information but also characteristics of the studies and their principal findings, which have been abstracted according to a standardized protocol. Using the database, evidence tables and figures can be generated or the data can be used for further analysis. This database will be uploaded at the Tobacco Free Japan's website,http//tobaccofree.jp, with a user manual.

The preparation of this report has involved the participation of many additional persons whose contributions merit our gratitude. In Japan, these include Akio Nakamura of Inks, Inc. for intensive direction and management of overall project including product development of this report and the accompanying Instruction Book, Guy Harris of Digital Medical Communications Inc. for scientific editing and coordination, and Fumiko Motegi of Medical Information & Secretary Service for reference management. We would also thank to the following individuals for project assistance; Mie Mori, Takako Morita, Reiko Watanabe and Naoko Tamaki.

From the Institute for Global Tobacco Control, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health in the United States, contributors include Carrie Mattson for project coordination, Erika Avila Tang for database management, Stephen Strathdee for database development, and Charlotte Gerczak for editing and manuscript preparation. We would also like to thank the following individuals for abstracting articles for the database; Nicole Ammerman, Oyelola 'Yomi Faparusi, Manuel Franco, Hope Johnson, Wadih Maalouf, and Khurram Nasir.

In closing, we emphasize again the importance of this moment for tobacco control in Japan and offer our expectation that this report will help to make Japan tobacco free.

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The editors would like to thank our advisory board, comprised of individuals from prestigious and distinguished medical and public health institutions in Japan. Their commitment has been critical to this project and to the future of tobacco control in Japan.

The editors are especially grateful to the authors whose dedication and expertise will help readers all over the world to understand the unique tobacco control situation in Japan. Their conscientious drafting, reviewing, and editing have made this report both comprehensive and powerful.

Introduction to the Report

Worldwide, tobacco use is a leading cause of preventable disease and premature death. For a century, large corporations have manufactured and sold cigarettes, a highly, addictive tobacco product. Today, over 1 billion people smoke. In recent decades, as smoking has declined in developed countries, the multinational tobacco companies have aggressively sought new markets in the developing countries.

In Japan, tobacco smoking is one of the main avoidable causes of disease and death. The majority of men smoke and because Japanese men have smoked increasing numbers of cigarettes across recent decades, the burden of smoking caused disease can be expected to rise. Fortunately, most women in Japan do not smoke; however, smoking is rising in young women who are the target of tobacco advertising and promotion.

Experience in many countries has shown that tobacco use can be reduced by broad strategies that incorporate education, media, regulation, and taxation. Successful implementation of such strategies requires collaboration and linkages among governmental agencies or offices concerned with tobacco control and nongovernmental agencies that can advocate for tobacco control and counter the influence of the tobacco industry. With the adoption of the Framework Convention on Tobacco Control (FCTC) by member states of the World Health Organization (WHO) in May 2003, there is now a global platform for tobacco control and an agreed-to agenda for action.

Although the need for tobacco control in Japan has long been evident, activities have been limited and local, rather than organized and national. Tobacco control may be uniquely difficult in Japan because the Japanese tobacco industry is governed by Japanese government. In fact, the Tobacco Industry Law of 1984 calls for activities that promote the development of tobacco in Japan and tobacco sales provides the government with substantial tax revenues. In sharp contrast, there is presently not an office specifically for tobacco control in the government.

In 2004, Japan is thus at a pivotal point for curbing its epidemic of tobacco use. The majority of men who smoke will need to quit, if the disease epidemic caused by smoking is to be slowed for the short term, and effective prevention is needed for the long term, particularly to assure that smoking does not increase among young women. A variety of strategies proven effective elsewhere could be adopted for Japan and the FCTC offers a framework and an impetus for moving forward.

This report has been prepared in recognition of this critical moment for tobacco control in Japan. The overall purpose is to offer a set of possible tobacco control measures for consideration by policymakers in Japan, as Japan prepares to advance its tobacco control agenda. Most appropriately, this type of report should be prepared by a governmental office for tobacco control, but there is presently not an entity with this charge in Japan. Consequently, authors from several organizations have joined together to produce this report. Their affiliations include: medical and public health organizations in Japan, and the Institute for Global Tobacco Control of the Johns Hopkins Bloomberg School of Public Health in the United States; a distinguished panel of advisors from organizations concerned with tobacco and health have provided guidance and review (see Preface for a listing).

Comprehensive reports on tobacco and health have played a prominent role in advancing tobacco control policies in several countries, including the United States and the United Kingdom. In preparing this report, we have turned to the model offered by the reports of the United States Surgeon General. The first of the Surgeon General's reports on tobacco and health was published in 1964 (DHEW 1964). The landmark report, which reached the conclusion that smoking caused lung cancer in men, offered a model for comprehensive, evidence-based reviews on public health issues. The panel that prepared the report gathered all relevant evidence, evaluated the quality of the evidence, and then weighed the evidence against criteria for causality of associations that remain in use for public health purposes. Subsequent reports have greatly expanded the list of diseases and other adverse health effects caused by smoking.

The finding of causal, adverse effects of active smoking offers a strong impetus for action to reduce smoking. The conclusions reached in the U.S. Surgeon General's reports have been closely tied to policy actions from the outset and other, similar reports have had comparable consequences in other countries. A similar sequence, leading from scientific evidence to action, can be traced for passive smoking as well. The 1986 Surgeon General's report on involuntary smoking (USDHHS 1986) supported a widespread call for smoke-free public places and workplaces; over the nearly two decades since the release of the report, remarkable progress has been made with many municipalities and some states banning smoking in all workplaces.

This report was prepared with a goal of identifying evidence critical to tobacco control planning in Japan, drawing on international literature as well as studies in Japan. Its approach is comparative, drawing "lessons learned" from experience elsewhere that may have applicability in Japan. The concluding chapter offers a listing of approaches meriting consideration as Japan weighs options for reducing the burden of smoking-caused morbidity and mortality.

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Chapter 1 TOBACCO SMOKING

1.1 Tobacco Smoking: a Global View

1.1.1 History of tobacco and the tobacco industry

Tobacco was first used and cultivated by the peoples of the pre-Columbian Americas, primarily for ceremonial and medicinal reasons. Brought to Europe from North America by Christopher Columbus, tobacco quickly became a widely cultivated crop throughout Europe. At the end of the 16th century, tobacco was introduced in Japan by the Portuguese and domestic cultivation of tobacco quickly spread throughout the country. Its leaves were consumed in many ways: as snuff, chewing tobacco, pipe tobacco, cigars, and cigarettes (Lock et al. 1998; Winter 2001). Tobacco use in the form of cigarettes was relatively small compared to the other forms until the late 19th century when the first automatic cigarette-making machine was developed and the first large cigarette manufacturing company was started in the United States by James “Buck” Duke. By the early 20th century, his American Tobacco Company had captured more than 90 percent of the world's sales. The introduction of the cigarette dramatically changed smoking habits in Western Europe, the Americas and Japan. In 1911, Duke's company was broken up under the Sherman Anti-Trust Act in the United States, which prohibited the formation of monopolies. The dissolution of the American Tobacco Company lead to the emergence of American Tobacco Co., R.J. Reynolds, Liggett and Myers Tobacco Company, Lorillard, and British-American Tobacco.

From its beginnings, the cigarette industry has been notable for its centralization. Large companies have dominated the global markets and many countries, such as Japan, have had national, state-owned companies, and, in some instances, monopolies. Indeed, in 1904 in Japan, tobacco leaf processing and sale

were brought under government control as a national monopoly. Not until 1985 was the monopoly turned into a private company, Japan Tobacco Inc. (hereafter JT). However, the government still owns a half of JT's company shares

Tobacco all over the world is big business: tobacco can be produced relatively inexpensively, making revenues from cigarette sales substantial. Governments further profit by taxes on cigarettes, which can be incremented without substantially reducing purchases by addicted smokers. In recent decades, large multinational companies, challenged by declining western markets, have expanded to the developing world, particularly countries in Asia, to find new customers. The companies have aggressively partnered with national companies and used their well-honed marketing tactics to capture market share. In addition to China National Tobacco, the world's largest companies now include Philip Morris, British American Tobacco, and JT.

1.1.2 The global epidemic of tobacco use

With the introduction of the manufactured cigarette in the early 20th century, global tobacco consumption has risen steadily. While tobacco consumption has been decreasing in some regions of the world, it is rapidly increasing in others; overall, global tobacco consumption is on the rise, along with tobacco-related deaths. Today there are an estimated 1.1 billion smokers (Jha and Chaloupka 1999). By 2025 it is estimated that there will be 1.6 billion smokers. The death toll will have risen from 4 million in the year 2000 to 10 million by 2030 (Peto and Lopez 2003). The overall increase in consumption is driven largely by two factors: population increase and tobacco industry marketing and advertising in low-income countries.

Tobacco-related disease, morbidity, and mortality have created a global epidemic that is moving from the developed countries to the less developed countries. The World Health Organization (WHO) has identified four stages of the tobacco epidemic. The paradigm allows health officials and policymakers to see where their country is currently located in relation to the larger pandemic and to better predict future smoking prevalence and associated tobacco-related morbidity and mortality (Figure 1.1) (Lopez et al. 1994). The four stages are characterized as:

Stage 1: Smoking prevalence in men below 20%; very low prevalence in women.

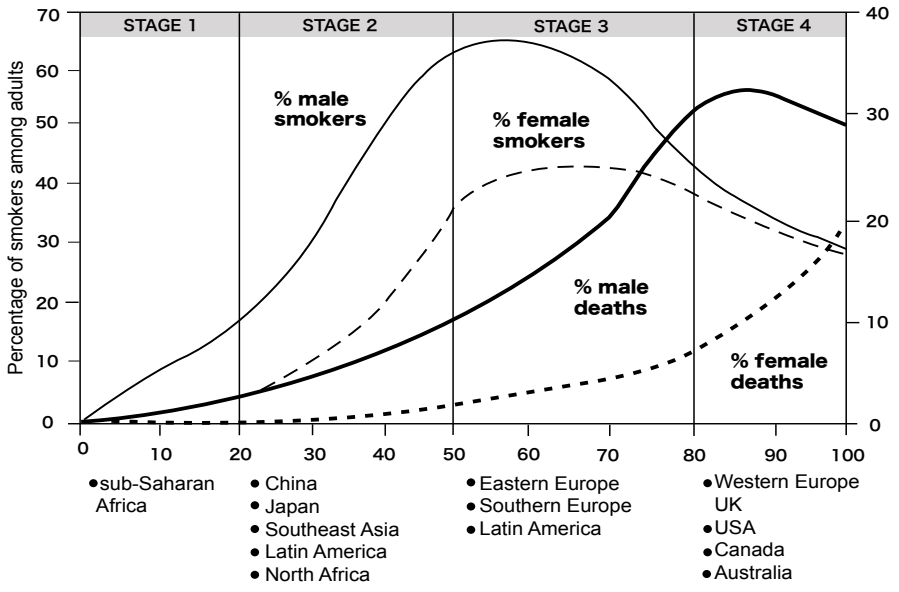
Stage 2: Smoking prevalence in men above 50%; increase in prevalence in women.

Stage 3: Reduced smoking prevalence in men; gradual decrease in prevalence in women; increase in smoking-related disease and mortality.

Stage 4: Reduced prevalence in men and women; deaths attributable

to smoking peak to 40-45% of deaths in middle aged men; deaths attributable smoking in women increase to 20-25% of all deaths.

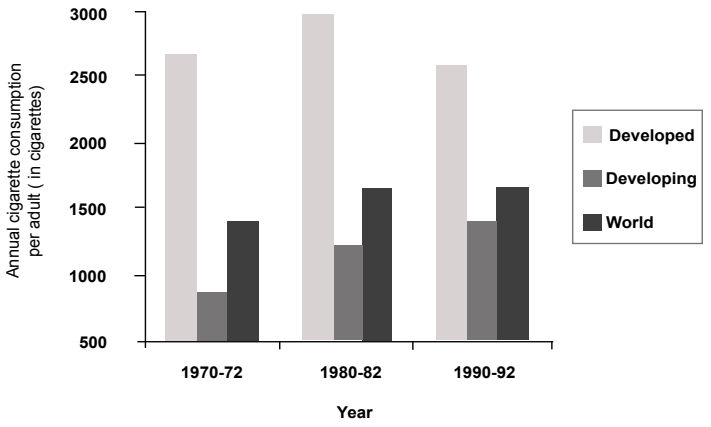
Figure 1.1 Four Stages of the Tobacco Epidemic



Source: Lopez et al. 1994

Japan, along with China, Southeast Asia, and Latin America is currently in Stage 2 of the epidemic. Thus, Japan will bear the health impacts of smoking for many decades to come. As shown in Figure 1.1, although the pandemic is lessening in severity in some developed countries, it is just beginning to erupt in less developed regions of Southeast Asia and Latin America (Lopez et al. 1994). The burden of the epidemic is therefore shifting to countries that are less prepared to manage the epidemic, as they lack national tobacco control infrastructure and a sufficient level of economic development to be able to direct resources towards tobacco control. In addition, the burden of disease is shifting from men in high-income countries to women in high-income countries, as well as to men in low-income countries. Figure 1.2 (WHO 1997) depicts the increasing trend in *per capita* adult cigarette consumption in developed and developing countries. During the same period that smoking decreased in higher-income countries, it increased in low-income countries.

Figure 1.2. Trends in *per capita* Adult Cigarette Consumption



Source: World Health Organization 1997

Table 1.1 shows regional patterns of smoking by both men and women (WHO 1997). Low- to middle- income countries comprise 82% of the world's smokers who will ultimately be forced to bear the catastrophic economic consequences related to tobacco related health care costs. Important also to note is that Table 1.1 shows the disparate rates of smoking prevalence in male and female populations in some regions. Tobacco advertising is increasingly targeting women as the tobacco industry sees tobacco use by women as a means to offset the global decline in male smoking prevalence. Asian women are a particularly critical target for the tobacco industry, given their large numbers and their presently low prevalence of smoking (Samet and Yoon 2001).

Table 1.1 Regional Patterns of Smoking: Estimated Smoking Prevalence by Gender and Number of Smokers in Populations Aged 15 and Above,by World Bank Region,1995

World Bank Region	Smoking prevalence			Total smokers (millions)	(% of all smokers)
	Males	Females	Overall		
East Asia and Pacific	59	4	32	401	35
Eastern Europe & Central Asia	59	26	41	143	13
Latin America & Caribbean	40	21	30	95	8
Middle East & North Africa	44	5	25	40	3
South Asia (cigarettes)	20	1	11	86	8
South Asia (bidis)	20	3	12	96	8
Sub-Saharan Africa	33	10	21	67	6
Low/Middle Income	49	9	29	933	82
High Income	39	22	30	209	18
World	47	12	29	1,142	100

Note: Numbers have been rounded.
Source: World Health Organization 1997

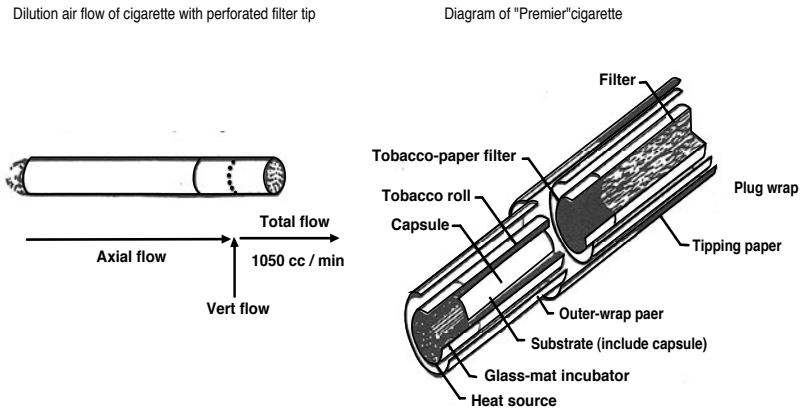
1.1.3 The cigarette as a product and a nicotine delivery system

The cigarette is a highly engineered and manipulated product designed to deliver nicotine to the smoker. Cigarettes cannot be considered as simple agricultural products as 10% of the cigarette is comprised of chemicals and other additives. Manufacturers know that people smoke to obtain the desirable pharmacological effects of nicotine. Because of this, manufacturers manipulate levels of nicotine through various tobacco grades, cultivation, additives, filter design, and other methods. The cigarette is not only tailored to meet consumer tastes and needs but is also designed to fall within permissible limits of tar and nicotine when measured by machine-measured cigarette test methods, such as the Federal Trade Commission (FTC) method and the International Organization Standardization (ISO) method (WHO 2001).

1.1.3.1 What is a cigarette?

Figure 1.3 (Hoffmann and Hoffmann 1997) outlines the basic components of a cigarette. Typically, a cigarette is composed of tobacco leaf and stem that have been conditioned and cured by the addition of chemicals and additives (reconstituted tobacco). A single cigarette may contain up to 150 additives used to enhance flavor and to control nicotine delivery (WHO 2001). A cigarette may include a filter with ventilation holes designed to modify the level of nicotine and tar received by the smoker.

Figure 1.3 Technologies of Modern Cigarettes



Source: Hoffmann et al. 1997

1.1.3.2 Controlling nicotine levels

Nicotine is recognized by the tobacco industry as being the "primary pharmacological agent in cigarette smoke." Industry documents reveal that cigarette manufacturers know that the most critical ingredient in tobacco is nicotine and that a certain level of nicotine from each cigarette is necessary to sustain addiction. A tobacco industry executive testified, "While it is apparent that the manufacturers of cigarettes view themselves as being in a business where nicotine is the primary product, their principal mission is to deliver it to humans. They are in the nicotine delivery business. Clearly this dictates that they develop technologies and strategies to control and manipulate nicotine release from the delivery device (WHO 2001)." Indeed, the industry has done extensive research on the optimal level of nicotine and on how to deliver adequate levels of nicotine while at the same time registering low tar and nicotine levels when measured by the FTC test machines (WHO 2001). Cigarette manufacturers control and manipulate the level of nicotine using some of the following key ways.

Cultivation

Tobacco plants can be cultivated in such a way to increase nicotine levels. One such method is to cut a portion of the plant early in the harvesting cycle so that as the remaining plant continues to grow it has an increased amount of nicotine in the roots and the leaves.

Reconstituted tobacco

Reconstituted tobacco is a combination of tobacco leaves and tobacco stems, which are typically high in nicotine and harsh in taste. Reconstituted sheet tobacco is a cheap filler paper used by most major tobacco companies to control burn rates and adjust tar and nicotine levels.

Ammonia additive technology

Ammonia is an additive used to increase the pH of cigarette smoke. The addition of ammonia increases the availability of free or unbound nicotine, thereby making nicotine more biologically available and increasing the speed at which nicotine reaches the smoker. Cigarettes that use both ammonia technology and reconstituted tobacco have nearly 50 percent higher nicotine delivery than cigarettes made of tobacco leaf only (Liberty Science Center 2003).

Filters

Filters and filter ventilation holes are designed to dilute the amount of smoke a smoker receives, thereby reducing the amount of nicotine and tar. However, the tobacco industry knows that smokers often cover or block the filter

ventilation holes with their fingers in order to receive the desired amount of nicotine. Thus, filtered cigarettes when machine measured will yield low tar and nicotine levels but these levels are often underestimated and inconsistent with the actual intake of a smoker.

1.1.3.3 Cigarette testing methods

In the 1960s, in response to changes in the cigarette, the FTC developed a standardized testing protocol for assessing tar, nicotine, and carbon monoxide yields, most commonly known as the FTC method. The FTC method was developed with the intention of providing smokers with a meaningful, comparable and consistent way of ranking levels of tar and nicotine from different cigarettes. Testing is performed by machines that are calibrated to take one puff of 2-second duration and 35-mL volume every minute. Cigarettes are smoked to a butt length of 23 mm. This protocol is based on observations of smokers dating well back into the 20th century. A total of 100 cigarettes of a particular brand and type are smoked by the machine to produce an official tar, nicotine, and carbon monoxide rating (Pillsbury 1996).

The FTC method provides a uniform protocol for comparing different brands with each other and can be easily replicated in different laboratories. In its original or in a modified format, it is in use around the world. While it does allow smokers to compare machine-measured yields of tar and nicotine of different brands, its results have now been shown to be of little direct relevance to human smoking. The FTC method does not reflect current human smoking patterns as smokers tend to alter their smoking behavior to obtain the desired amount of nicotine from each puff, especially when smoking low-tar or low-nicotine brands. This is often described as compensatory smoking behavior, characterized by taking larger puff volumes, more frequent puffs, inhaling more deeply, blocking filter vents, or smoking more cigarettes per day. These dynamic aspects of smoking are not captured by the static FTC protocol. On the issue of compensatory smoking behavior, one industry expert said:

> "The delivery of any cigarette will depend on the way in which it is smoked. The term compensation is used to describe the tendency for a smoker to obtain a similar delivery, intake and uptake of smoke constituents on a daily basis, from a variety of products with differing standard (machine-smoked) deliveries... Smokers have been found to be unsatisfied by nicotine-low or free cigarettes and will modify their smoking pattern in order to regulate their nicotine intake." (WHO 2001).

Many smokers switching from higher- to lower-yield products will adopt several of these compensatory behaviors simultaneously and will maintain these

behaviors for as long as they continue to smoke lower-yield cigarettes. Thus, a smoker engaging in compensatory smoking behavior can increase his or her intake several times above the FTC measured predicted yields—a desirable outcome for maintaining nicotine addiction. Several published studies, including studies funded by the tobacco industry, show little relationship between biomarkers for smoke components and tar and nicotine yield as measured by the FTC protocol (Yach and Bialous 2001).

In Japan, the Tobacco Institute of Japan (TIOJ), a tobacco industry group, is authorized to measure tar and nicotine content and to verify values as stated on cigarette packs sold in Japan. The TIOJ uses the International Organization for Standardization (ISO) standards for tobacco and tobacco products (ISO 1991) to measure tar and nicotine yields. The ISO is an alternative protocol for determining tar and nicotine yield, but does no better in estimating biologically relevant doses than the FTC method. In fact, there are only slight differences between the ISO and the FTC methods, with both using a smoking machine to derive a ranking of tar and nicotine yield across different brands of cigarettes. Both the ISO and FTC methods were developed based on scientific evidence and recommendations provided by the Cooperative Centre for Scientific Research Relative to Tobacco (CORESTA), a tobacco research organization whose membership is dominated by the tobacco industry (Yach and Bialous 2001). Neither the FTC nor the ISO methods for determining tar and nicotine yield are based on scientific studies of human smoking behavior (WHO 2001). As such, these methods provide smokers with inaccurate predictive values for assessing the health risks of different products and are offered as a foundation for using misleading labels, such as 'light.'

Recognizing the limitations of the FTC and ISO test methods, alternative protocols have been developed by Canada and Massachusetts state. The Canadian method aims to provide smokers with more meaningful values to estimate levels of toxicity. The Canada method mandates that all tobacco products provide a comprehensive listing of all toxic constituents and all ingredients in the product (including whole tobacco, filter paper, tube, and additives). Under this protocol all tobacco emissions are tested, both mainstream and sidestream smoke, to provide a list of all toxic and carcinogenic emissions such as tobacco-specific nitrosamines, aromatic amines, phenolics, etc (WHO 2001). The Massachusetts testing method aims to better replicate actual smoking conditions and reflect compensation techniques by increasing the amount of smoke inhaled with each puff by the smoking machine (puff volume), reducing the amount of time between puffs (puff interval), and requiring that 50% of the cigarette ventilation holes in the filter be covered. By adjusting the smoking machine's parameters to those that more accurately reflect human smoking conditions and adjusting for compensatory behavior, the Massachusetts testing for nicotine yield produces numbers twice as

high as those found by the FTC method (American Cancer Society 2003).

1.1.4 Changes in product design and marketing of cigarettes

1.1.4.1 Industry manipulation of product design

The 1950s saw the emergence of scientific evidence undisputedly linking smoking with lung cancer and other adverse health effects. Responding to the public's increased concern about the dangers of smoking, and fearful of reduced sales, the tobacco industry began manufacturing and marketing cigarettes with lower machine-measured yields of nicotine and tar and touted these as a form of 'health protection.' New cigarette brands, with labels such as 'Mild,' 'Light,' and 'Ultra Light' steadily became more and more prevalent in the market. Since the late 1950s, the use of filter, reduced tar, and low-yield nicotine cigarette products has increased significantly, and in most countries, few people smoke unfiltered cigarettes similar to those used up through the 1950s. Lower machine-measured emissions of tar and nicotine were accomplished by product engineering by the tobacco industry, most notably through the use of highly efficient filter tips, filter tip ventilation, reconstituted tobacco, and porous cigarette paper (Hoffmann et al. 1996). Specific design features such as filter ventilation, use of reconstituted tobacco, and ammonia additive technology interact with smoking behavior (puff volume/puff interval) to produce low yields of tar and nicotine when measured by cigarette testing machines but result in higher yields by the smoker (Kozlowski et al. 2001). Consequently, despite the many changes in the packaging, design, and labeling of various cigarette brands, the disease risks from smoking these products have not changed (USDHHS 2004).

1.1.4.2 Marketing of low-yield cigarettes

Despite the industry's knowledge that cigarettes with low machine-measured yields of tar and nicotine may have no real impact on biological exposure, they aggressively marketed these new products as a form of 'health protection.' One brand's advertising read: “filter gives greater protection against nicotine and tars than any other cigarette on the market today” (WHO 2001). Another brand advertised the 'Magic of the Filter Tip' even though the manufacturer increased the amount of tar by 40% and nicotine by 70% after the filter had been introduced (WHO 2001).

The tobacco industry's advertising worked: over the decades, smokers have gradually shifted their cigarette product choice, unwittingly believing that low-yield varieties were less risky. By 1979, 91.7% of Americans used filter-tipped cigarettes compared with 1.4% in the early 1950s. Mild Seven, launched

in Japan in 1977, has since become the most popular brand in the country. And in the market today is a proliferation of low-yield cigarette brands labeled 'Light,' 'Ultra Light,' 'Mild,' and 'Medium' which the industry uses to shape consumers' perceptions of their health risks.

1.1.4.3 Cigarette labeling, product choice, and the FCTC

Categorizations of 'Light,' 'Ultra Light,' and 'Mild' cigarettes are loosely based on the FTC machine-measured protocols. The labeling of various cigarette brands as low-tar and low-nicotine have little value for the smoker as the levels of actual intake and exposure will vary from smoker to smoker. Because smokers tend to engage in compensatory behaviors when smoking low-yield products, the FTC rating can severely underestimate the amount of actual exposure of a smoker. Thus, these labels provide misleading guidance on actual intake and associated health risks. Studies conducted to explain the motives for switching to 'Light' or 'Mild' cigarettes consistently show that smokers believe that these products are somehow less harmful to health. Consumers who choose these varieties over higher-yield tar and nicotine brands do so because they are concerned about their health and/or interested in trying to quit.

The labeling of cigarettes as 'Light,' 'Ultra Light,' or 'Mild' inherently deceives the consumer into thinking that these products are less harmful. Most importantly, smokers may switch to these brands rather than undergo serious quit attempts. The Parties to the Framework Convention for Tobacco Control (FCTC) acknowledge that labeling of cigarette products can be misleading, and to that effect bind governments to implement effective measures to ensure that:

> "····tobacco product packaging and labeling do not promote a tobacco product by any means that are false, misleading, deceptive or likely to create an erroneous impression about its characteristics, health effects, hazards or emissions, including any term, descriptor, trademark, figurative or any other sign that directly or indirectly creates the false impression that a particular tobacco product is less harmful than other tobacco products. These may include terms such as 'low tar,' 'light,' 'ultra-light,' or 'mild.'"

1.1.5 No safe cigarette

As the manufacturing of cigarettes changed after the 1950s, the US Congress issued a directive to convene a working group to study the relative health effects of varying levels of tar, nicotine, and cigarette additives. The conclusions of this working group are summarized in the 1981 Surgeon General's Report entitled, "The Health Consequences of Smoking: The Changing Cigarette."

The report unequivocally concludes that the search for a less hazardous cigarette has not yielded a product which can be considered as 'safe' (USDHHS 1981). While the report concedes that there may be some harm reduction when a smoker switches to lower-yield cigarettes, the health benefits are small. More importantly, the report cautions smokers to not turn to these lower-yield products as a 'safer' alternative and forgo smoking cessation, for which there is a proven reduction in health risks. Important recommendations from the report include: the promotion of broad-based programs aimed at smoking cessation programs and smoking initiation; the need to monitor changes in cigarette composition and product design and their impacts on health; the requirement of the tobacco industry to completely disclose cigarette ingredients and additives; and the necessity of stronger health warnings on tobacco products.

This historical overview of smoking provides a brief background of the global expansion of the tobacco industry, the rise in smoking, and the subsequent rise in smoking-related all cause mortality. This section is meant to set the stage for subsequent chapters on health effects and tobacco control measures.

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1.2 Tobacco Smoking in Japan

1.2.1. Historical background and current picture of tobacco in Japan

1.2.1.1 The evolution of cigarettes in Japan

Tobacco was introduced into Japan from Portugal at the end of the 16th century. Domestic cultivation of tobacco began as the custom of smoking spread. In time, smoking became a symbol of scoundrels and ruffians, leading the shogunate of the Edo period (17th to mid-19th century) to prohibit both the growth and use of tobacco. Smoking and cultivation nonetheless continued, spreading widely among the people and rendering the prohibition ineffective during the end of 17th century.

The characteristic Japanese method of smoking finely-cut tobacco in long-stemmed, thimble-bowled pipes known as *kiseru* is also believed to date from approximately the same era. In the years after 1868 (Meiji era), when Japan once again became open to cultural input from other parts of the world, new kinds of tobacco products were imported from abroad and their popularity rapidly spread. In particular, the introduction of cigarettes dramatically changed Japanese smoking habits.

The domestic tobacco industry flourished as never before. In 1904, the Meiji-era government, recognizing the value of tobacco as a potential source of revenue, brought tobacco leaf processing and sale under government control as a national monopoly. In spite of a general shortage of goods, the smoking rate among male adults increased during World War II because tobacco was distributed to soldiers. In 1985, the monopoly was reestablished as a private company, Japan Tobacco Inc. (hereafter JT), and two years later, the importation and distribution of

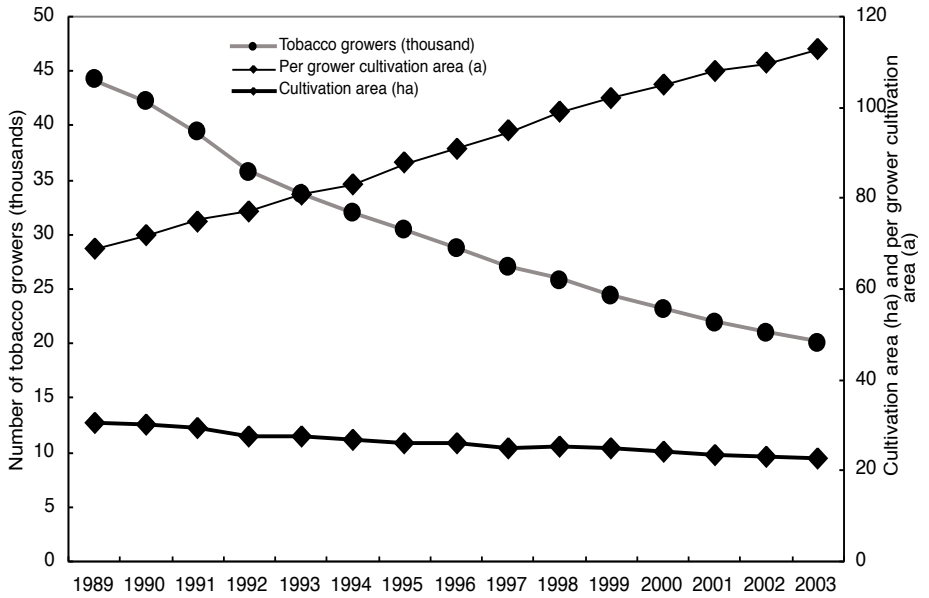
foreign tobacco were liberalized.

To date, most data on the cultivation of tobacco, tobacco products and smoking prevalence in Japan have been provided by JT. Data from a nationwide survey on smoking conducted in 1999 by the Ministry of Health, Labour and Welfare (MHLW) have also been published (MHLW 2000).

1.2.1.2 Tobacco agriculture, manufacture and sales

Tobacco leaf has been cultivated in 42 of the 47 prefectures of Japan, from Aomori in the north to Okinawa in the south. The number of farmers who cultivate tobacco and the total area under cultivation have decreased in the last 15 years, but cultivation area per farmer has increased (cultivation area/farmer engaged in tobacco production) (Figure 1.4). All domestically produced leaf tobacco is purchased by JT, at a price of 1,600-2,500 yen/kg ($15.20-23.80; $1=105 yen) in 2002.

Figure 1.4 Trends in the Number of Tobacco Growers, Cultivation Area, and Per Grower Cultivation Area in Japan



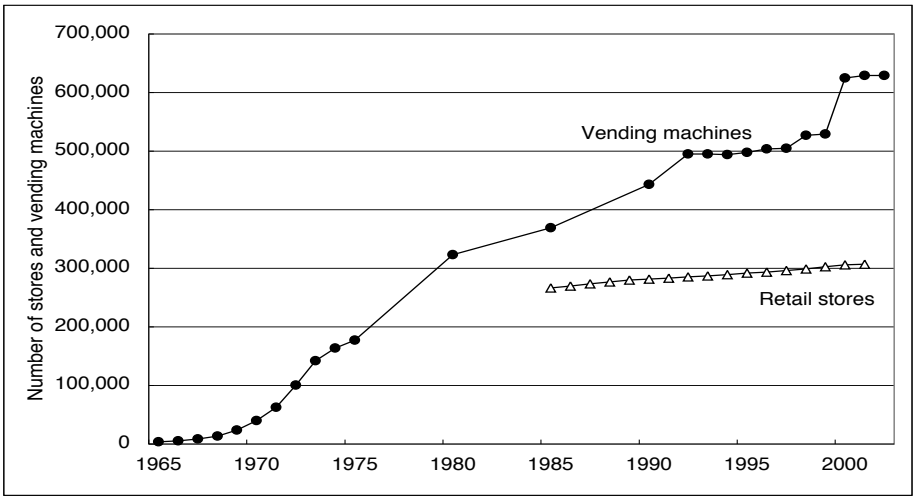
Source: Data from the Japan Tobacco Growers Association (http://www.jtga.or.jp)

Advertising expenses for tobacco products were 26.8 billion yen in fiscal 1998. Expenditure has more recently trended down, to 23.7 billion yen in 1999, 23.1 billion yen in 2000 and 17.8 billion yen in 2001. The proportion of advertising expenses to total sales in 2001 was 0.65%.

Japanese smokers purchase their cigarettes mainly from vending machines, convenience stores and tobacconist shops. The number of cigarette

vending machines increased rapidly during 1970s and 1980s, and more steadily since the early 1990s, reaching over 600,000 in 2000. The number of cigarette retail stores has also gradually increased to about 300,000 (Figure 1.5).

Figure 1.5 Trends in the Number of Vending Machines and Retail Stores in Japan



Source: Data from the Japan Vending Machine Manufactures Association (http://www.jvma.or.jp)

1.2.1.3 Self-regulation of the sale of cigarettes

In 1996, the tobacco retail industry instituted a program to stop sales from cigarette vending machines at night (from 11 pm to 5 am). It extended this self-regulation to cover all vending machines in 1998, and in 2003 introduced new machines that prevent sales to minors through the use of personal IC identification cards. These are scheduled to replace all current machines by 2008. Additional self-regulation came in April 1998 with a permanent moratorium on commercial television advertising before 10:54 pm Further, since 1985, the industry has refrained from advertising in magazines aimed at minors (although the definition of magazines for minors is left ambiguous).

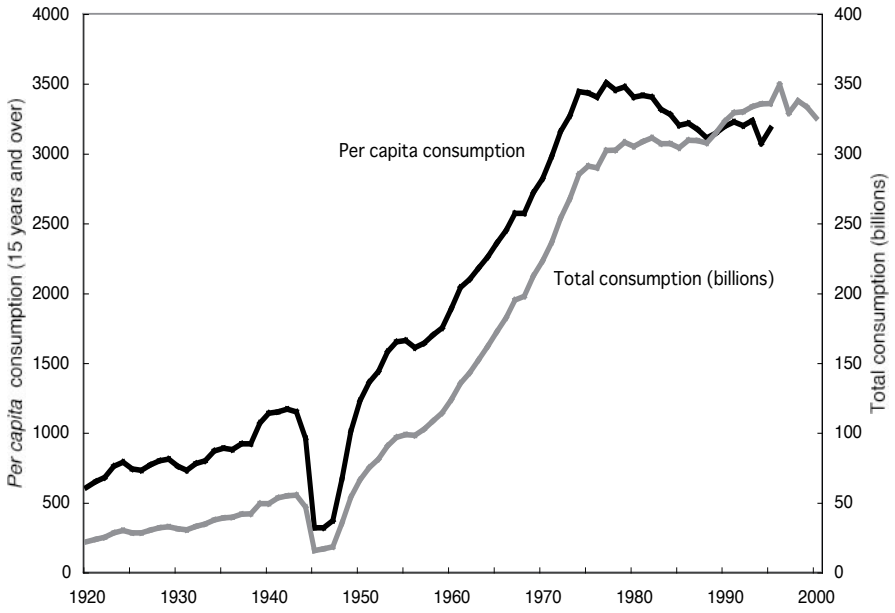
Information on self-regulation is available from the home pages of the Japan Vending Machine Manufacturers Association (http://www.jvma.or.jp/) and JT (http://www.jti.co.jp/JTI/tobacco/index.html).

1.2.1.4 Sales of tobacco products

From 1920 until about 1943 the per adult consumption of manufactured cigarettes increased slowly from 2 to 3 cigarettes per day. Daily consumption decreased sharply towards the end of World War II, but thereafter resumed its increase until the late 1970s when it reached a peak of nearly 10

cigarettes before decreasing to 9 cigarettes by the 1990s. Echoing this trend, the consumption of all tobacco products per adult was about 4 g per day from 1920 to 1944, dropping to 2 g in 1945, then increasing after the war to nearly 10 g by the late 1970s. Consumption then decreased to 9 g per adult per day by 1984, after which estimates cannot be made. Since 1920 almost all tobacco has been consumed in the form of cigarettes, with negligible consumption of other products. In 1925, 54% of tobacco was consumed in manufactured cigarettes and 46% in hand-rolled cigarettes. Since the 1970s virtually all tobacco has been consumed as manufactured filtered cigarettes. The total sales of cigarettes and per capita cigarette consumption increased steadily after World War II until 1975. Sales then continued to increase but with a gentler slope until about 1998, whereas per capita cigarette consumption decreased (Figure 1.6).

Figure 1.6 Trends in Total and *per capita* Cigarette Consumption in Japan



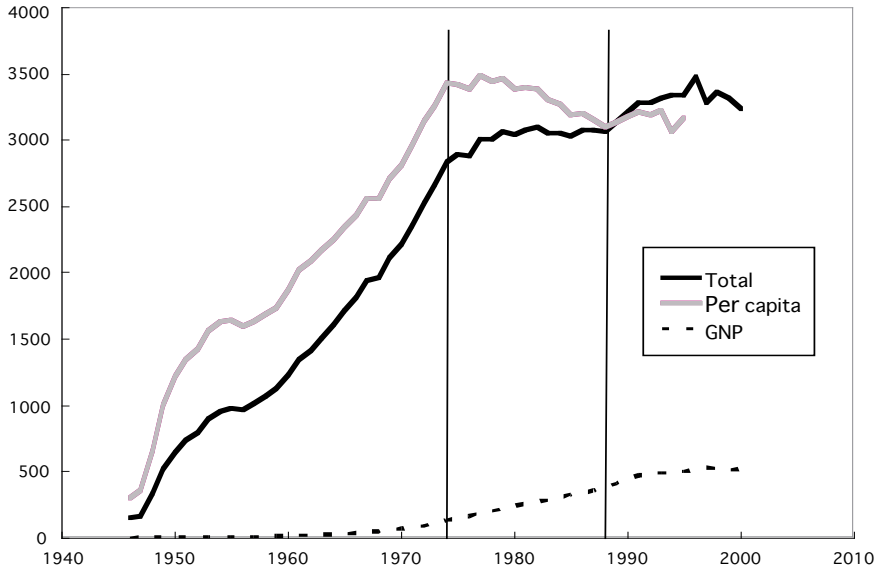
Source: Foundation for Health Promotion and Fitmess (http://www.health-net.or.jp/tobacco/product/pd070000.html)

JT sold a total of 229 billion cigarettes in 2002, a decline from 1998. In contrast, foreign brands sold 83.6 billion that year (from a base of near-zero when the market opened in 1986), giving total sales in 2002 of 312.6 billion, a slight decrease from 1998. As the market share of foreign brands has increased, to 26.7% in 2002, JT has developed its own international tobacco business, and in 2002 exported 207.8 billion cigarettes to a number of countries in Asia, the Middle East, Africa and Russia. Total domestic sales through vending machines were 19,766.5 billion yen in 2002, corresponding to 28.3% of total sales.

1.2.2 Trend in tobacco consumption in Japan

Current risks associated with smoking in Japan largely reflect smoking in the decades since World War II, during which cigarette consumption quickly accelerated. Visual assessment of these data suggests three different periods, as indicated by patterns of total sales and per capita consumption (Figure 1.7. See Figure 1.6 for the pattern extending to the pre-War era). The first period began right after the war and continued until around 1974, during which total sales as well as per capita consumption both dramatically increased in parallel with rapid economic growth. The second period began in the mid-1970s and lasted until 1988, when total sales appeared to plateau and per capita consumption decreased somewhat. Subsequent to 1988 and seemingly continuing to the present, both total sales and per capita consumption have increased again, although far more slowly than during the 1950s and 1960s. Analysis of these temporal trends can provide insights into factors determining cigarette consumption in Japan. Factors potentially influencing these changes are now considered.

Figure 1.7 Post-war Growth in Cigarette Consumption and GNP in Japan

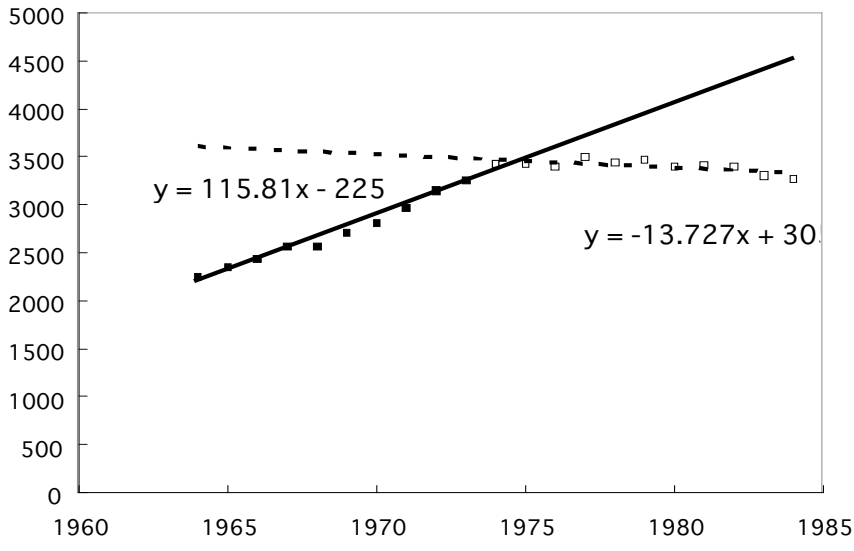


The slowing of tobacco consumption in the early 1970s may partially reflect a number of economic factors, including global and national economic conditions and cigarette costs. In 1973, the so-called 'Oil Shock' brought a sudden economic crisis to Japan and many other countries. Economic growth slowed and even reversed. This slowing led to price increases for many goods and services, including tobacco, which had been hitherto supported by the government. What caused cigarette consumption to slow in 1975? The answer appears to be the approximately 50% increase in tobacco price consequent to changes in

governmental financing. Curiously, this increase in price and its impact on tobacco consumption do not seem to have been widely discussed, possibly because it is only one of many societal changes happening around that time.

The changes in price were substantial. In 1974, when a total of 287 billion cigarettes were sold, 'hi-lite' was the leading brand, with a 27% market share, followed by 'Seven Stars' (20%), 'Cherry' (15%) and 'Hope' (10%). For these major brands, the price per single cigarette was raised from 4 to 6 yen for 'hi-lite', and from 5 to 7.5 yen for 'Seven Stars', 'Cherry' and 'Hope', an approximately 50% increase on average. Annual per capita consumption stopped increasing at this time. By linear regression, consumption decreased by 13 cigarettes per year after 1975, after having increased by an estimated 116 cigarettes per year previously when cigarettes were relatively inexpensive (Figure 1.8). In fact, the cost of cigarettes as a percentage of total household expenditure decreased from 3.8% in 1950 to 1.8% in 1974 (Ministry of Finance 1976). Cigarettes in that year cost 80 to 100 yen per pack for major brands, in sharp contrast to prices in other counties: 216 yen (308 yen/dollar) per pack in the United States ('Winston', 'Kent'), 152 yen (69 yen/franc) in France ('Gitanes'), 271 to 307 yen (118 yen/mark) in West Germany (domestic brands), and 200 to 288 yen (625 yen/pound) in the United Kingdom (domestic brands).

Figure 1.8 Sizable Change in per capita Cigarette Consumption in 1975 in Japan

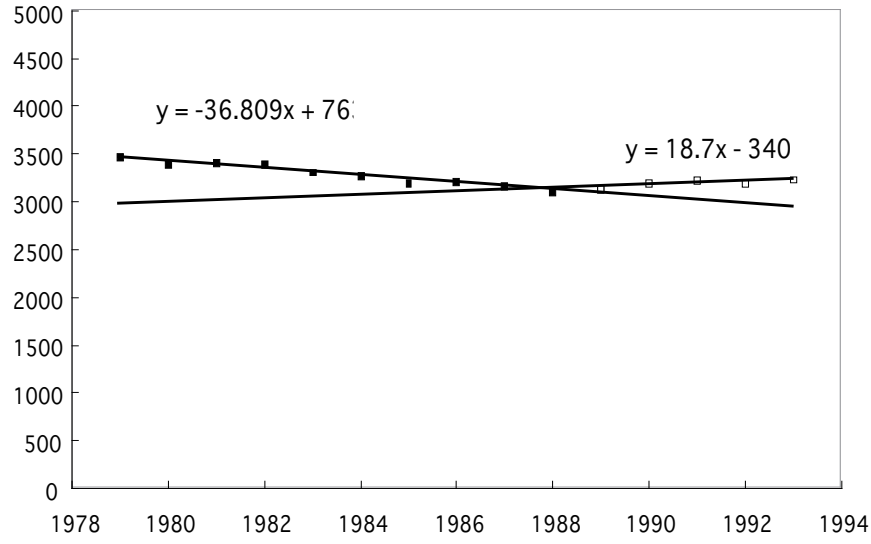


The decision to increase the price was made by the Ministry of Finance (remembering that all cigarettes were produced by the government at that time). An explicit rationale cannot be found, although the harmful health effects of tobacco had of course been well documented overseas by that time. Earlier, in

1972, the Ministry of Finance had placed the first warning labels on cigarettes sold in Japan, as described in the postscript to this volume (Levin 2004), but this did not slow the rise in consumption. Importantly, the experience of the 1970s shows that cigarette consumption in Japan is responsive to price, as the 1975 price increase was followed by declining consumption for the next 10 years (Figure 1.7). Figure 1.8 shows two regression lines that further describe the change in consumption. The solid line gives the time trend of change up to 1975 and the dotted line, the trend after 1975. Comparison of the two regression lines shows that *per capita* consumption changed from an increase of 116 cigarettes a year to a decrease of 14 cigarettes, a net change of 130 cigarettes or an approximately 3.8% annual decrease in relation to the *per capita* annual consumption of 3,432 cigarettes in 1975. This drop indicates the potential for reducing tobacco consumption through price increases in Japan.

Several factors are likely to have been involved in the increase in consumption which began in the late 1980s (Figure 1.9). In 1985, the Ministry of Finance decided to privatize the Japan Tobacco and Salt Public Corporation (JTSPC) and change its name to Japan Tobacco Inc. (JT). This was followed by the abolition of the tariff on imported tobacco in 1987. At the same time, and after a long silence, Japan began to develop its first initiatives in tobacco control, with the Ministry of Health and Welfare issuing its first white paper on smoking and health to coincide with the Sixth World Conference on Smoking and Health, held in Tokyo in 1987. In 1988, the public movement toward a tobacco-free society seemed to accelerate. The First World No Tobacco Day Symposium was held in Tokyo in 1989 and in the same year JT undertook a series of voluntary restrictions on TV advertising. In spite of these encouraging steps, however, tobacco consumption began to rise, even as the economy entered a long recession.

Figure 1.9 Change in *per capita* Cigarette Consumption in 1989 in Japan



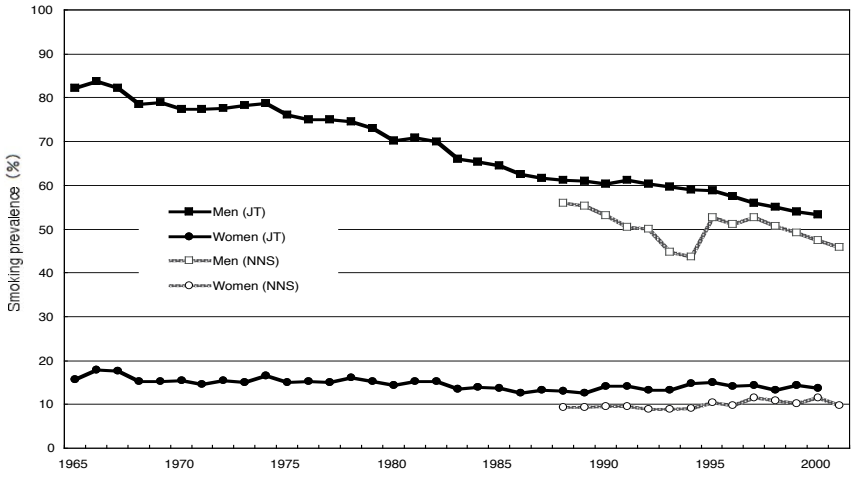
Why did consumption rise at the same time that tobacco control began and the economy slowed? Only speculation can be offered, centered largely on the increasing aggressiveness of JT, now a private company. JT strengthened its marketing efforts to counteract public pressure to reduce tobacco consumption. Internal company documents show that it tried to expand its business via an integrated corporate strategy (JT 2003). Tobacco sales could be strengthened by three distinct efforts: the power of products, the power of advertising, and the power of marketing. To overcome the reduced effectiveness of its advertising brought on by the voluntary restrictions, JT seems to have redirected efforts towards strengthening the power of its marketing. Part of this effort involved the deployment of marketing managers to individual retail stores throughout the country.

1.2.3 Smoking prevalence in Japan

1.2.3.1 Temporal trends in smoking

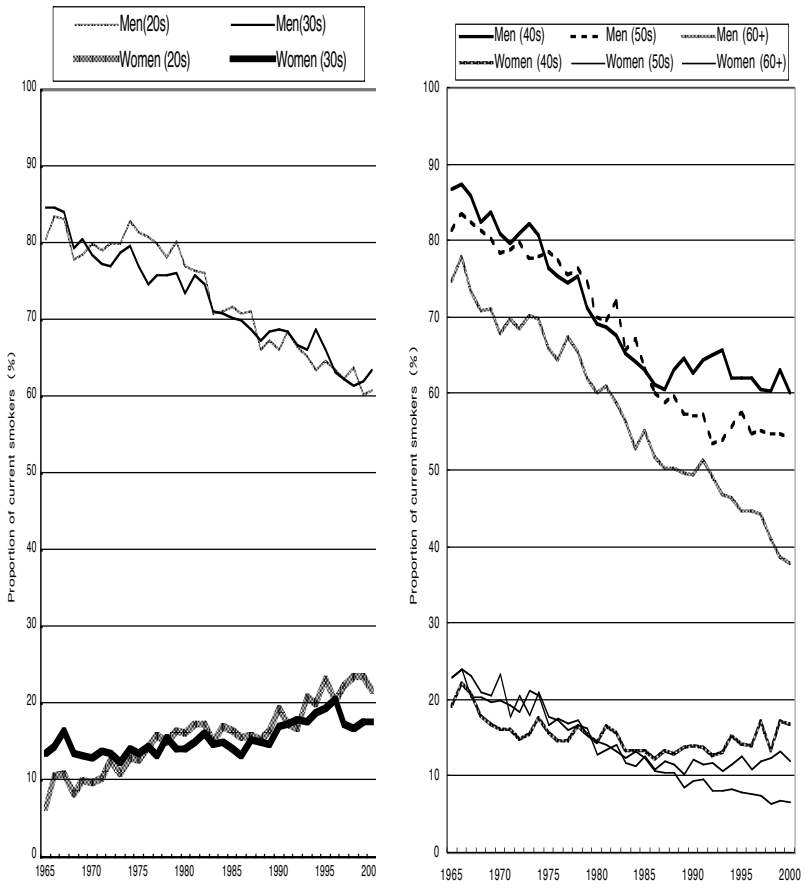
JT has monitored the adult smoking rate since 1965. In that year, prevalence among men was 82.3% (http://www.jti.co.jp/JTI/tobacco/index.html). It has since gradually decreased, reaching 50% in the 1990s and continuing down to 49.1% in 2002. The Ministry of Health, Labour and Welfare has monitored adult smoking prevalence since 1986 as part of its National Nutrition Survey. The results show lower prevalence than the JT survey, with respective ratio for adult men from 1998 to 2001 of 50.8%, 49.2%, 47.4% and 45.9% vs. 55.2%, 54.0%, 53.5% and 52.0% in the JT survey (Figures 1.10, 1.11).

Figure 1.10 Trend in Smoking Prevalence by Survey



Source: Data from MHLW and JT

Figure 1.11 Trend in Smoking Prevalence by Gender and Age Group



Source: Data from JT

Among adult women, smoking prevalence in 1965 was 15.7%, increasing to 17-18% in 1966-67 and then decreasing slightly to stabilize at around 13-14% during the 1990s. Viewed by age group, however, prevalence reveals tremendous changes, with rates increasing steadily among women in their twenties and thirties but decreasing in those aged 60 years or older. Data from the National Nutrition Survey do not describe any particular trend in smoking rate among women, but prevalence was again lower than in the JT survey. For example, prevalence rates from 1998 to 2001 were 13.3%, 14.5%, 13.7% and 14.7% in the JT survey, but only 10.9%, 10.3%, 11.5% and 9.9% in the National Nutrition Survey.

The methods used in these two surveys may have limitations, and the details of the sampling method and survey procedure used in the JT survey have not been disclosed. Further, the response rate in the National Nutrition Survey has not been reported.

1.2.3.2 Current picture of smoking

In 1999, the Ministry of Health and Welfare (MHW) conducted the first nationwide survey on smoking behavior in Japan (MHW 1999). The survey was well-designed and its methods were well-described. Smoking prevalence among men was 52.8%. By age, the highest rate was 62.1% among those aged 30-39, followed by 60.0% at 40-49 and 57.9% at 20-29. Among those aged over 40, prevalence decreased with age, being 51.6% at 50-59, 46.8% at 60-69, and 30.8% at 70 years and older. With regard to the age at which smoking was begun, 55.5% of current male smokers smoked their first cigarettes while still minors. Among current smokers, those smoking 11-20 cigarettes per day were the most prevalent (51.8%), followed by 21-30 (19.6%) and 1-10 (14.9%). The number of cigarettes smoked per day increased with age to a peak in the fifties, after which it decreased. Inquiry showed that 24.8% of current male smokers answered "I would like to quit smoking", while the proportion reached 63.1% when the response "I would like to reduce the number of cigarettes smoked" was included.

The data from the 1999 Ministry of Health and Welfare Survey for women showed a smoking prevalence of 13.4% (Table 1.2). The age group-specific rate was highest at 23.2% among women in their twenties, followed by 19.8% at 30-39 years and 15.5% at 40-49 years. This decreasing tendency with age continued: rates were 10.1% at 50-59, 7.2% at 60-69, and 5.0% at 70 years and over. As for the age at which smoking was begun, 44.1% of current female smokers smoked their first cigarettes when still minors. Among current smokers, those smoking 11-20 cigarettes per day were most prevalent, (46.4%), followed by 1-10 (42.7%) and 21-30 (8.2%). No remarkable tendency in the number of cigarettes smoked was observed in women smokers by age. Inquiry showed that 34.9% of current female smokers answered "I would like to quit smoking", with this proportion reaching 69.6% when the response of "I would like to reduce the number of cigarettes smoked" was included.

Table 1.2 Smoking Prevalence (%) in Japan, National Survey on Smoking and Health, 1999

	Age (years)					
	20-29	30-39	40-49	50-59	60-69	70+
Men	57.90%	62.1	60	51.6	46.8	30.8
Women	23.20%	19.8	15.5	10.1	7.2	5

Source: MHW 1999

According to the 1999 national survey, 47% of current smokers and 49.9% of ex-smokers smoked their first cigarettes as minors (under 20 years of age) (Table 1.3). Age at becoming a regular smoker among current smokers was

less than 20 (41.5%) or 20-29 years (53.3%). A total of 55.5% of current male smokers started smoking as minors, and 41.6% of current male smokers became regular smokers as minors (Table 1.4). Further, 44.1% of current female smokers started smoking as minors, and 35.3% became regular smokers as minors.

Table 1.3 Age Distribution (%) of First Smoking Experience among Current Smokers, National Survey on Smoking and Health, 1999

	Age at which smoking was first tried						
	under 12	12-14	15-17	18,19	20-29	30+	Total
Men	2	6.3	20.5	26.7	43.1	1.4	100
Women	1.4	5.6	14.7	22.4	45.2	10.7	100

Note: Legal smoking age is 20. Underage smoking is prohibited by law.
Source: MHW 1999

Table 1.4 Age Distribution (%) of Initiation of Regular Smoking among Current Smokers, National Survey on Smoking and Health, 1999

	Age at which regular smoking was initiated				
	-19	20-29	30-39	40-49	50+
Men	41.6	54.9	2.6	0.6	0.2
Women	35.3	49.2	9.6	4.1	1.8

Note: From response to the question "At what age did you become a regular smoker?"
Source: MHW 1999

The proportion of people in the 1999 national survey who reported that they are frequently subjected to passive smoking was very high (Table 1.5). When questioned, 45.5% of respondents answered "I am subject to passive smoking at home sometimes or almost every day", and 56.4% of men answered "I am subject to passive smoking at my workplace or school sometimes or almost every day". For men, 38.7% reported that passive smoking was a regular experience at home, and 72.1% reported it was common at the workplace or school.

Table 1.5 Prevalence (%) of Daily Exposure to Second Hand Smoke by Setting, National Survey on Smoking and Health, 1999

	Setting				
	Home	Workplace or school	Restaurant	Amusement center	Other
Men	38.7	72.1	58.9	29.9	35.1
Women	50.9	40.3	39.4	10	29.8

Note: From response to the question "How often are you exposed to others' smoking in the following settings?" (every day, sometimes, never, no chance to visit)
Source: MHW 1999

To determine the level of passive smoking, the survey measured cotinine concentration in the saliva of the non-smokers. A dose-response relationship by frequency of passive smoking at home, workplace or school, restaurant, and amusement facility was observed. For example, in the case of passive smoking in

the home, the proportion of non-smokers with saliva cotinine levels of 5 ng/ml or more was 21.6% for people subject to passive smoking almost every day, 14.9% for those subject to it sometimes, and 10.9% for people not subject to passive smoking. Respective ratios in the case of passive smoking in the workplace or school were 17.2%, 12.3% and 10.2%. For women, 50.9% reported that passive smoking at home was a regular experience, this ratio being higher than that for men. Further, 40.3% reported regular passive smoking in the workplace or school, which was lower than among men.

On questioning, 24.8% of current male smokers answered "I would like to quit smoking," and 38.3% answered "I would like to reduce the number of cigarettes I smoke." (Table 1.6). The respective ratios for current female smokers were 34.9% and 34.7%, the former being higher than that among men.

Table 1.6 Prevalence (%) of Willingness to Quit among Current Smokers in Japan, National Survey on Smoking and Health, 1999

	Willingness to quit			
	Want to quit	Want to reduce no. of cigarettes smoked	Don't want to quit	Not sure
Men	24.8	38.3	26.8	10.1
Women	34.9	34.7	17.5	12.9

Source: MHW 1999

1.2.3.3 Smoking by children

Two nationwide surveys on smoking behavior among Japanese junior and senior high school students have been conducted, in 1996 (Osaki et al. 2003) and 2000 (Osaki et al. 2004) (Table 1.7). Experimentation rate, current smoking rate (smoking on at least one of the preceding 30 days), and daily smoking rate (smoking on each of the preceding 30 days) increased with school grade in both sexes. Smoking prevalence among boys was higher than among girls. Comparison of these two surveys showed that smoking experimentation rate decreased among junior high school boys, while current and daily smoking rate increased slightly among girls. An increase in the number of cigarettes smoked per day was observed, but a downward shift in the age of first smoking experience was seen.

Table 1.7 Smoking Prevalence (%) among Japanese High School Students ,1996 and 2000

	High school	Grade	Experimenters		Current smokers		Daily smokers	
			1996	2000	1996	2000	1996	2000
Boys	Junior	1	29.9	22.5	7.5	5.9	0.7	0.5
		2	35.1	28	10.8	8.2	1.9	1.9
		3	38.7	35.4	14.4	14	4.6	5.2
	Senior	1	47.7	45	24.7	24.3	10.8	12.4
		2	52.6	51.3	31	29.5	18.3	18
		3	55.6	55.7	36.9	36.9	25.4	25.9
Girls	Junior	1	16.7	16	3.8	4.2	0.4	0.4
		2	20.4	20.5	5.4	5.7	0.7	1
		3	22.7	23.5	5.5	6.9	1	1.8
	Senior	1	29.2	30.6	9.2	10.9	2.4	3
		2	33.6	34.2	13.3	13	4.5	5.3
		3	38.5	36.7	15.6	15.8	7.1	8.2

Note: Experimenters, students who had tried smoking at least once
Current smokers, students who smoked ≥1 day of the 30 days preceding the survey
Daily smokers, students who smoked every day of the 30 preceding the survey
Source: Osaki et al. 2003, 2004

1.2.3.4 Smoking by special populations

Smoking prevalence among physician members of the Japan Medical Association was surveyed in 2000 (Ohida et al. 2001). The prevalence of cigarette smoking among physicians was 27.1% for men and 6.8% for women, about half the age-adjusted prevalence rates among the general Japanese population. Smoking prevalence among female nurses in national hospitals in Japan was 18.6% (Ohida et al. 1999a). Prevalence among nurses in Mie Prefecture, including nurses working in private clinics, public hospitals and private hospitals, was 75.5% for men and 14.6% for women (Ohida et al. 1999b). Prevalence among teachers at public schools in Mie Prefecture was 44.7% for men and 3.1% for women (Ohida et al. 2000).

Notwithstanding the importance of research into smoking behavior among minority groups, there are no scientific papers on this subject in Japan. In the near future, surveys are planned on smoking behavior in Ainu (an ethnic minority), foreign people living in Japan, people of lower socioeconomic status, people in isolated islands including Okinawa, people in distinct communities and others.

1.2.3.5 Prevalence of tobacco dependence

The distribution of values in screening for tobacco dependence syndrome in current and ex-smokers shows a higher ratio of people with high dependency among current smokers than among ex-smokers (MHW 1999). Further, the earlier they became regular smokers, the greater was the ratio of

people with high dependency. From these results, 53.9% of current smokers were determined on screening as having tobacco dependence syndrome. In other words, the number of people among all Japanese aged 15 and over with tobacco dependency according to the WHO International Classification of Injuries and Diseases (5 or more points on tobacco dependency screening) is estimated at 18 million.

1.2.4 Characteristics of Japanese cigarettes

1.2.4.1 Tobacco and additives

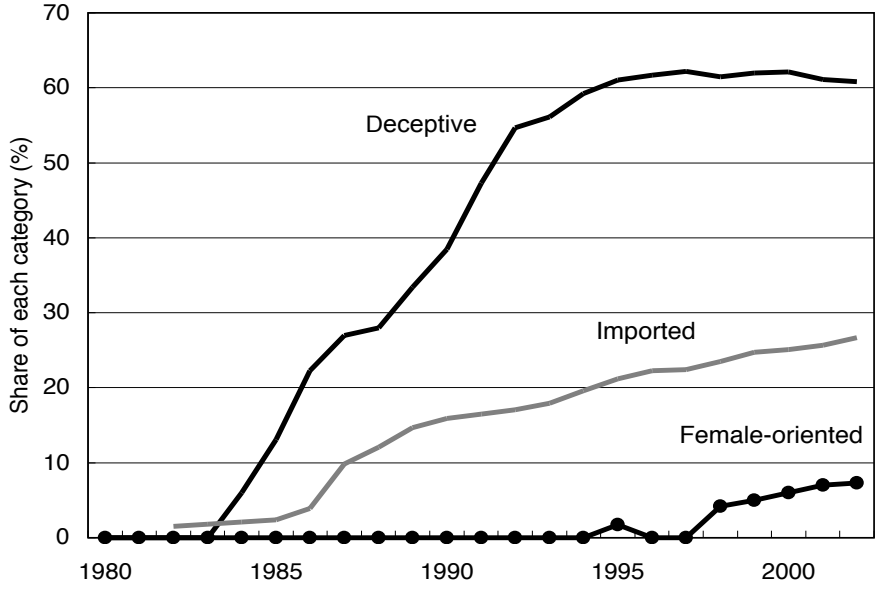
Many additives, both natural and synthetic, are added to cigarettes to enhance flavor and prevent desiccation. Various books and articles mention figures indicating that cigarettes contain any of up to several hundred types of additives but, since JT has not disclosed this information, it is not possible to know the details of any additive used, in terms of either nature or quantity (Ministry of Health and Welfare 1998).

1.2.4.2 General design

The first Japanese style of tobacco product was the *kiseru*, the small pipes mentioned above. The *kiseru* period lasted about 300 years. The first cigarette without a filter was produced in 1873, in the Meiji era, and was made from paper and one kind of tobacco leaf only. In 1888, a new type of cigarette containing spices (but still no filter) was produced. Filters were subsequently added to meet consumer preference for a lighter tasting tobacco. The first such filtered brand was 'Hope,' marketed in 1957. Beginning around 1965, cigarettes containing a blend of several types of tobacco leaf were introduced, and the development of lighter tasting cigarettes proceeded in step with progress in filter technology. Recently, a new type of cigarette which produces almost no smoke or ash has been developed; this maintains flavor without burning the leaf through the use of a special type of charcoal on the top end of the cigarette. A second recent type uses rolled paper made from components of tobacco leaf to decrease side-stream smoke, while a third reduces the smell of tobacco by using special flavors.

The market share of cigarettes branded with descriptors deceptively conveying an impression of lesser risk, such as 'light' or 'mild,' increased from 1985 to 1995, while the share of brands with words targeted towards women such as 'menthol' or 'slim' increased after 1999 (Figure 1.12). The market share of imported brands has steadily increased since 1987, when the market was opened to them.

Figure 1.12 Share of Brands with Deceptive Descriptors and Female-oriented Descriptors among the Top 10 or 20 Brands by Sales in Japan



Note: Deceptive descriptors means 'light' or 'mild' in the brand name. Female-oriented descriptors means 'menthol' or 'slim' in the brand name.
Source: Tobacco and Salt Newspaper 1995, 1998-2002

1.2.4.3 Types of filters and ventilation

The first brand of cigarette with a filter, 'Hope,' was launched in 1957, and the first with a charcoal filter, 'Seven Stars,' was marketed in 1969. Cigarettes marketed by JT are classified into four types according to filter characteristics, namely those with single-material filters, charcoal filters, menthol filters, and those without filters. Types of filter include plain filters (single layer of acetate), dual filters (double layer of acetate + charcoal and acetate), triple filters (triple layer of acetate, charcoal and acetate), and recessed filters (single layer of acetate and a cavity). Recently, JT produced a new cigarette with a filter that is biodegradable and decomposes naturally.

Some brands of cigarette have a ventilated filter. The filter has columns of small holes which decrease the combustion qualities of the cigarette and maintain combustion temperature, leading to a decrease in the production of carbon monoxide. Usually, however, smokers of this type block the holes with their fingers and lips, leading to the inhalation of more nicotine, tar and carbon monoxide levels than the rated values on the cigarette package. As a consequence, ventilated filters do not contribute to reducing nicotine, tar and carbon monoxide in the smoke inhaled by the smoker.

1.2.4.4 Smoke components

In 2000, the Ministry of Health, Labour and Welfare asked a Canadian laboratory (Labstat International Inc.) to analyze components of the mainstream and sidestream smoke of the seven major cigarette brands produced in Japan and sent 13 cartons of each for analysis. The analyses were conducted according to the methods of Health Canada.

The mainstream smoke contained nicotine, CO, tar, formaldehyde, acetaldehyde, acetone, acrolein, propionaldehyde, crotonaldehyde, methylethylketone, butyraldehyde, benzopyrene, NO, NOx, hydrogen cyanide, ammonia, 1,3-butadiene, isoprene, acrylonitrile, benzene, toluene, N-nitrosonornicotine, 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone, N-nitrosoanatabine, and N-nitrosoanabasine.

Table 1.8 Difference in Testing Methods for 'Standard' and 'Average' Regimens

	Standard	Average
Amount of smoke per puff	35 ml	45 ml
Duration of puffs	60 sec	30 sec
Inhalation time	2 sec	2 sec
Ventilation holes on the filter	open	half closed

To investigate tar and nicotine levels, the laboratory adopted two examination methods, those of the Canadian Ministry of Health and the Massachusetts Department of Health in the USA. To analyze mainstream smoke, two conditions were applied, a 'standard' and an 'average' condition. Side-stream smoke was analyzed according to the 'standard' condition only. The characteristics of these two methods are listed below (Table 1.8). Quantities of nicotine and tar listed on the cigarette pack are measured using the former (standard) method, but it is the latter (average) method which is closer to actual smoking conditions.

1.2.4.5 Changing yields

A trend has been evident over recent years of a decrease in the sales-weighted values of tar and nicotine given on cigarette packaging. Whether these reflect actual values, however, cannot be determined easily. In market share by brand, 12 of the top 20 (and 9 of the top 10) include the words 'mild,' 'light,' 'extra light,' 'ultra mild' or 'super light' in their name. The proportion of top 10 brands

marketed as lower yield has in fact increased: ratios were 20% in 1983, 40% in 1985 and 60% in 1990.

1.2.4.6 Relationship of machine yield to actual dose

Among Japanese brands, machine-measured tar and nicotine yields (ISO conditions; rated value on the cigarette package) were much lower than those measured under actual conditions (i.e. conditions reflecting actual smoking behavior). Mainstream smoke analysis under 'standard' conditions gave respective per cigarette ranges for nicotine, tar and CO of 0.12-1.44 mg, 1.44-16.3 mg and 2.02-14.7 mg. Respective values under 'average' (i.e. actual) conditions, however, were 0.48-2.66 mg, 6.65-31.4 mg and 10.3-24.4 mg, and thus much higher than standard conditions. With regard to side-stream smoke, respective per cigarette values for nicotine, tar, and CO under standard conditions were 3.54-5.79 mg, 19.1-25.6 mg and 43.2-51.1 mg. Concentrations of other components in sidestream smoke were also much higher than in mainstream.

1.2.5 Summary

The data on smoking rates in Japan are mixed with regard to implications for tobacco control. For adults, smoking prevalence among men has steadily decreased, whereas that among young women (20-39 years of age) is showing a tendency to increase. For adolescents, smoking prevalence among senior high school boys has reached a level similar to that in western countries, whereas that among girls is lower than in western countries, although still slightly increasing. The still relatively high smoking prevalence among medical professionals also needs to be addressed, as this is an opportunity to offer a smoke-free role model.

The market share of brands with 'light' or 'mild' in their brand name has increased. The test method used leads to the underestimation of actual tar and nicotine doses to smokers. The number of cigarette vending machines has increased and now exceeds 600,000.

A further national survey on smoking behavior in Japan is needed. This should be followed by an ongoing series of periodic surveys and smoking among key groups, particulary youths of both sexes and young women, needs to be closely tracked. The addition of biomarkers of dose, particularly cotinine, would be useful. Evidence will guide the development of countermeasures to reduce total cigarette consumption in Japan.

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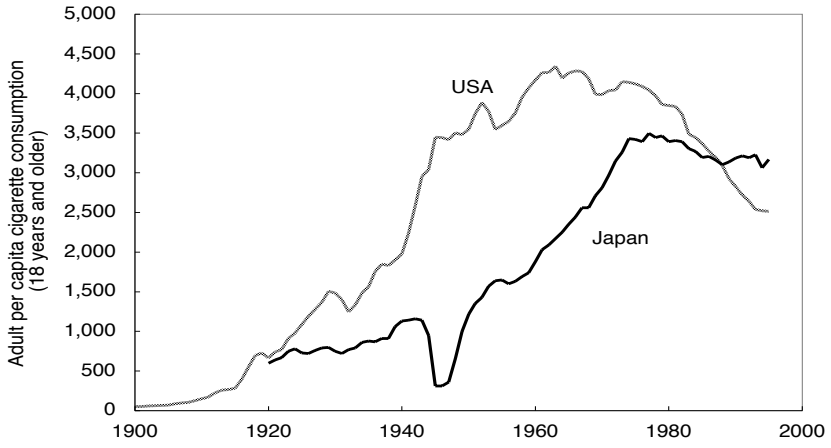
1.3 Tobacco in Japan and Other Countries: Brief Comparisons

1.3.1 Tobacco consumption

Although tobacco was first introduced into Japan in the 16th century, the current nationwide tobacco epidemic started in the 1950s after World War II. This contrasts with the situation in the US and many European countries, which began to experience epidemics of tobacco use in the 1920s, after World War I, approximately 30 years earlier than Japan. For example, *per capita* cigarette consumption in the US reached 3,000 cigarettes per year in 1940s, whereas that in Japan did not reach this level until the 1970s, as shown in Figure 1.13. This difference in timing is central in comparing the situation in Japan to other countries. As discussed later in this chapter, the chronic health effects of smoking in Japan began with a time lag of approximately 30 years.

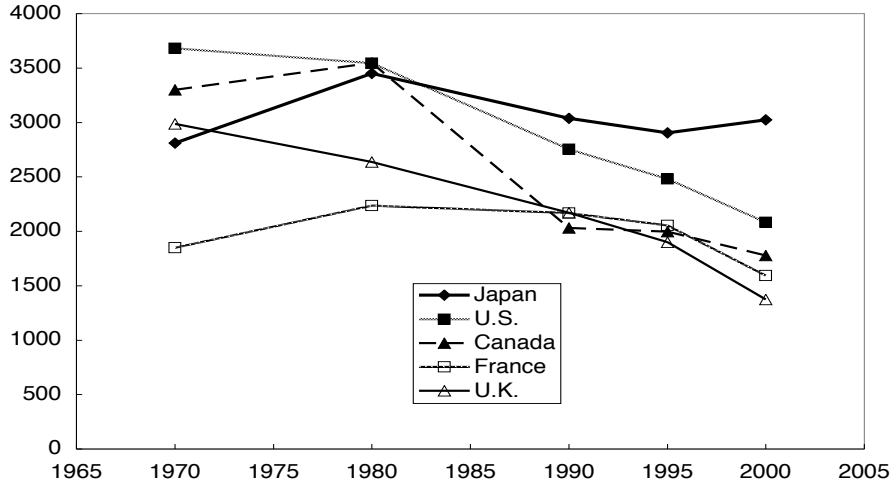
Figure 1.13 Comparison of *per capita* Cigarette Consumption in Japan and the USA



Source: USDHHS 2000, Japanese data is available from Foundation for Health Promotion and Fitness (http://www.health-net.or.jp/tobacco/product/qd070000.htm)

The time trend in *per capita* cigarette consumption from 1970 to 2000 is illustrated in Figure 1.14 for Japan, the United States, Canada, France and the United Kingdom. While the other four countries successfully reduced *per capita* consumption, for example, to 1,374 cigarettes in the United Kingdom and to 2,082 in the United States, *per capita* consumption in Japan remains at the much higher level of 3,023. There is even an increase after 1995. Thus, while other countries have enjoyed at least some success in combating the tobacco epidemic, Japan has not yet realized a decrease in consumption. The underlying differences in tobacco control policy are discussed in the policy chapter of this report.

Figure 1.14 Comparison of *per capita* Tobacco Consumption in Different Countries



1.3.2 Filters, yield, and cigarette types

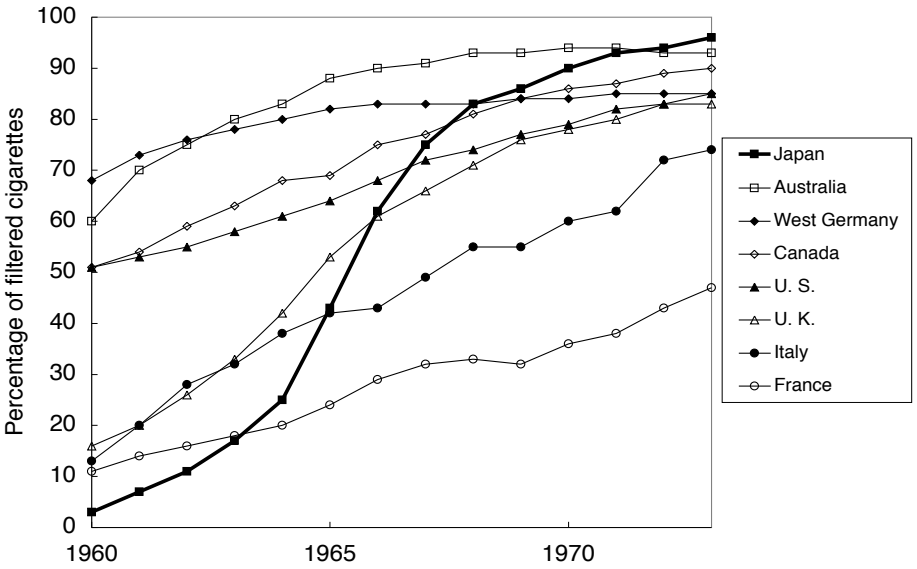
As detailed in section 1.1, the cigarette is a highly engineered product. Various techniques are used to ensure the efficient delivery of nicotine to the smoker, including filter design and additives. Since Japan Tobacco's brands dominate the Japanese market (69.2% in 2000), the cigarettes smoked by Japanese may differ from those in other countries with regard to the yield of nicotine and tar, and to the contents of other substances, including additives. The magnitude and character of the health risks faced by Japanese smokers may likewise differ to those in other countries.

1.3.2.1 Filters

Although the first filtered cigarette brand, 'Hope,' was introduced into the Japanese market as early as 1957, the share of filtered cigarettes began to increase rather late. The increase in market share of filtered cigarettes from 1960 to 1973 is compared to that in major countries in Figure 1.15. In 1960, it

was only 3% in Japan, compared to 68% in West Germany, 60% in Australia, and 51% in the US and Canada. It increased more rapidly than in the other countries, however, reaching 96%, as compared to 85% in West Germany, 93% in Australia, 85% in the US and 90% in Canada. A total of 38 new brands of filtered cigarette came onto the Japanese market between 1960 and 1973 (Ministry of Finance 1976).

Figure 1.15 Increase in Proportion of Filtered Cigarettes in Different Countries, 1960-1973



A major difference between filtered cigarettes in Japan and other countries is the use of charcoal filters in Japan. In fact, almost all filtered cigarettes sold in Japan, not only domestic but also imported brands, use charcoal filters. In contrast, the market share of charcoal-filtered cigarettes is less than 1% in the US. The health consequences of this difference are unclear and net extensively investigated. A comparative case-control study conducted in Japan and the US which examined differences in lung cancer risk in association with differences in filter produced inconclusive results (Stellman et al. 2001).

1.3.2.2 Additives

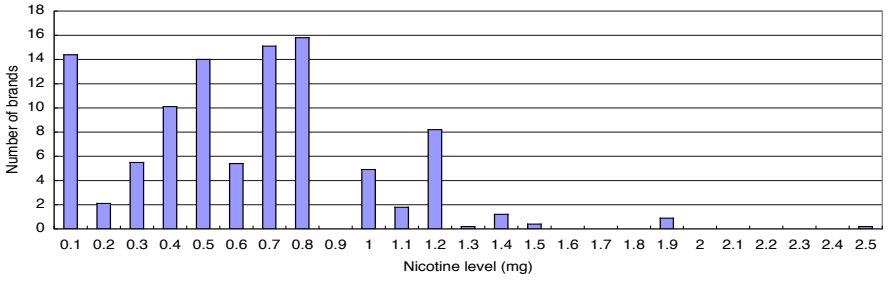
Additives are used to make cigarettes more acceptable to smokers. They include humectants (moisturisers) to prolong shelf life; sugars to make the smoke seem milder and easier to inhale; and flavourings such as chocolate and vanilla. While some of these may appear to be quite harmless in their natural form, they may become toxic when combusted in combination with other substances. Further, when additives are burned, new products of combustion are formed and these may be toxic.

Additives can be found in cigarettes in Japan and other countries. In the United States, ammonia has long been added to tobacco to increase the pH of the cigarette smoke, thereby increasing the delivery of nicotine to the smoker. Whether ammonia is also used in cigarette manufacture in Japan has not been disclosed by JT.

1.3.2.3 Yields

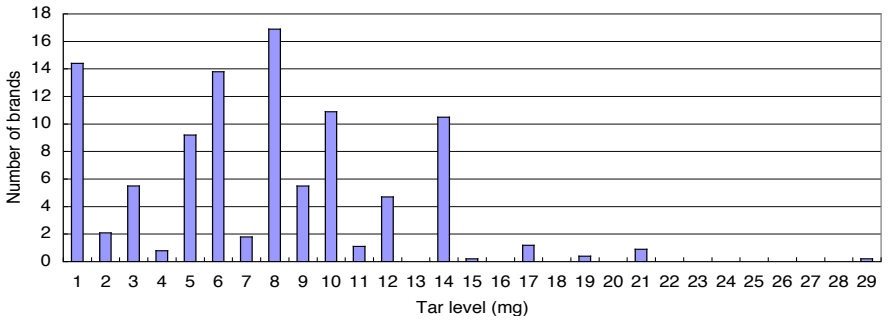
The Tobacco Institute of Japan (TIOJ) measures the yield of cigarettes sold in Japan by the International Organization of Standardization (ISO) method, and the results have been presented on package labels since 1971. The distribution of nicotine and tar levels is displayed in Figures 1.16 and 1.17. It should be noted that, as of 2002, 14.4% of brands sold in Japan report a value of 0.1 mg for nicotine and 1 mg for tar. The median values are 0.6 mg for nicotine and 7 mg for tar. For comparison, the distribution of nicotine and tar levels of 50 major cigarette brands sold in Canada in 1996 is displayed in Figures 1.18 and 1.19.

Figure 1.16 Nicotine Levels Presented on the Packge Labels of 100 Major Cigarette Brands Sold in Japan in 2002



Source: Tobacco Institute of Japan

Figure 1.17 Tar Levels Presented on the Package Label of 100 Major Cigarette Sold in Japan in 2002



Source: Tobacco Institute of Japan

Figure 1.18 Nicotine Levels Presented on the Package Label of 50 Major Cigarette Brands Sold in Canada 1996

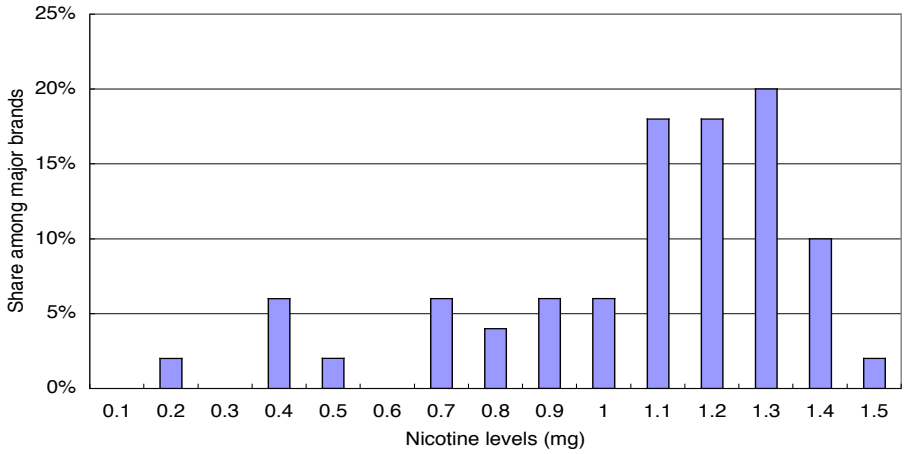
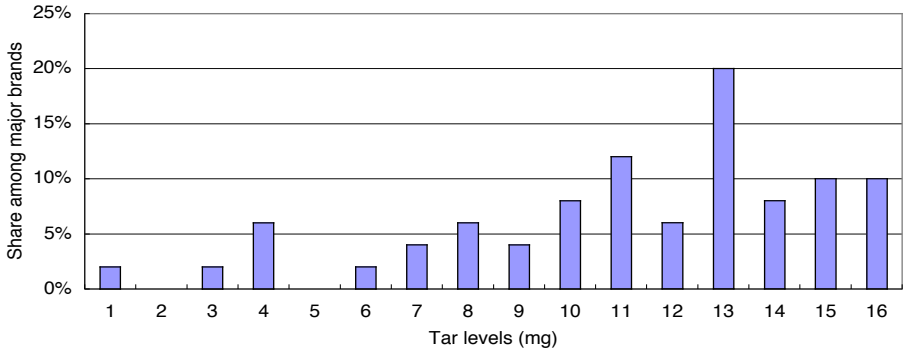


Figure 1.19 Tar levels Presented on the Package Label of 50 Major Cigarette Brands Sold in Canada in 1999



The distribution of tar levels of the Japanese cigarettes was not close to that in Canada, with only 1.3% of brands below 3 mg, in contrast to 12.9% above 15 mg. Notwithstanding that the figures are from different years, there are nevertheless large differences in both nicotine and tar yields between cigarettes in Japan, Canada and the US, and these might reflect the preference for low-yield cigarettes among Japanese smokers. Differences in machine testing methods between countries are not likely explanation. Cigarette testing methods have gone through relatively little change in the past four decades and the methods used in Japan an dht US are similar. In Japan, the ISO has established standard ranges for the measurement of nicotine, tar and carbon monoxide. A machine is used to determine levels by simulating the smoking of a cigarette. A similar method is used in the US and is authorized by the Federal Trade Commission (FTC).

The validity of these measurements as an indicator of the doses of toxins in cigarette smoke delivered to the lungs of a smoker has been questioned, because a machine smokes a cigarette very differently to an actual smoker. Smokers block the ventilation holes in the filter with their fingers, which a machine does not do, thus making the measurement an inaccurate indicator of the

dose actually delivered to the smoker. In reaction to this problem, the Japanese Ministry of Health, Labour and Welfare requested that a Canadian laboratory test seven major cigarette brands sold in Japan in 1999. The results were reported in 2000. The testing method used for this analysis was the standard method used by the Department of Health, Canada, and also by the State of Massachusetts. Two different machine smoking regimens were adopted, a standard and an average regimen, with the average smoking regimen designed to be closer to actual smoking patterns, especially when low-nicotine cigarettes are smoked. Details of testing methods are show in Table 1.8 and the results in Tables 1.9 and 1.10. For both nicotine and tar, the values obtained by both the average and standard smoking regimens were in general higher than those presented on the package labels. This is not surprising given the difference in measurement protocols. However, the results also show that a cigarette, when smoked to obtain more nicotine, will deliver more tar and other substances to smokers (results not shown). More detailed results were obtained for 50 major cigarette brands sold in Canada as of 1996; as shown in Figures 1.20 and 1.21, the values obtained under intensive smoking conditions, which reflect the smoker's compensatory smoking pattern adopted by the smoker to obtain the highest possible level of nicotine, tend to be higher than the values presented on the package label.

Table 1.9 Comparison of Nicotine Levels as Measured under Different Conditions and Printed on the Label

Brand	Standard smoking regimen		Average smoking regimen		Label	Standard to label	Average to label
	Mean	SD	Mean	SD			
Frontier Light	0.12	0.013	0.48	0.036	**0.1**	1.2	4.84
Mild Seven Extra Light	0.3	0.028	0.97	0.053	**0.3**	1.01	3.23
Mild Seven Superlight	0.44	0.026	1.16	0.056	**0.5**	0.88	2.32
Marlboro Menthol Light	0.6	0.039	1.41	0.048	**0.8**	0.75	1.76
Cabin Mild	0.66	0.029	1.43	0.063	**0.7**	0.94	2.04
Mild Seven	0.96	0.059	1.97	0.1	**0.8**	1.2	2.46
Seven Stars	1.44	0.088	2.66	0.205	**1.2**	1.2	2.22

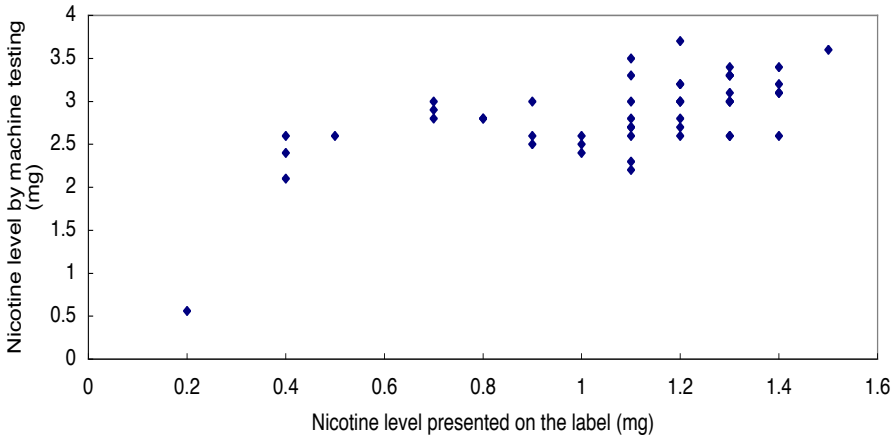
Source: MHLW 2002

Table 1.10 Comparison of Tar Levels as Measured under Different Conditions and Printed on the Label

Brand	Standard smoking regimen		Average smoking regimen		Label	Standard to label	Average to label
	Mean	SD	Mean	SD			
Frontier Light	1.44	0.447	6.65	0.74	**1**	1.44	6.65
Mild Seven Extra Light	3.19	0.428	11.7	0.787	**3**	1.06	3.9
Mild Seven Superlight	5.24	0.281	15.9	1.14	**6**	0.87	2.65
Marlboro Menthol Light	7.48	0.397	19.6	0.868	**12**	0.62	1.63
Cabin Mild	8.7	0.411	19.9	1.31	**8**	1.09	2.49
Mild Seven	11.8	0.634	25.1	1.2	**10**	1.18	2.51
Seven Stars	16.3	0.747	31.4	1.76	**14**	1.16	2.24

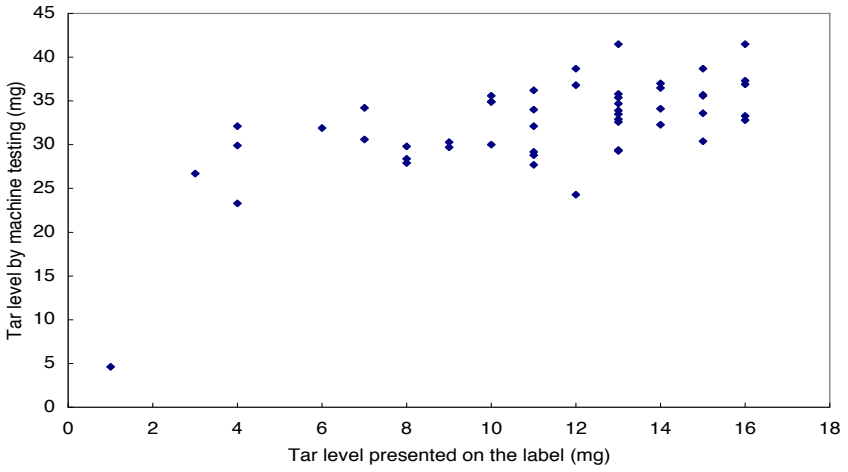
Source: MHLW 2002

Figure 1.20 Nicotine Levels of 50 Major Cigarette Brands sold in Canada in 1996



Note: Values presented on the label versus machine-tested values under intensive smoking conditions

Figure 1.21 Tar Levels of 50 Major Cigarette Brands Sold in Canada in 1996



Note: Values presented on the label versus machine-tested values under intensive smoking conditions

1.3.2.4 Marketing of low-yield cigarettes

Since the mid-20th century the tobacco industries in both Japan and other countries including the US have manufactured and marketed products touted as 'mild,' 'ight,' and 'ultra light' to give the impression that they are less harmful to the smoker's health. Filters, tar reduction, low-yield products, ammonia additives, reconstituted tobacco, and porous paper are design elements that have been manipulated in many countries to alter smoking behavior. In Japan, the three major brands are 'Mild Seven Light,' 'Mild Seven Superlight' and 'Mild Seven,' whose sales together constituted one-quarter of the Japanese market in 2002. Out of 20 major brands sold in Japan in 2002, 12 had 'mild,' 'light,' 'superlight' or 'extralight' in their names.

1.3.3 Tobacco consumption and health risks

The disease risks of smoking are both immediate and delayed. Risks for the major diseases caused by smoking arise only after several decades of continued smoking. Historical patterns of smoking are thus predictive of future disease risks and the present occurrence of smoking-related diseases needs to be considered in the context of past smoking patterns. In this regard, Japanese men, while presently smoking at a high rate, did not smoke large numbers of cigarettes equivalent to the present pattern until approximately the 1970s. Such high rates of consumption were reached decades earlier in the United States, the United Kingdom and other western countries. Thus, the present rates of tobacco-caused diseases in Japan should not be interpreted as reflecting a lesser risk from the smoking of Japanese cigarettes by Japanese smokers. Fortunately, only a small percentage of Japanese women are currently smoking but experience in other countries indicates that girls and young women can be quickly reached by the tobacco industry and that smoking rates among women can quickly rise.

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Chapter 2 HEALTH RISKS OF SMOKING

2.1 The Establishment of Causality: Mission Accomplished

2.1.1 Evidence on the health effects of tobacco smoking

Evidence on the health effects of tobacco smoking, both active and passive, and of using smokeless tobacco has been central in driving initiatives to control tobacco use throughout the world. This chapter introduces that evidence and the conclusions that have been reached over a half-century concerning the causation of disease by smoking, and sets a framework for interpreting the studies on smoking and disease risk in Japan.

Although there were writings on the dangers to health of tobacco use centuries ago, the research that constitutes the foundation of our present understanding of tobacco as a cause of disease dates approximately to the mid-20th century. Even earlier in the 20th century, clinicians began to question the role of smoking in causing lung cancer as they provided care for increasing numbers of cases, primarily in smokers (Arkin and Wagner 1936; Ochsner and DeBakey 1939; Ochsner et al. 1945; Ochsner et al. 1947a, b). Pearl (1938) documented reduced life expectancy in smokers in a report in Science that was published in 1938. Case-control studies on smoking and lung cancer were carried out in Germany in the 1930s (Proctor 1999).

The key initial observations were made in epidemiologic studies that had been carried out to understand changing patterns of disease across the first half of the 20th century, particularly the rise of lung cancer, coronary heart disease and stroke, and chronic obstructive lung disease, including bronchitis and emphysema. These studies compared disease risks in smokers to disease risks in nonsmokers, as the health risks of smoking could not be ethically or feasibly examined in experiments. Beginning in the mid-20th century, there was a flood of evidence as

case-control studies were carried out on lung cancer and other cancers, and cohort studies were initiated to prospectively document the risks of smoking by follow-up of large groups of smokers and nonsmokers. Because of the strength of smoking as a cause of disease, the cohort studies quickly provided prospective documentation of increased risk in smokers to complement the retrospective case-control studies.

There were many landmark investigations—the early case-control studies of lung cancer (Doll and Hill 1950; Levin et al. 1950; Wynder and Graham 1950), and the large cohort studies such as the Framingham study (Dawber 1980), the British Doctors' Study (Doll and Hill 1954), and the cohort studies initiated by the American Cancer Society (Hammond 1966). These initial observations quickly sparked complementary laboratory studies on the mechanisms by which tobacco smoking caused disease. Even by 1950, however, cigarette smoke was know to contain benzo[a]pyrene, an established carcinogen, and attempts had been previously made to produce cancers in animals by exposing them to tobacco smoke. By 1953, Wynder et al. (1953) had shown that painting the skin of mice with cigarette smoke condensate caused tumors. The key epidemiologic findings on the major tobacco-related diseases were quickly replicated over the 1950s and 1960s. The ease of replication derived from the strength of smoking as a cause of many diseases.

By the early 1960s, the mounting evidence was sufficient to warrant formal review and evaluation by government committees. Even in the 1950's, there was sufficient evidence on lung cancer and smoking to lead to a near consensus view in the scientific community that the association was causal (White 1990), a view even echoed in some tobacco-industry documents now available from that time (Hurt and Robertson 1998). In the United Kingdom, the 1962 report of the Royal College of Physicians of London concluded that smoking was a cause of lung cancer (Royal College of Physicians of London 1962). In the United States, the 1964 report of the Advisory Committee to the Surgeon General offered the conclusions that smoking was a cause of lung cancer in men and of chronic bronchitis and emphysema (USDHEW 1964). Until recently, a US Surgeon General's report was required annually by law and these periodic reports added to the list of diseases caused by smoking. The International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) reviewed the evidence on smoking and cancer in 1986 (IARC 1986) and again in 2002 (IARC 2004). The Royal College of Physicians in the United Kingdom has also continued to release periodic reports and the United Kingdom's Scientific Committee on Tobacco reported findings on active and passive smoking in 1998 (Scientific Committee on Tobacco and Health 1998).

These reports and other expert syntheses of the evidence have proved to be an effective tool for translating the findings on smoking and disease into policy.

The systematic review process, involving review of the evidence and application of criteria for causality, has resulted in an unassailable series of conclusions on the causal associations of smoking with specific diseases and other adverse health effects. Table 2.1 provides a listing of the diseases and conditions found to date to be causally associated with smoking, based on the various reports of the Surgeon General and the 2002 review of the IARC (IARC 2004). The table also provides the date on which a causal conclusion was first reached by the US Surgeon General or the IARC for each disease or other adverse effect.

Table 2.1 Diseases Caused by Smoking, as Concluded in the Reports of the US Surgeon General

Disease	Statement	Surgeon General's Report
Atherosclerosis/Aortic Aneurysm	"Cigarette smoking is **the most powerful risk factor** predisposing to atherosclerotic peripheral vascular disease.	1983
	"[Cigarette smoking is] **a cause and most important risk factor** for atherosclerotic peripheral vascular disease."	1989
Bladder Cancer	"Smoking is a **cause** of bladder cancer; cessation reduces risk by about 50% after only a few years, in comparison with continued smoking."	1990
Cerebrovascular Disease	"Cigarette smoking is a **major cause** of cerebrovascular disease (stroke), the third leading cause of death in the United States."	1989
Chronic Obstructive Pulmonary Disease (COPD)	"Cigarette smoking is the most important of the causes of chronic bronchitis in the United States, and increases the risk of dying from chronic bronchitis."	1964
	"Cigarette smoking in **the most important of the causes** of chronic non-neoplastic bronchopulmonary diseases in the United States. It **greatly increases the risk of dying** not only from both chronic bronchitis, but also from pulmonary emphysema."	1967
Coronary Heart Disease	"Additional evidence not only confirms the fact that cigarette smokers have higher death rates from coronary heart disease, but also suggest how these deaths may be **caused** by cigarette smoking. There is an increasing convergence of many types of evidence concerning cigarette smoking and coronary heart disease which strongly suggests that cigarette smoking **can cause death** from coronary heart disease."	1967
Esophageal Cancer	"Cigarette smoking is a **major cause** of esophageal cancer in the United States."	1982
Laryngeal Cancer	"Cigarette smoking is **causally associated** with cancer of the lung, larynx, oral cavity, and esophagus in women as well as in men..."	1980
Lung Cancer	"Cigarette smoking is **causally related** to lung cancer in men; the magnitude of the effect of cigarette smoking **far outweighs all other factors**. The data for women, though less extensive, point in the same direction."	1964
	"Additional epidemiological, pathological, and experimental data not only confirm the conclusion of the Surgeon General's1964 Report regarding lung cancer in men but strengthen the **causal relationship** of smoking to lung cancer in women."	1967
Oral Cancer	"Epidemiological studies indicate that smoking is a **significant causal factor** in the development of oral cancer."	1979
	"Cigarette smoking is **causally associated** with cancer of the... oral cavity... in women as well as in men..."	1980
	"Cigarette smoking is a **major cause** of cancers of the oral cavity in the United States."	1982
Pancreatic Cancer	"Cigarette smoking is a **contributory factor** in the development of pancreatic cancer in the United States. The term 'contributory factor **by no means excludes** the possibility of **a causal role** for smoking in cancers of this site."	1982
Peptic Ulcer Disease	"The **relationship** between cigarette smoking and death rates from peptic ulcer, especially gastric ulcer, **is confirmed**. In addition, morbidity data suggest a similar relationship exists with the prevalence of reported disease from this cause."	1967
	"The finding of a **significant dose-related excess mortality** from gastric ulcers among both male and female Japanese cigarette smokers, in a large prospective study, and in the context of the genetic and cultural differences between the Japanese and previously investigated Western populations, **confirms and extends the association** between cigarette smoking and gastric ulcer mortality."	1973
Diminished Health Status/ Respiratory Morbidity	"Relationships between smoking and cough or phlegm are **strong and consistent**; they have been amply documented and are judged to be **causal.**"	1984
	"Consideration of evidence from many different studies has led to the conclusion that cigarette smoking is **the overwhelmingly most important cause** of cough, sputum, chronic bronchitis, and mucus hypersecretion."	1984

The table provides a remarkable picture of the extent to which active smoking damages health and causes disease. Most leading causes of death worldwide are caused by active smoking: cancers, cardiovascular diseases, chronic respiratory diseases, and respiratory infections. Not surprisingly, smokers have a substantially reduced lifespan in comparison with never smokers. Smoking also causes diminished health generally and several problems such as cataract and gingival disease. Smoking by women adversely affects nearly all aspects of reproduction. Even though the health effects of active smoking have been under investigation for decades, new adverse health effects are still being identified. As recently as 2002, the list of cancers caused by smoking was expanded to include cancers of the liver, stomach, and cervix, along with acute leukemia. The 2004 Report of the US Surgeon General added cataract, respiratory infections, some other specific diseases and conditions, and diminished health generally (USDHHS 2004).

While there were scattered clinical reports on passive smoking earlier, the first epidemiological studies on passive smoking and health were reported in the late 1960s (Cameron 1967; Colley and Holland 1967; Cameron et al. 1969). The initial investigations focused on parental smoking and lower respiratory illnesses in infants; studies of lung function and respiratory symptoms in children soon followed (USDHHS 1986; Samet and Wang 2000). The first reports on passive smoking and lung cancer in nonsmokers were published in 1981 (Hirayama 1981; Trichopoulos et al. 1981).

The US Surgeon General's reports began to express concern about passive smoking and health as early as 1971 (USDHEW 1971) and the topic was considered in multiple subsequent reports across the 1970s and 1980s. By 1986, the evidence supported the conclusion that passive smoking was a cause of lung cancer in non-smokers (IARC 1986; National Research Council (NRC) 1986; USDHHS 1986). The evidence on child health and passive smoking was also reviewed in 1984 and 1986 by the US Surgeon General and in 1986 by the US National Research Council (Table 2.2). Subsequently, a now-substantial body of evidence has continued to identify new causal associations with specific diseases and other adverse effects of passive smoking (Table 2.2) (California Environmental Protection Agency 1997; Scientific Committee on Tobacco and Health 1998; WHO 1999; Samet and Wang 2000). A new review is now in progress for an upcoming report of the US Surgeon General(USDHHS 2004).

Table 2.2 Adverse Effects of Exposure to Tobacco Smoke

Health effect	SG 1984 (1)	SG 1986 (2)	EPA 1992 (3)	CalEPA 1997 (4)	UK 1998 (5)	WHO 1999 (6)	IARC 2002 (7)
Increased prevalence of respiratory illnesses	Yes/a	Yes/a	Yes/c	Yes/c	Yes/c	Yes/c	
Decrement in pulmonary function	Yes/a	Yes/a	Yes/a	Yes/a		Yes/c	
Increased frequency of bronchitis, pneumonia	Yes/a	Yes/a	Yes/a	Yes/c		Yes/c	
Increase in chronic cough, phlegm		Yes/a				Yes/c	
Increased frequency of middle ear effusion		Yes/a	Yes/c	Yes/c	Yes/c	Yes/c	
Increased severity of asthma episodes and symptoms			Yes/c	Yes/c		Yes/c	
Risk factor for new asthma			Yes/a	Yes/c			
Risk factor for SIDS				Yes/c	Yes/a	Yes/c	
Risk factor for lung cancer in adults		Yes/c	Yes/c	Yes/c	Yes/c	Not addressed	Yes/c
Risk factor for heart disease in adults				Yes/c	Yes/c	Yes/a	Yes/c

Note: Yes/a, association; Yes/c, cause
(1) US Department of Health and Human Services (USDHHS). The health consequenses of smoking - chronic obstructive lung disease. A report of the Sergeon General. Washington, DC. US Government Printing Office, 1984.
(2) US Department of Health and Human Services (USDHHS).
(3) US Environmental Protection Agency (EPA). Respiratory heallth effects of passive smoking. Lung cancer and other diseases. Washington, DC. US Government Printing Office. 1992; EPA/600/006F.
(4) California Environmental Protection Agency (Cal EPA) and Office of Environmental Health Hazard Assessment. Health effects of exposure to environmental tobacco smoke. California Environmental Protection Agency. 1997.
(5) Scientific Committee on Tobacco and Health and HSMO. Report of the Scientific Committee on Tobacco and Health. The Stationary Office. 1998;

As for active smoking, the evidence now supports a number of conclusions with regard to the causation of disease (Table 2.2). Passive smoking causes lung cancer and coronary heart disease in adults. The respiratory health of children is harmed, particularly if the mother smokes. The effects include reduced lung function, increased respiratory illnesses and symptoms, higher risk for asthma and for worsening of asthma, and acute and chronic ear disease. For a number of other adverse effects, there is substantial evidence, though not yet reaching the threshold for an inference of causality.

2.1.2 Evidence evaluation: the criteria for causality

The systematic review process in the United States, involving evaluation of the evidence and the application of criteria for causality, has resulted in a series of conclusions on the causal association of active smoking with specific diseases and other adverse health effects (Table 2.1). As set out in the 1964 Surgeon General's report (USDHEW 1964), the review of evidence proceeds at three sequential levels: 1) assessment of the validity of individual scientific reports; 2) judgment as to the validity of the interpretations and conclusions reached by investigators; and 3) judgments needed to formulate overall conclusions. The 1964 report commented on the need to evaluate all relevant lines of evidence, including not only epidemiological studies but also clinical, pathological and experimental evidence.

In 1964, the Advisory Committee to the Surgeon General (USDHEW 1964) set out criteria for judging the causal significance of an association, including the association's consistency, strength, specificity, temporal relationship, and coherence. The 2004 Report of the US Surgeon General (USDHHS 2004) further considered causal inference and offered a uniform set of descriptors for characterizing the strength of evidence available for causal inference. Consistency refers to the similarity of findings in separate studies involving different populations. Comparability of findings across studies of different groups, using different methods, argues for causality. Stronger associations are more likely to reflect an underlying causal link, as the possibility that bias from uncontrolled confounding or other sources is responsible becomes less tenable with increasing strength of association. Since specificity, which refers to a unique exposure-disease association, is not applicable to most chronic diseases caused by smoking, this criterion has generally been set aside in assessing associations of smoking with cancer. Of course, smoking precedes disease onset, meeting the criterion offered for the proper temporal relationship, i.e., exposure should come before the disease. Finally, coherence refers to the overall cohesion of the evidence, including the fit between population patterns of smoking and disease occurrence and the biological plausibility of the claim that an association reflects an underlying causal relationship. Assessment of coherence involves the evaluation of all relevant data, including experimental evidence, as well as the consideration of mechanisms.

In offering these criteria, the 1964 Committee both recognized that they were not rigid guidelines for the interpretation of evidence and commented on the complexity of defining 'cause' for multifactorial complex diseases. The Committee summarized its definition as follows: "The word *cause* is the one in general usage in connection with matters considered in this study and it is capable of conveying the notion of a significant, effectual, relationship between an agent and an associated disorder or disease in the host."

The principles set forth in the 1964 Surgeon General's Report have continued to guide the evaluation of evidence on tobacco use and health, in the Surgeon General's reports and elsewhere, and are relevant to the evidence from Japan considered in this report. Studies carried out in Japan that replicate associations found elsewhere are useful, not only for documenting consistent findings in Japan, but for indicating the magnitude of the risk in Japanese smokers. With regard to coherence, there is little basis for postulating differing mechanisms of disease causation in Japanese and non-Japanese smokers. Similarly, for most diseases caused by smoking, the distribution of modifying factors should not be so dramatically different between Japanese and non-Japanese smokers as to qualitatively affect the risk of smoking.

2.1.3 Toxicology of tobacco smoke

Tobacco smoke is generated by the burning of a complex organic material, tobacco, along with the various additives and paper, at a high temperature, reaching several thousand degrees centigrade. The resulting smoke, comprising numerous gases and also particles, includes myriad toxic components that can cause injury through inflammation and irritation, asphyxiation, carcinogenesis and other mechanisms (Table 2.3). Active smokers inhale mainstream smoke (MS), the smoke that is drawn directly through the end of the cigarette. Passive smokers inhale smoke that is often referred to as environmental tobacco smoke (ETS) or secondhand smoke (SHS), comprising a mixture of mostly sidestream smoke (SS) given off by the smoldering cigarette and some exhaled MS. In indoor environments, concentrations of SHS are far below the levels of MS inhaled by the active smoker, but there are qualitative similarities between SHS and MS (USDHHS 1986). Based on these similarities, the evidence on MS, coming from studies of active smokers and laboratory research on its toxic effects, can be reasonably extended to passive smoking.

Table 2.3 Concentrations of Selected Active Agents in Nonfilter Cigarette Mainstream Smoke

Smoke constituent	Concentration/cigarette
Total particulate matter	15-40 mg
Carbon monoxide	10-23 mg
Nicotine	1.0-2.3 mg
Acetaldehyde	0.5-1.2 mg
Hydrogen cyanide	110-300 mg
Benzene	20-50 mg
N-Nitrosonornicotine	200-3000 ng
N-Nitrosopyrrolidine	0-110 ng
Vinyl chloride	1.3-16 ng
Benzo[a]pyrene	20-40 ng
4-Aminobiphenyl	2.4-4.6 ng

Source: US Department of Health Education and Welfare (USDHEW) 1964

Both active and passive smokers absorb tobacco smoke components through the lung's airways and alveoli and many of these components, like the gas, carbon monoxide, then enter into the circulation and are distributed generally. There is also uptake of some components, like benzo[a]pyrene, directly into the cells that line the upper airway and the lung's airways. Some of the carcinogens undergo metabolic transformation into their active forms (Hecht et al. 1993). The genitourinary system is exposed to toxins in tobacco smoke through the excretion of these compounds in the urine. The gastrointestinal tract is exposed through the

deposition of smoke in the upper airway and the clearance of smoke-containing mucus from the trachea through the glottis into the esophagus. Not surprisingly, tobacco smoking has proved to be a multisystem cause of disease.

A large scientific literature is available on the mechanisms by which tobacco smoking causes disease (USDHHS 1990, 2001,2004; IARC 2004). This literature includes characterization of the many toxic components in smoke (Table 2.3), some having well-established toxicity, like hydrogen cyanide, carbon monoxide, and nitrogen oxides. The toxicity of smoke has been studied by exposing animals to tobacco smoke, in cellular and other laboratory toxicity assays, and by assessing smokers for evidence of injury by tobacco smoke using biomarkers such as tissue changes and levels of damaging enzymes and cytokines. The data from these studies amply document the powerful toxicity of tobacco smoke. Young smokers in their twenties, for example, already have evidence of permanent damage to the small airways of the lung and to their arteries (Niewoehner et al. 1974; PDAY Research Group 1990) and lavage of the lungs of smokers shows increased numbers of inflammatory cells and higher levels of markers of injury, in comparison with non-smokers (USDHHS 1990). With the new tools of molecular and cellular biology, we now have evidence at the molecular level of changes specific to tobacco-smoke carcinogens (Denissenko et al. 1996; Hussain and Harris 1998; Hecht 1999; Caporaso 2002; Shields 2002).

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2.2 Health Effects of Smoking in Other Countries

2.2.1 Active smoking

2.2.1.1 Introduction

This section of the report provides a broad overview of the health consequences of active smoking and then considers each of the main diseases caused by smoking. Of necessity, the review is brief and selective in its coverage of the literature. Extensive summaries can be found in the Reports of the Surgeon General and the 2004 report from the International Agency for Research on Cancer (IARC) (IARC 2004).

The US Surgeon General (USDHHS 1990a), the Royal College of Physicians of London (1962), the IARC (IARC 1986), the United Kingdom's Scientific Committee on Tobacco and Health (Scientific Committee on Tobacco and Health 1998), and other expert groups have identified causal associations of smoking with disease and other adverse effects (Table 2.1). These associations can be grouped into the broad categories of cancer, cardiovascular disease, acute respiratory infections, chronic respiratory diseases, and adverse effects on reproduction. There are additional effects of concern, including general health status and some more specific effects, such as cataract and osteoporosis. For each of these associations, the evidence is extensive and comprehensively reviewed in the key reports. Other recent reports that provide valuable compilations of the epidemiologic and other data include monographs in a series prepared by the US National Cancer Institute (NCI 1996, 1997) and a 1996 issue of the British Medical Bulletin (Doll 1996).

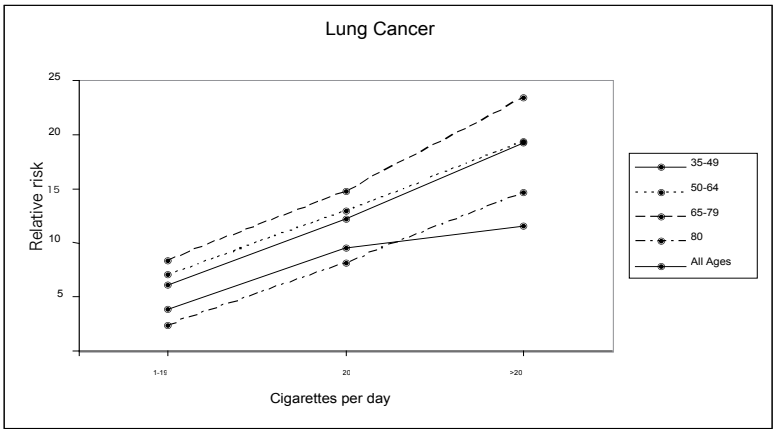
Table 2.4 Changes in Cigarette-related Mortality Risks between Cancer Prevention Study I (1959 through 1965) and Cancer Prevention Study II (1982 through 1988) and Percentage of Deaths Attributable to Active Cigarette Smoking

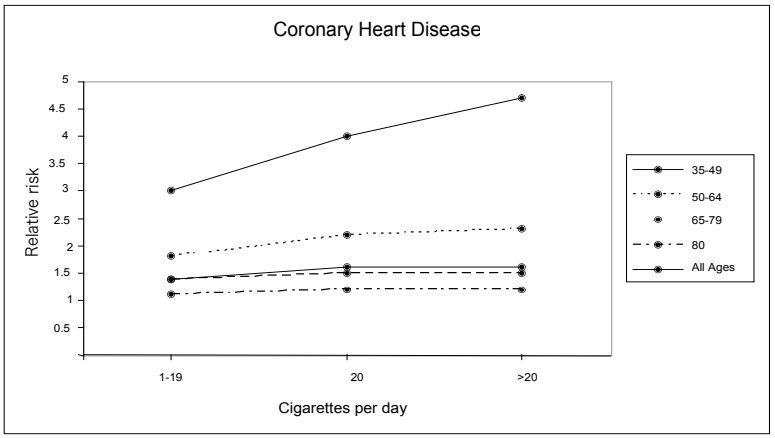
	CPS I		CPS II	
	Men			
	Relative risk	Percent	Relative risk	Percent
Overall mortality	1.7	42.2	2.3	57.1
Lung cancer	11.9	91.6	23.2	95.7
Coronary heart disease	1.7	41.5	1.9	46.2
Chronic obstructive pulmonary disease	9.3	89.2	11.7	91.4
Stroke	1.3	21.9	1.9	46.8
Other smoking-related cancers	2.7	63.4	3.5	71.2
	Women			
	Relative risk	Percent	Relative risk	Percent
Overall mortality	1.2	18.7	1.9	47.9
Lung cancer	2.7	63.4	12.8	92.2
Coronary heart disease	1.4	27	1.8	45.1
Chronic obstructive pulmonary disease	6.7	85	12.8	92.2
Stroke	1.2	15.2	1.8	45.7
Other smoking related cancers	1.8	45	2.6	60.8

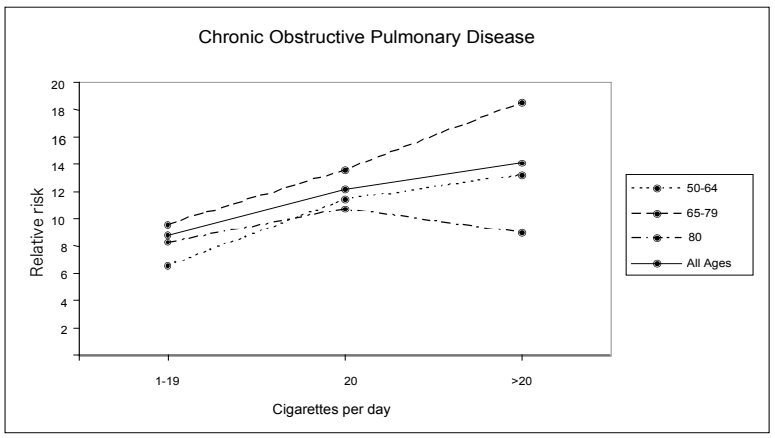
Note: Other smoking-related cancers include larynx, oral cavity, esophagues, bladder, kidney, other urinary, and pancreas.
Source: Thun et al. 1997

Table 2.4 provides relative risks for dying from major smoking-caused diseases obtained in two studies, each of one million persons, conducted by the American Cancer Society (Thun et al. 1995). These studies are sufficiently large to provide statistically stable estimates of the increased risk associated with smoking for each of the diseases caused by smoking. Mortality from a particular disease is the outcome measure considered, rather than incidence. For some diseases, e.g., lung cancer, incidence and mortality are comparable, but for others, e.g., coronary heart disease, incidence is much higher than mortality and the relative risk for mortality may be an imperfect indicator of the relative risk for incidence. There is a wide range of relative risk values, reflecting the strength of smoking as a cause of the different diseases; for some, like lung cancer the relative risks are extremely high whereas those for cardiovascular diseases and some other cancers are lower. The high relative risks for lung cancer, reflect the continuing direct exposure of the lung to inhaled carcinogens in tobacco smoke and the dominant role of smoking in causing most cases in developed countries. The lower relative risks for coronary heart disease stem from the multifactorial etiology of this condition. For the principal chronic diseases associated with smoking, the effect of smoking on disease risk is manifest only after a substantial latent period, which represents the time needed for the underlying injury to be sufficient to cause disease. For smoking and lung cancer, for example, incidence rates rise after about 20 years of active smoking (Burns et al. 1997a).

Figure 2.1 Relative Risks for Disease Mortality and the Number of Cigarettes Smoked per Day among White Male Participants in the American Cancer Society's Cancer Prevention Study (CPS) I







Source: Burns et al. 1997b

The relative risk values generally rise with indicators of exposure to tobacco smoke, including numbers of cigarettes smoked and the duration of smoking, and fall after successful cessation. This pattern is strongly indicative of a causal

association, as it cannot be readily explained by the actions of another factor. Figure 2.1 illustrates the relationship between lung cancer, coronary heart disease, and chronic obstructive pulmonary disease (COPD) mortality and the number of cigarettes smoked per day among white male participants in the American Cancer Society's Cancer Prevention Study (CPS) I; risks increase progressively with the number of cigarettes smoked (Burns et al. 1997b). These risk estimates decrease with increasing years of smoking cessation for all levels of cigarette smokers (Table 2.5) (Burns et al. 1997b; Thun et al. 1997).

Table 2.5 Mortality Rate Ratios for White Male Former Smokers by Duration of Cessation and Level of Cigarette Consumption in the USA - Comparison with the Never-Smoker Group Weighted to Match Former Smokers for Person-Years of Observation for Each (age × duration × cigarettes per day) Cell

Cigarettes per day	Duration of cessation (years)							
	2-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39
				Lung cancer				
1-9	2.83	1.68	1.22			0.58	1.38	1.89
10-19	7.96	3.50	2.91	2.04	0.96	2.16	1.68	
20	11.68	10.49	5.03	2.22	1.86	1.12	1.55	4.10
21-29	14.30	9.18	4.85	4.88	2.04		4.13	3.69
≥40	27.88	12.36	7.77	3.74	3.99	0.89		
Combined	13.12	8.44	4.61	2.89	2.04	1.19	1.84	3.18
				Coronary heart disease				
1-9	1.55	1.36	1.38	1.08	0.71	1.01	0.83	0.46
10-19	2.53	1.56	1.26	0.93	0.93	0.92	0.77	0.62
20	3.00	1.56	1.20	1.09	0.97	0.98	1.13	0.70
21-29	2.65	2.03	1.55	1.29	1.13	1.09	0.95	0.56
≥40	2.96	1.68	1.72	1.15	1.02	0.98	1.25	0.39
Combined	2.66	1.64	1.37	1.13	0.99	0.96	0.93	0.55
				Chronic obstructive pulmonary disease				
1-9		6.46	2.25	2.67	3.29			
10-19	21.03	12.35	9.02	2.07	0.95	0.85	1.01	2.49
20	41.10	15.27	11.85	7.05	3.75	1.13	2.89	
21-29	31.00	28.14	11.39	5.57	1.40	1.98		
≥40	57.03	34.25	10.33	9.37	4.00		4.99	
Combined	36.14	18.89	10.33	5.64	2.80	1.42	2.28	2.49

Source: Burns et al. 1997b

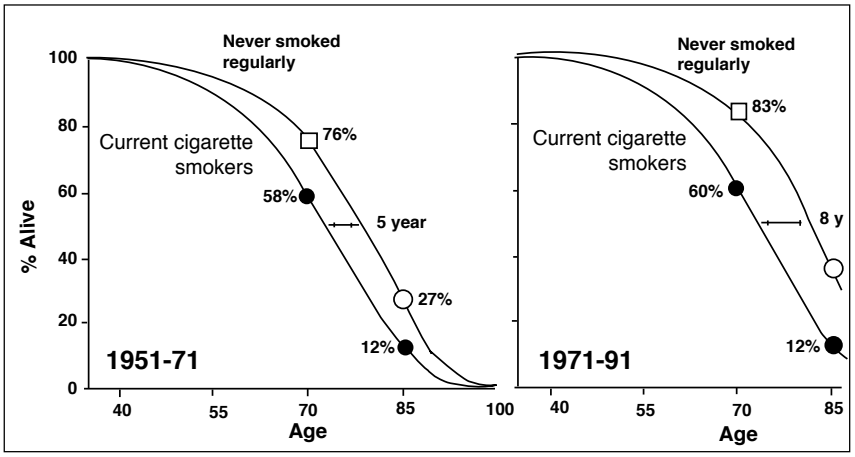
For the cancers caused by smoking, the relative risks tend to decline slowly as the number of years since quitting increases (USDHHS 1990a); by contrast, there is an immediate decline in the relative risk for cardiovascular disease and the levels of former smokers tend to reach those of never smokers after 5 to 10 years of successful cessation. Chronic obstructive pulmonary disease results from sustained excessive loss of lung function in smokers. Fortunately, after cessation, the rate of decline of lung function quickly returns to that of never smokers (USDHHS 1990a).

Smoking by the mother also adversely affects reproduction. Smoking during pregnancy reduces birth weight by approximately 200 grams on average (USDHHS 1990a), and the degree of reduction is dose-related. With successful

cessation by the third trimester, much of this weight reduction can be avoided. Smoking also increases rates of spontaneous abortion, placenta previa, and perinatal mortality, and smoking during pregnancy is now considered to be a cause of sudden infant death syndrome (SIDS) (Table 2.2). There is more limited evidence suggesting that smoking by the mother may increase childhood cancer incidence and congenital defects (Charlton 1996; Scientific Committee on Tobacco and Health 1998).

Cigarettes have changed substantially over the last 50 years (USDHHS 1981; NCI 1996). Filter cigarettes dominate the market and tar and nicotine yields, as assessed by smoking machines, have declined substantially. However, tar and nicotine deliveries to smokers have little relationship to the machine-measured levels (Benowitz and USDHHS 1996). Epidemiologic evidence shows slight reduction in risk for some cancers, particularly lung cancer, and for total mortality, comparing smokers of lower delivery and higher delivery products, but no reduction for myocardial infarction (Samet 1996). In fact, rising relative risks of smoking have been documented across the recent decades when the lower delivery products came into widespread usage (Doll et al. 1994; Burns et al. 1997a). In the cohort study of British doctors, there was a substantial increase in mortality for smokers, comparing the second 20 years of follow-up with the first (Figure 2.2) (Doll et al. 1994). These studies in western countries have not addressed charcoal filters, which are not widely used in Europe and North American but are the most common type of filter in Japan.

Figure 2.2 Survival after Age 35 among Cigarette Smokers and Non-smokers in the First Half (left) and Second Half (right) of the British Doctors' Study



Note: For ages 35-44 rates for the whole study are used in both halves since little infromation on these is available from the second half.
Source: Doll et al. 1994

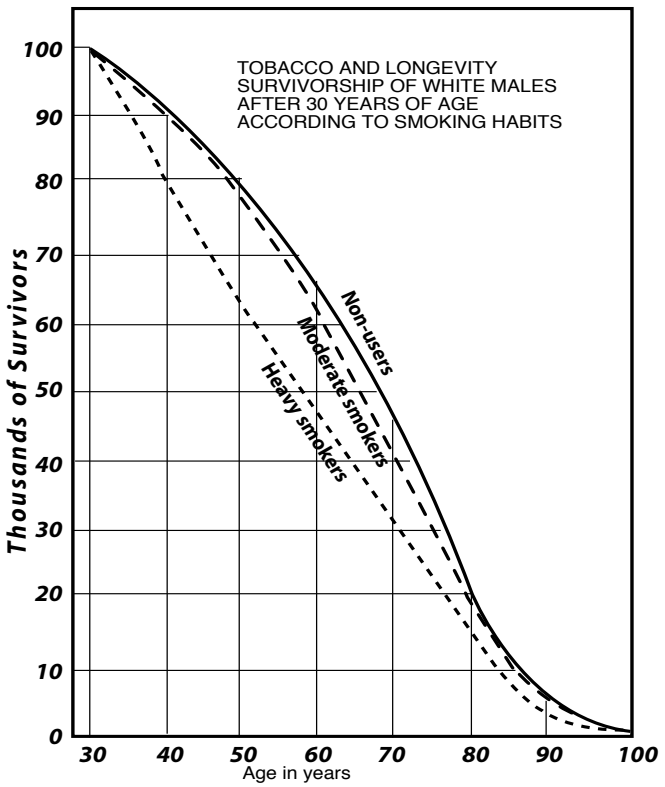
Several panels have reviewed the evidence on declining yields of tar and nicotine, as measured by machines (Stratton et al. 2001; USDHHS 2001,2004; IARC 2004). These groups have found little evidence for benefit to public health

from the declining yields and expressed concern that the availability of cigarettes labeled as 'light' or 'ultra light' may dissuade some smokers from quitting and encourage others to start, because of the inherent message that risks are lessened.

Although cigarette smoking causes many of the principal chronic diseases and smokers have reduced life expectancy compared with non-smokers, active cigarette smoking has been associated with reduced risk for selected diseases and conditions (Baron 1996; Scientific Committee on Tobacco and Health 1998). These inverse associations include Parkinson's disease, endometrial carcinoma, ulcerative colitis, and extrinsic allergic alveolitis. There is also suggestive evidence of an inverse association for Alzheimer's disease. While these inverse associations are of little public health consequence, they do indicate opportunities for exploring disease pathogenesis and seeking therapeutic approaches. Nicotine has been examined as a therapy for ulcerative colitis and anti-estrogenic effects of smoking have been considered as the likely explanation for the reduced risk of endometrial carcinoma.

2.2.1.2 All cause mortality

Figure 2.3 Raymond Pearl's Survival Curve: Tobacco and Longevity
The survivorship lines of life tables for white males fall into three categories relative to the usage of tobacco A.Non-users(solid line); B.Moderate smokers (dash line); C.Heavy smokers (dot line).



Source: Pearl 1938

Tobacco use was first linked with all cause mortality in 1938, when Raymond Pearl published a figure illustrating a sharp decrease in survivorship after the age of 30 years in male heavy tobacco users compared to non-tobacco users (Figure 2.3) (Pearl 1938). In 1964, the US Surgeon General's Report on smoking and health stated that cigarette smoking was "associated with a 70 percent increase in the age-specific death rates of males, and to a lesser extent with increased death rate in females." It was also noted that the mortality rates for men increased as the number of cigarettes smoked per day increased (USDHEW 1964).

Since Dr. Pearl's publication, several large cohort studies have provided data that both complement and expand upon the association he noted between tobacco use and all-cause mortality (NCI 1997). The relative risk of mortality among the Cancer Prevention Study I participants was found to increase with the number of cigarettes smoked per day for both men and women. The risk of mortality among current smokers compared to never smokers participating in CPS-II was 2.3 (2.3-2.4) for men and 1.9 (1.9-2.0) for women (NCI 1997). After 40 years of follow up from the British doctors' study, the mortality rate ratio for current smokers compared to subjects who never used tobacco was 2.29 for cigarette smokers and 1.24 for users of other forms of tobacco (Doll et al. 1994).

2.2.1.3 Cancer

Lung cancer

Lung cancer is the label given to primary carcinomas arising in the lung including the four principal histologic types (squamous cell carcinoma, small cell carcinoma, adenocarcinoma, and large cell carcinoma) and several other less frequent types. These cancers arise in the airways and alveoli (air sacs) of the lung, causing symptoms as they grow and compromise the surrounding lung or spread to distant sites. Survival is poor with only approximately 14% of lung cancer patients in the United States surviving 5 years following diagnosis (USDHHS 1995; Wingo et al. 1999). The lung is the principal site of deposition of the carcinogens in smoke. As inhaled smoke contacts the airways and alveoli of the lung, these carcinogens are deposited. Some require metabolic transformation by enzymes before taking a carcinogenic form, while others are inherently carcinogenic (Hecht 1999). We now have evidence supporting the long-held hypothesis that cancer results from a multi-step process involving multiple injuries to the genes which control the growth and differentiation of cells, including tumor suppressor genes, such as *p53*, and oncogenes, such as *ras*. Cells of the airways of smokers show changes indicating that the cells have been affected and are moving from normal toward being cancerous (Auerbach et al. 1970, 1979). These

changes are visible under the microscope but can now also be confirmed with more sophisticated techniques of molecular and cellular biology. Specific patterns of mutation have been found in the lung cells of smokers, in comparison with non-smokers (Wistuba et al. 1997). Additionally, several studies show the binding of benzo[a]pyrene, an active tobacco smoke carcinogen, to sites on the *p53* gene that are typically mutated in lung cancers found in smokers (Denissenko et al. 1996). This result offers an insight at the molecular level of the mechanisms by which the deposited components of tobacco smoke components cause disease.

The epidemiologic evidence on smoking and lung cancer is now voluminous, having accumulated across the last century. Several case-control studies were carried out in Germany before 1950. However, the most prominent and cited early reports were published in 1950: three landmark case-control studies, all showing strong associations of lung cancer with cigarette smoking (Doll and Hill 1950; Levin et al. 1950; Wynder and Graham 1950). The US study by Wynder and Graham and the British study of Doll and Hill showed that smokers experienced approximately a ten-fold increased risk for lung cancer when compared to lifelong non-smokers. Across the 1950s, additional case-control studies were conducted and the results of the first cohort studies of smoking and disease also became available. For men, the evidence uniformly showed an increased risk of lung cancer in smokers; the data for women were similar, although the degree of elevation of risk in women smokers was not as great at the time as in men. The epidemiologic evidence has also shown consistent evidence for dose-response relationship between lung cancer risk and numbers of cigarettes smoked per day and the duration of smoking. The relative risk of lung cancer falls following smoking cessation, although the absolute risk does not appear to reach that of persons who never smoked (USDHHS 1990b). Evidence from Western countries indicates a possible small reduction in risk for lung cancer, comparing smokers of filtered and unfiltered cigarettes (Alberg and Samet 2003).

Laryngeal cancer

Laryngeal cancers arise from the vocal cords, the fibrous structures that generate speech. Typical symptoms of laryngeal cancer include cough, coughing blood, and hoarseness. These symptoms often occur in the early stages of the disease and the majority of cases can be treated by surgery, often combined with radiation. The underlying mechanisms for lung cancer and laryngeal cancer are likely to be similar. The larynx is lined with a cellular membrane similar to that of the lungs and carcinogens are deposited in both during smoking.

As with lung cancer, the evidence on laryngeal cancer derives from case-control and cohort studies. The 1964 Report of the Advisory Committee to the Surgeon General listed ten case-control studies and seven cohort studies on cancer of the larynx. The report concluded that "····cigarette smoking is

a significant factor in the causation of laryngeal cancer in the male" (USDHEW 1964). Subsequent evidence has strengthened this conclusion, showing that risk for laryngeal cancer increases with the amount and duration of smoking and falls with successful smoking cessation. Together, alcohol and cigarette smoking are synergistic in increasing risk, which means those with heavy alcohol intake are more susceptible to cigarette smoke as a cause of laryngeal cancer. In fact, most cases of laryngeal cancer arise from these two agents.

Oral cancer

Oral cancers are squamous cell cancers that arise in the mouth and throat. The surfaces of the oral cavity are lined with a cellular membrane that undergoes changes related to smoking. Non-malignant lesions termed leukoplakia are associated with smoking and as genetic damage continues, oral cancers may result. Typically, oral cancers are detected as lumps, often with symptoms of pain or bleeding, and surgical removal may lead to cure, although at the cost of disfigurement. The oral cavity is a site of direct deposition of the particles and gases in tobacco smoke. Presumably this direct exposure and the resulting uptake of carcinogens by the exposed cells lead to cancer. Oral cancers are also caused by the use of smokeless tobacco (Gupta et al. 1996). As with laryngeal cancer, smoking and alcohol intake are synergistic for oral cancer.

Esophageal cancer

Esophageal cancers, predominantly squamous carcinomas, arise in the esophagus, which links the oral cavity to the stomach. These cancers arise from the lining of the surface of this organ and cause symptoms arising from blockage of the esophagus by the cancer and pain as the cancer spreads into surrounding tissues. Survival is poor. Epidemiologic studies show that the risk of esophageal cancer is elevated approximately five-fold in smokers compared with those who have never smoked. At the time of the 1964 report, the evidence was not sufficient to result in a causal conclusion. However, the data were judged to meet the criteria for causality in the 1979 Report of the Surgeon General (USDHEW 1979). At present, there is an unexplained shift in patterns of esophageal cancer with a rise in adenocarcinoma of the distal esophagus. Both types, squamous cell and adenocarcinomas are considered to be caused by smoking (USDHHS 2004).

Stomach cancer

Stomach cancer remains one of the most common cancers around the world, in spite of a steadily declining incidence presumed to reflect better food storage and differing preservation and cooking practices across the decades. We also now know that a bacterium, *Heliobacter pylori*, figures in its causation (IARC 2004). Smokers have been consistently found to have a modestly increased risk

for stomach cancer, and in 2004, both the US Sergeon General and the IARC concluded that smoking is a cause of stomach cancer (USDHHS 2004; IARC 2004).

Cancer of the pancreas

The pancreas is a secretory organ situated at the rear of the abdominal cavity, behind the stomach. It secretes digestive enzymes, which travel in the pancreatic duct to be released into the intestine. The pancreas also secretes insulin and other hormones into the blood. Adenocarcinoma, a cancer of the glandular cells, is the principal type of cancer that occurs in the pancreas. Because of its location and the symptom picture of typical cases, most pancreatic cancers are detected at an advanced stage and survival is poor.

A number of cohort and case-control studies show increased risk for pancreatic cancer in smokers. Compared to never smokers, smokers tend to have an approximately two-fold increase in risk for pancreatic cancer. The risk tends to rise with the number of cigarettes smoked per day and to fall with smoking cessation. Recent reviewing groups, including the IARC (IARC 2004) and the US Surgeon General (USDHHS 2004) have concluded that smoking causes cancer of the pancreas. Causes other than smoking have yet to be identified, although risk appears to be increased by chronic pancreatitis.

Kidney cancer

Kidney cancers arise from the body of the kidney itself (adenocarcinoma of the kidney) and from the renal pelvis, the collecting funnel for the urine formed in the tubules of the kidney. The clinical pictures of these two types of cancers are somewhat distinct with adenocarcinomas tending to spread early and cancers of the renal pelvis causing symptoms primarily by blockage of urine and bleeding. The kidney, as a major excretory organ, is bathed in the tobacco smoke carcinogens, which are in the blood and then concentrated in the urine.

The major cohort studies show evidence of increased mortality from kidney cancer in smokers, as do case-control studies. The increase in risk for smokers compared to never smokers is modest and there is little evidence of a change in risk following smoking cessation. Nonetheless, the data have been judged as showing a causal association between smoking and cancer of the renal pelvis and body. As mentioned above, the 1986 IARC monograph concluded that smoking causes cancer of the renal pelvis. and Doll has extended the causal association to take in adenocarcinoma as well (Doll 1996), a similar conclusion being reached more recently by IARC (IARC 2004) and the US Sergeon General (USDHHS 2004).

Cervical cancer

Cervical cancer remains one of the most common cancers among women worldwide, even though incidence and mortality have fallen sharply in the

developed world where screening programs have been implemented. Over the last two decades there has been a major advance in our understanding of the etiology of cervical cancer with identification of the human papilloma virus (HPV) as the cause of most cases (IARC 2004). Cervical cancer risk is strongly associated with particular genetic strains of the virus (IARC 2004). Even though HPV appears to be a necessary agent for most cases, cigarette smoking also contributes to the development of cervical cancer. Cigarette smoke carcinogens and nicotine have been found in cervical mucus. Many case-control and some cohort studies have examined smoking as a risk factor for cervical cancer but only recently have studies of smoking incorporated assays for HPV. Several studies now show that HPV-positive women who smoke have increased risk for cervical cancer, compared with nonsmokers. In 2004, the IARC classified smoking as a cause of cervical cancer (IARC 2004).

Acute leukemias

The leukemias comprise both acute and chronic leukemias, having differing cells of origin and clinical pictures. For the acute leukemias, the clinical course was poor until recent decades and mortality and incidence rates were close. Increased risk for acute leukemias in adults has been documented in both case-control studies (Severson 1987; Brownson 1989; Severson et al. 1990; Brownson et al. 1991; Brown et al. 1992; Mele et al. 1994) and cohort studies (Weir and Dunn Jr 1970; Paffenbarger Jr et al. 1978; Kinlen and Rogot 1988; McLaughlin et al. 1989; Garfinkel and Boffetta 1990; Mills et al. 1990; Friedman 1993; Doll et al. 1994; Engeland et al. 1997; Tulinius et al. 1997). Risk tends to increase with increasing duration of exposure. Tobacco smoke contains benzene, a well-established occupational cause of leukemia, and smokers have increased levels of benzene in their blood (Hecht 2002). In 2002, the IARC concluded that smoking causes acute leukemia in adults (IARC 2004).

Cancer of the urinary bladder

Cancers of the bladder arise from the cells that cover the bladder's surface. Bleeding is one of the earliest symptoms of bladder cancer. If metastasis (spread) occurs, the disease can be fatal. The bladder, of course, is the site for the storage of urine, which contains carcinogens that have been absorbed, metabolized, and excreted by the kidneys. The urine of smokers has been shown to contain tobacco-specific carcinogens and also has a generally higher level of mutagenic activity, an indicator of the potential to cause genetic damage to cells. Both cohort and case-control studies show increased risk of bladder cancer in smokers compared with non-smokers, generally several-fold. Risks generally tend to increase with the number of cigarettes smoked per day and to fall with cessation. The 1990 Report of the Surgeon General (USDHHS 1990b) concluded

that smoking causes bladder cancer, as did the earlier 1986 report of the IARC (IARC 1986).

2.2.1.4 Cardiovascular diseases

The cardiovascular diseases caused by smoking include coronary heart disease (CHD), arteriosclerotic peripheral vascular disease or atherosclerosis and cerebral vascular disease (stroke) (USDHHS 1983). Coronary heart disease has the clinical manifestations of myocardial infarction (heart attack), angina pectoris (chest pain attributable to inadequate oxygen delivery to the heart muscle), and sudden cardiac death. These conditions have in common the narrowing of the coronary arteries, the blood vessels that carry blood to the heart. Most cases of myocardial infarction result from blockage of the narrowed coronary arteries by thrombus or blood clot. Smoking not only is a cause of the atherosclerosis which tends to narrow the coronary arteries but also increases the tendency of the blood to clot. Myocardial infarction occurs when oxygen delivery to the heart muscle is compromised and the heart muscle damaged. Angina pectoris refers to pain arising from a lack of oxygen without permanent damage to the heart muscle (ischemia).

Atherosclerosis also affects the arteries of the body, compromising blood flow. Symptoms of atherosclerosis arise when blood flow delivers insufficient oxygen for the demands of the muscle it serves or complete blockage occurs leading to tissue damage. The aorta is the major artery of the body, coursing from the heart down through the thoracic and abdominal cavities before dividing. Aortic aneurysm refers to an abnormal dilatation of the aorta. Rupture of an aneurysm can lead to death.

Stroke and cerebrovascular accident are general terms that refer to the clinical consequences of bleeding within the brain or brain tissue death resulting from inadequate oxygen delivery. Strokes can occur if a blood vessel is occluded by a blood clot that has arisen locally or moved from a distant site, or from bleeding within the brain. The mechanisms by which smoking causes stroke are similar to those that lead to myocardial infarction.

The epidemiologic evidence on the cardiovascular diseases is massive, coming from case-control studies and a number of cohort studies, including the renowned Framingham Study (USDHHS 1990b) and the Nurses' Health Study (Stampfer et al. 2000). Risk for the cardiovascular diseases increases with the number of cigarettes smoked per day and with the duration of smoking. For example, in the Nurses' Health Study the rate of fatal coronary heart disease among participants who never smoked was 5 per 100,000 person-years. This rate increased to 8, 19, and 27 deaths per 100,000 person-years for current

smokers who smoked 1-14, 15-24, and ≥25 cigarettes per day, respectively. For women who smoked ≥25 cigarettes per day, the adjusted relative risk for fatal coronary heart disease compared to never smokers was 5.4, and it was reported that 81% of the coronary heart disease deaths among these heavy smokers were attributable to cigarette smoking (Willett et al. 1987). Smoking cessation reduces the risk of the cardiovascular diseases. For coronary heart disease, the risk tends to decline rapidly immediately following cessation. After one year of not smoking, the risk to the former smoker has been reduced by about half from the risk to the current smoker, and with continued abstinence reaches that of the never smoker after about five years. Smoking cessation also reduces risk for stroke. For the cardiovascular diseases, smoking lower tar and nicotine cigarettes has not been shown to affect risk. The cardiovascular diseases have causes other than smoking, including, for example, hypertension and elevated cholesterol. After taking these factors into account, many epidemiologic studies still have identified an independent effect of smoking on disease risk; thus, the increased risk for cardiovascular disease in smokers does not reflect confounding by some aspect of lifestyle not taken into account in these studies.

2.2.1.5 Repiratory diseases

Chronic obstructive pulmonary disease (COPD)

COPD is a clinically used diagnostic label that refers to the permanent loss of lung function that affects some cigarette smokers, resulting in shortness of breath, impaired exercise capacity, and frequently a need for oxygen therapy (American Thoracic Society et al. 1987). In the past, the term 'emphysema' was often the diagnostic label for the same disease, but COPD is more widely applied today. COPD is characterized by slowed emptying of air from the lung, reflecting underlying narrowing of the airways of the lung and a loss of elasticity from the development of emphysema. Emphysema properly refers to permanent destruction of the alveoli, the air sacs of the lung. COPD is currently a rising cause of mortality in the United States, accounting for over 117,000 deaths annually (American Lung Association 2003). The current increase is likely to reflect past patterns of smoking and also the declining rates of mortality from cardiovascular disease, which have left a larger pool of persons with COPD at risk for respiratory death.

This disease develops progressively in a minority of smokers (USDHHS 1984, 1990b). Its appearance reflects an acceleration of the usual age-related loss of lung function (Fletcher and Peto 1977). In some smokers, this loss is accelerated and eventually lung capacity becomes reduced to a level at which functioning is affected and the symptoms of COPD occur. Cigarette smoking causes inflammation of the lungs, with the migration of inflammatory cells into

the lungs and release of enzymes that can destroy the lung's delicate structure. Smoking activates the inflammatory process and reduces the efficacy of defenses against inflammation. Unchecked inflammation, sustained over many years, underlies the development of COPD (USDHHS 1984).

Relevant epidemiologic evidence comes from research on the level of lung function in smokers and nonsmokers and on changes in the degree of lung function over time in relation to smoking; mortality from COPD has been described in cohort studies as well (USDHHS 1984, 1990b). The studies of lung function show that smokers, in comparison with nonsmokers, have a lower level of function on average and that the level of function declines as the number of cigarettes smoked per day increases. Smokers, followed over time, have a faster decline in lung function, on average, than non-smokers. The decrement is an approximate doubling for smokers overall, compared with nonsmokers, but some susceptible smokers loose lung function at an even faster rate. The rate of decline in smokers reverts to that of non-smokers following successful quitting. Unfortunately, the damage prior to cessation is mostly irreversible. Mortality rates for COPD are elevated in smokers compared with non-smokers by approximately ten-fold. Former smokers tend to have particularly high mortality from COPD, because the development of lung disease leads many of them to quit. There is no consistent evidence that risk for this disease is associated with the tar and nicotine yield of the cigarettes smoked.

Only a few of the factors that place smokers at increased risk for COPD have been identified, beyond the cumulative amount of smoking. One relatively uncommon genetic disorder, alpha-1-antitrypsin deficiency, markedly increases risk for early development of COPD in homozygotes. Occupational exposures may heighten risk by also accelerating the decline in lung function.

Respiratory morbidity

Respiratory infections, including influenza and pneumonia, remain a leading cause of morbidity and mortality worldwide. The scope of respiratory infections extends from the common cold, caused by viruses, to fatal pneumonias, sometimes caused by exotic organisms. The most common types of respiratory infections, colds and the lower respiratory tract infections - laryngitis, bronchitis, and pneumonia - are primarily caused by various respiratory viruses, but bacteria and other types of organisms can also cause pneumonia, particularly in the elderly. Persons with the smoking-caused conditions COPD and coronary heart disease are particularly susceptible to the development of more severe respiratory infections. Moreover, respiratory infections are often the cause of death in persons with underlying COPD and in older people generally. Respiratory infections are also one of the most frequent causes of morbidity in the general population and even healthy persons have several respiratory infections per year.

There is voluminous epidemiologic evidence on respiratory health and health status in relation to smoking. Many studies have described the association of smoking with respiratory symptoms, respiratory infections, and several indicators of reduced health status generally. Epidemiologic data from cross-sectional and cohort studies provide convincing evidence that smoking increases the occurrence of the cardinal respiratory symptoms - cough (i.e., 'smoker's cough'), sputum production, wheezing, and dyspnea (shortness of breath). Symptom rates are substantially higher in smokers in comparison with those who have never smoked and tend to increase in frequency with the number of cigarettes smoked per day. The Surgeon General's Reports have commented on these associations and described the relationship between smoking and cough and phlegm as causal (Table 2.1).

There is also mounting and consistent evidence that smoking increases risk for respiratory infection (USDHHS 2004). In a number of the prospective cohort studies, mortality from respiratory infections was higher in smokers than in those who never smoked. Other studies show increased incidence of respiratory infections in smokers as well. Smokers have thus been shown to have more respiratory infections than nonsmokers and possibly more severe respiratory infections as well.

This increased risk for respiratory infections in smokers may partially explain the generally poorer health status of smokers in comparison with nonsmokers. In comparison with nonsmokers, smokers have greater utilization of health care services, higher rates of absenteeism from work, and poorer self-reported health status. There is evidence of improvement in these indicators with smoking cessation. The 1990 Surgeon General's Report commented on the better health status of former smokers in comparison with current ones (Table 2.1) (USDHHS 1990b).

Considered in its entirety, there is a substantial body of epidemiologic evidence on respiratory morbidity and respiratory infections, and on morbidity and health status generally in smokers. Since respiratory infections are a principal cause of morbidity and mortality at all ages and consequently, the complementary sets of evidence on respiratory morbidity and mortality and impaired health status generally can be considered together. The extensive and consistent evidence shows increased risk for respiratory infections and morbidity and for poorer health status generally in smokers compared with nonsmokers. Dose-response relationships have been demonstrated between these outcomes and numbers of cigarettes smoked per day. The biologic basis for these associations appears to lie in the diverse effects of smoking on the lung and on defenses against respiratory pathogens. The Surgeon General's Reports have repeatedly commented on respiratory morbidity in smokers and also on the poorer health status of smokers (USDHEW 1964, 1971, 1979; USDHHS 1980, 1984, 1990a).

2.2.1.6 Reproductive outcomes

Smoking by the mother adversely affects reproduction. Smoking during pregnancy reduces birth weight by approximately 200 grams on average (USDHHS 1990a), and the degree of reduction is related to the amount smoked. If a mother who smokes gives up this behavior by the third trimester, much of this weight reduction can be avoided. Smoking also increases rates of spontaneous abortion, placenta previa, and perinatal mortality, and smoking during pregnancy is now considered to be a cause of sudden infant death syndrome (SIDS). There is more limited evidence suggesting that smoking by the mother may increase childhood cancer incidence and risk for congenital defects (Charlton 1996; Scientific Committee on Tobacco and Health 1998).

2.2.1.7 Gastrointestinal disease

Peptic ulcer

Peptic ulcers are disruptions (ulcers) of the lining of the stomach and the duodenum (the first part of the small intestine). Peptic ulcers are usually characterized by abdominal pain and bleeding. Although peptic ulcers are a relatively uncommon cause of death, they remain a substantial source of morbidity. For uncertain reasons, morbidity and mortality from peptic ulcer disease have declined sharply in the last decades.

Smoking has multiple effects on the gastrointestinal tract that may be relevant to peptic ulcer disease. The 1990 Report of the Surgeon General (USDHHS 1990b) reviewed the effects of smoking on gastrointestinal physiology. Smoking increases gastric acid secretion and tends to increase duodenogastric reflux (reflux of bile from the duodenum into the stomach). *Helicobacter pylori*, a bacterium, is now recognized to be a major cause of peptic ulcer disease (Kurata and Nogawa 1997). The 1990 Report notes that smoking is associated with peptic ulcer disease in persons with gastritis caused by this organism.

The association of smoking with peptic ulcer disease has been thoroughly documented in the Reports of the Surgeon General and smoking is considered to be a cause of peptic ulcer disease. The evidence has also indicated that smoking retards the healing of peptic ulcers and the 1990 Report of the Surgeon General concluded that smokers who stop smoking may improve the clinical course of peptic ulcer disease in comparison with those who continue to smoke following the diagnosis.

2.2.1.8 Effects on children

The 1994 Surgeon General's Report (USDHHS 1994) considered the

epidemiologic findings on active smoking and respiratory health of children, covering respiratory symptoms, lung function, and general respiratory morbidity. These studies documented increased respiratory symptoms in children smoking actively, in comparison with those who did not smoke. Symptoms included increased respiratory morbidity, and adverse effects on lung function - effects similar to those in adults. However, COPD is not observed in children, as many years of sustained smoking are generally needed to cause this condition. Evidence cited in the 1994 report and more recent reports (Gold et al. 1996) show that active smoking slows the rate of lung growth during adolescence. The evidence in the report also indicates less favorable lipid profiles in children who smoke.

2.2.1.9 Implications for smoking and disease risk in Japan

This literature review covers the range of causal conclusions that have been reached on active and passive smoking (Tables 2.1 and 2.2). These conclusions have been reached through careful, evidence-based reviews that have evaluated the evidence against rigorous criteria for causality. While epidemiological research has been central in reaching these conclusions, there is substantial supporting experimental evidence as well, and the mechanisms by which smoking causes a number of disease have been well worked out.

This deep understanding of the causation of disease by smoking offers a strong foundation for confidently extending the causal conclusions on active and passive smoking to Japan. Neither the Japanese nor Japanese cigarettes have such unique characteristics that the consequences of active and passive smoking would differ qualitatively in Japan from what has been observed elsewhere. Risks might quantitatively differ to some extent because of differing patterns of other risk factors for some diseases, comparing Japan and other countries, and possibly because of some differences in the characteristics of the cigarettes.

For some diseases caused by active smoking, risks might be expected to be somewhat lower in Japan compared to western countries. This expectation reflects historical patterns of smoking; while smoking was common in Japan among men after the Second World War, the numbers of cigarettes smoked were relatively small until more recent decades. As risks rise for most chronic diseases with increasing numbers of cigarettes smoked, the lighter smoking of the past predicts lower relative risks for the present, particularly for cancer and perhaps COPD. Unfortunately, today's present heavy smoking in Japan predicts rising relative risks from cancer. These risks may also rise as the age at which smoking is started drops to younger and younger ages. Because risks for many cancers rise exponentially with increased duration of smoking, an earlier age of starting to smoke also predicts rising cancers caused by smoking.

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2.2.2 Health effects of passive smoking

2.2.2.1 Terminology of passive smoking

The inhalation of tobacco smoke by nonsmokers has been variably referred to as passive smoking or involuntary smoking. Cigarette smoke contains both particles and gases generated by the combustion of tobacco, paper and additives at high temperatures. The smoke inhaled by nonsmokers that contaminates indoor spaces and also outdoor environments has often been referred to as secondhand smoke (SHS) or environmental tobacco smoke (ETS). This smoke is a mixture of sidestream smoke (SS) released by the smoldering cigarette and the mainstream smoke (MS) that is exhaled by the smoker. Sidestream smoke, generated at lower temperatures and more reduced conditions than MS, tends to have higher concentrations of many of the toxins in cigarette smoke (US Department of Health and Human Services (USDHHS) 1986).

2.2.2.2 Health effects

Evidence on the health risks of passive smoking comes from epidemiological studies which have directly assessed the associations of SHS exposure with disease outcomes, and also from knowledge of the components of SHS and their toxicities. Judgments as to the causality of association between SHS exposure and health outcomes are based not only on this epidemiological evidence, but also on the extensive evidence derived from epidemiological and toxicological investigation of active smoking. Additionally, studies using biomarkers of exposure and dose, including the nicotine metabolite cotinine and white cell adducts, document the absorption of SHS components by exposed nonsmokers, adding to the plausibility of the observed associations of SHS with adverse effects. The adverse effects of passive smoking extend across the lifespan.

Secondhand smoke exposure of the infant and child has adverse effects on respiratory health, including increased risk for more severe lower respiratory infections, middle ear disease, chronic respiratory symptoms, and asthma and a reduction in the rate of lung function growth during childhood. There is more limited evidence suggesting that SHS exposure of the mother reduces birth weight and that child development and behavior are adversely affected by parental smoking (Eskenazi and Castorina 1999; World Health Organization 1999). There is no strong evidence at present that SHS exposure increases childhood cancer risk (Boffetta et al. 2000; International Agency for Research on Cancer (IARC) 2004).

In adults, SHS exposure has been causally associated with lung cancer and with ischemic heart disease. The association of SHS with lung cancer has now been evaluated in about 50 epidemiological studies. The first major study to find

an association was, of course, Dr. Hirayama's cohort study in Japan (Hirayama 1981). The 2002 IARC meeting summarizes the data on lung cancer and SHS as follows:

More than 50 studies of involuntary smoking and lung cancer risk in never smokers, especially spouses of smokers, have been published during the last 25 years. These studies have been carried out in many countries. Most showed an increased risk, especially for persons with higher exposures. To evaluate the information collectively, in particular from those studies with a limited number of cases, meta-analyses have been conducted in which the relative risk estimates from the individual studies are pooled together. These meta-analyses show that there is a statistically significant and consistent association between lung cancer risk in spouses of smokers and exposure to secondhand tobacco smoke from the spouse who smokes. The excess risk is on the order of 20% for women and 30% for men and remains after controlling for some potential sources of bias and confounding. The excess risk increases with increasing exposure. Furthermore, other published meta-analyses of lung cancer in never smokers exposed to secondhand tobacco smoke at the workplace have found a statistically significant increased risk of 16 to 19 per cent. This evidence is sufficient to conclude that involuntary smoking is a cause of lung cancer in never smokers. The magnitudes of the observed risks are reasonably consistent with predictions based on studies of active smoking in many populations (IARC 2004).

An epidemiological report considered inconsistent with the causal conclusion (Enstrom and Kabat 2003) does not provide sufficient scientific evidence to reverse the IARC position (Hackshaw 2003). Since 1986, other expert groups have also found SHS to be a cause of lung cancer in nonsmokers (US Environmental Protection Agency (EPA) 1992; Australian National Health and Medical Research Council 1997; California Environmental Protection Agency 1997; Scientific Committee on Tobacco and Health 1998; IARC 2004). Coronary heart disease has also been causally associated with ETS exposure, based on observational and experimental evidence (Taylor et al. 1992; Glantz and Parmley 1995; California Environmental Protection Agency 1997; Scientific Committee on Tobacco and Health 1998). In a 1997 meta-analysis, Law and Hackshaw (1997) estimated the excess risk from ETS exposure as 30% (95% CI 22-38%) at age 65 years. There is also evidence linking ETS to other adverse effects, including exacerbation of asthma, reduced lung function, and respiratory symptoms, but the associations have not yet been judged causal (California Environmental Protection Agency 1997; Scientific Committee on Tobacco and Health 1998; Samet and Wang 2000).

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2.3 Health Effects of Smoking in Japan

2.3.1 Health effects of active smoking

2.3.1.1 All cause mortality

Data are available on all cause mortality from a number of cohort studies. Hirayama (1990), in describing the characteristics of a 1965 census-based large-scale cohort study consisting of a community population of 265,000 subjects from six prefectures (Six Prefecture Cohort Study), summarized the 17-year follow-up results in his monumental work, "Life-Style and Mortality" in 1990. The results demonstrated significantly higher age-standardized mortality rates for daily smokers compared to non-smokers. The relative risk (RR) (90% CI) of daily smokers was 1.29 (1.26-1.32) for men and 1.31 (1.27-1.36) for women, and thus quite close between the sexes.

These results were further stratified according to the number of cigarettes smoked per day. Among men, the relative risks were 1.35 (1.30-1.41), 1.25 (1.22-1.29) and 1.29 (1.25-1.33) for smokers of 1-9, 10-19 and 20 or more cigarettes per day, respectively. Among similar groups of women, it was 1.30 (1.24-1.36), 1.32 (1.25-1.38) and 1.40 (1.26-1.56), respectively.

When stratified by the age when individuals first took up smoking, the relative risk for men was 1.35 (1.30-1.41) when smoking began at 19 years of age or younger, and 1.27 (1.23-1.30) for those who started smoking at 20 years of age or later. Respective values for female smokers were 1.33 (1.12-1.59) and 1.29 (1.24-1.34). The relative risk values were thus somewhat elevated for those who started smoking early.

To evaluate the effect of smoking cessation on relative risk, follow-up

data on ex-smokers were stratified according to the duration (years) of smoking cessation. For male ex-smokers, the relative risk was 1.31 (1.21-1.42), 1.17 (1.05-1.31) and 0.91 (0.82-1.02) after a tobacco-free period of 1-4 years, 5-9 years, and 10 years or longer, respectively; and for female ex-smokers, it was 1.63 (1.31-2.02), 1.32 (0.95-1.84) and 1.57 (1.16-2.12), respectively, after the same number of years. Among men in particular, the relative risk decreased with the duration of smoking cessation.

Hirayama observed that although cigarette smoking increased the risk of dying from diverse causes, the extent of the increase was also determined by age. Using age-specific mortality rates of the above Six Prefecture Cohort Study cited by Akiba and Mizuno (1998), and substituting the relative risks for their mortality ratios, among male smokers in the age groups of 40-49, 50-59, 60-69 and 70-79, these were 0.92, 1.12, 1.29 and 1.40 for smokers of 1-14 cigarettes per day; 0.79, 1.09, 1.20 and 1.36 for smokers of 15-24 cigarettes per day; and 0.92, 1.17, 1.22 and 1.26 for smokers of 25 or more cigarettes per day, all respectively. While unexpectedly low in the youngest group (RRs $\leqq$ 1.00), they systematically increased for all age groups among men. For women, higher relative risks were observed for those in their fifties and among heavy smokers. These findings indicate how age may affect the risk of smoking.

Toshima et al. (1995) reported the results from the Seven Countries study in Japan for 1958 to 1985. The subjects were 1,010 men at baseline ages of 40 to 59 years. The relative risk of smokers of 15 to 20 cigarettes per day was 1.24 to 1.34, which was calculated by using the coefficients in a Cox multivariate regression model. With the inclusion of changes in risk factors over the first 10 years, the relative risk of a smoker of 10-20 cigarettes per day was estimated to be 1.13 to 1.29. These estimates are in general agreement with those of the above Six Prefecture Cohort Study.

Tomita et al. (1991), following an occupational cohort of younger men (n=37,646) from 1975 to 1985, obtained the following relative risks (95% CI): 1.95 (1.51-2.51), 1.59 (1.31-1.94), 1.38 (1.08-1.76), 1.41 (1.02-1.92) and 1.49 (0.47-2.27) for smokers of 1-14, 15-24, 25-34, and 35 or more cigarettes per day, and ex-smokers, respectively. The relative risks were higher in this cohort than in the six-prefecture study cited above, although the dose-response relationship with the number of cigarettes smoked was not particularly clear.

Kawaminami et al. (2003) followed up to the year 1999 subjects whose baseline data were collected in the National Cardiovascular Survey in 1980 (n=10,546). This study was carried out for all household members 30 years or older in 300 districts throughout Japan. The relative risks for male smokers were reported as 1.19 (0.98-1.45), 1.45, 1.31 (1.10-1.56), 1.52 (1.23-1.89) and 1.58 (1.04-2.41) for ex-smokers, all smokers, and smokers of up to 20, 21-40 and 41

or more cigarettes/day, respectively. For female smokers, the relative risks were 1.10 (0.75-1.59), 1.24, 1.27 (1.02-1.58), and 1.98 (1.05-3.74) cigarettes/day, respectively (no woman smoked more than 40 cigarettes/day). For male smokers overall, the relative risk was elevated to 1.45.

Ito et al. (1997) followed 929 male and 1,424 female residents in a rural region in Japan from 1986 to 1994, and reported relative risks of 1.47 and 1.32 for current male smokers and ex-smokers, respectively, and 1.41 and 3.06 for their female counterparts, respectively.

Morioka (1996) followed 1,308 male residents in a rural region from 1988 to 1994 and reported that the relative risks for male smokers were 1.40 (0.94-2.08), 1.60 (1.04-2.44) and 2.12 (1.28-3.51) during the follow-up periods of 1989-1994, 1990-1994 and 1991-1994, respectively. The relative risk values were elevated, with higher values in the later periods.

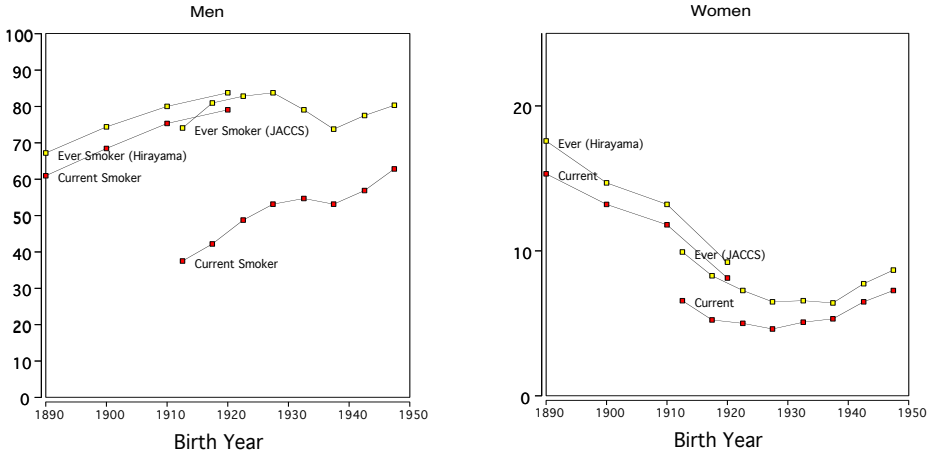
Following 7,662 rural residents from 1990 to 1997, Takezaki et al. (1999) reported that the relative risks by smoking category were 1.27 (smokers) and 2.15 (ex-smokers who quit smoking within the past year) for men and 1.72 (smokers) and 1.81 (tobacco-free for less than one year) for women. In this cohort study, never-smokers and ex-smokers who had quit for more than one year were aggregated.

Hara et al. (2002) followed 19,950 men and 21,534 women aged 40 to 59 years in a population-based prospective study from 1990 to 1999. The relative risks for male and female smokers were 1.66 (1.40-1.95) and 2.03 (1.52-2.73), respectively. With regard to dose-response, relative risks for men were 1.00, 0.95 and 0.96 for 1-19, 20-29 and 30 or more cigarettes per day, respectively (with 1-19 cigarettes/day used as a reference point). The highest relative risk for men was observed in those smoking the fewest cigarettes per day. The relative risks for women were 1.00, 1.27 and 2.20, respectively.

In summary, the relative risks of smoking appear to have increased in recent decades with respect to all causes of death among both men and women. With regard to dose-response, relationships with number of cigarettes smoked were inconsistent in men but apparent in women. In men, the highest relative risks were sometimes observed for those smoking the fewest cigarettes smoked per day.

Figure 2.4 describes smoking prevalence by birth cohort in the Hirayama data and afterwards (Research Group on Evaluation of Risk Factors for Cancer by Large-Scale Cohort Study 1996). These patterns, along with numbers of cigarettes smoked, are relevant background to interpreting the all-cause mortality risk. While the prevalence of ever-smoking has been relatively stable among men, the number of cigarettes smoked has increased. Unexpectedly, however,

Figure 2.4 Smoking Prevalence (%) by Birth Cohort in Japan

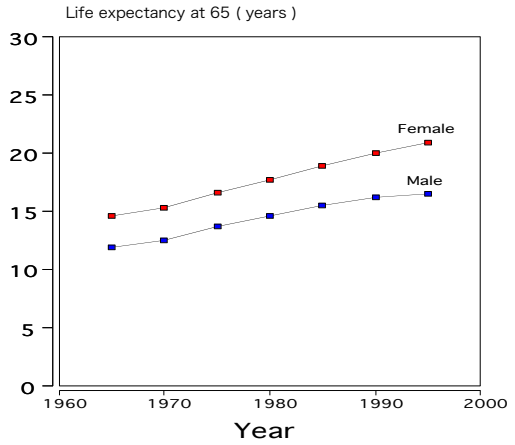


Source: Research Group on Evaluation of Risk Factors for Cancer by Large-Scale Cohort Study 1996

the relative risk for lung cancer in the most recent cohort study was almost the same as in Hirayama's cohort.

In spite of the heavy smoking among men, their life expectancy improved from 1960 on (Figure 2.5). Of course, multiple factors determine life expectancy and fortunately the balance of these factors contributed to rising life expectancy in Japanese men, even as their smoking increased. Undoubtedly, smoking contributes to the male-female gap in life expectancy.

Figure 2.5 Increase in Life Expectancy at Age 65 in Japan



Note: Data from vital statistics of Ministry of Health, Labour and Welfare (http://www.mhlw.go.jp)

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2.3.1.2 Cancer

Based on studies in many countries throughout the world, including Japan, tobacco smoking is a well-established cause of cancers of multiple organs (International Agency for Research on Cancer (IARC) 2004; USDHHS 2004). This chapter reviews reports on smoking and cancer in Japan with the overall goal of comparing the evidence on smoking and cancer in Japan with evidence obtained in other countries around the world. For this purpose, the chapter's authors carried out a comprehensive search for reports on smoking and cancer in Japan. A literature search carried out in March, 2003, identified 1,246 reports through PubMed, using the search terms ((smoking OR smoker OR smoke OR tobacco) AND Japan*) AND (cancer OR tumor OR neoplasm) AND human) , then restriction with ((cohort OR case OR epidemiol*) NOT case report) left 763 reports. The reviewing authors (I.Y. and T.S.) selected 288 reports for examination, including case-control and cohort studies. Additionally, studies of multiple sites, second primary cancers, and cancer genetics were also included.

The findings of these studies are summarized in an extensive series of evidence tables (Appendix B). These tables provide design features and quantitative results. Further description of individual studies is provided as an appendix to this chapter (Appendix A) and the studies are further described, along with their findings, in a database prepared for this report. Approximately 200 reports were referenced in this chapter and in the database.

(1) Specific cancer site

Head and neck cancers

Head and neck cancers have been studied in Japan, as elsewhere, with both case-control and cohort approaches. Cancers of the neck and head include a number of anatomically distinct loci: the lip, the oral cavity, the sinonasal cavity, the pharynx, and the larynx. These have been grouped by investigators in a number of ways because of the relatively similar effects of smoking and of alcohol in increasing cancer risks across these sites. These cancers have also been combined with esophageal cancer in a grouping often referred to as "upper aerodigestive" cancers. Lung cancer has been added by some researchers in an even broader grouping referred to as "aerodigestive."

Tobacco use and alcohol consumption are well-characterized causal factors for these cancers, and the combined effect of these two agents is synergistic, explaining most of the occurrence of these cancers around the world (IARC 2004). This synergism implies that the impact of smoking in causing these cancers depends on the pattern of alcohol use among smokers. The studies in Japan span from the 1960s through the 1990s. The point estimates for smokers

compared to non-smokers are around two in the various studies for cancers of the oral cavity, pharynx, and upper aerodigestive grouping. Esophageal cancer risks were much higher. In general, strong dose-response relationships are evident with the number of cigarettes smoked or cumulative smoking, e.g. pack-years. A few studies showed lower risk in former smokers compared with current smokers. Because of the shared risk factors for the individual head and neck cancer sites, second primary tumors frequently involve the aerodigestive sites. Smoking has been shown to increase risk for second primary tumors of these sites (Kobayashi et al. 1990; Hiyama et al. 1992; Nakamizo et al. 1993; Morita et al. 1994).

Esophageal cancer

Risk factors for esophageal cancer, like head and neck cancer, include tobacco smoking and alcohol use. Some studies included this site in the grouping upper aerodigestive. Hirayama's cohort study showed early and clear evidence linking tobacco smoking to esophageal cancer (Hirayama 1990). In a 1990 report, among male smokers, he found that the relative risk was more than doubled (RR=2.24, 94% CI 1.72-2.91) and was similarly elevated for female smokers (RR=1.75, 94% CI 1.21-2.51). The study provided clear evidence of a dose-response with the number of cigarettes smoked per day in both men and women. Compared to non-smokers, men smoking 1 to 9, 10-19 and more than 20 cigarettes per day had significantly increased risks for esophageal cancer of 1.62, 2.04, and 2.69, respectively. The strength of the association was similar for women.

Subsequent studies have provided confirmatory evidence with relative risks tending to be somewhat higher than those estimated earlier in the cohort study carried out by Hirayama (Nakachi et al. 1988; Kinjo et al. 1998; Takezaki et al. 2000). Takezaki et al. (2000) reported odds ratios for current cigarette smoking and esophageal cancer of 3.5 (95% CI 2.1-5.8) from a case-control study conducted among men in Nagoya. Another case-control study also found a significantly increased risk in women (OR 2.30, 95% CI 1.02-5.17) but not in men (OR 2.37, 95% CI 0.99-5.69) (Nakachi et al. 1988).

Dose-response relationships with numbers of cigarettes smoked and with duration of smoking were documented in some of these studies. The increased risk is well documented for both men and women. In the cohort study by Takezaki et al. (2000), the odds ratio for men was more than three times higher for those smoking 1 to 9 and more than 20 cigarettes per day compared to never-smokers (Takezaki et al. 2000). Results from the Hirayama study showed that men smoking 1 to 14 cigarettes per day and 15 or more had odds ratios of 2.3 (95% CI 1.5-3.3) and 2.7 (95% CI 1.8-3.8), respectively. Women smoking less than 14 cigarettes per day also had an increased risk of esophageal cancer (OR 1.8, 95% CI 1.1-3.0) (Kinjo et al. 1998).

A cohort study conducted in Hawaii among Japanese-Americans showed a much higher risk of developing upper aerodigestive tract cancer, including esophageal cancer, among those who smoke cigarettes and drink alcohol (Kato et al. 1992; Chyou et al. 1995). However, a case-control study conducted in Japan (Hanaoka et al. 1994) did not observe a synergistic effect of alcohol drinking and cigarette smoking for esophageal cancer, although full details were not given.

Stomach cancer

The epidemiologic characteristics of stomach cancer in Japan differ from those in many western countries (Nomura 1996). The incidence rate is substantially higher (69.20 for males and 28.64 for females in Japan vs 7.61 for males and 3.62 for females in the US (Ferlay et al. 2001), as the figure for Japan includes gastric ulcers, which are viewed as a significant source of gastric carcinoma in Japan, but not in the West (Nomura 1996).

Also differing significantly is the location of the tumors (Ekstrom et al. 1999; Okabayashi et al. 2000; Blaser and Saito 2002): a study in Japan using national registry data found that as few as 18% of stomach cancers were located in the cardia (Blaser and Saito 2002), while in some western countries, the estimate for cancers in the cardia is as high as 45% (Ekstrom et al. 1999). The majority of stomach cancers in Japan are located in the middle and distal thirds of the stomach (82%) (Blaser and Saito 2002).

Studies in Japan generally show relative risks similar to those carried out elsewhere; some studies show no indication of association, while other studies show risks in smokers to be two-fold or more compared with never-smokers. Evidence comes from both cohort and case-control studies, beginning with the Hirayama cohort (Hirayama 1990), which showed an increased risk in stomach cancer in both males (RR 1.45, 95% CI 1.33-1.57) and females (RR 1.18, 95% CI 1.05-1.33). Subsequent case-control studies have generally provided similar results with dose-response relationships, with numbers of cigarettes smoked reported in some studies. Several studies have examined the association of smoking with cancers of different locations within the stomach, as well as with stratification by histologic type. In one study, the association with smoking was stronger for cancers of the gastric cardia (Inoue et al. 1994). Kato et al. (1990) did not find differences in risk by histologic type. Sasazuki et al. (2002) found some variation in risk by histologic type and location. They observed twice the increase in risk of developing differentiated distal gastric cancer in both current and former smokers compared to never-smokers. The strength of the association was similar to smoking status for cigarettes per day, age started smoking, and pack-years of smoking. The authors observed a negative association for the undifferentiated type of distal gastric cancer. For cardia cancer, an increased although not statistically significant risk was observed for former (RR 1.6, 95% CI 0.5-5.5) and current (RR

2.4, 95% CI 0.8-7.1) smokers compared to never-smokers. They also found similar results for cigarettes per day, age started smoking, and pack-years of smoking.

While the association of smoking with stomach cancer has long been noted and investigated, only recently has the association been designated as causal (IARC 2004).

Colorectal carcinoma and adenoma

Only recently has substantial evidence accumulated on smoking and colorectal cancer and adenoma (Giovannucci 2003). As adenomas are considered to be precursor lesions for carcinoma, evidence on the association of adenoma with smoking is relevant to colorectal cancer generally. The evidence on colorectal carcinoma and smoking was recently reviewed by the International Agency for Research on Cancer (IARC)'s Working Group, which did not find the evidence sufficient to warrant a causal conclusion (IARC 2004). The findings of the 2004 Surgeon General's Report were similar (USDHHS 2004).

The evidence from Japan, both for colorectal adenomas and carcinomas, is mixed, consistent with findings elsewhere. Five case-control studies were identified on colorectal adenomas and cigarette smoking. Several showed significantly increased risk for adenomas with dose-response relationships with numbers of cigarettes smoked. On the other hand, other studies did not show significant associations. Case-control and cohort studies of colorectal cancer provided a similarly mixed body of evidence.

Liver cancer

Liver cancer has several well-established causes, including infection with hepatitis B and C viruses, exposure to aflatoxin, and alcohol consumption. In characterizing the association of smoking with tobacco use, confounding by alcohol is of particular concern, given the higher rate of alcohol use by smokers.

The studies carried out in Japan, which included both case-control and cohort studies, have considered these other factors to a varying extent. Across the collective evidence, risk for liver cancer was shown to be increased by smoking, with possible confounding by alcohol and/or hepatitis B or C, considered in several of these studies. The risk tended to be greater for those smoking more heavily. The relative risk values, ranging up to a value of two, are comparable to those observed in other populations.

Pancreatic cancer

Pancreatic cancer, while considered to be caused by smoking (IARC 2004), is not strongly associated with tobacco use. Relative risk values tend to be two or less comparing smokers to never-smokers. Generally, the risks in studies from Japan are in this range, with substantially greater risks observed for heavy

smokers. The evidence for dose-response with increasing number of cigarettes smoked is inconsistent.

Lung cancer

Lung cancer has been studied extensively in Japan with substantial data available from cohort and case-control studies. Additionally, there is substantial recent work on lung cancer in Japan using "molecular epidemiology" approaches. These studies have not been systematically reviewed here.

In Japan the relative risks, comparing smokers to never-smokers, range as high as ten with values typically around five for males. For women, the data are more limited; the relative risks tend to be lower than in men with values ranging from approximately two to four.

For former smokers, the anticipated pattern of greater risk than for never-smokers but lower risks than for current smokers is found. This pattern was observed in studies of men and also of women. Additionally, the anticipated pattern of increasing relative risk with number of cigarettes smoked, duration of smoking, and pack-years was also observed (Ando et al. 2003).

A number of studies have examined relative risk by histologic type of lung cancer. In other countries, squamous cell and small cell carcinoma have been the histologic types most strongly associated with smoking, with a lesser effect for adenocarcinoma. However, more recent studies in the United States have shown rising relative risk for adenocarcinoma, coincident with the shift towards adenocarcinoma as the most common histology type (Alberg and Samet 2003).

The studies from Japan, carried out during the 1980s and 1990s, show a strong association of smoking with squamous cell carcinoma. Increased risks were also found, in a smaller number of studies, for small-cell and large-cell carcinomas.

Seven case-control studies examined the relationship between adenocarcinoma and current smoking. For men, five showed a significant increase; for women, three of the seven found an increased risk. In general, similar to patterns observed historically in other countries, the relative risks tended to be lower than for squamous-cell carcinoma and small-cell carcinoma.

Breast cancer

Only limited data have been reported on smoking and breast cancer risk in Japan. Overall, the evidence worldwide does not indicate increased risk for smokers compared with never-smokers (IARC 2004). The eight studies in Japan provide evidence consistent with the worldwide synthesis by the Oxford pooling project (Hamajima et al. 2002). A few point estimates were significantly elevated, but only modestly.

Cervical cancer

For cervical cancer, we now know that human papilloma virus (HPV) is likely a necessary causal agent (Bosch et al. 2002). Thus, the risks of cervical cancer in smokers are best studied by following cohort HPV-positive women to assess whether smoking increases risk for pre-neoplastic lesions or carcinoma. The studies in Japan have been of the case-control design and have not specifically controlled for HPV infection, nor considered the causal role of this agent that is now considered to be well established. Consistent with studies carried elsewhere, subject to the same methodological limitation, the studies in Japan showed increased risk for cervical cancer in smokers compared to non-smokers.

Ovarian cancer

Ovarian cancer has not been associated with smoking in studies in other countries. The one study carried out in Japan, a case-control study, showed an increased, but not significant, risk (RR= 1.60 94% CI 0.78-3.7).

Prostate cancer

Worldwide, smoking has been associated with increased prostate cancer mortality, but not incidence. This pattern may be explained by differences in the screenings between use of screening of smokers and non-smokers, or alternatively reflect different biologic behavior in prostate cancer in smokers and non-smokers. Two case-control studies in Japan do not show increased risk.

Bladder cancer

Bladder cancer has been studied with case-control and cohort designs. The studies consistently show increased risks in smokers, along with evidence of dose-response with amount smoked. Morrison et al. (1984) carried out parallel case-control studies in Japan, the United States, and England. In all three study's areas a history of cigarette smoking was associated with an increased risk for bladder cancer. The relative risk for bladder cancer in Nagoya, Japan was 1.7 (95% CI 1.1-2.9) for men and 4.3 (95% CI 2.0-9.2) for women. The authors observed similar results for Boston, US but not for Manchester, UK. The risk of bladder cancer in Manchester was slightly higher (RR 2.2, 95% CI 1.4-3.5) for men and lower for women (RR 1.3, 95% CI 0.8-2.0). Among men, a dose-response relationship for bladder cancer and packs smoked per day was observed in the three study areas. Japanese men had lower relative risks than American or English men.

Hematopoietic disorders

Increasing evidence in the last two decades has associated smoking with acute leukemias, leading to the recent conclusion by the IARC (IARC 2004) that

smoking causes myeloid leukemias. Several studies in Japan provide evidence for increased risk as well.

Combined sites

Several cohort studies provide data on risk of cancer overall, combining all sites. Not surprisingly, given the many sites of cancer causally associated with smoking, risk for cancer overall is increased in smokers.

(2) Population attributable risk

Population attributable risk estimates, which can be made for both morbidity and mortality (Fellows et al. 2002; Hyland 2003), provide indexes of disease burden for motivating tobacco control and for tracking. In the United States, such estimates are periodically reported, providing emphasis to the existence of an ongoing epidemic. For example, the current mortality estimate stands at 440,000 persons dying annually from a cigarette smoking-attributable illness (Fellows et al. 2002).

To make estimates of population attributable risk, data are needed on the relative risks associated with smoking (overall or by disease), and the distribution of smoking in the population. This information can be used to estimate the percentage of disease attributable to smoking, or -by using the number of deaths (total or from the disease of interest) -, the number of attributable deaths. Similar calculations can be made for smokers alone.

Only a few Japanese studies have provided information on the population-attributable risk of cancers associated with smoking. However, the results of these studies are fairly consistent (Table 2.6). Hirayama estimated that after 17 years of follow-up in a large Japanese cohort, 32.33% of all cancers in men and 4.57% of all cancers in women were attributable to smoking (Hirayama 1990). In a separate Japanese cohort conducted nearly a decade after the end of the Hirayama follow-up, Hara and colleagues estimated that 24.7% of all cancers in men and 4.2% of all cancers in women were attributable to smoking (Hara et al. 2002). Using data collected from Japanese-American males participating in the Honolulu Heart Program from 1965-1990, Chyou et al. estimated that 29% of all cancers in men were attributable to smoking (Chyou et al. 1992).

The percentage of lung cancer cases reported to be attributable to smoking has been examined in several studies. Hirayama estimated that in his cohort, 71.55% of lung cancer cases in men and 15.60% of cases in women were the result of smoking (Hirayama 1990). Prospectively collected data provided by Sobue and colleagues were used to estimate an attributable risk from smoking of 64.5% of male and 15.8% of female lung cancer cases (Sobue et al. 2002).

Table 2.6 Population Attributable Cancer Risk Estimates from Selected Studies

Reference	Study design/ Population	Cancer site	Population attributable risk (%)
Hirayama 1990	PROSPECTIVE COHORT STUDY	All Sites	
	1965-1982	(Men)	32.33
	122,261 Japanese men and	(Women)	4.57
	142,857 Japanese women	Buccal/Pharynx	
		(Men)	60.78
		(Women)	0
		Esophagus	
		(Men)	47.84
		(Women)	8.7
		Stomach	
		(Men)	25.13
		(Women)	3.48
		Intestine	
		(Men)	17.33
		(Women)	-2
		Rectum	
		(Men)	15.22
		(Women)	0.86
		Bile Duct/Gall Bladder	
		(Men)	15
		(Women)	2.92
		Liver	
		(Men)	28.26
		(Women)	8.72
		Pancreas	
		(Men)	28.33
		(Women)	6.06
		Larynx	
		(Men)	95.83
		(Women)	22.22
		Lung	
		(Men)	71.55
		(Women)	15.6
		Prostate	
		(Men)	-2.8
		Kidney	
		(Men)	0
		(Women)	-6.25
		Bladder	
		(Men)	30.69
		(Women)	11.43
		Breast	
		(Women)	4.42
		Cervix	
		(Women)	7.22
		Ovary	
		(Women)	6
Chyou et al. 1992	PROSPECTIVE COHORT STUDY	All Sites	29
	Honolulu Heart Program	Lung Cancer	85
	1965-1990	Oral, Larynx, Esophagus, Pancreas, Kidney, Ureter or Bladder	46
	7,760 Japanese-American men living in Hawaii		
Parrish et al. 1993	ECOLOGICAL STUDY	Buccal Cavity and Pharynx	84.5 *
	Japanese vital statistics records and census data	Esophagus	86.3 *
	1985-1989 (buccal cavity and pharynx); 1990 (esophagus)		
	2,835 Japanese men (buccal cavity and pharynx); 5,753 Japanese men (esophagus)		
Hara et al. 2002	PROSPECTIVE COHORT STUDY	All Sites	
	Japan Public Health Center Cohort I	(Men)	24.7
	1990-1999	(Women)	4.2
	19,950 Japanese men and 21,534 Japanese women		
Sobue et al. 2002	PROSPECTIVE COHORT STUDY	Lung Cancer	
	Japan Public Health Center Cohort I and Cohort II	(Men)	64.5 **
	1990-1999	(Women)	15.8 **
	44,533 Japanese men and 48,281 Japanese women		
Yokoyama et al. 2002	CASE-CONTROL	Esophageal Cancer	53.6
	2000-2001		
	Japanese men		
	Cases: 234		
	Controls: 634		
Ando et al. 2003	PROSPECTIVE COHORT STUDY	Lung Cancer	
	Japan Collaborative Cohort study	(Men)	52.2
	1988-1997	(Women)	11.8
	45,010 Japanese men and 55,724 Japanese women		

*Population attributable risk for cigarette smoking and alcohol consumption; † Calculated using Levin's formula for PAR and assuming a 52% prevalence of current smokers for men (RR4.5) and 5.9% for women(RR4.2)(numbers obtained from(Sobue et al.2002)

Ando et al. (2003) reported that the percentage of lung cancer cases that were attributable to smoking was 52.2% for men and 11.8% for women participating in a Japanese cohort study. In a cohort of Japanese-American men, smoking was found to account for 85.0% of lung cancer cases (Chyou et al. 1992)

The risk of upper aerodigestive tract cancers attributable to smoking in Japan has also been estimated by several researchers. Data from Hirayama's cohort were used to estimate that 47.84% and 8.70% of esophageal cancer cases in men and women, respectively, were attributable to smoking (Hirayama 1990). Yokoyama and colleagues used information collected from a case-control study to estimate an attributable risk of 53.6% of esophageal cancer cases in Japanese men (Yokoyama et al. 2002). An ecological study conducted by Parrish et al. indicated that 86.3% of male esophageal cancer cases were attributable to smoking and drinking combined (Parrish et al. 1993). Sixty percent of buccal/pharyngeal cancers in men were attributed to smoking in Hirayama's cohort (Hirayama 1990), and Parrish's ecological study estimated that 84.5% of such cancers were the result of drinking and smoking combined (Parrish et al. 1993).

Another measurement of disease burden that can be calculated for tobacco is years of life lost (YLL). Shibuya (1999) estimated in 1995 that 10% of the total YLL were attributable to tobacco in Japan. The author concluded that smoking was the "single most important cause of YLL in Japan."

(3) Passive smoking and cancer

Hirayama's 1981 report in the British Medical Journal (Hirayama 1981) was one of the first studies on passive smoking and lung cancer risk. Although extensively critiqued, including many comments by tobacco industry consultants, the study's findings of an association of marriage to a smoker with increased risk could not be explained by bias, including confounding. Within five years of this first report, passive smoking was classified as a cause of lung cancer (National Research Council (NRC) 1986; US Department of Health and Human Services (USDHHS) 1986).

Subsequent to Hirayama's landmark report, there have been numerous studies of passive smoking and lung cancer in Japan. In general, the studies show increased risk for never-smokers, particularly for the exposure measure of marriage to a smoker. The observed risks are fully consistent with the most recent meta-analysis, which showed an approximate 20% increase in lung cancer risk for never-smoking women married to a smoker compared with similar women married to never-smokers (Hackshaw 2003).

Hirayama's cohort study revealed evidence of increased risk for cancer of other sites in nonsmokers married to smokers compared to nonsmokers married to nonsmokers. Sites with increased risk included nasal sinus, brain, and

breast cancer, as well as all sites combined. However, these cancers have yet to be causally linked to passive smoking (IARC 2004).

(4) Factors modifying the effect of smoking on cancer risk

A number of factors, both environmental and genetic, may modify the risks of cancer in smokers. Epidemiologists refer to such factors as effect modifiers; they may act to increase risk (synergism) or to decrease risk (antagonism). There are methodological complexities in assessing effect modification that are well described in the recent IARC monograph (IARC 2004) and in epidemiological texts (Rothman and Greenland 1998).

Effect modification should be considered when comparing cancer risk for smokers in Japan to smokers elsewhere. Substantial differences in major effect modifiers could lead to differences in risks to Japanese smokers. Effect modifiers considered in studies of smokers include occupational agents such as asbestos, dietary factors and other lifestyle-associated exposures and the presence of chronic diseases such as chronic lung diseases. To date several important effect modifiers for the risk of smoking have been identified. These include heavy alcohol consumption for head and neck cancers as well as esophageal cancer, several occupational agents for lung cancer (asbestos, radon, and others), and low intake of fruits and vegetables for a number of sites (IARC 2004). Increasing research is identifying and addressing genes that may determine risks to smokers.

Several epidemiological studies in Japan have explored effect modification by these and other factors. Given the methodological difficulties of assessing effect modification, it would be difficult to identify patterns of effect modification that differ substantially in Japan from other locations. Studies have been reported related to alcohol, diet, environment and occupation, and other factors.

Alcohol intake

Studies that have assessed the combined effects of smoking and alcohol consumption are presented in Table 2.7. Among a cohort of Japanese-American men living in Hawaii, the risk of upper aerodigestive tract (ADT) cancers was examined by smoking and drinking habits (Kato et al. 1992). Compared to never-smokers who drank less than 30 ml alcohol per day, ever-smokers (former and current smokers) who also drank less than 30 ml alcohol per day had an age-adjusted RR of 3.3 (1.3-8.04). Never-smokers who drank greater than or equal to 30 ml alcohol per day had a RR or 8.6 (2.1-36.0), and men who had ever smoked and drank greater than or equal to 30 ml alcohol per day had a RR of 17.3 (6.7-44.2). These risk estimates suggested that alcohol synergistically modifies the risk of upper ADT cancers in smokers; however, interaction was not formally

assessed in this publication.

Several years later, Chyou and colleagues performed a more thorough assessment of the interaction between alcohol intake and smoking on the risk of upper ADT cancers using data from this same cohort (Chyou et al. 1995). Risk estimates for upper ADT cancers were calculated by the ounces of alcohol consumed per month, stratified by both cigarettes per day and by years smoked. A similar pattern of increasing risk estimates with increasing drinking and smoking was observed. For the men who never smoked but consumed more than or equal to 14 oz of alcohol per month, the age-adjusted relative risk for upper ADT cancers was 6.50 (1.63-26.00); for men who did not drink but smoked moree than 20 cigarettes per day the risk was 3.20 (0.76-13.39). The risk of upper ADT cancers in the men who both drank more than or equal to 14 oz alcohol per month and smoked moree than 20 cigarettes per day was 14.35 (4.35-47.35). Again, these results suggested that alcohol may be an effect modifier of smoking on the risk of upper ADT cancers; however, the authors stated that none of the tests for interaction was statistically significant.

A case-control study of Japanese men with incident esophageal cancer examined the combined effects of alcohol intake and cigarette smoking using three categories: high alcohol consumption (>414 grams per week), smoking ≥ 20 cigarettes per day, and smoking and high alcohol consumption (Hanaoka et al. 1994). The authors stated that "the results showed no combined effects of alcohol drinking and cigarette smoking" on the risk of esophageal cancer; however, the risk estimates were not provided in the text.

Diet

Studies that have assessed the effects of smoking and diet are summarized in Table 2.8. Data from Hirayama's large Japanese cohort were used to perform an extensive analysis of smoking by meat and vegetable intake and the risk for different cancers (Hirayama 1986). Daily vegetable intake was inversely associated with the risk for lung cancer among smokers. Compared to male nonsmokers who did not green-yellow vegetables daily, the mortality rate ratio for male nonsmokers who did eat daily vegetables was 0.90. For male daily smokers who did not eat daily vegetables, the RR for lung cancer was 5.38, while or daily smokers who also ate vegetables daily, the RR was 4.6. There was no relationship between smoking status and meat and vegetable fintake in the risk for cancers of the mouth/pharynx, esophagus, stomach, liver, pancreas, nasal sinus, larynx, prostate and bladder and the risk of malignant lymphoma; however, interaction was not statistically assessed in this publication. Daily vegetable intake did appear to modify the risk for lung cancer among ex-smokers. Compared to never-smokers who ate vegetables daily, the risk for lung cancer among ex-smokers who had quit for 1-4 years who ate vegetables daily was 1.4, while for those ex-smokers of 1-4

Table 2.7 Selcted Studies That Have Asseaaed the Combined Effects of Smoking and Alcohol Consumption on Cancer Risk

Reference	Cancer Site	Study Design/ Population	Outcome	Exposure	Risk Estimate	Comment
(Kato et al. 1992)	Upper ADT (oral-pharynx, esophagus, larynx)	PROSPECTIVE COHORT • Hawaii • 1965-1990 • 6,701 American men of Japanese ancestry, born between 1900-1919	• Diagnosis of incident cancer • 75 upper ADT outcomes (21 oral-pharynx, 26 esophagus, 24 larynx, 4 other)	Smoking Status: • Never smokers • Ex- and current smokers Alcohol Intake: • <30ml/day • ≥30ml/day	**Never smokers:** *<30ml/day:* **RR:** 1.0 [reference] *≥30ml/day:* **RR:** 8.6 [2.1-36.0] **Ex- and current smokers:** *<30ml/day:* **RR:** 3.3 [1.3-8.4] *≥30ml/day:* **RR:** 17.3 [6.7-44.2]	• Adjusted for age • RR calculated using Cox proportional hazards regression
(Hanaoka et al. 1994)	Esophagus	CASE-CONTROL STUDY • Japan • 1989-1991 • **CASES:** 141 men with incident esophageal cancer • **CONTROLS:** 141 male hospital controls, individually matched on age and prefecture; men with alcohol- or tobacco-related diseases were excluded	• Diagnosis of incident esophageal cancer	The combined effects of alcohol drinking and cigarette smoking were examined using 3 categories: • High alcohol consumption (>414g/week) • Smoker (≥20 cig/day) • Smoker and high alcohol consumption	"The results showed no combined effects of alcohol drinking and cigarette smoking." [Data were not shown.]	• Conditional logistic regression analysis was used
(Chyou et al. 1995)	Upper ADT	PROSPECTIVE COHORT • Hawaii • 1965-1993 • 7,9995 American men of Japanese ancestry, born between 1900-1919	• Diagnosis of incident cancer • 92 upper ADT outcomes	Cigarettes/Day: • 0 cig/day • >0 - ≤20 cig/day • >20 cig/day Years Smoked: • 0 years • >0 - <30 years • ≥30 years Ounces/Month Alcohol: • 0 oz./month • >0 - <14 oz./month • ≥14 oz./month	**0 cig/day:** *0 oz/month:* **RR:** 1.00 [reference] *>0 to <14 oz/month:* **RR:** 1.27 [0.26-6.30] *≥14 oz/month:* **RR:** 6.50 [1.63-26.00] **>0 to ≤20 cig/day:** *0 oz/month:* **RR:** 2.99 [0.79-11.26] *>0 to <14 oz/month:* **RR:** 1.91 [0.48-7.66] *≥14 oz/month:* **RR:**10.66[3.21-35.44] **>20 cig/day:** *0 oz/month:* **RR:** 3.20 [0.79-13.39] *>0 to <14 oz/month:* **RR:** 4.57 [1.18-17.71] *≥14 oz/month:* **RR:**14.35[4.35-47.35] **0 years smoked:** *0 oz/month:* **RR:** 1.00 [reference] *>0 to <14 oz/month:* **RR:** 1.26 [0.25-6.25] *≥14 oz/month:* **RR:** 6.47 [1.62-25.86] **>0 to <30 years:** *0 oz/month:* **RR:** 1.97 [0.44-8.81] *>0 to <14 oz/month:* **RR:** 2.42 [0.60-9.73] *≥14 oz/month:* **RR:** 9.24 [2.67-31.91] **≥30 years smoked:** *0 oz/month:* **RR:** 4.20 [1.14-15.52] *>0 to <14 oz/month:* **RR:** 3.27 [0.85-12.64] *≥14 oz/month:* **RR:**14.22[4.37-46.25]	• Adjusted for age • RR calculated using Cox proportional hazards regression • "None of the tests on the effect of interaction was statistically significant ($p > 0.45$)."
(Yokoyama et al. 1996)	Upper ADT (esophageal, gastric, oropharyngo-largyngeal)	CROSS-SECTIONAL • Japan • 1993-1995 • 1,000 Japanese male alcoholics ≥40 years old	• Diagnosis of prevalent cancer by upper gastro-intestinal endoscopy • 53 prevalent upper ADT cancers (36 esophageal, 17 gastric, 9 oropharyngo-largneal, 8 multiple)	Pack-years of smoking: • <50 p-y • ≥50 p-y	"Patients who had triple combination of inactive ALDH2, stronger beverage choice, and 50+ pack-years were more common among the multiple-cancer patients (62.5%, 5/8, p , 0.005) than among those with esophageal cancer alone (7.1%, 2/28)." **Pack-years smoked:** Esophageal Cancer: *<50 pack-years:* **OR:** 1.0 [reference] *≥50 pack-years:* **OR:** 2.8 [1.4-5.7] Gastric Cancer: *<50 pack-years:* **OR:** 1.0 [reference] *≥50 pack-years:* **OR:** 2.0 [0.7-5.4] Oropharyngo-laryngeal Cancer: *<50 pack-years:* **OR:** 1.0 [reference] *≥50 pack-years:* **OR:** 5.1 [1.3-19.5] Multiple Cancer: *<50 pack-years:* **OR:** 1.0 [reference] *≥50 pack-years:* **OR:** 11.8 [2.3-60.7] All Cancers: *<50 pack-years:* **OR:** 1.0 [reference] *≥50 pack-years:* **OR:** 2.0 [1.1-3.7]	• Adjusted for age, daily alcohol consumption, and stronger alcoholic beverage choice • OR calculated using multiple logistic regression

years who did not eat vegetables daily, the risk was 4.49. Further, for ex-smokers who quit ≥5 years ago, the risk of lung cancer was 1.40 and 2.63 for those who did and did not eat daily vegetables, respectively. Again, interaction was not formally assessed.

Several years later, data from this same cohort were used to investigate the relationship between smoking and meat intake and the risk of pancreatic cancer (Hirayama 1989). For non-smoking men who ate meat daily, the risk of death due to pancreatic cancer was 1.25 (0.59-2.75), compared to the non-smoking men who did not consume meat daily. For daily smokers, the risk of pancreatic cancer among those who did not eat meat daily was 1.53 (1.18-1.99), while for those who did eat meat daily the risk was 1.89 (1.34-2.75). As with the previous publication from this cohort, interaction was not statistically assessed

Sasaki and colleagues investigated the relationship between smoking and eating salty foods on the risk for esophageal cancer using 201 men and women with incident diagnoses and 403 hospital controls (Sasaki et al. 1990). Although interaction was not formally assessed, intake of salty foods did modify the risk between smoking and esophageal cancer. Compared to nonsmokers who did not eat salty foods, nonsmokers who did report eating salty foods had an odds ratio of 0.6, while smokers had odds ratios of 1.5 and 4.5 for those who did not and did report eating salty foods, respectively.

A separate Japanese case-control study examined the risk of lung cancer by smoking status and fruit and vegetable intake using 282 hospital-based case-control pairs (Gao et al. 1993). The daily intake of fruit, raw vegetables, green vegetables, lettuce, and cabbage all decreased the odds of lung cancer among current smokers by more than half. For examples, compared to never-smokers who did not eat raw vegetables daily, the odds ratio for current smokers who also did not eat raw vegetables daily was 13.83; for current smokers who did eat daily vegetables this risk was reduced to 6.5. However, interaction was not formally assessed.

A population-based case-control study conducted in Hawaii with both Caucasian and Japanese men and women examined the risk of lower urinary tract cancer in relation to smoking status and quantile of total fluid intake (Wilkens et al. 1996). After multivariate adjustment, the risk of cancer among ever-smokers was reduced to unity or below unity for men and women in the highest quantiles of total fluid intake, total fluid intake excluding alcohol, and tap water intake. Compared to never-smokers in the lowest tertile of total fluid intake excluding alcohol, the odds ratio for ever smokers in the same tertile was 8.1 (1.8-36.2). The risk estimate was reduced to 1.0 (0.6-1.6) for ever-smokers who were in the highest tertile of fluid intake (excluding alcohol). Again, interaction was not formally assessed.

Table 2.8 Selected Studies That Have Assessed Combined Effects of Smoking and Diet on Cancer Risk

Reference	Cancer Site	Study Design/ Population	Outcome	Exposure	Risk Estimate	Comment
(Hirayama 1986)	• All sites • Mouth and pharynx • Esophagus • Stomach • Liver • Pancreas • Nasal sinus • Larynx • Lung • Prostate • Bladder • Malignant lymphoma	PROSPECTIVE COHORT • Japan • 1965-1981 • 265,118 men and women ≥40 years old	Death due to cancer	Years after smoking cessation: • 1-4 years • ≥5 years Lifestyle factors (Yes/No) • Daily smoking • Daily drinking • Daily meat intake • Daily green-yellow vegetable intake	YEARS QUIT SMOKING: **Never smoker:** *Daily vegetable intake:* **$RR_{Lung\ Cancer}$:** 21.2/21.2 = 1.00 *Non-daily vegetable intake:* **$RR_{Lung\ Cancer}$:** 28.9/21.2 = 1.36 **≥5 years quit:** *Daily vegetable intake:* $RR_{Lung\ Cancer}$: 30/21.2 = 1.4 *Non-daily vegetable intake:* **$RR_{Lung\ Cancer}$:** 55.8/ 21.2 = 2.63 **1-4 years quit:** *Daily vegetable intake:* $RR_{Lung\ Cancer}$: 29.7/21.2 = 1.40 *Non-daily vegetable intake:* **$RR_{Lung\ Cancer}$:** 95.3/21.2 = 4.49 **Current smoker:** *Daily vegetable intake:* $RR_{Lung\ Cancer}$: 99.3/21.2 = 4.68 *Non-daily vegetable intake:* **$RR_{Lung\ Cancer}$:** 109.4/21.2 = 5.16	• Mortality rates were age-standardized • When only mortality rates were provided, I divided them to estimate the mortality rate ratio (RR); this math work is shown • Numbers of deaths due to lung cancer are available for nonsmoking women exposed to secondhand smoke from their husbands, stratified by green-yellow vegetable intake (but mortality rates are not provided)
(Hirayama 1989)	Pancreatic Cancer	PROSPECTIVE COHORT • Japan • 1966-1982 • 265,118 Japanese men and women ≥40 years old	Death due to pancreatic cancer	Smoking Status: • Non-smoker • Daily smoker Meat Consumption: • Daily • Others	**MEN:** **Non-smokers:** *Daily meat:* **RR:** 1.25 [0.59-2.75] *Others:* **RR:** 1.00 [reference] **Daily smokers:** *Daily meat:* **RR:** 1.89 [1.34-2.75] *Others:* **RR:** 1.53 [1.18-1.99]	• Age-standardized • RRs calculated using logistic regression • Interaction was not formally assessed
(Sasaki et al. 1990)	Esophageal Cancer	CASE-CONTROL • Japan • 1974-1979 • **CASES:** 201 men and women with incident cancer of the esophagus • **CONTROLS:** 403 male and female hospital controls, individually matched on age, gender, hospital, and time of admission	Incident diagnosis of esophageal cancer	The following exposures are indicated by -/+ (it is unclear exactly what these symbols mean) • Smoking • Sake drinking • Salty foods	**MEN:** **(-) smoking:** *(-)Sake drinking & (-) salty foods:* **OR:** 1.0 *(-) Sake drinking & (+) salty foods:* **OR:** 0.6 *(+) Sake drinking & (-) salty foods:* **OR:** 3.8 (p<0.01) *(+) Sake drinking & (+) salty foods:* **OR:** 12.3 (p<0.05) **(+) smoking:** *(-)Sake drinking & (-) salty foods:* **OR:** 1.5 (p<0.01) *(-) Sake drinking & (+) salty foods:* **OR:** 4.5 (p<0.01) *(+) Sake drinking & (-) salty foods:* **OR:** 8.8 (p<0.01) *(+) Sake drinking & (+) salty foods:* **OR:** not stated	
(Gao et al. 1993)	Lung Cancer	CASE-CONTROL • Japan • 1988-1991 • **CASES:** 282 men with lung cancer • **CONTROLS:** 282 male hospital controls, individually matched on age, gender, and time of first visit to hospital	Diagnosis of lung cancer	Smoking Status: • Nonsmoker • Ex-smoker • Current smoker Fruit and Vegetable Intake: • Almost none and sometimes • 3-4 times per week • Every day	See next page	• Crude odds ratios were calculated from numbers provided in the article

Occupational and environmental exposures

The effect modification of cigarette smoking by occupational and environmental exposures on cancer risk has not been thoroughly studied in Japan. The few studies that have examined such relationships have yielded very limited data (Table 2.9). A hospital-based case-control study conducted by Minowa and colleagues investigated the risk of lung cancer mortality in men by smoking status and asbestos exposure level (as reported by family member proxies) (Minowa et al. 1991). Compared to non-smoking men unexposed to asbestos, men who

were smokers (but also not exposed to asbestos) had an age-adjusted odds ratio of 3.38 for lung cancer death, while the odds ratio associated with smoking and asbestos exposure was 8.28. However, interaction was not formally assessed in the analysis. Hiraoka et al. investigated the association between cigarette smoking and asbestos bodies per gram of lung tissue on the odds of lung cancer in a case-control study conducted in Japan; however, the data were inconclusive and interaction was not formally assessed (Hiraoka et al. 1990).

Table 2.9 Selected Studies That Have Assessed the Combined Effects of Smoking and Occupational Exposures on Cancer Risk

Reference	Cancer Site	Study Design/ Population	Outcome	Exposure	Risk Estimate	Comment
(Hiraoka et al. 1990)	Lung Cancer	CASE-CONTROL • Japan • 1979-1988 • **CASES:** 476 men and women with lung cancer • **CONTROLS:** 369 male and female hospital controls	Histologically confirmed lung cancer	Cigarettes per day: • <15cig/day • ≥15cig/day Asbestos bodies (AB) per gram lung tissue: • 0-19 AB/g • 20-199 AB/g • ≥200 AB/g	**<15 cig/day:** *0-19 AB/g:* **OR:** 1.00 [reference] *20-199 AB/g:* **OR:** 0.94 *≥200 AB/g:* **OR:** 0.76 **≥15 cig/day:** *0-19 AB/g:* **OR:** 1.40 *20-199 AB/g:* **OR:** 2.10 *≥200 AB/g:* **OR:** 2.86	• I calculated the odds ratios myself • Interaction was not assessed
(Minowa et al. 1991)	Lung Cancer	CASE-CONTROL • Japan • 1978-1982 • **CASES:** 96 men with fatal lung cancer • **CONTROLS:** 86 hospital controls who died from causes other than cancer, pneumoconiosis, accident, or suicide	Primary lung cancer confirmed histologically or by cytological examinations of smears, surgical specimens, or autopsy specimens	Smoking Status: • Nonsmokers (never smokers plus ex-smokers who had quit 10 or more years) • Smokers Asbestos Exposure: • Not exposed • Suspected • Exposed	**Nonsmokers:** *Not exposed:* **OR:** 1.00 [reference] *Suspected exposure:* **OR:** 2.33 *Exposed:* **OR:** -- **Smokers:** *Not exposed:* **OR:** 3.38 *Suspected exposure:* **OR:** 4.84 *Exposed:* **OR:** 8.28	• All information was obtained from family members • Age-adjusted • Interaction was not assessed
(Yamaguchi et al. 1992)	Lung Cancer	CASE-CONTROL • Japan • 1989-1990 • **CASES:** 144 men and women with lung cancer • **CONTROLS:** 676 male and female hospital controls. individuallv matched on hospital ward, age, gender, and hospital	Histologically confirmed lung cancer	Smoking Status: • Never smoker • Ex-smoker • Current ≤20 cig/day • Current >20 cig/day Work Categories: • Shipbuilding • Ironworks • Building construction • Road construction • Steel manufacturing • Coal mining • Other plants	"The combined effects of employment in at-risk work categories and smoking were evaluated by including interaction terms in the logistic regression equations. The relative risks thus obtained were then compared with the risk estimates calculated under the assumptions of additive and multiplicative effects. The increase in the relative risk among workers in the "other plants" category was closer to the multiplicative model, while that among workers in ironworks looked closer to the additive model."	• The numbers are not provided to calculate these odds ratios
(Tsuda et al. 1995)	Lung Cancer	HISTORICAL COHORT • Japan • 1959-1992 • 454 people who lived in an arsenic-polluted area	Death due to lung cancer	Smoking Status: • Nonsmokers • Smokers Arsenic concentration: • <0.05 ppm • 0.05-0.99 ppm • ≥1 ppm	Crude Mortality Rate/ 1,000 person-years: **Nonsmokers:** *<0.05ppm:* 0 [0-0.91] *0.05-0.99ppm:* 0 [0-2.68] *≥1ppm:* 0.55 [0.03-3.16] **Smokers:** *<0.05ppm:* 0 [0-1.26] *0.05-0.99ppm:* 1.17 [0.06-6.74] *≥1ppm:* 5.29 [2.48-10.84]	"The synergic excess fraction for ingested arsenic exposure (≥0.05 ppm) and smoking was up to 0.92. These results suggest that synergism between ingested arsenic exposure and smoking exists in the development of lung cancer."

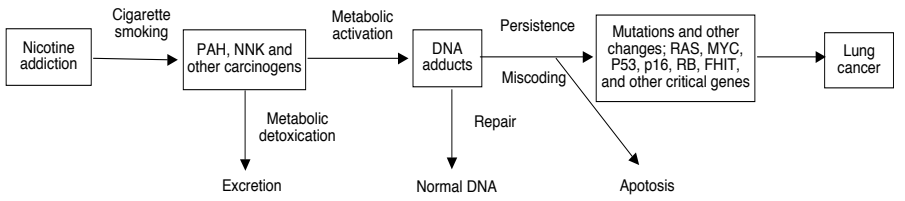
Yamaguchi and colleagues examined the odds of lung cancer by smoking status and occupational category using the case-control method and found only a possible interaction associated with working in "other plants" (Yamaguchi et al. 1992). Finally, Tsuda et al. examined arsenic levels and smoking status on the

risk of lung cancer in a historical cohort (Tsuda et al. 1995). The authors stated that their data suggested a synergistic relationship between smoking and arsenic exposure; however, there were so few lung cancer deaths among the nonsmokers that a clear estimation of the risks could not be evaluated.

(5) Genetic polymorphism

Cigarette smoke, and tobacco smoke more generally, is a complex mixture that contains many specific carcinogens as well as many agents that may act nonspecifically to increase cancer risk. A wide range of genes can be reasonably postulated as affecting risk of cancer in smokers (Caporaso et al. 1995; Hecht 1999). Hecht has offered a schema for considering these genes (Figure 2.6), which include genes involved in carcinogen activation and detoxification, genes determining mutagen sensitivity and DNA repair, and oncogenes and tumor suppressor genes. There is a rapidly growing literature on these genetic factors, with many studies carried out in Japan. Few clear patterns have been identified in Japan, as in other countries. These studies are not specifically reviewed in this report, but a bibliography is included as Appendix at the end of this section.

Figure 2.6 Genetic Mechanism of Cancer from Smoking



Source: Hecht 1999

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2.3.1.3 Cardiovascular diseases

A total of 475 references on tobacco and cardiovascular disease were retrieved through PubMed on March 14, 2003 using the search terms (smoking OR smoker OR smoke OR tobacco OR tobacco on title or abstract) AND (Japan*) AND [stroke OR (cerebrovascular disease) OR (heart disease) OR (heart attack) OR (cardiovascular disease) OR (heart failure) OR aneurysm OR atherosclerosis OR arteriosclerosis] AND [(relative risk) OR (hazard ratio) OR (odds ratio) OR (attributable risk)]. In-press papers and papers in the Japanese-language literature were also reviewed. Two reviewers read all the papers and selected a total of 66 references for the following review on the effect of smoking on cardiovascular diseases.

Ischemic heart disease

Evidence on tobacco and ischemic heart disease in Japanese populations is available from three case-control and 13 cohort studies.

A worksite case-control study showed that regular smokers had four- to five-fold higher odds of sudden death than the rest of the group including occasional, former or never-smokers combined (Owada et al. 1999). A subsequent case-control study showed that compared with never-smokers, current smokers of more than 20 cigarettes per day had four-fold higher odds of nonfatal acute myocardial infarction among middle-aged subjects, and three-fold higher odds among the elderly (Miyake 2000). A dose-response relationship was found between pack-years of smoking and the odds ratios of fatal and nonfatal myocardial infarction (Kashihara et al. 2000).

The findings of the 13 cohort studies showed a consistent relationship between smoking and the risk of ischemic heart disease among Japanese men (Kimura 1977; Hirayama 1981; Kono et al. 1985; Konishi et al. 1987, 1990; Kiyohara et al. 1990; Kodama et al. 1990; Benfante et al. 1991; Fujishima et al. 1992; Sato et al. 1992; Goldberg et al. 1995; Research Group on Health Risk Evaluation for Disability and Death due to Stroke 1995; Jacobs et al. 1999; Irie et al. 2001; Yamagishi et al. 2003) and Japanese American men (Yano et al. 1988; Benfante et al. 1991; Goldberg et al. 1995), and among Japanese women (Hirayama 1981; Benfante et al. 1991; Research Group on Health Risk Evaluation for Disability and Death due to Stroke 1995; Irie et al. 2001). Most of the cohort studies showed that the multivariate relative risk of ischemic heart disease for current smokers compared with never-smokers or ex-smokers was approximately 2 to 3 in both sexes. Nine studies reported a dose-response relationship between the number of cigarettes currently smoked and the risk of ischemic heart disease (Kono et al. 1985; Konishi et al. 1987; Yano et al. 1988; Kiyohara et al. 1990; Kodama et al. 1990; Fujishima et al. 1992; Jacobs et al. 1999; Irie at al. 2001;

Yamagishi et al. 2003). The relative risk (RR) of coronary heart disease for current smokers was similar between Japanese living in Japan and Japanese Americans (Yano et al. 1988; Konishi et al. 1990; Goldberg et al. 1995). The Hirayama study (1981), the largest cohort study using mortality as an endpoint, showed a significant but weaker association, with age-adjusted relative risk for daily smokers compared with non-smokers of 1.78 (95% CI 1.55-2.04) in men and 1.33 (95% CI 1.07-1.66) in women. The weaker effect of smoking may have been in part due to misdiagnosis of coronary heart disease as the cause of death. Hirayama (1981) also examined the effect of environmental tobacco smoke in this study, and found an age-adjusted relative risk for non-smoking wives of husbands who smoked 20 or more cigarettes per day compared with those of non-smoking husbands of 1.30 (95% CI 1.06-1.60).

A number of studies showed that the risk of ischemic heart disease was lower among ex-smokers than current smokers (Research Group on Health Risk Evaluation for Disability and Death due to Stroke 1995; Jacobs et al. 1999; Irie et al. 2001; Yamagishi et al. 2003), suggesting that smoking cessation lowers this risk, but this has not been confirmed in broad-based cohort studies or clinical trials. Research in this field is warranted.

Cerebrovascular diseases

Evidence on tobacco and cerebrovascular disease is available from two case-control and 17 cohort studies. Both the case-control (Kubota et al. 2001; Ohkuma et al. 2003) and nine of the cohort studies (Kagan et al. 1980; Stemmermann et al. 1984; Abbott et al. 1986; Uchiyama et al. 1992; Naito et al. 1997; Nakayama et al. 1997; Sankai et al. 1999; Nakayama et al. 2000; Tanizaki et al. 2000; Ueshima 2001; Rodriguez et al. 2002; Yamagishi et al. 2003) showed significant associations, but the eight other cohort studies did not (Hashimoto et al. 1970; Okada et al. 1976; Kimura 1977; Tanaka et al. 1982, 1985; Shimozato et al. 1996; Irie et al. 2001). An association between tobacco and the risk of subarachnoid hemorrhage was found in both case-control (Kubota et al. 2001; Ohkuma et al 2003) and two cohort studies (Hirayama 1981; Sankai et al. 1999), with smokers having two- to four-fold higher odds or risk than non-smokers. However, no association was seen between tobacco and the risk of intraparenchymal hemorrhage (Nakayama et al. 1997).

The inconsistent findings on the relation between tobacco and the risk of total and ischemic stroke may be because this association is weaker than that between tobacco and the risk of ischemic heart disease. The Hirayama study (1981) showed that the age-adjusted relative risk of total stroke for current daily smokers compared with non-smokers was 1.13 (95% CI 1.07-1.20) in men and 1.21 (95% CI 1.10-1.34) in women, which tended to be lower than the respective

estimated risk values for ischemic heart disease, which were 1.78 (95% CI 1.55-2.04) in men and 1.33 (95% CI 1.07-1.66) in women. A recent follow-up report of the NIPPON DATA 80 study, a cohort of national representative samples aged 30 or over, showed that heavy male smokers (more than 40 cigarettes per day) had a significant multivariate relative risk of ischemic stroke compared with non-smokers (RR 2.2), but that light-to-moderate male smokers had no significant excess risk. Most of the other Japanese studies also reported a relative risk of ischemic stroke associated with current smoking of around 1.5 or less, none of which were statistically significant (Okada et al. 1976; Kimura 1977; Tanaka et al. 1982, 1985; Shimozato et al. 1996; Nakayama et al. 2000; Irie et al. 2001).

The Honolulu Heart Study (Abbott et al. 1986) of Japanese American men produced multivariate relative risk estimates for current smokers compared with non-smokers of 2.5 (95% CI 2.0-3.3) for total stroke, 2.5 (95% CI 1.8-3.5) for thromboembolic stroke (ischemic stroke) and 2.8 (95% CI 1.7-4.8) for hemorrhagic stroke. No dose-response relation between the number of cigarettes smoked and risk of ischemic stroke was found. A recent report from the Hirayama study showed a significant multivariate relative risk of lacunar infarction for current smokers compared with non-smokers (RR 2.2; 95% CI 1.3-3.9), but no association with the risk of total ischemic stroke, atherothrombotic infarction or cardioembolic infarction (Tanizaki et al. 2000). Another recent Japanese cohort study showed a significant association between current smoking and the risk of ischemic stroke among hypertensive men (Yamagishi et al. 2003).

The risk of total or ischemic stroke was lower among ex-smokers than current smokers (Uchiyama et al. 1992; Yamagishi et al. 2003), which suggested that smoking cessation lowers this risk. As with the case of cessation and ischemic heart disease, however, this has not been confirmed in broad-based cohort studies or clinical trials, making further research in this field warranted.

Atherosclerosis

Autopsy studies in Japan showed that cigarette smoking was positively associated with atherosclerosis in coronary arteries (Okumiya et al. 1985) and the aorta (Reed et al. 1987), and with the degree of ischemic myocardial lesion (Burchfiel et al. 1996). Angiography studies also showed that cigarette smoking was associated with atherosclerosis in coronary arteries (Hiyamuta et al. 1990; Inoue et al. 1995; Kato et al. 2001) and the thoracic aorta (Inoue et al. 1995). Two studies using echosonography also showed that cigarette pack-years was associated with carotid atherosclerosis (Mannami et al. 1997; Kitamura et al. 2000). An angiography study showed that smoking was also associated with atherosclerosis in the basilar and middle cerebral arteries (Yasaka et al. 1993) whereas a second study showed no association with atherosclerosis in middle

cerebral arteries (Takahashi et al. 1999). A significant association was seen with the prevalence of periventricular hallucination (Fukuda et al. 1996), but not with that of silent brain infarction (Yamashita et al. 1996; Shintani et al. 1998).

Population-attributable risk percentage

Population-attributable risk percentage of ischemic heart disease was estimated to be 35% to 51% in men and 12% to 21% in women, given that relative risk was 2 to 3 in both sexes (Kimura 1977; Hirayama 1981; Kono et al. 1985; Konishi et al. 1987, 1990; Kiyohara et al. 1990; Kodama et al. 1990; Benfante et al 1991; Fujishima et al. 1992; Sato et al. 1992; Goldberg et al. 1995; Research Group on Health Risk Evaluation for Disability and Death due to Stroke 1995; Jacobs et al 1999; Irie et al. 2001; Yamagishi et al. 2003), and that the prevalence of current smokers among middle-aged men and women was 53%, and 13%, respectively (Ministry of Health and Welfare 1999). These estimates imply that approximately one-third to one-half of ischemic heart disease in men and one-fifth in women could be preventable by smoking cessation. Population-attributable risk percent for subarachnoid hemorrhage was 35% to 61% in men and 12% to 27% in women, given that relative risk was 2 to 4 in both sexes (Sankai et al. 1999; Kubota et al. 2001; Ohkuma et al. 2003;). Population-attributable risk percent for total or ischemic stroke was 21% to 35% in men, given that relative risk was 1.5 to 2 (Hirayama 1981; Abbott et al. 1986; Yamagishi et al. 2003), while the corresponding estimation for women was not done due to insufficient data. However, population-attributable risk percent for total stroke was estimated to be 3% from the Hirayama study (1981). The number of patients was estimated at 123,800 for ischemic heart disease and 364,900 for total stroke according to a 1999 National Hospital Survey. The number of annual deaths was 70,100 from ischemic heart disease and 132,500 from total stroke.

If conservative estimates of the population-attributable risk percent are used, i.e. 20% for ischemic heart disease and 10% for total stroke in men and women combined, the estimated number of patients due to smoking is approximately 25,000 for ischemic heart disease and 36,000 for stroke. The respective estimated number of deaths is 14,000 and 13,000. Because approximately 25% of surviving stroke patients are dependent, the estimated number of dependent stroke patients attributable to smoking is about 9,000, and given that approximately 10% of surviving stroke patients develop dementia, the number of stroke patients with dementia attributable to smoking is estimated to be about 3,600.

Mechanisms of tobacco's effect on cardiovascular disease

1) Ischemic heart disease and ischemic stroke

The mechanisms by which smoking causes ischemic heart disease and ischemic stroke include the short-term effects of accelerated thrombus formation through increased plasma fibrinogen (Iso et al. 1996), increased platelet aggregability (Hioki et al. 2001), increased hematocrit (Wannamethee et al. 1994), decreased fibrinolytic activity (Hioki et al. 2001; Minami et al. 2002), and decreased blood flow in the myocardium and brain due to vasoconstriction (Nobuyoshi et al. 1992; Isaka et al. 1993; Sugiishi and Takatsu 1993; Takaoka et al. 2000); and for coronary heart disease, cardiac arrhythmia (Peters et al. 1995). A longer-term effect is the enhancement of atheroma formation through direct injury to endothelial cells (Nagy et al. 1997) and low HDL-cholesterol levels (Minami et al. 2002).

2) Subarachnoid hemorrhage

The mechanism by which smoking induces subarachnoid hemorrhage is not clear, but there is some evidence that it increases the release of proteinases from activated pulmonary macrophages, which exacerbate the fragility of cerebral aneurysms (Weitz et al. 1987), and that it increases hemodynamic stress on the Circle of Willis through enhanced atherosclerosis in basal cerebral and carotid arteries (Handa et al. 1983).

Conclusion

Although relative risk associated with active and passive smoking was smaller for cardiovascular disease (RR = 2-3 for ischemic heart disease, and 1.5-2 for total stroke) than for lung cancer (RR = 4-6), the number of patients with ischemic heart disease or stroke is 18-fold higher than that of lung cancer, and the number of cardiovascular deaths is four-fold higher than that of lung cancer. The public health burden of smoking and environmental tobacco smoke on cardiovascular disease is therefore substantially greater in terms of the number of patients and deaths.

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2.3.1.4 Respiratory diseases

A literature search carried out in May 28, 2003, identified 1,260 reports through PubMed using the search terms "((tobacco OR smoke OR smoking) AND Japan AND epidemiology AND human." Reports on respiratory diseases were selected for review and the findings are described below.

Asthma

In 1967, as part of an investigation of respiratory diseases in cooperation with a US telephone company, Comstock et al. (1973) interviewed a total of 592 male employees of NTT in Tokyo, Japan. The outcomes investigated included morning cough in winter, persistent winter cough, morning phlegm in winter, persistent winter phlegm, persistent cough and phlegm, respiratory episodes, recent chest illness, chronic wheeze, persistent nasal catarrh, breathlessness, mean sputum volume and ventilatory function (assessed as one-second forced expiratory volume or FEV_1). The results were presented adjusted for age, place of birth, past and present place of residence, and present place of work. The authors constructed an adjusted rank score of asthma-like respiratory symptoms to summarize the different outcomes. A dose-response relationship was observed with the adjusted rank score and number of cigarettes per day.

A study of the effects of air pollution on the health of 805 households (617 fathers, 716 mothers and their children) in areas along a trunk road in Tokyo was conducted in 1986 (Ono et al. 1990). The prevalence rates of asthma-like symptoms in non-smoking and smoking fathers were 0.0% and 0.2%, respectively, while those in non-smoking and smoking mothers were 1.3% and 1.2%, respectively. However, statistical tests and adjustment for confounding factors were not specifically carried out to assess the significance for smoking in these test groups.

To elucidate factors contributing to hard metal-associated asthma, the entire workforce (n=703) of a corporation producing hard metal tools was examined (Kusaka et al. 1996). The result showed a statistically significant increased prevalence rate of asthmatic symptoms in ever-smokers compared to non-smoking male employees. This difference was diminished, however, after adjustment for age, atopy and concentration of exposed airborne cobalt

These three reports, although not directly addressing an association between smoking and asthma, show that active smoking increases the prevalence of asthma-like symptoms in Japan.

Wheeze

In their study of telephone workers, Comstock et al. (1973) found that the prevalence of wheeze tended to increase as the smoking rate increased. Ono

et al. (1990) reported that the prevalence of wheeze tended to increase in both male and female smokers, although the increase was not statistically significant and adjustment was not made for potential confounding variables.

Kagamimori et al. (1996) followed a total of 5,344 primary and junior high school children from 1972 until 1990 to determine the relationship between allergy in childhood and respiratory symptoms as adults. Information about smoking pattern was obtained at the end of the study, and the analyses were conducted cross-sectionally. This cohort was divided into three groups according to age at the start of follow-up, namely 6 to 8 years, 9 to 11 years and 12 to 24 years. The relative risk of wheeze associated with smoking increased in all three groups. However, the increase was not statistically significant and adjustment was not made for potential confounding variables, including results for allergic reaction.

These reports indicate that smoking may increase the risk of wheeze. However, the estimates were not statistically significant and adjustment for potential confounding variables was not made.

Cough

Comstock et al. (1973) observed that the occurrence of morning cough in winter, persistent winter cough, and persistent cough and phlegm tended to increase as cigarette consumption increased. Although results of a trend test for a dose-response relationship were not presented, the prevalence rates of winter cough in non-smokers were significantly lower than the mean. Ono et al. (1990) reported that the prevalence rates of persistent cough as well as cough and phlegm persisting for two or more years tended to increase in smokers. However, the increases were not statistically significant, and adjustment for confounding variables was not made. Kagamimori et al. (1996) observed an increased risk of persistent cough in winter among smokers compared to non-smokers. The crude relative risk (RR) for those individuals aged 18-22, 21-29 and 24-31 years of age at the end of the follow-up, in each cohort as noted above, were 2.3 (95% Confidence Interval (CI), 0.6-6.6), 3.7 (95% CI, 2.1-11) and 3.3 (95% CI, 1.3-8.1), respectively. Adjustment for potential confounding variables was not made .

Kumagai et al. (1993) investigated male employees of the Department of Waterworks and related departments in 119 municipalities in Japan. The prevalence rates of respiratory symptoms (cough, phlegm and breathlessness) in 322 conduit repair workers were compared with a control group consisting of 345 clerical or engineering workers. A simple correlation analysis revealed a non-significantly higher rate of cough in smokers compared to non-smokers. The prevalence rate of cough after adjustment for age and duration of employment was higher in smokers than in non-smokers and ex-smokers, although tests of

statistical significance were not presented the comparison by smoking status.

Comstock et al. (1973), Kumagai et al. (1993) and Kagamimori et al. (1996) found that the occurrence of cough increased with smoking, although adjustment for potential confounding was not made.

Phlegm

Comstock et al. (1973) found that the presence of morning phlegm in winter, persistent winter phlegm, and persistent cough and phlegm as well as mean sputum volume tended to increase as cigarette consumption increased. Although test trend results were not presented, the prevalence rates of winter phlegm in non-smokers were significantly lower than the mean. Ono et al. (1990) reported that the percentage of individuals with persistent phlegm as well as cough and phlegm persisting for two or more years tended to increase in smokers. However, the increases were not statistically significant, and adjustment for potential confounding variables was not conducted. In the study by Kumagai et al. (1993), a simple correlation analysis revealed that the percentage of individuals with phlegm was higher in smokers than non-smokers in both conduit repair workers and clerical/engineering workers ($p<0.05$). After adjustment for age and duration of employment, the occurrence of phlegm was higher in smokers than in non-smokers and ex-smokers, although the results of significance testing were not presented for this comparison.

In the study by Kagamimori et al. (1996), a significant increase ($p <0.01$) in the prevalence of persistent phlegm was observed in all three cohort groups.

An increase in the prevalence of phlegm and in mean sputum volume was associated with smoking in all four reports. The reports did not include formal statistical tests and did not adjust for potential confounding variables.

Breathlessness

In the telephone workers study, Comstock et al. (1973) reported that there was no relationship between the prevalence rate of breathlessness and cigarette smoking.

Ono et al. (1990) found that prevalence tended to increase in smokers. However, the increase was not statistically significant. In the study by Kumagai et al. (1993), a simple correlation analysis revealed that the prevalence rate of breathlessness was significantly higher ($p<0.05$) in smokers than in non-smokers. The prevalence of breathlessness, adjusted for age and duration of employment, was higher in smokers than in non-smokers and ex-smokers. Results of significance tests were not presented for comparison by smoking status.

All three reports suggest a relationship between smoking and breathlessness, but statistical testing of significance and adjustment for confounding variables was not done in any of them.

Common cold

In the one report on this topic, Ono et al. (1990) did not find an effect of smoking on the prevalence rate of severe common cold, accompanied by phlegm. Evidence is limited on whether smoking increases the risk of common cold. This topic has received little investigation in Japan, as elsewhere.

Respiratory function

Comstock et al. (1973) found no relationship between cigarette consumption and one-second forced expiratory volume expressed as a percentage of the individual's value based on age and standing height.

Baba et al. (1985) conducted a cohort study of 176 dust discharge workers. Cross-sectional results showed a relationship between smoking pattern at the start of follow-up and respiratory function. There was no significant relationship between smoking and $FEV_{1.0}$/FVC or $\dot{V}_{25}$/H.

Katoh et al. (2001) conducted a cross-sectional study and follow-up survey to investigate the effects of smoking on pulmonary function. A total of 1,739 residents from farming areas in Miyazaki Prefecture for whom a health survey and pulmonary function tests could be performed were enrolled. In the cross-sectional component, there was a significant difference in both %FVC and % $FEV_{1.0}$ to the predicted values between smokers and non-smokers. In the longitudinal component, the decrease in the adjusted annual change FVC, for both men and women, and the decrease in adjusted annual change $FEV_{1.0}$ in males tended to be greater in both former and current smokers as compared to never-smokers.

Thus, decreased respiratory function in smokers has been identified in both large-scale cross-sectional and longitudinal studies.

Idiopathic spontaneous pneumothorax

Nakamura et al. (1983) reported the results of a case-control study conducted by the Spontaneous Pneumothorax Study Group of National Hospitals. The case group consisted of 2,793 male patients with idiopathic spontaneous pneumothorax recruited by the Study Group, and the control of 1,994 male employees of a major Japanese company. Results showed that the Brinkman Index was significantly higher in the idiopathic spontaneous pneumothorax group ($p<0.05$).

The study by Nakamura suggests that smoking and duration of smoking are associated with idiopathic spontaneous pneumothorax in Japan.

Chronic Obstructive Pulmonary Disease (COPD)

The prevalence of emphysema in 7,847 general inhabitants and its

correlates were analyzed from data obtained during screening for lung cancer with low-dose spiral computed tomography in Nagano Prefecture. Prevalence increased with smoking dose, but the increase was not statistically significant (Wang et al. 2001). Additionally, the authors found that smoking indices were significant factors for the development of emphysema ($p < 0.01$).

Nawa et al. (2002) investigated the prevalence of emphysema by low-dose spiral computed tomography in employees belonging to an employee health insurance cooperative. Prevalence was 2.2% in non-smokers and 14.6% in subjects with smoking experience, but confounding factors including age were again not adjusted for.

Other respiratory symptoms

The report by Comstock et al. (1973) also included prevalence rates for recent chest illness and persistent nasal catarrh. No relationship between these conditions and cigarette consumption was observed.

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2.3.1.5 Adverse effects on reproduction

A literature search carried out on May 28, 2003, identified 1,260 reports through PubMed using the search terms "((tobacco OR smoke OR smoking) AND Japan AND epidemiology AND human)." Reports on the adverse effects of smoking on reproduction were selected from among the papers returned.

Low birth weight

A case-control study conducted in Gunma Prefecture in 1979 compared mothers of low birth weight (LBW) infants (<2,500 g) to mothers of control infants with birth weights of 3,000 to 4,000 g. Infants were matched for sex, geographical area of birth and period of birth (Kitamura 1984). Data were collected through home visits by public health nurses. Mothers of multiple births were excluded from analysis. The relative risk (RR) of LBW associated with smoking was 2.12 ($p<0.001$). Important confounding variables such as mother's age, education level and socioeconomic factors were not considered.

Between 1987 and 1995, Maruoka et al. (1998) investigated factors involved in LBW in a total of 23,132 mothers and their 1-month-old infants at scheduled postnatal health examinations in Fukuoka City. The relative risk of LBW associated with maternal smoking after adjustment for live birth order and history of LBW infants was 1.30 (95% CI 0.94-1.80). The report mentioned the interaction between maternal smoking and birth order and indicated that being the second live birth increased the risk of LBW, although there was no description of the dose-response relationship and birth order.

Matsubara et al. (2000) provided results of a cohort study conducted in Nagoya City. In this study, a self-administered questionnaire on lifestyle including smoking habits was collected at the initial report of pregnancy, and mothers were also asked to report the outcome of delivery by mail. Response rate was 56.7%, and the analysis was carried out with exclusion of multiple pregnancies. Birth weight was significantly greater in infants of mothers who had abstained from smoking after becoming aware of their pregnancy.

As for the smoking pattern of the mother, infants born to actively smoking mothers were on average 96 g lighter than those of non-smoking mothers, this difference being significant. The relative risks for LBW and intrauterine growth retardation (IUGR) were 1.89 (95% CI 1.09-3.26) and 1.79 (95% CI 1.05-3.04), respectively, in actively smoking mothers compared with non-smoking mothers. Among actively smoking mothers, a significant trend towards lower mean birth weight and a higher relative risk of both LBW and IUGR was evident as daily cigarette consumption increased. Mean birth weight of infants born to mothers who had quit smoking was significantly greater than that of infants of non-smoking mothers.

Three relevant reports on the relationship between active smoking and LBW have been published. Matsubara et al. (2000) indicated that smoking by the mother leads to a significant decrease in mean birth weight and significant increases in the relative risk of LBW and IUGR. However, neither this nor the other two studies (Kitamura 1984; Maruoka et al. 1998) were adjusted for socioeconomic factors.

Pre-eclampsia

Ioka et al. (2003) conducted a cohort study of 493 pregnant women making their first visit to Osaka Prefectural General Hospital between September 1997 and April 1998. A self-administered questionnaire focusing on lifestyle was conducted during pregnancy, and pregnancy outcome information was obtained from medical records. After adjustment for secondhand smoke (SHS) exposure and alcohol intake, results showed no significant difference in the morbidity of pre-eclampsia associated with smoking.

Miscellaneous

Matsubara et al. (2000) reported that mean gestational age and relative risk of preterm birth were not significantly different between smoking and non-smoking mothers. The Human Embryo Center for Teratological Studies, Kyoto University has collected embryo obtained from induced abortions since 1961. Matsunaga et al. (1977) compared 103 case samples of holoprosencephalus (craniofacial malformations) from this collection with parity-matched 206 control samples of embryo. No significant difference was observed in the rate of holoprosencephalus in embryos from smoking and non-smoking mothers.

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2.3.1.6 Other diseases

A literature search carried out on May 28, 2003, identified 1,260 reports in PubMed using the search terms "((tobacco OR smoke OR smoking) AND Japan AND epidemiology AND human)." The category of "other diseases" includes those not dealing with respiratory diseases, malignant neoplasma, reproduction, and cardiovascular diseases.

(1) Gastrointestinal diseases

Peptic ulcer

Between 1977 and 1981, Araki and Goto (1985) conducted an epidemiological study for peptic ulcer involving 348 male employees of a plastic processing factory in Tokyo who underwent X-ray and endoscopic screening examinations of the stomach. Of these, 74 were considered to be positive for peptic ulcer. Male employees of the same factory were selected as controls for each case by matching for sex (all males), age (same 5-year span), type of work and job position. The odds ratio (OR) for risk of peptic ulcer associated with smoking was 2.7 ($p<0.05$).

Hamajima et al. (1987) conducted a study using records from a local government in Aichi Prefecture to identify 54 individuals absent from work due to gastric ulcer. One employee of the same local government was randomly selected as a control for each patient after matching for year of birth ($\pm$ 1 year) and type of job. With adjustments for depression, anxiety, timing of meals, and duration of sleep, unconditional logistic analysis showed that the relative risk associated with smoking less than 10 or 10 or more cigarettes per day was 11.9 (95% Confidence Interval (CI), 1.6-89.4) and 9.9 (95% CI 2.6-37.7), respectively, compared with non-smokers.

Between 1980 and 1990, upper gastrointestinal endoscopy was done in a total of 1,792 persons, comprising 1,264 Japanese, 503 Korean and 25 of unknown ethnicity, in a single institute in Kyoto City. Among these, Watanabe et al. (1992) conducted a case-control study in 257 patients with open gastric ulcer, 179 with open duodenal ulcer and a control group consisting of 588 patients without endoscopic findings. The odds ratio of gastric ulcer associated with smoking after adjustment for age, sex, salty food consumption and alcohol consumption was 3.10 (95% CI 2.08-4.62), while that of duodenal ulcer associated with smoking after adjustment for age, sex, spice consumption and coffee consumption was 1.90 (95% CI 1.24-2.92). The results of analysis by ethnic group were not presented.

In a study by Hirayama (1985), the risk of death from peptic ulcer was 1.5 times higher among subjects who smoked daily compared to non-smokers.

Both gastric and duodenal ulcers were associated with smoking in men; however, a stronger association was seen with gastric ulcer (Kato et al. 1990). With regard to atrophic gastritis, a positive association with smoking was not observed (Kato et al. 1990, Namekata et al. 2000).

In summary, these studies in Japan show that the risk of peptic ulcer, in terms of peptic ulcer as a whole as well as gastric and duodenal ulcer separately, has been shown to increase with smoking.

Stomach pain

A questionnaire survey was conducted in 5,523 male taxi drivers in Osaka Prefecture to investigate their working conditions, characteristics of their daily life and a variety of health issues. The prevalence of stomach pain was increased in association with cigarette consumption (Ueda et al. 1989); however, a formal analysis was not presented and potential confounding factors were not addressed. Additionally, the symptom of stomach pain is non-specific, and this report is not necessarily indicative an association between smoking and peptic ulcer disease.

Ulcerative colitis (UC)

Higashi et al. (1991) conducted a case-control study in 50 UC patients from three hospitals in Kyoto, Osaka and Hyogo. All were individuals undergoing health screening in Kyoto City and Osaka City and were matched for sex and age. Smoking habit in the year prior to the onset of the disease was investigated. An association was not observed for UC and smoking status for men. There were no female cases among everyday smokers and ex-smokers. The validity of selecting controls from among subjects undergoing health screening is questionable.

Between 1988 and 1990, the Epidemiology of Intractable Diseases Research Committee of the Ministry of Health and Welfare of Japan performed a case-control study for UC. A total of 384 patients receiving financial aid for treatment of the disease were compared with 384 age- and sex-matched controls in the same public health center jurisdiction (Nakamura and Labarthe 1994). Data on lifestyle, including smoking pattern, were collected for the year prior to the onset of the disease. Compared with never-smokers, former smokers were at an increased risk of UC (OR=1.67; 95% CI 0.97-2.88), whereas current smokers were at a decreased risk (OR=0.30; 95% CI 0.18-0.5). Dose-response relationships in terms of daily cigarette consumption, duration of smoking (years) and Brinkman index were statistically significant.

A multi-site, hospital-based case-control study examined the risk of UC in relation to several factors including smoking. Information prior to the onset of the disease was obtained from self-administered questionnaires. A total of 101 UC

patients and 143 hospital controls were compared (Kurata et al. 1994). Compared with never-smokers, current smokers tended to have a decreased risk of UC. The odds ratios for 1 to 20 cigarettes per day and more than 20 were 0.60 (95% CI 0.2-1.7) and 0.70 (95% CI 0.2-2), respectively. An increased risk was observed in former smokers (OR=2.40; 95% CI 1-6) compared to never-smokers.

In a total of three studies reported on this subject, Nakamura and Labarthe (1994) reported a decreased risk in current smokers and an increased risk in former smokers. The study conducted by the Epidemiology Group of the Research Committee of Inflammatory Bowel Disease in Japan supported this result, though it showed no statistical significance (Kurata et al. 1994).

Gallstone and gallbladder disease

Between 1986 and 1990, Kono et al. (1992) investigated risk factors leading to gallstone disease in male self-defense officials undergoing retirement examination at the Self-Defense Fukuoka Hospital, Fukuoka. Of 2,739 men, gallbladder ultrasonography revealed gallstone disease in 61 and previous removal of the gallbladder in 38. The overall prevalence of gallbladder disease was 3.6%. With adjustment for BMI, alcohol use, glucose tolerance status, military rank and hospital, none of the diagnoses were significantly associated with smoking.

Among 2,228 men aged 49 to 55 examined at one of three hospitals of the Japan Self Defense Forces between 1991 and 1992 (Kono et al. 1995), ultrasonography revealed 41 with gallstones, 31 with a history of cholecystectomy and 2,044 with a normal gallbladder. Smoking habit was ascertained by self-administered questionnaire. After controlling for alcohol use, exercise, glucose tolerance, BMI, hospital and rank, smoking was not related with either gallstones or a history of cholecystectomy.

Kono et al. (2002) subsequently expanded the scale of this survey and between 1986 and 1994 investigated a further 7,637 men aged 48 to 59 years undergoing retirement examination at four hospitals of the Self Defense Forces. The study included 174 patients with gallstones as diagnosed by ultrasonography, and 104 post-cholecystectomy and 6,906 control subjects with a normal gallbladder. Smoking habit was ascertained by self-administered questionnaire. After adjustment for BMI, alcohol use, glucose tolerance status, rank and hospital, cigarette smoking was not associated with either the prevalence of gallstones or postcholecystectomy state, nor with either newly diagnosed or known gallstone disease.

Chronic pancreatitis

To examine the association of alcohol drinking and nutritional intake with chronic pancreatitis, 91 male patients newly diagnosed with chronic pancreatitis were recruited between 1997 and 1998 to a case-control study. One

hundred and seventy-five controls were individually matched by gender, age, hospital and time of first hospital visit. Information on demographic characteristics, smoking, drinking and dietary habits were collected by self-administered questionnaire. The proportion of current smokers was higher among patients than controls ($p<0.05$). In addition to smoking, education level and alcohol consumption were also associated with chronic pancreatitis.

(2) Infectious diseases

Helicobacter pylori infection

Helicobacter pylori (H. pylori) infection is now an established cause of peptic ulcer disease and also of gastric cancer. Smoking could increase risk for these diseases by increasing risk for this infection. In a cross-sectional study of 566 men aged 50 to 55 years undergoing retirement examinations at the Self Defense Force Fukuoka Hospital between 1993 and 1994, Shinchi et al. (1997) examined the association of lifestyle variables including smoking with *H. pylori* infection. Results showed that smoking was not related to the prevalence of infection. An epidemiological study investigating the relationship of *H. pylori* to food intake and smoking habit was conducted among 283 subjects, of whom 68.2% were aged 50 years or over (Toyonaga et al. 2000). Smoking was not related to the seroprevalence of *H. pylori*. In a study by Ogihara et al. (2000), the relationship between seropositivity for *H. pylori* and lifestyle factors including smokingwas investigated in 8,837 textile company workers. Current smokers had a 0.82-fold (95% CI 0.74-0.91) greater risk of seropositivity for *H. pylori* than those who had never smoked. Current cigarette consumption showed a significant dose-dependent (p trend<0.001), negative association for seropositivity. The association between smoking and *H. pylori* infection was strong in younger subjects.

Although two of these three reports indicate no relationship between smoking and *H. pylori* infection, the larger study by Ogihara et al. (2000) shows a negative relationship in a younger population based on analysis by age. In the former two, age might have been adjusted due to a small sample size, or the subjects might have been predominantly older.

Tuberculosis

Une and Esaki (1993) conducted a case-control study on the relationship between socioeconomic factors and tuberculosis in a former coal mining area of Northern Kyushu. The cases were newly registered tuberculosis patients at the Iiduka Health Center District, while controls were randomly selected from a resident directory and matched for sex, age and place of residence. After adjustment for occupation, experience in coal mining, marital status, education,

source of income, drinking, irregular mealtimes and unbalanced diet, smoking status was not significantly associated with the onset of tuberculosis.

(3) Diabetes mellitus

To investigate the association between psychological stress and HbA1c level, and the possible role of catecholamine as mediators of this association, Kawakami et al. (1995) measured mood status (Profile of Mood States, POMS), urinary catecholamines (adrenalin, noradrenalin and dopamine) and fasting plasma glucose in 63 male employees of an electric company. After adjustment for age, occupation, POMS value and respective catecholamines, the number of cigarettes smoked per day was positively associated with HbA1c level ($p<0.01$).

To evaluate the association between smoking and lifestyle risk factors, a case-control study comparing three case groups (53 patients with non-insulin dependent diabetes mellitus (NIDDM), 130 with dyslipidemia and 58 with co-morbidity) was done (Wang et al. 2002). An age- and sex-matched control group consisted of city office workers in Tokyo. After adjustment for parental history of diabetes, stress of life events, history of hypertension, weight (obesity), and daily intake of meat, green vegetables and fiber, odds ratios of NIDDM, dyslipidemia and the co-morbidity associated with smoking were 2.50 (95% CI 1.11-5.68), 1.98 (95% CI 1.43-4.52) and 3.36 (95% CI 1.56-10.01), respectively.

Nakanishi et al. (2002) examined 2,953 male Japanese office workers aged 35 to 59 years without impaired fasting glucose (IFG), NIDDM, medication for hypertension or a history of cardiovascular disease. Fasting glucose concentrations were measured at annual health examinations from 1994 through 2000. Smoking was associated with IFG or NIDDM by white blood cell (WBC) count categories, with the relative risk for IFG or NIDDM and smoking decreasing as the WBC count category increased.

The effects of smoking on the incidence of NIDDM over an 8-year period (1984-1992) were investigated in a cohort of 2,312 male employees of an electric company (Kawakami et al. 1997). After controlling for age at baseline, BMI, physical activity, alcohol consumption, family history, education, work shift and occupation, a proportional hazard regression analysis indicated that those who were currently smoking 16-25 cigarettes per day had a 3.27-fold (95% CI 1.18-9.09) higher risk of developing NIDDM during the follow-up period than non-smokers ($p<0.05$). The hazard ratio was similar (3.21, 95% CI 1.05-9.83)) for those currently smoking 26 or more cigarettes per day.

A cohort of 2,573 non-diabetic subjects in Tokyo was followed for 16 years to evaluate the risk of developing diabetes mellitus (Sugimori et al. 1998). After adjustment for age, BMI, alcohol consumption, eating no breakfast, dairy intake, hypertension, hypercholesterolemia, hyperuricemia, family history and

fasting blood sugar (FBS), the hazard ratio of smoking was significantly elevated. The adjusted risk of developing diabetes mellitus for current smokers was 1.37 (95% CI 1.03-1.82) for men and 1.42 (95% CI 1.1-1.83) for both sexes, compared to non-smokers.

To assess the impact of cigarette smoking on the incidence of NIDDM in middle-aged Japanese, Uchimoto et al. (1999) enrolled 6,250 healthy male employees of a company in Osaka. Subjects were followed for 4 to 16 years (60,904 person years). After adjustment for age, BMI, alcohol consumption, physical activity, parental history of diabetes, fasting plasma, glucose, total cholesterol, triglycerides, HDL cholesterol and hematocrit, the relative risk of NIDDM among current smokers compared with non-smokers was 1.47 (95% CI 1.14-1.92). Men who smoked 30 cigarettes or more per day had a risk of 1.73 (95% CI 1.2-2.48) compared with non-smokers. The number of cigarettes smoked daily and pack-year values were positively and dose-dependently correlated to the development of NIDDM (p for trend=0.0026 and 0.001, respectively).

In these studies in Japan, smoking was a risk factor for the development of NIDDM independent of other factors such as family history and obesity.

Renal complications of diabetes mellitus

To investigate factors contributing to renal failure in NIDDM, Takei et al. (1995) compared 37 NIDDM patients on dialysis and 37 without dialysis (control) in Tokyo. The two groups were similar in terms of age and disease duration. Smoking rate was slightly higher in the patients on dialysis, although the difference was not statistically significant. HbA1c levels in control patients at 6 months before the start of the study were higher than those in patients on dialysis at 6 months before the start of dialysis.

Considering that early-onset NIDDM patients (diagnosed before age 30) can develop diabetic end-stage renal failure (ESRF) in their thirties, Yokoyama et al. evaluated the incidence of diabetic nephropathy and its relationship to basic characteristics in 426 NIDDM patients (Yokoyama et al. 1998). The patients were followed for a mean of 6.8 years. The hazard ratio of ESRF associated with smoking was 1.15 (95% CI 0.60-2.22) by univariate analysis.

To clarify risk factors for the progression of microalbuminuria in Japanese NIDDM patients, a cohort study was conducted over 10 years in 67 outpatients with NIDDM, all showing no overt proteinuria at baseline (Oue et al. 1999). Multiple logistic regression analysis was conducted with control for age, duration of diabetes, HbA1c, blood pressure, BMI, serum lipid and alcohol consumption. In analyses at baseline and again at 10 years of follow-up, smoking was not associated with the progression of microalbuminuria.

Ikeda et al. (1997) investigated the relationship between renal involvement and cigarette smoking in 148 men with NIDDM. The odds ratio for

the prevalence of micro- or macroalbuminuria associated with smoking was 4.5 (95% CI 1.9-11.6) in smokers and 2.0 (95% CI 0.6-6.7) in ex-smokers. Handling of confounders is not clearly described.

A total of 5,174 male company workers were included in a cross-sectional study to examine the relationship between HbA1c level and the prevalence of proteinuria (Hashimoto et al. 1999). After adjustment for age, BMI, BP, change in HbA1c, total cholesterol, and family history of DM and hypertension, smoking was associated with proteinuria in all subjects (OR=1.18, 95% CI 0.77-1.80) and in those with high HbA1c levels (OR=11.53, 95% CI 1.44-92.19).

Although most studies do not support smoking as an increased risk factor for renal insufficiency in DM patients, the study by Hashimoto et al. (1999) involving close analysis of a large number of subjects indicates that smoking increases the prevalence of proteinuria in DM patients.

(4) Neurodegenerative diseases

Dementia

A follow-up study (Nojiri et al. 1991) to an original 1965 cohort study conducted in a farming village in Shizuoka Prefecture was done to investigate the prognosis and occurence of dementia in the surviving subjects. A relationship between dementia and smoking was not found for 405 male patients.

Yamada et al. (2003a) investigated the association between midlife risk factors and the development of vascular dementia or Alzheimer's disease 25 to 30 years later in 1,772 A-bomb survivors born in Hiroshima before 1932. No dementia was documented in 1,660 subjects, but was newly diagnosed in 114 from 1992 to 1997. Criteria were based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition(DSM- Ⅳ). After adjustment for age and education, smoking was shown to not significantly affect the prevalence of vascular dementia or Alzheimer's disease in either sex.

Parkinson's disease

Watanabe (1994) conducted a case-control study in Hokkaido in which 95 patients with primary Parkinson's disease were compared with 190 controls matched by age, sex and area of residence. The results of this study suggest an association between Parkinson's disease and smoking. In men, smokers were 2 times (95% CI 0.94-4.79) more likely of having Parkinson's disease than non-smokers. A negative association between smoking and Parkinson's disease was reported for women (OR=0.79, 95% CI 0.25-2.52).

(5) Otorhinologic diseases

Idiopathic sudden deafness

Nakamura et al. (2001) investigated the relationship between idiopathic sudden deafness and smoking, alcohol intake and sleep duration in a case-control study involving consecutive patients diagnosed with idiopathic sudden deafness between 1996 and 1998 at collaborating hospitals in Japan. Controls were obtained from a nationwide database of pooled controls matched for age, sex and residential district. The authors wrote: "there was extremely weak evidence of association between daily tobacco intake and sudden deafness." No significant association was observed in idiopathic sudden deafness, as a whole or by type (high-frequency, low-frequency, flat-type and profound).

Hearing loss

The association of cigarette smoking with the development of hearing impairment (loss of 30 dB at 1000 Hz and 40 dB at 4000 Hz) on 5-year follow-up was studied in 1,554 non-hearing-impaired Japanese male office workers aged from 30 to 59 years (Nakanishi et al. 2000). After controlling for BMI, alcohol consumption, mean blood pressure, serum total cholesterol level, high-density lipoprotein cholesterol level, triglyceride level, fasting plasma glucose level and hematocrit at study entry, the relative risk of hearing loss in the high-pitch range associated with smoking more than 30 cigarettes per day and more than 40 pack years were 2.2 (95% CI 1.09-4.2) and 2.45 (95% CI 1.28-4.7), respectively. A similar tendency was observed in the low-pitch range but this was not statistically significant.

In order to determine the risk factors for hearing loss in the elderly, 496 subjects with hearing loss (loss of 30 dB at 1000 Hz and 40 dB at 4000 Hz) and 2,807 age-matched subjects without hearing disturbance were recruited. The subjects all participated in an automated multiphase health screening examination, and their lifestyle and medical data were analyzed (Itoh et al. 2001). After adjustment for sex, age, BMI, %VC, hemoglobin, TC, FPG (Fasting Plasma Glucose), AST, ALT, and GTP, current smokers showed a significantly elevated risk of hearing loss compared with non-smokers (OR=2.10, 95% CI 1.46-2.87).

Mizoue et al. (2003) examined the synergistic effects of smoking and noise exposure on hearing acuity. The data used were derived from periodic health examinations for 4,624 male steel company workers and included audiometry testing and information on smoking. Occupational exposure to noise was determined based on company records. Smoking was dose-dependently associated with increased odds of high-frequency hearing loss, independent of occupational noise exposure.

These studies suggest an association of smoking with hearing loss, an

association that has received little attention to date.

(6) Ophthalmological diseases

Neovascular form of age-related macular degeneration

A case-control study conducted between 1990 and 1992 at five university-affiliated hospitals in the Tokyo metropolitan area compared 56 male patients aged 50 to 69 years, all with the neovascular form of age-related macular degeneration of less than 3 years' duration, to 82 controls randomly selected from persons visiting one of these five hospitals for a general health examination (Tamakoshi et al. 1997). The relative risk of the neovascular form of age-related macular degeneration associated with smoking was 2.97 (95% CI 1.0-8.84). This risk was significantly higher in those subjects who smoked cigarettes without the use of a filter, deeply inhaled, started smoking at 20 years or younger, had been smoking for 40 years or longer, or had a Brinkman index of 700 or higher as compared with the other subjects. It is possible that the controls, selected from subjects visiting a university-affiliated hospital for health examinations, were not representative of healthy subjects.

Intraocular pressure

Yoshida et al. (2003) evaluated the association between lifestyle-related factors and intraocular pressure (IOP) in 569 residents aged 29 to 79 years in Ibaraki Prefecture. After adjustment for BMI, alcohol consumption, age and diastolic blood pressure, cigarette consumption was found to have a significantly positive association with IOP in men. The association was also seen in women, but this was not significant.

(7) Endocrine diseases

Graves' disease

Between 1994 and 1995, Yoshiuchi et al. (1998) compared 228 patients with Graves' disease (46 men and 182 women) with controls, the latter described as "sex- and age-matched (within 5 years) healthy control subjects, randomly selected from our database." After adjustment for stress, the risk of Graves' disease associated with smoking was significantly increased in women but not in men. Women smoking less than 10, 11 to 20 and 21 to 40 cigarettes per day had an odds ratio of developing Graves' disease of 3.7 (95% CI 1.3-11), 3.5 (95% CI 1.2-10), and 5.1 (95% CI 1.0-27), respectively. Since the control subjects were insufficiently described (e.g. type and size of database), it is difficult to evaluate the validity of these results. The difference by gender may relate to the small size of the male case group.

(8) Dental diseases

Caries

To assess the relationship between smoking, oral hygiene habits and dental caries, 575 adults aged 20 to 29 years who visited dental clinics in Chiba City were interviewed orally and by questionnaire, then given an oral examination (Tada and Hanada 2002). In women, smokers presented with more tooth decay, missing teeth and filled teeth than non-smokers. No such smoking-related increases were seen in men. Even after adjustment for age, employment status, family composition and oral health status, female smokers had increased tooth loss and decay. This study did not use DMFT (Decayed, Missing and Filled teeth) as the index of caries prevalence. The results suggest that smokers were likely to leave their caries untreated. Further, the study took no consideration of diet (i.e. sucrose intake) as a potential confounding factor. Ogawa et al. (1998) conducted a cross-sectional study of hypertension and dental diseases in 2,000 workers at a petrochemical plant in Osaka. In this study, data were collected on the association between smoking and dental disorders (Community Periodontal Index of Treatment Needs (CPITNs), number of decayed and missing teeth, and number of filled teeth). Although the number of decayed and missing teeth was greater in smokers than non-smokers, analysis was limited and no consideration was taken of possible confounding factors such as sugar intake.

Periodontosis

In the study by Ogawa et al. (1998) mentioned above, the CPITN was higher in smokers in every age group tested. Shizukuishi et al. (1998) interviewed and administered questionnaires to 310 factory workers in Osaka as part of a study of differences in lifestyle designed to evaluate the effect of smoking on the Community Periodontal Index (CPI). After adjustment for age, sex, alcohol consumption, frequency of tooth brushing, diligence in brushing teeth at the cervical area and use of interdental cleaners, the odds ratio of CPI associated with smoking was 2.11 (95% CI 1.17-3.81).

(9) Postoperative complications

Postoperative pulmonary complications

Nakagawa et al. (2001) evaluated the effects of smoking on postoperative pulmonary complications (PPC) in patients undergoing pulmonary surgery between 1997 and 1998. The odds ratio of PPC after adjustment for age, sex, pulmonary function and duration of surgery was 1.03 (95% CI 0.47-2.26) in ex-smokers who abstained from smoking for at least 4 weeks prior to surgery compared to non-smokers. The odds ratio in recent smokers who abstained from

smoking for 2 to 4 weeks prior to surgery was 2.44 (95% CI 0.67-8.89), showing no difference from that in current smokers (OR=2.09, 95% CI 0.83-5.25). The type of surgery as a confounding variable was of interest, but no difference was observed among tumor enucleation, wedge resection, lobectomy and pneumonectomy.

(10) Allergic diseases

Allergic symptoms

Kuwahara et al. (2001) studied 426 community-dwelling women in Osaka to evaluate the effect of living environment on atopy and enhanced eosinophil activity. The relationship between smoking and these conditions was also evaluated. Atopic sensitization to house-dust mites and enhanced eosinophil activity were assessed by measuring serum levels of *Dermatophagoides pteronyssinus*-specific IgE and eosinophil cationic protein, respectively. For smoking, smoking habit of the subjects themselves and the number of family members who smoked was investigated. Active smoking was not associated with a significant increase in any of the indices tested.

(11) Autoimmune diseases

Systemic lupus erythematosus (SLE)

A case-control study of SLE was conducted by the Epidemiology of Intractable Diseases Research Committee of the Ministry of Health and Welfare of Japan between 1988 and 1990 (Nagata et al. 1995). A total of 282 newly registered female patients receiving financial aid for treatment were compared with a group of controls living in the same geographic area. All subjects underwent health examinations at the health center during the study period and were age-matched within 5-year differences. It was found that the risk of developing SLE was significantly increased in current smokers. Risk was also increased in those with a family history of asthma and those with a higher age of menarche, although no adjustment for these potentially confounding variables was made.

(12) Absenteeism due to illness and injury

A survey was conducted in 21,924 male workers at a chemical fiber manufacturing company to assess the relationship between smoking habit and leave from work due to morbidity (Muto and Sakurai 1992). Data used included statistics on sick leave and the results of a 1988 health survey. Adjustment was made for age, type of work, BMI, exercise and alcohol consumption. The odds ratio

of sick leave in current smokers and ex-smokers as compared with never-smokers was 1.4 ($p<0.01$) and 1.3 ($p<0.01$), respectively, both increases being significant. A dose-response relationship between cigarette consumption and sick leave was observed for respiratory disease, gastrointestinal disease and all other morbidity, but was significant for gastrointestinal disease only. The lack of significance may have been in part due to the possibility that smokers with a history of heavy cigarette consumption had already become ex-smokers. This hypothesis is supported by the fact that there was little difference between the odds ratio of sick leave in current and ex-smokers. Smoking in men increases the risk of leave due to morbidity.

(13) Sleep disturbance

Snoring

Kurono et al. (1993) conducted a study of snoring in 6,725 male workers at an iron-manufacturing company in Chiba. The incidence of snoring, determined present or absent by self-administered questionnaire, increased with increasing Brinkman index. The prevalence rate of snoring increased with age. Brinkman index also increased with age, and age should be considered a potential confounding variable; however, no adjustment for this or other confounders was made.

Excessive daytime sleepiness (EDS)

To estimate the prevalence of EDS and examine factors associated with it, Doi et al. (2002) investigated 3,909 male non-shift white-collar workers in the Tokyo metropolitan area between December 1999 and January 2000. After adjustment for age, marital status, education, type of work, sleep duration, sleep-wake schedule, DISD (difficulty in initiating and/or maintaining sleep), hypnotic medication use, alcohol, caffeine, depression, asthma, peptic ulcer and muscle pain, the prevalence rate of excessive daytime sleepiness showed an increased risk of 2.15 (95% CI 0.85-5.43) in those subjects smoking 2 or more packs of cigarettes per day.

Other sleep disorders

To clarify the effects of daily stress, regular exercise, alcohol consumption and smoking on the prevalence of sleep disorders, Kim et al. (1999) surveyed 3,030 Japanese subjects aged over 20 years by stratified random sampling using structured interviews. Smoking did not affect the prevalence of difficulty in initiating sleep, difficulty in maintaining sleep, early morning awakening or hypnotic medication use.

(14) Sudden death

Sudden death in adults

A study was conducted to identify the risk factors and triggers of sudden death in people whose cause of death was definitively identified at autopsy (Owada et al. 1999). The definition used was that proposed by the Sudden Death Project Team of the Ministry of Health and Welfare. Following the death and subsequent autopsy of 91 persons at the Department of Legal Medicine, Kitasato University School of Medicine laboratory, a telephone interview was conducted with available relatives. As control subjects, 1,167 persons who consulted the authors for a health check were used. After adjustment for age, sex, blood pressure, diabetes mellitus, hypercholesterolemia, heart disease, chest symptoms, autonomic disturbance, short- and long-term stress, drinking and occupation, smoking significantly increased the risk of sudden death (OR 1.91; 95% CI 1.02-3.59). Other factors also increasing this risk included short- and long-term stress, autonomic disturbance, heart disease, and chest symptoms. Although the validity of the definition of sudden death in Japan is questionable, an association with smoking was clearly demonstrated.

A nested case-control study was conducted among 164,017 male employees receiving annual medical checkups. The most recent medical checkup data of 242 sudden death patients were compared with corresponding data of 505 age-, workplace-, and job type-matched male controls (Kondo et al. 2001). The risk of sudden death tended to increase ($p=0.005$) commensurate with Brinkman index but potential confounding factors were not considered.

A question remains as to the definition of sudden death in Japan; nevertheless, the possibility that smoking may increase the risk of sudden death has been shown.

Sudden infant death syndrome (SIDS)

Tanaka et al. (1999) reported a case-control study of SIDS between 1996 and 1997. Control infants were matched by date and municipality of birth and an interview was performed in 1998. After adjustment for birth weight, gestational weeks, usual sleep position, sleep position on the day of death, mode of nutrition, room temperature and clothing/bedclothes, the odds ratio of SIDS associated with smoking by both the father and mother was 3.0 (95% CI 1.8-5.1). The odds ratio also showed a significant increase in incidence associated with smoking by either the father or mother (1.19; 95% CI 1.16-2.25).

(15) Bone Disorders

Bone mineral density

As part of a cohort study conducted in Wakayama Prefecture, bone mineral densities in the lumbar spine and femur neck were measured using dual energy X-ray absorptiometry (Ueda et al. 1996). Additional information on smoking habit was collected for some subjects. Results were reported only for male subjects with a high smoking rate. No change in bone mineral density associated with smoking was observed at either site in any age group. Results were presented by age group, reported for men only and not adjusted for confounding variables (Yoshimura et al. 1996).

As baseline for their cohort study, Yoshimura et al. examined 400 randomly selected subjects surveyed on bone mineral density of the lumbar spine and proximal femur and physical characteristics as well as smoking habit (Yoshimura et al. 1996, Egami et al. 2003). Results showed that bone mineral density was not related to smoking habit.

To investigate the association of lifestyle factors with bone mineral density among young men, Egami et al. (2003) measured bone mineral density of the second metacarpal bone in 143 male university students aged 18 to 22 years by computed X-ray densitometry. The subjects completed a lifestyle questionnaire which included amount of smoking. Spearman's rank correlation coefficient (ρ) between bone mineral density and daily cigarette consumption was -0.121 (p=0.148).

Hip fracture

A cohort study conducted in Hiroshima and Nagasaki focused on the occurrence of hip fracture not attributable to traffic accident in 4,573 atomic-bomb survivors (Fujiwara et al. 1997). A questionnaire including queries on smoking habit was administered between 1978 and 1981, and subjects were subsequently followed up for the occurrence of hip fracture through examination by physicians up to 1992; 55 cases of fracture occurred during the observation period but no association with smoking was seen.

Idiopathic osteonecrosis of the femoral head

The risk factors for idiopathic osteonecrosis of the femoral head were investigated in a nationwide multicenter case-control study comparing 118 patients with no history of systemic corticosteroid use with 236 controls matched for sex, age, ethnicity, clinic and date of initial examination (Hirota et al. 1993). After adjustment for alcohol consumption, occupational energy consumption, BMI and liver dysfunction, an increased risk was found for current smokers (OR=4.7,

95% CI 1.5-14.5). A dose-response relationship with daily cigarette consumption and the cumulative consumption of cigarettes was also observed (trend $p<0.05$).

In a cooperative hospital-based case-control study of idiopathic avascular necrosis of the femoral head, 64 men were compared to 128 matched controls without history of systemic corticosteroid use but with the same sex, age, ethnicity and medical institution (Shibata et al. 1996). After adjustment for drinking, flushing pattern, history of liver disease, occupational history and BMI, no significant difference was seen between the case and control groups for smoking pattern or daily and cumulative number of cigarettes smoked.

(16) Erectile dysfunction

To measure the prevalence of erectile dysfunction (ED) and to study its correlates, a random sample of men aged 40 to 70 years from Brazil, Italy, Japan and Malaysia were interviewed using a standardized questionnaire (Nicolosi et al. 2003). Among the four countries, age-adjusted prevalence of moderate and complete ED was highest in Japan. Heavy smoking was associated with an increased risk of ED, although Japan-specific data for this finding were not provided.

(17) Bulimia

To investigate the relationship of bulimia with alcohol abuse and smoking, Suzuki et al. (1995) surveyed 2,597 high school students. A group of bulimic students who fulfilled four of five DSM-III-R bulimia nervosa criteria were identified, and a control group reporting no experience with binge-eating experience was established. The prevalence of smoking was significantly higher among the bulimic women than the controls, but no significant difference in smoking experience was seen among the men.

(18) Obesity

Although smoking cessation is strongly associated with subsequent weight gain, it is not clear whether the initial gain after cessation remains over time. Cross-sectional analyses to investigate the relationship between BMI and the duration of smoking cessation were done using data from periodic health examinations of civil servants (Mizoue et al. 1998). Among former smokers who had smoked 25 cigarettes a day or more, odds ratio after adjustment for age, alcohol intake and sports activity for BMI>25 kg/m^2 was 1.88 (95% CI 1.05-3.35), 1.32 (95% CI 0.74-2.34), 0.66 (95% CI 0.33-1.31) for those with 2-4, 5-7 and

8-10 years of smoking cessation, respectively. The corresponding odds ratio among those who previously consumed less than 25 cigarettes a day was 1.06 (95% CI 0.58-1.94), 1.00 (95% CI 0.58-1.71) and 1.49 (95% CI 0.95-2.32). These results suggest that although heavy smokers may experience significant weight gains and weigh more than non-smokers in the few years after smoking cessation, they subsequently lose this weight and return to the level of never-smokers. In contrast, light and moderate smokers do not gain excess weight after smoking cessation.

Ishizaki et al. (1999) investigated the association between waist-to-hip ratio and life-style factors including smoking in 3,833 metal product workers. After adjustment for age and BMI, smoking was not associated with waist-to-hip ratio. The BMI of heavy smokers was found to increase after the cessation of smoking, but to return to the value before cessation after several years. For light smokers, changes were found in the BMI but not in the waist-to-hip ratio.

(19) Laboratory findings

Proteinuria

To analyze the effects of obesity and smoking on the development of proteinuria, 5,403 subjects who participated in health screening examinations in Okinawa in 1997 and 1999 and who had normal renal function and negative proteinuria in 1997 were studied (Tozawa et al. 2002). After adjustment for obesity, hypertension, diabetes mellitus, age, sex, hypercholesterolemia, hypertriglyceridemia, anemia, hyperuricemia, drinking habit and exercise habit, the incidence of proteinuria was positively associated with the number of cigarettes smoked per day ($p<0.05$). The relative risk of developing proteinuria was 1.32 (95% CI 1.00-1.74) for smokers.

A total of 5,174 male company workers were included in a cross-sectional study examining the relationship between HbA1c level and the prevalence of proteinuria (Hashimoto et al. 1999). After adjustment for age, BMI, BP, change in HbA1c, total cholesterol and family history of DM and hypertension, smoking was associated with proteinuria in all subjects (OR=1.18, 95% CI 0.77-1.80) and in those with high HbA1c levels (OR=11.53, 95% CI 1.44-92.19). Smoking was not associated with proteinuria in subjects who had a HbA1c level of less than 5.9%.

Hemoglobin (Hb) level

Yamada et al. (2003b) analyzed a Japanese population over a 40-year period, adjusting for the effects of sex, birth cohort, smoking and anemia-associated diseases. Hb levels in ever-smokers were significantly elevated over those in non-smokers ($p<0.0001$).

Hyperuricemia

Kono et al. (1994) examined behavioral and biological correlates of serum uric acid in 2,487 men undergoing retirement health examinations at the Self Defense Force Fukuoka Hospital between 1986 and 1990. Subjects using medication for hyperuricemia, hypertension or hyperlipidemia were excluded. After adjustment for age, BMI and serum creatinine, past smoking was positively associated with serum uric acid levels. The authors suggested that this relationship might have been due to the effects of unconsidered confounding factors.

In Osaka, hyperuricemia-free male office workers aged 30 to 54 years were examined for six successive years (Nakanishi et al. 1999). Subjects who were found to be hyperuremic or who started medication for hyperuricemia during these repeated examinations were defined as incident cases. Among the 1,365 final subjects, the adjusted hazard ratio for the development of hyperuricemia with past and current smoking compared with never-smoking was 0.90 (95% CI 0.60-1.35) and 0.65 (95% CI 0.46-0.92), respectively. The authors could not clearly explain this finding but pointed out that the increase in body weight during the follow-up period was 1.19 kg in never-smokers but 0.60 kg in ex-smokers and 0.09 kg in current smokers ($p<0.001$, analysis of variance).

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2.3.2 Health effects of passive smoking

2.3.2.1 Cardiovascular disease

Evidence from Japan on the effect of passive smoking on the cardiovascular system is limited, but the Hirayama cohort study showed that the relative risk of mortality from ischemic heart disease attributable to secondhand smoke (SHS) among non-smokers was 1.3 (90% CI 1.06-1.60) (Hirayama 1990). Given that the proportion of passive smokers was estimated at 27% in the 1999 National survey, the population-attributable risk percent is approximately 7%. Thus, ischemic heart disease morbidity and mortality attributable to passive smoking is about 9,000 hospitalizations and 5,000 deaths, making passive smoking a potentially important cause of cardiovascular disease.

2.3.2.2 Cancer

A number of investigators have examined the increased risk of lung cancer for non-smokers living with tobacco-smoking family members. The case-control study of Akiba et al. reported an approximately 50% increase in risk among non-smoking women with smoking husbands (Akiba et al. 1986). Hirayama estimated the excess risk of lung cancer in women exposed to household SHS as similarly moderate (mortality rate ratio: 1.78; 15.50/8.70) (Hirayama 1981). In contrast, Sobue examined several forms of indoor air pollution and found only a weakly significant association of lung cancer with passive smoke (Sobue 1990a, b). Shimizu et al. (1988) compared the risk of lung disease from household passive smoke by relationship to the smoker. Results showed that risk was strongest for non-smoking women living with smoking mothers or fathers-in-law (Shimizu et al. 1988). Interestingly, in a Japanese study that demonstrated an increased risk of passive smoke-associated lung cancer, the histopathological subtype of such tumors was skewed toward adenocarcinomas, as compared to the expected predominance of squamous cell carcinomas typical among smokers (Akiba et al. 1986). The association between passive smoking and lung cancer was higher, although not statistically significant, for the adenocarcinoma subtype compared to squamous cell carcinoma and small cell lung carcinoma (Katada et al. 1988), so a difference in the histopathological subtype of lung cancer attributable to SHS exposure is of potential mechanistic significance.

With respect to malignancies at sites other than the lung, the data on disease among nonsmokers in smoking households have suggested a slightly increased risk for oropharyngeal and urinary tract malignancies, but lesser increases in the risk of malignancy at other common sites of cancer. The prospective cohort studies of Hirayama suggested that non-smoking women with

smoking husbands are at an increased risk of cancers of the lung, nasal sinus, brain, and all sites combined, but not of the stomach, for example (Hirayama 1984, 1985). Squamous cell neoplasms of the maxillary sinus have been found at a higher incidence in both smoking and non-smoking women, with the rate significantly related to the number of smokers in the household (Fukuda et al. 1990). Cancer incidence was marginally elevated (relative risk (RR)1.75, 95% CI 0.94-3.1) among SHS exposed non-smoking women at all sites previously implicated in studies of active smoking-related cancers (Nishino et al. 2001). Incidence for breast cancer was somewhaat decreased in passively exposed women (RR 0.58, p=0.078), a notable result given Hu et al.'s similar previous finding that the incidence of breast cancer among women with smoking husbands was slightly but nonsignificantly decreased (odds ratio (OR) 0.67 (0.43-1.06)) (Hu et al. 1997).

Interestingly, *in utero* exposure (maternal smoking during pregnancy) was associated with a significantly increased risk of neuroblastoma (OR≥1.4, p<0.05) compared to all other cancers. The association for benign or 'details unknown' teratoma (OR≥1.4) and hepatoblastoma (OR≥2) was not statistically significant (Kobayashi et al. 1990).

In summary, studies in Japan show increased risk for several cancers in association with passive smoking. The risks are moderate relative to those of active smoking. As in other countries, consideration needs to be given to measurement error and confounding in interpreting these data.

2.3.2.3 Respiratory diseases

On behalf of the Research Committee of the Prevalence of Asthma in Children, Society of Bronchial Asthma of Children in Western Japan, Nishima reported the prevalence of bronchial asthma in school children in western Japan (Research Committee of the Prevalence of Asthma in Children, Society of Bronchial Asthma of Children in Western Japan 1983). This study, with a total of 55,388 respondents, was conducted in children from 11 primary schools from all prefectures in Kyushu as well as Yamaguchi, Hyogo and Kagawa Prefectures. When family history of major allergy and bronchial asthma were taken into account, the presence or absence of smoking family members did not markedly affect the rate of asthma or of people in remission.

The relationship between indoor air pollution, including SHS exposure, and air cooling or heating was evaluated in 7,916 children aged 3 undergoing age-scheduled health examinations in Aichi Prefecture (Tominaga and Itoh 1985). The prevalence of asthmatic bronchitis was significantly higher in children with a smoking mother than in those without smoking family members. An opposite (but not significant) trend was observed for bronchial asthma. This pattern

might be explained by abstention from smoking by members of a family with an asthmatic child. In family situations where there was both a smoking mother and family members with cough and sputum, the prevalence of asthmatic bronchitis in children was unusually high. This was statistically significant compared to the prevalence in children with either a smoking mother or family members having cough and sputum.

Ono et al. (1990) investigated the prevalence of respiratory diseases and SHS exposure in children. The prevalence of asthma tended to increase with increasing SHS exposure. However, the authors did not test for statistical significance or adjust for potential confounding variables to determine the impact of smoking on asthma.

A study on asthma, wheeze and remission using the revised Japanese version of the ATS-DLD questionnaire was conducted in 10,137 children from 17 primary schools in Okinawa (Okuma 1994). In families with one or more smoking members, 55.0% had a child without wheeze or asthma, whereas 58.8%, 43.9% ($p<0.01$), 55.1% and 62.0% ($p<0.01$) had a child with active asthma, asthma in remission, active PDA (physician-diagnosed asthma) and PDA in remission, respectively.

To elucidate factors contributing to pediatric bronchial asthma in urban communities, Nakajima et al. (1998) conducted a case-control study in 210 patients with atopic asthma, 24 with non-atopic asthma and 180 controls. The controls were selected from children attending a different hospital from the patients but had no history of allergic symptoms or asthma. The presence or absence of smoking family members as well as the smoking habits of the father, mother and other family members were investigated. There was no difference in asthma rate in families with one or more smoking members regardless of relationship to the child, while the percentage of smoking fathers was lower in children with non-atopic asthma and the percentage of smoking mothers was lower in children with atopic asthma. In addition to the smoking habit of family members, extensive investigations were conducted into the home environment, such as window ventilation, air cooling and heating, mold growth, indoor sanitation and house-dust mite allergens, although the relationship between ETS and asthma was not specifically analyzed. The controls were selected from a hospital environment different from that of the case subjects, but the effect of this difference was not discussed.

Takemura et al. (2001) conducted a case-control study comparing 2,315 asthmatic patients and 21,513 controls in Saitama Prefecture to determine the relationship between asthma in children and junior high school students and their infant nutrition. The smoking habits of the father and mother were also investigated. After adjustment for age, sex, family history of asthma and the mode

of infant nutrition, no significant association between parental smoking habit and the child's asthma was observed.

Most studies evaluating the relationship between SHS and asthma did not focus directly on the effect of passive smoking, although the analyses of Tominaga and Ito (1985) and Takemura et al. (2001) are considered appropriate. SHS exposure, especially due to smoking by the mother, was shown to increase the prevalence of asthmatic bronchitis in the former, but not in the latter.

Wheeze

Nishima reported that the presence of wheeze, as well as of major allergy or bronchial asthma, was higher in individuals exposed to SHS than those who were not (Research Committee of the Prevalence of Asthma in Children, Society of Bronchial Asthma of Children in Western Japan 1983). However, statistical testing of significance and adjustment for confounding variables were not done.

Ono et al. (1990) found no relationship between the presence of wheeze and SHS exposure (absence, presence with a non-smoking mother, or presence with a smoking mother). Again, however, statistical testing of significance and adjustment for confounding variables were not done.

Okuma (1994) found no significant difference between a wheezing and a control group on evaluation for one or more smoking family members. No adjustment was made for confounding variables.

These studies suggest that smoking increases the risk of wheeze. However, in these studies consideration was not given to potential confounding factors.

Cough

Ono et al. (1990) found no relationship between the prevalence of cough and SHS exposure (absence, presence with a smoking mother, or presence with non-smoking mother). Formal statistical analyses were not presented.

Phlegm

Ono et al. (1990) found no relationship between the incidence of phlegm and SHS exposure (absence, presence with a smoking mother, or presence with non-smoking mother). Statistical testing of significance and adjustment for confounding variables were not done.

Common cold

Tominaga and Itoh (1985) reported that the prevalence of frequent common cold was lowest in children without smoking family members, higher in those with a smoking father and highest in those with a smoking mother, although

the association with passive smoking was not significant. Ono et al. (1990) found no significant difference in the prevalence of severe common cold accompanied by phlegm, although no adjustment for potential confounding variables was made. No conclusive evidence that passive smoking increases the risk of common cold has been obtained.

2.3.2.4 Reproduction

Matsubara et al. (2000) examined children of smoking and non-smoking fathers and reported that the mean gestational age of infants born to these men was not significantly different. Among continuously smoking fathers, infants with fathers who smoked more than 20 cigarettes per day were significantly shorter at gestational age than those with fathers who smoked less than 20 cigarettes per day. There were no differences in mean gestational age between children of women exposed to SHS, whether at home, work, or elsewhere, and children of non-exposed women. No increase in the relative risk of preterm birth was observed in association with father's smoking and SHS exposure. Further, no significant increase in the relative risk of LBW was observed in association with father's smoking or SHS exposure. Infants born to non-smoking mothers exposed to SHS were 19 g lighter ($p<0.05$), but no dose-response relationship was observed.

Ioka et al. (2003) conducted a cohort study of 493 women whose first antenatal visits were between September 1997 and April 1998 at Osaka Prefectural General Hospital. A self-administered questionnaire focused on lifestyle was done during pregnancy, and pregnancy outcome information was obtained from medical records. No relationship was found between the morbidity of pre-eclampsia and the exposure of pregnant women to household smoke.

2.3.2.5 Allergic dieases

Kuwahara et al. (2001) found that atopic sensitization to house-dust mites and eosinophil activity were not increased as a result of SHS exposure.

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2.4 Comparison of Health Effects of Smoking in Japan and Other Countries

2.4.1 Introduction

This report has summarized the major studies in Japan on active and passive smoking and health, including several hundred papers from many individual epidemiological studies using case-control, cohort, and cross-sectional designs. Not surprisingly, these studies show that smoking increases risk for many diseases in Japan as elsewhere in the world. The data from these studies are included in an extensive series of evidence tables, which we summarize qualitatively below. There is a smaller number of studies from Japan on passive smoking, but these studies have been a critical component of the broader base of evidence on passive smoking and disease, particularly for lung cancer.

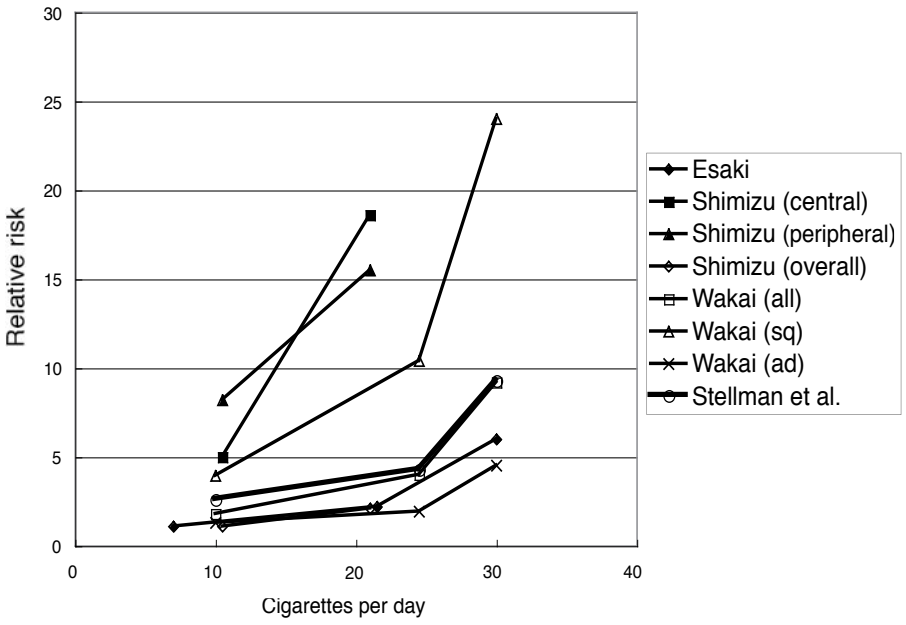
2.4.2 Health effects of active smoking

2.4.2.1 Lung Cancer

Lung cancer has been studied extensively using both case-control (n=8) and cohort (n=4) approaches. There is consistent evidence for increased risk when smokers are compared with never-smokers and for a dose-response with the number of cigarettes smoked. Risks are lower for former smokers than for current smokers. Increased risks are documented in both men and women and for all major histologic types of lung cancer. In general, the relative risks are lower than those observed in western countries during the same time intervals, but have tended to increase over time. Relative risks measured over the last decade are approximately half those observed in major studies in western countries,

which indicate relative risks above 20, comparing smokers with never-smokers. An increase in the relative risk of lung cancer has been reported in relation to the daily number of cigarettes smoked in three studies, as shown in Figure 2.7. Compared to the dose-response relationship observed in the Cancer Prevention Study II (CPS II), the rise in risk in Japan is less steep, possibly reflecting differences in historical smoking patterns between Japan and western countries. The cumulative dose, which reflects the total number of cigarettes smoked in one's life, is lower among those Japanese smokers now developing lung cancer, as compared to smokers in western countries, since the average number of cigarettes smoked by Japanese increased rapidly only after 1950, as shown by Figures 1.6 and 1.7. One parallel case-control study in the US and Japan (Stellman et al. 2001) compared dose-response relationships in the two countries. The findings need to be interpreted with caution because of the particularly high relative risks in the US component. Nonetheless, the dose-response relationships were substantially weaker in the Japanese data, a finding interpreted by the authors as possibly reflecting differences in the cigarettes smoked in the two countries.

Figure 2.7 Quantitative Analysis of Cigarette Smoking and Lung Cancer Risk



To show the difference in cumulative dose between smokers in the US and Japan, a 50-year cumulative consumption index was formulated as the summation of *per capita* cigarette consumption over the past 50 years (Figure 2.8). The period of 5 years was chosen to reflect the duration of smoking from age 20 to 70. This index correlates reasonably with lung cancer mortality rates for age 65 to 74 in both sexes (Figure 2.9). Interestingly, it shows a slight decrease in the

1990s, coincident with an actual decrease in lung cancer mortality rate in the US during the same period. Although the index is only an approximate indicator of cumulative dose, Figure 2.9 suggests that the difference in relative risks for Japan and the US may reflect differences in cumulative dose. For example, the relative risk of lung cancer estimated by Hirayama's cohort study, 4.5, was about half that estimated from American cohort studies conducted at the same time, and quite close to the difference in the cumulative consumption index shown in Figure 2.9. For 1970-80 in Japan, the follow-up interval for the Hirayama cohort study, the index in Japan was about half the US value.

Figure 2.8 Comparison of *per capita* Cigarette Consumption

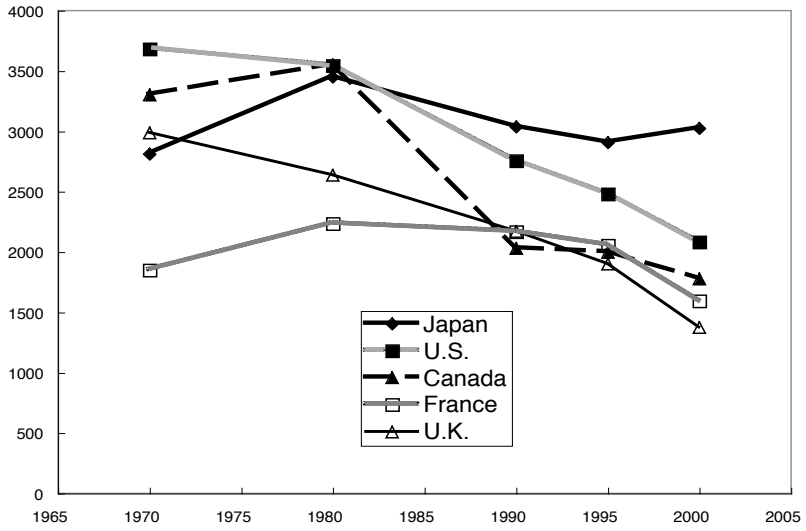
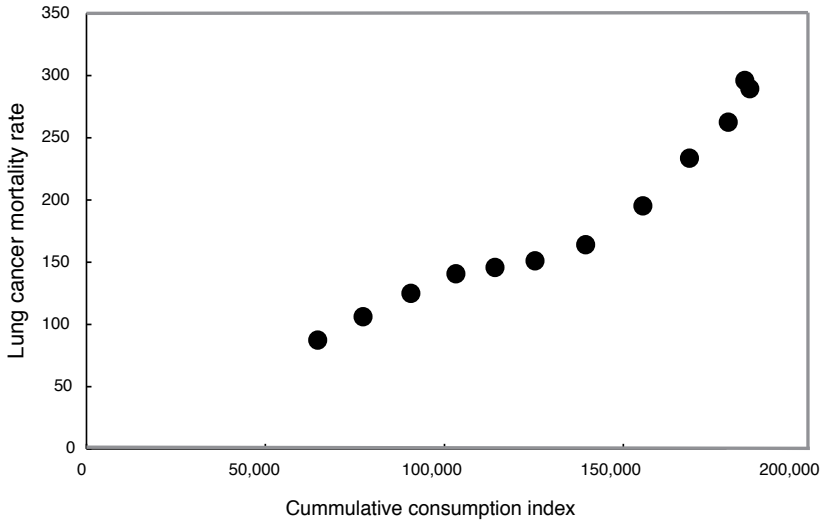


Figure 2.9 Cumulative Consumption and Lung Cancer Mortality Rate



2.4.2.2 Other cancers

For other cancer sites, the review of Japanese studies clearly indicates qualitative similarities in risks between Japan and other countries, although quantitative comparisons were not possible because of the inadequate numbers of studies. As suggested by the cumulative dose analysis above, the relative risk for some cancer sites tended to be smaller than the values reported in other countries, where cumulative doses were higher than in Japan.

For cancers of the oral cavity, pharynx, and larynx, data are available only from two case-control studies and a single cohort study, that by Hirayama. The studies show a two-fold increase in relative risk, comparing smokers with never-smokers. For laryngeal cancer, findings from case-control and cohort studies showed greatly increased risks in smokers.

For cancer of the esophagus, two cohort and one case-control study were identified. Smoking was associated with a doubling of the risk for esophageal cancer.

For cancer of the pancreas, the evidence base includes two case-control and two cohort studies. As observed elsewhere, the risk was increased by 50% to 100%.

For cancer of the stomach, relevant data were found in four cohort and seven case-control studies. In general, risks were increased for smokers compared with never-smokers, with the magnitude of increase much greater in men, around 100% in most studies, than in women, around 25% to 50%.

For cancer of the liver, relatively extensive data are available, including eight cohort studies and five case-control studies. In general, they show increased risk associated with smoking, although the range of increase was quite wide. Separate estimates for men and women were not provided.

For cancer of the urinary bladder, data were provided by four case-control and three cohort studies. Smoking increased the relative risk approximately two- to three-fold. One parallel case-control study, carried out in the late 1970s, demonstrated comparable relative risks in Boston, USA, and Nagoya, Japan.

For cancer of the kidney, only two studies were identified, neither showing evidence for an association between smoking and risk for this cancer.

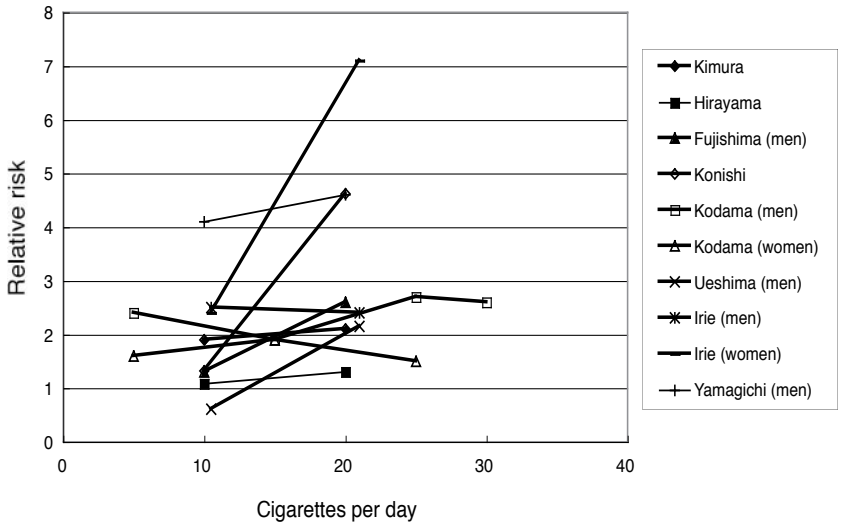
For leukemia, only two studies were identified, one not showing an association and the other showing a positive association and evidence for a dose response.

2.4.2.3 Cardiovascular diseases

For coronary heart disease, evidence from 12 cohort, three cross-

sectional and four case-control studies was reviewed. These studies uniformly show increased risks overall for male smokers compared with never-smokers; the magnitude of increase, approximately two-fold on average, is consistent with risks observed in other countries. Risks also increase with the number of cigarettes smoked and tend to be lower in ex-smokers. The increase in risk for studies in Japan included in the data base is plotted against the number of cigarettes smoked per day in Figure 2.10. There is clear evidence of increasing risk with an increasing number of cigarettes smoked. As compared to the dose-response curve observed in the CPS I study (Figure 2.1), the increases in risks observed in Japan are somewhat lower. This difference in relative risks might also be explained, at least in part, by the lower cumulative consumption index, shown in Figure 2.9. The studies in Japan span from the 1960s to the 1990s, with some indication of rising relative risks over that time. This increase might also be explained by the increasing cumulative consumption index over time, as shown in Figure 2.9. For women, the data are sparse but several recent studies show increased risk for smokers.

Figure 2.10 Quantitative Analysis of Cigarette Smoking and CHD Risk



For cerebrovascular disease, evidence from 17 cohort, two case-control and two cross-sectional studies was reviewed, and provide a consistent indication of an association of smoking with increased risk in both men and women. The range of effects extended to about a three-fold increase comparing smokers with never-smokers. Variation over time was not evident.

For atherosclerosis, evidence comes from five cross-sectional and one case-control studies. The limited data identified show an association of smoking with various measures of atherosclerosis.

2.4.2.4 Chronic obstructive pulmonary disease (COPD)

Smoking is associated with respiratory symptoms and an increased rate of loss of lung function, the development of COPD, and mortality from COPD. Even though COPD is now a leading cause of smoking-related death in the United States and some other western countries, it has received little investigation in Japan. Only eight studies were identified for this review; a variety of designs were used, including cross-sectional and cohort approaches. In general, the studies indicated greater risk in smokers, with evidence for a dose response with the number of cigarettes smoked. The risks were not as high as observed in studies in western countries. The lower cumulative dose of tobacco use in Japan may explain this lower risk in Japan. Japanese epidemiologists have not paid much attention to this disease, possibly because of this lower relative risk.

2.4.2.5 Reproductive outcomes

A wide range of reproductive effects of smoking has been identified, but these outcomes have received little investigation in Japan. Several studies show that infants of Japanese mothers who smoke are at risk for low birth weight. This lack of attention to reproductive risk might reflect, at least in part, the lower smoking prevalence among Japanese women.

2.4.2.6 Summary for active smoking and health

The evidence from studies in Japan is convincing in showing associations of active smoking with the many diseases already causally linked to smoking. The relative risks for some diseases are quite comparable to those in other countries, specifically for coronary heart disease and some cancers. The various forms of chronic lung disease caused by smoking have received little investigation in Japan. Similarly, the adverse reproductive effects of smoking in Japan have not been extensively investigated, perhaps reflecting the low prevalence of smoking among women. The observed risks for lung cancer are notably lower than risks in studies carried out at the same time in the US and Europe, even though comparable risks were found for laryngeal cancer, bladder cancer and stomach cancer. Risks for cerebrovascular disease were higher in some studies than have been found in other countries. Research on mechanisms, while not a topic of this review, has indicated no basis for thinking that these differences in risk are due to any differences in pathogenic mechanism between Japanese and other smokers. The studies reviewed in this chapter lead to the conclusion that active smoking causes the same diseases and other adverse health effects in Japan as elsewhere in the world.

On the other hand, we do note differences between Japan and other countries when we compare the magnitude of health effects identified as relative risks by epidemiologic studies in Japan and overseas. These differences likely reflect the historical patterns of tobacco use in Japan compared to other countries. We have attempted to quantitatively analyze the relationship between cigarette consumption and its health effects by constructing a simple index for cumulative dose, namely a 50-year cumulative consumption index. Focusing on the historical difference in cigarette consumption between Japan and the US, we attempted to compare the difference in lung cancer risk between the two countries in relation to cigarette consumption pattern. We found a similarity in the quantitative relationship between cigarette consumption and disease risk, further strengthening the rationale for the implementation of effective tobacco control policy as promptly as possible to limit the epidemic of tobacco-caused lung cancer.

2.4.3 Health effects of passive smoking

Studies on passive smoking and disease have also been carried out among children and adults in Japan. In fact, Hirayama was the first to document an association between passive smoking and lung cancer risk in his 1981 report in the British Medical Journal; his cohort study was also a key source of information on passive smoking and risk for coronary heart disease (Hirayama 1981). Because of the high rates of smoking among Japanese men, passive smoking is highly prevalent in Japan's homes and workplaces, as well as in other key places. Women and children, constituting a non-smoking majority of the population, are unable to avoid exposure.

There is particularly abundant evidence for passive smoking and lung cancer, including not only Hirayama's studies but subsequent case-control and cohort studies. These studies generally show increased risk in nonsmokers exposed to tobacco smoke. Hirayama's cohort study has also provided evidence for increased mortality from coronary heart disease for passively-exposed never-smokers. A number of studies have addressed respiratory morbidity in children in association with passive smoking. While the number of studies is limited, there is clear indication of the adverse effects of smoking on asthma and wheezing disorders.

To date, there has been limited quantitative characterization of passive smoking in Japan. The high smoking prevalence of active smoking among men implies a high rate of passive smoking. The available epidemiological evidence documents increased lung cancer risk in passively exposed nonsmokers as well as adverse effects on children. As for active smoking, the available evidence, interpreted in the context of the information already available on the risks of passive smoking, supports the conclusion that passive smoking causes adverse effects in Japan, as elsewhere.

2.4.4 Bridging between scientific findings and policy making procedures

When the US Surgeon General's Report was published in 1964, it had an impact in Japan, drawing the attention of Japanese researchers and also policy makers. One consequence was the initiation of a prospective cohort study, led by Dr. Hirayama at the National Cancer Center with funds from the Ministry of Health and Welfare of Japan. This study has contributed substantially to characterizing the risks of tobacco smoking, and not only among Japanese. Rather, its findings have had worldwide implications. Most notably, this study, along with the case-control study in Athens by Trichopoulos and colleagues, provided the first evidence of an increased risk of lung cancer by passive smoking (Trichopoulos et al. 1981). However, these and other findings from the cohort were reported about 20 years after the 1964 Surgeon General's report. The first Japanese white paper on smoking and health comparable to the US Surgeon General's report in 1964 was published in 1987. In the intervening years, *per capita* cigarette consumption in Japan almost doubled, as shown in Figure 3.6, while *per capita* consumption in the United States decreased substantially during the same period. Even though this evidence from the Hirayama cohort and other studies in Japan was reported and showed a growing epidemic of tobacco-caused disease, little emphasis was placed on tobacco control until recently. In many other countries, similar findings evoked increasingly strong attempts to control tobacco use.

The structural gap that led to this delay lies in the previous lack of tobacco control entities within and outside of the government. Epidemiological research provided a warning but a response mechanism was not in place. In fact, the unique relationship between the domestic tobacco industry and the government was most certainly a barrier to translation of the emerging evidence into action. For the future, Japan needs ongoing research to document the risks of smoking in order to track the epidemic and to maintain the scientific foundation for tobacco control.

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Chapter 3 SOCIOECONOMIC IMPACT OF SMOKING

3.1 Socioeconomic Impacts of Smoking: an Overview

3.1.1 Introduction

In most countries of the world, tobacco manufacturing and sales represent a significant amount of economic activity. While tobacco is a widely grown crop, it is a substantial component of agriculture in only a few countries, e.g., Malawi, Zimbabwe, and Indonesia. Beyond the direct economic activities associated with the tobacco industry, there are a multitude of adverse economic and societal consequences. Although governments gain revenues through taxation, they may lose considerably more through increased health care expenditures and loss of productivity from premature death and disability. Other consequences of smoking may go beyond the individuals who smoke to their families, as expenditures for cigarettes and other tobacco products may contribute to poverty and poor health outcomes for children (Thomson et al. 2002). This brief summary discusses some of the major concerns about the impact of tobacco use on populations and individuals.

3.1.2 Impact of tobacco use on populations

3.1.2.1 Economic impact (employment and revenues)

Governments are often hesitant to institute tobacco control for fear of adverse economic impacts that might directly and indirectly affect their populations. This reluctance may be, at least in part, fostered by the tobacco industry (Thomson et al. 2002). The tobacco industry commonly argues that tobacco agriculture, manufacturing, distribution, and sale of tobacco products are essential for economic viability and that controlling tobacco use would lead to job

loss and declines in tax revenues (Jha and Chaloupka 1999).

Research funded by the tobacco industry often inflates the potential number of jobs that may be lost and overestimates the amount of lost government revenues (Jha and Chaloupka 1999). Economic theory states that when resources are no longer devoted to a given economic activity, they do not disappear but are redirected to other economic functions (Warner 2000). In other words, if people stop spending money on tobacco, they usually spend it on other things, generating alternative jobs to compensate for any loss in the tobacco area. In most instances, countries can proceed with strong tobacco control without damage to the economy (Jha and Chaloupka 1999). For example, a study in the UK found that jobs increased by more than 100,000 full time equivalents when former smokers replaced their tobacco purchases with purchases of luxury items and any decline in tax revenue was offset by taxes raised on other goods and services. (Jha and Chaloupka 1999).

However, individual countries may experience short-term social and political difficulties as they transition their economies but there is research to indicate that even low-income countries can obtain benefits from this transition. For example, in Bangladesh, one of the world's poorest countries it is estimated that an 18.7% increase in employment could be gained if domestic consumption expenditures on tobacco was eliminated and individual smokers spent their funds on other goods and services (Van der Merwe 1998). However, job losses could be possible in countries that are extremely dependent on tobacco exports, especially where farming is the primary employment sector. Loss of tobacco agriculture would affect rural communities and households, necessitating support for farmers who would need to transition to alternative crops. An example of a country in this category is Zimbabwe, where it is estimated that a loss of 12.4% in employment would be expected if all domestic tobacco consumption and production of tobacco were eliminated (Jha and Chaloupka 1999).

3.1.2.2 Impact on healthcare costs

Tobacco smoking leads to substantial cost expenditures, arising from damage to materials and cleaning costs, lost productivity, and above all, the causation of disease and the diminution of health status. Economists are still debating the extent of this burden, from extreme to more modest; however, most developed countries devote a significant portion of their medical expenditures to treating tobacco-related diseases (Warner et al. 1999). The health costs reflect those needed for the management of the many diseases specifically caused by smoking, along with the additional costs incurred for providing medical care for smokers, who are generally less healthy than nonsmokers. These costs can be estimated using various econometric approaches that are based in the

epidemiologic principle of attributable risk. In order to estimate the health costs of smoking, data are needed to calculate the smoking-attributable fraction (SAF) of health care costs. One approach is to extend the attributable risks for smoking as a cause of disease to health care expenditures. For example, if 90% of lung cancer cases are attributable to smoking, then 90% of the costs of lung cancer treatment are also attributed to smoking. If the needed data are available, that is information on disease diagnoses and related costs, along with health care expenditures, than econometric techniques can be used to calculate the SAF. In the United States, a 1987 national study, the National Medical Expenditure Survey (NMES) has been used for this purpose. With these data, it is possible to calculate the excess expenditures for smokers resulting from their being smokers rather than nonsmokers. Analyses of the NMES data show that substantial costs result from smoking through the nonspecific diminution of health in smokers, as well as from the specific smoking-caused diseases. Recent estimates attribute about 5-7% of health care expenditures in the United States to smoking. While this figure differs across countries, in all cases it likely remains a substantial amount. For many countries, these expenditures are expected to escalate along with the increase in length of time of tobacco use and increased consumption rates (Warner et al. 1999).

With fewer tobacco-related health care costs, countries would have the resources to fund other health and social welfare issues (Warner 2000). Although the differences may be less of an argument for developing countries where governments do not assume much responsibility for health care costs for their populations, all governments must recognize the enormous burden smoking exerts on the public's health. A recent study from Korea confirms some of these economic impacts by quantifying the significant burden that tobacco use exerts on Korean society. The study provides compelling evidence for the development of a national tobacco control policy (Kang et al. 2003).

The proposition has been advanced that smokers, over their lifetimes, actually pose a lesser economic burden to society generally and to governments than do nonsmokers. Support for this cynical argument, sometimes referred to as the “death benefit” argument, has been found in the shorter life spans of smokers and their equivalent contributions to various forms of insurance and pensions. However, real health expenditures do occur because of smoking and the possibility of having a net economic gain to society from the premature deaths of smokers is an ethically repugnant basis for not initiating tobacco control.

3.1.2.3 Impact on smuggling

Worldwide, about a quarter of exported cigarettes end up as part of the illicit smuggling trade, estimated at 400 trillion cigarettes annually. Smuggling is related to lost revenues for governments of about US $25-30 trillion and is therefore an economic and public health problem (WHO 2001).

Controlling smuggling is one of the few supply-side measures that are effective in reducing tobacco use. It should be noted that increased smuggling is not solely related to an increase in the price of cigarettes: organized crime and other criminal networks are often involved in smuggling, and government corruption and the tobacco industry itself are implicated in smuggling. The tobacco industry needs to ensure that their exported products arrive in the "end-user market," instead of becoming contraband products (WHO 2001). Spain serves as an example of a country that reduced the rate of smuggling. Spain had a serious smuggling problem even though the price of cigarettes in that country was relatively low. By focusing their efforts on reducing organized crime, the government reduced smuggling from 15% to 5%, and governmental revenues increased after this effort (Joossens and Raw 1995). Canada also faced an increase in smuggling following a tax increase, but rather than focus on direct efforts to reduce smuggling Canada rolled back some of the tax increase and lowered the cost of cigarettes. The lowering of cigarette prices lead directly to an increase in consumption and a loss of government revenue (Sweanor and Martial 1994).

3.1.3 Impact of tobacco use on individuals

3.1.3.1 Impact on nonsmokers

Smokers not only harm themselves but also impose physical harm and maybe even financial harm on nonsmokers, especially their own family members. Substantial evidence supports the increased risk of disease for both non-smoking adults and children associated with exposure to second-hand smoke. For example in the US, exposure to secondhand smoke is estimated to be responsible for 3,000 lung-cancer deaths among nonsmokers each year; 35,000 heart disease deaths among nonsmokers each year; and 250,000 children experiencing lung and bronchi infections each year (Smoke-free restaurant and bar laws do not harm business 2003). Nonsmokers are also burdened with increased physical irritation cause by exposure to a toxic substance as well as the costs associated with cleaning clothes, household goods and the removal of cigarette litter. There is evidence that smoking is a major contributor to indoor air pollution, increases the incidence of fires, and impacts on the global environment through the deforestation which stems from tobacco cultivation and processing.

3.1.3.2 Impact on the poor

In developed countries it is the lowest socio-economic groups which suffer most from tobacco use; they also spend a higher proportion of their household income on tobacco. While it is well established that raising taxes on tobacco products lowers consumption, an argument against taxing tobacco is that it will further hurt the poorest segment of the population. In contrast, evidence from the US and UK suggests that low income smokers are more price-sensitive and will cut back on their tobacco consumption when the price increases (Chaloupka 1991; Townsend et al. 1994; Farrelly and Bray 1998). Poor smokers may indeed experience greater costs from tobacco control than richer smokers. This argument is not unique for tobacco control and exists for other public health initiatives such as child immunization and family planning. The poor have more difficulty gaining access to health care and may have to travel further or wait longer, thus losing income in the process (Thomson et al. 2002). However, health care officials do not usually point out these disparities and do not devalue the health benefits gained from these important health services. Tobacco control is cost effective and in the long run will benefit the poor in society (Jha and Chaloupka 1999).

3.1.3.3. Impact on children's health and survival

Studies indicate that tobacco spending is related to poverty: in households with extremely limited incomes, funds are used to purchase tobacco instead of food or other essential items (Jha and Chaloupka 1999). In developed countries, such as the US, children from low socio-economic households of smokers have poorer nutrition (Thomson et al. 2002). In developing countries, such as Bangladesh, tobacco spending affects child survival rates and is a cause of malnutrition. A study from Bangladesh estimated that 10.5 million fewer people would suffer from malnutrition if poor people did not use tobacco products (Efroymson et al. 2001). In New Zealand, a recent study estimated that households in the low socio-economic category and with smokers expended more than 14% of household income on tobacco. Governments who seek to reduce poverty and improve the lives of their citizens should work to reduce tobacco use (Efroymson et al. 2001). Children need to be protected from the financial harm caused by tobacco use in their households, and if governments devoted a small percentage of their cigarette taxes to tobacco control and smoking cessation efforts, the result could be beneficial effects for child health and welfare (Thomson et al. 2002).

3.1.3.4 Impact on farmers

The transition from tobacco agriculture is mostly a problem for the poor farmer in developing or low-income countries, especially economies that are heavily dependent on agriculture. Studies of farmers in high-income countries have found that most economies have diversified and farmers have been making economic adjustments in their crops for decades. In the US, farmers have received monies to transfer to other crops. A survey conducted with farmers in the US found about 50% of the population surveyed was aware of alternative profitable crops. Farmers who were better educated were more aware of these alternative crops and were more likely to consider crop substitution as a viable option. In addition, one-third of the farmers indicated that they would advise their children not to continue to grow tobacco. According to the World Bank report, governments in low-income countries would need to consider transition assistance for their farmers for social, economic and political reasons. It has been suggested that tax increases could be used to fund the transition costs. Alternative government action could include encouraging sound agricultural and trade policies, the provision of broad rural development programs, assistance with crop diversification, rural training, and other safety-net systems (Jha and Chaloupka 1999).

3.1.4 Conclusion

Tobacco control requires high-level political support and cannot be accomplished solely through health sector policy initiatives since the complex socio-economic components of tobacco control require a broader policy context. For countries such as Japan, government ownership of tobacco company shares presents a significant barrier to securing political commitment for tobacco control. However, in diverse and strong economies, such as Japan, strong tobacco control policies, such as increased taxes, is a win-win situation that will not only secure higher government revenues but also reduce smoking rates. In many countries, it is the financial and economic sectors that wield the power, and promoting a healthy economy is the priority. There may be little political will or support for public health issues, including tobacco control. The SARS epidemic highlighted how the health and economic sectors are interrelated since this health emergency had far-reaching effects on the economies of numerous countries. With 4 million people killed by tobacco each year and the looming pandemic of 10 million annual deaths only decades away, the need for action is imperative.

The tobacco industry has been able to use its economic and political clout to pressure governments not to enact known effective tobacco control strategies. To control tobacco use effectively, governments must also garner

popular support. This will involve more of a collective ownership of the problem and the solution. Governments, civil society, the private sector, and interest groups must come together to form a broad coalition with the power to implement and sustain tobacco control (Jha and Paccaud 2000).

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3.2 Smoking and Economics in Japan

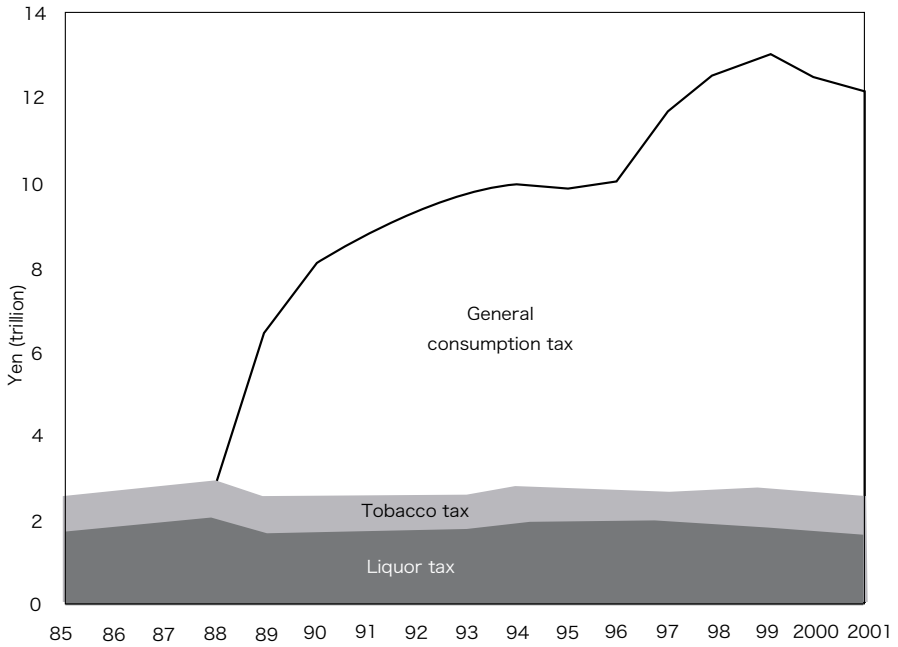
3.2.1 Background

Tobacco was first 'imported' into Japan in the late 16th century by Portuguese merchants, together with other western cultural practices such as Christianity, various scientific disciplines, and products such as rifles. Although wary at first, the Japanese quickly adopted the exotic custom of smoking. The feudal government, fearing declines in rice production, periodically banned the growing of tobacco, sometimes under heavy penalty. Despite suppression, smokers and the number of farmers growing tobacco steadily increased, and the government eventually withdrew its bans on tobacco in the middle of the feudal age. After Japan was modernized through the Meiji Restoration, a revolution which threw down feudalism and revived imperialism, smoking was hailed as symbol of the new modernity. The government was quick to grab this potentially lucrative source of revenue and began to levy a tobacco tax in 1876, which the tobacco industry effectively evaded by bootlegging and smuggling. In 1904, the government introduced a government monopoly, partially to generate war funds for the forthcoming war with Russia and partially to prevent industry takeover by foreign concerns. From a socioeconomic standpoint, tobacco was clearly viewed as a national asset rather than a burden by both the government and the people. Under a social atmosphere such as this, it would have been difficult to argue against smoking, let alone the tobacco industry.

In discussing the importance of the tobacco industry in Japan's economy, one should be aware of a peculiarity of its tax system. Japan has heavily relied on direct taxation: direct tax accounted for 74.2% of total tax revenue in 1989, versus 55% in the UK, 53.2% in Germany and 39.1% in France. To the

surprise of western economists, Japan did not have an all-encompassing general indirect tax until 1989. As Figure 3.1 vividly suggests, tobacco tax was one of Japan's mainstay indirect tax revenues and it is little wonder that the government wanted to protect this valuable source of revenue at any cost.

Figure 3.1 Trend in Japan's indirect taxation



Note: Other indirect taxes omitted
Source: National Tax Agency

With this in mind, the “importance” of the tobacco industry should be interpreted more as a means of levying taxation than as a source of production or employment. The relative importance of tobacco as a source of indirect tax has undoubtedly declined considerably, particularly since the introduction of the general consumption tax in 1989 and its subsequent expansion in 1997.

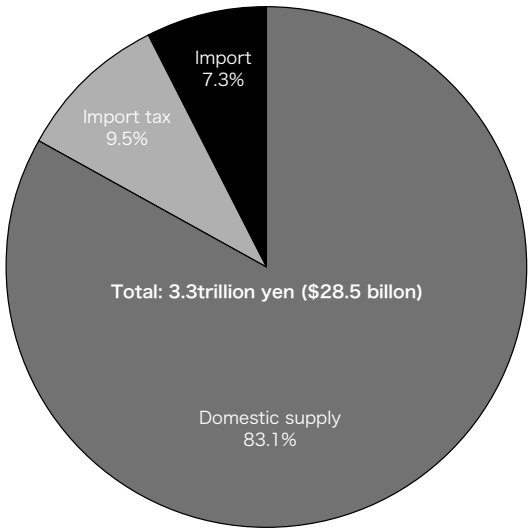
Closer socioeconomic analysis reveals somewhat perplexing aspects of smoking and the tobacco industry. For example, despite its large contribution to the national treasury, the tobacco industry makes relatively little contribution to national employment. Negative income elasticity as observed in an economics survey would also shed a different light on the socioeconomic impact of smoking and the tobacco industry. The introduction of the general consumption tax in 1989 was accompanied by a nationwide outcry, particularly against the regressive nature of indirect taxation under which the poor have to shoulder a heavier burden. If tobacco taxation is the most regressive tax of all, it can be argued that it would be wise for the Japanese to quit smoking if only for tax minimization purposes.

3.2.2 The tobacco industry in Japan's economy

Japan's tobacco industry has been a government monopoly since the establishment of Japan Tobacco and Salt Public Corp. in 1949, which was later privatized to Japan Tobacco Inc. (hereafter JT) in 1985. JT is even today endowed with the exclusive right to tobacco manufacture in Japan, pursuant to the Tobacco Industry Law, which also mandates that all tobacco leaves produced in Japan must be purchased by JT. A total of 60,000 tons of leaf were purchased in 2000 (Institute for Health Economics and Policy 2002). In that year, 23,128 farmers were engaged in tobacco production, predominantly in the northeastern part of the country. Although the total sale of tobacco has been relatively constant, the market share of JT, which was as high as 97.6% in 1985, has been nibbled away by aggressive foreign tobacco manufacturers and stood at 74.9% in 2000. The sale of tobacco in Japan is characterized by its ready availability: as shown in Figure 3.5, in 2000 there were 625,000 vending machines, twice the approximately 300,000 licensed retailers.

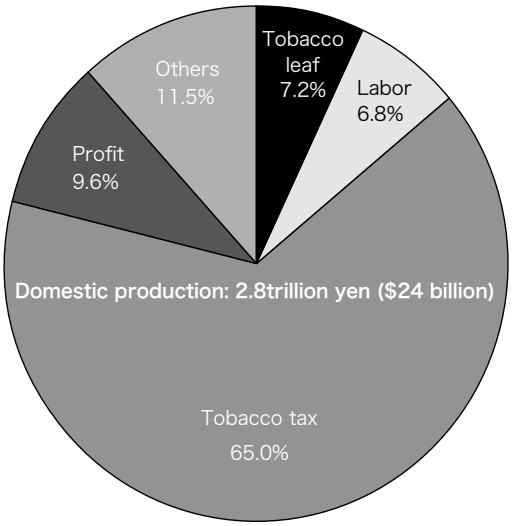
According to the latest I/O (input and output) table, the size of the tobacco market was estimated at 3.3 trillion yen ($31.4 billion; $1=105 yen) in 1999, of which 2.77 trillion yen (83.1%) represented domestic product and the rest imports (Economy, Trade and Industry Statistics Association 2002). The US is by far the largest exporter of tobacco to Japan (93.7%). About 2/3 of the retail tobacco price is tobacco tax. (Figures 3.2, 3.3, 3.4).

Figure 3.2 Tobacco market of Japan, 1999



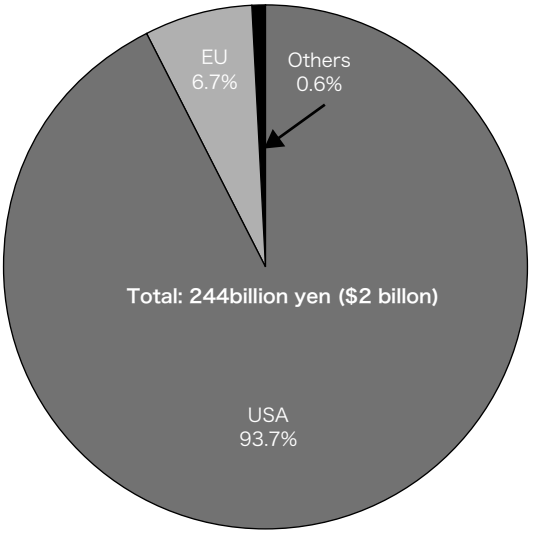
Source: 1999 I/O table

Figure 3.3 Cost structure of tobacco in Japan, 1999



Source: 1999 I/O table

Figure 3.4 Imports of tobacco into Japan, 1999



Ikeda used an I/O analysis to estimate the impact of the removal of the tobacco industry on Japan's economy. He estimated the impact coefficient of the tobacco industry to be 0.7, signifying that removal would have only a small ripple effect on other industry sectors (Ikeda et al. 2000). He also demonstrated through macro-economic analysis that the economic impact would be minimal even if the final consumption of tobacco were eliminated.

3.2.3 The government's stake in the tobacco industry

The Japanese government has traditionally relied heavily on tax revenue generated by tobacco smoking. It still retains a heavy stake as the largest shareholder of JT (64.5% of outstanding stock, released to 50% on June 11, 2004), which might explain the reluctance of the Ministry of Finance toward the promotion of tobacco control (Usuda et al. 2002). After the privatization of the Japan Tobacco and Salt Public Corp., the tobacco market was liberalized and opened to foreign capital. Honjo et al. points out that the US government forced the Japanese government to lift the trade tariff on tobacco under threat of invoking Section 301 of the 1974 Trade Act (Honjo et al. 2000). They summarized that the entrance of foreign companies, coupled with their aggressive promotion, has reversed the declining trend in tobacco consumption that existed in Japan prior to 1987.

In general, both industry and economists welcome deregulation, because it enhances productivity by reducing prices. In 1999, the Economic Planning Agency sponsored an economic research project to evaluate the effect of deregulation on Japan's economy (Economic Planning Agency Institute of Economics 1999). The project revealed that a 1% productivity increase in the retailing industry due to deregulation would boost tobacco consumption by 11% in the short term and 45% in the long term. If the productivity of all five industries studied (energy, retailing, finance, transportation and telecommunication) were improved by 1% due to deregulation, tobacco consumption would increase by as much as 74% in the long term.

3.2.3.1 Tobacco tax and government revenue

Tobacco prices in Japan are relatively cheap in comparison with most developed countries. A typical package costing 250 yen includes 153.34 yen indirect tax (including 5% consumption tax applicable to all goods and services), or 61.3% of the price. Through tobacco tax, the government raised approximately one trillion yen ($9.5 billion; $1=105 yen) as tax revenue in FY 2001. Local governments receive the same amount as local tobacco tax, which is why local governments welcome tobacco sales with the hope of increasing tax revenue.

3.2.3.2 Impact of increased tobacco taxation

As of July 1, 2003, the tobacco tax was raised to increase the price of tobacco by 20 yen per pack (or approximately 1 yen per cigarette). This measure was taken after careful deliberation of the pros and cons of increased tobacco taxation. Aburaya and Mochizuki forecast the economic impact of raising tobacco

tax (Institute for Health Economics and Policy 2002). After reviewing evidence from abroad, they concluded that tobacco is a "merit product," the demand for which rises commensurate with increases in personal income. But it is also price-inelastic, in that tobacco is a necessary product for smokers. They recommended a tax hike because it would reduce the smoking rate without decreasing the tax revenue. Whether the tax hike will bring about the expected outcome remains to be seen.

3.2.4 Social cost of tobacco smoking

The Institute for Health Economics and Policy (hereafter IHEP) first studied the social costs associated with tobacco smoking in 1994 (IHEP 1997). The IHEP (1997) study relied heavily on a cohort study conducted by Hirayama between 1966 and 1982. The greatest limitation of the IHEP study was that the attributable risk of smoking was on mortality, not on incidence, which is more appropriate for estimating social cost. However, attributable risk on incidence was not available. The IHEP (1997) study estimated social cost in terms of both direct (health care) and indirect costs. Indirect cost includes loss of income due to hospitalization and loss due to fire, such as property damage and death or injury. The study estimated the direct cost (excess health care cost) as 1.3 trillion yen and the indirect social cost as 5.8 trillion yen as of 1999. According to the National Household Survey (Statistics Bureau, Ministry of Public Management 2003), a sampling survey to record all income and expenditures of households conducted by the national government, an average household with 2.65 members spent 1,296 yen (approximately $11) per month, or approximately 0.5% of the monthly expenditure of 271,579 yen (approximately $2,263) on tobacco in FY 2001.

With regard to other items, an average household spends 8,023 yen for electricity, 5,026 yen for gas and 3,066 yen for liquor. Although 1,296 yen for tobacco appears small in comparison, note that this is the overall mean which includes households with no smokers. Average monthly expenditure for tobacco would of course be higher if the denominator were limited to households with smokers. However, tobacco shows unique economic characteristics of negative income elasticity and marginal propensity. Negative elasticity denotes that as the cost of living expenditures of a household increase by 1%, expenditure on tobacco decreases by 0.36% (income elasticity); or its corollary, marginal propensity - a household spends 16 yen less for tobacco for every 10,000 yen increase in its living expenditure. No other item shows such negative income elasticity and marginal propensity except house rent, which is anticipated because wealthy families are more likely to be homeowners and hence free from rent.

3.2.5 Health care cost of tobacco smoking

IHEP (1997) defines the direct cost associated with smoking as "excessive health care cost" derived from both direct exposure to smoking and passive smoking. These researchers applied the population-attributable risk of mortality of each smoking-related disease to the National Health Care Expenditure (NHCE) figures published by the national government every year. They define the following diseases as associated with direct smoking (relative risk of mortality): cancer (1.52), hypertension (1.46), ischemic heart disease (1.8), cerebrovascular disease (1.11), bronchitis and chronic obstructive lung diseases (1.41), asthma (2.39), stomach and duodenal ulcer (2.03), and liver diseases (1.28), as well as low birth weight. They attributed only lung cancer to passive smoking, the risk of which was cited from a 1992 report by the US Environmental Protection Agency.

Their consequent estimate of the health care costs associated with smoking was approximately 1.3 trillion yen (10.8 billion dollars), or 4.2% of the NHCE. They also estimated the health care cost of lung cancer associated with direct smoking by applying the incidence-attributable risk derived from a cohort study conducted by the government and reached almost the same estimate: 43.1 billion yen by incidence-attributable risk versus 38.7 billion yen by mortality-attributable risk. Given the high case fatality rate of lung cancer, the two estimates approximate each other well, but it was concluded that the discrepancy between estimates by mortality-attributable versus incidence-attributable risk should be carefully weighed.

IHEP (1997) based its estimate on macro-level data, not on micro-level health records or claims data. Some researchers have attempted micro-level analyses to estimate the economic impact of smoking, but the mixed results have long confused Japanese health economists.

Izumi et al. (2001) proved that smokers spend 11% more on health care than nonsmokers over 30 months' follow-up in a community-based cohort study (n=43,408). The primary difference behind the higher *per capita* health care cost was the higher inpatient costs of smokers (82 vs. 62 pounds for men and 53 vs. 49 pounds for women between smokers vs. nonsmokers, *per capita* monthly cost). For outpatient costs, the opposite was shown: expenditures were less for smokers than nonsmokers (88 vs. 92 pounds for men and women).

These somewhat contradictory findings were replicated by two other studies, involving company workers (n=4,795, in- and outpatient plus dental patients; Yamamoto et al. 1996) and community subjects (n=966, outpatient only; Ozasa et al. 1994), both of which showed lower costs for smokers than nonsmokers. In the Yamamoto study, nonsmokers had 40% higher *per capita* inpatient costs. A number of reports from within Japan and overseas also show lower health care costs for smokers, but the evidence is mixed with findings

likely variyig with population characteristics and the nature of the health care delivery system. In one US study, Haynes et al. (2002) confirmed that smokers and nonsmokers do not differ as to *per capita* health care cost, but that BMI, blood pressure or cholesterol levels were associated with increased health care costs.

One study reported similar findings for passive smoking. Shimizu et al. (1988) matched health survey records and claims for non-smoking women and children in smoking households and found that women in smoking households spend less per capita on health care than their counterparts in nonsmoking households, although costs for their children (under 20 years) are comparatively higher (geometric mean of *per capita* cost was 26,558 yen for children of nonsmoking households as opposed to 33,713 yen in smoking households).

These findings based on health insurance claims in smokers and nonsmokers appear to provide evidence against greater health care costs for smokers and have long puzzled researchers. They could lead to the misinterpretation that tobacco control will not bring cost savings and perhaps may explain why policy makers in Japan have not implemented tobacco control for the purpose of containing health care costs.

3.2.6 Research implications

As the new Health Promotion Law authorizes health insurers to conduct health promotional activities as well as insurance operations (Sec. 16), health insurers are expected to monitor long-term utilization and spending patterns in relation to smoking behavior. Health insurers accumulate claims submitted by health care providers, which include itemized information on medical care services rendered but do not report smoking and other behavioral information. Linking claims and health screening records, which include smoking and other behavioral data, could identify associations between behavioral factors and medical services received. However, unless care is taken, the findings from such research may lead to misinterpretation, in extreme cases justifying smoking for health care cost containment purposes!

A crucial limitation in conducting research on lifestyle-related diseases is the impossibility of conducting randomized controlled trials: we cannot randomly assign participants to smoking and nonsmoking subgroups and must rely instead on observational data. Differences between smokers and nonsmokers need to be taken into account, including patterns of health care utilization and other lifestyle factors. Estimates from observational studies are then made after careful adjustment for confounding factors.

Appropriate interpretation requires the evaluation of health care costs related to smoking, not of overall costs. To enable this, a detailed and objective

classification system for estimating disease-specific costs is required.

Macro level analysis is appropriate to estimating the direct medical costs of smoking using attributable risk percent (ARP). As a recent IHEP report (2002) notes, ARP should be the risk of 'incidence,' not 'mortality' if it is to avoid underestimating costs. However, incidence is difficult to monitor for some diseases and most research published in and out of Japan uses the ARP of mortality. The incidence of cancer (to take one disease) could be estimated using cancer registries, but the same information may be obtained at lower cost and with less effort from health insurance claims. Since municipal governments (insurers of the National Health Insurance program) are authorized by the HPA to collect incidence data of cancer and cardiovascular diseases, a centralized registry body to help promote such activities by municipal governments is required.

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3.3 International Comparison of the Economic Impact of Tobacco

3.3.1 Background

In the preamble to the Framework Convention on Tobacco Control (FCTC), it is proudly stated that "signatory countries resolve to give priority to their right to protect public health". The adoption of this convention reaffirms the importance of protecting health, which often occupies a position of lesser importance within governments as compared with the economic, development or financial sectors (Usuda et al. 2002, 2003). The importance of the FCTC, especially for those countries which have yet to introduce full-scale tobacco regulation, is the intent " to control tobacco use and reduce exposure to tobacco smoke to protect the health of people of the current and next generations." This goal is assured by the FCTC, albeit to varying degrees and speed.

Tobacco use has been epidemiologically proved the greatest single health hazard of the 20th century, but social, political and economic systems have come to rely on tobacco agriculture, manufacturing, production and consumption. Despite the urgency of the problems associated with tobacco use and the fact that many smokers have become pharmacologically dependent on tobacco even as tobacco dependency had spread through society, many governments have been less than willing to prioritize tobacco control in health policy. It maybe harder for governments to control tobacco use by implementing counter measures because the consequences of smoking do not become apparent for many decades.

Before a government's decision makers acknowledge that long-term tobacco use carries serious health hazards and has a negative effect on the

national economy, the country will be affected in phases: Further, whether a government reflects the negative effects of tobacco in policy at the time they are acknowledged or forecast depends on the maturity and transparency of the country's policy-making procedures. That is, in those countries where policy making is implemented in clear public view by valuing scientific evidence based on the "precautionary principle," tobacco control measures tend to be taken relatively early, even in the presence of competing political issues (e.g. infectious diseases). In the opposite circumstances, the tobacco industry exerts tremendous political and economic pressure on governments even though epidemiological knowledge linking tobacco use to disease is well established. It can be said that the international agreement by WHO member states to the Framework Convention on Tobacco Control has been helpful in correcting the gap in perception among nations. The purpose of this section is to briefly examine, from an economic perspective, how the government, industries, and public have influenced policy making, and to interpret the circumstances facing Japan in an international context.

3.3.2 Economic factors behind tobacco issues

A tobacco tax, imposed in most countries in which tobacco is consumed, is cash revenue generated immediately upon the sale of the product. The economic costs of health hazards, in contrast, such as the excess medical costs of long-term tobacco use are harder to visualize. Likewise, in terms of labor productivity loss, it is difficult to estimate future lost profits. In those countries where tobacco is sold by a state-run monopoly, governments earn direct and stable profits, a situation which has hampered any policy shift toward the control of tobacco consumption. The Japanese monopoly system for tobacco sales was initially established to increase tax revenue after the Sino-Japanese War and to raise funds for the military expenses of the Russo-Japanese War. It was subsequently established as a permanent system which made a reliable financial contribution to the national coffers (Fujimoto 1990).

In Japan, the tobacco monopoly system was abolished in 1985, but the structure of the system was maintained by the Tobacco Industry Law of 1984, promulgated by the Ministry of Finance. The Tobacco Industry Law stipulates that "This law, upon abolition of the tobacco monopoly and taking into consideration the role tobacco-related tax plays in financial income, intends to control (1) production and purchase of domestic tobacco leaf required in manufacturing tobacco products, and (2) production and sales of tobacco products. This law thereby allows for the sound growth of Japan's tobacco industry, and thus intends to maintain a stable financial income and allow for the sound growth of the public

economy." Given this, it has been pointed out that there is a conflict of logic between promoting health, which the Framework Convention on Tobacco Control is trying to achieve, and the lack of political will and support for public health issues by governments (Usuda et al. 2002, 2003).

Although Europe and Asia have maintained similar tobacco monopoly systems, the number has decreased since the 1980s. The collapse of the Soviet Union in the 1990s triggered a further decrease. In the late 1990s, the IMF pressured Korea, the Republic of Moldova, Thailand and Turkey to privatize state-run companies as a condition of the provision of loans. Nevertheless, 40% of total world cigarette consumption (of which China accounts for 30%) is sold under such monopoly systems (Mackay and Eriksen 2002).

3.3.3 International comparison of tobacco production and sales

Table 3.1 Unmanufactured Tobacco Production, Trade and Consumption in Leading Countries, 2002

Production	(1000t)	(share)
World total	5,688	100%
China	1,980	35%
India	575	10%
Brazil	570	10%
USA	372	7%
Zimbabwe	172	3%
Indonesia	145	3%

Exports	(1000t)
World total	2,096
Brazil	448
USA	163
Zimbabwe	148
China	118
India	105
Malawi	105

Import	(1000t)
World total	2,073
Russian Federation	308
USA	300
Germany	257
UK	119
Japan	91
Netherland	65

Consumption	(1000t)
World total	6,473
China	2,633
USA	500
India	476
Russina Federation	309
Germany	180
Indonesia	155

Ending Stocks	(1000t)
World total	5,043
China	1,492
USA	1,473
Turkey	371
Japan	220
Brazil	217
Italy	134

Source: USDA 2003

Tobacco-related industries exist in every country where people smoke, but it is not always the case that the country has production, manufacturing and distribution companies. In addition, the involvement of the government and political influence exerted by the tobacco industry varies among countries. Particularly in those countries where the tobacco industry occupies a significant position within overall agricultural policy, tobacco growers have gained strong influence through protectionism, and tobacco control for health development tends to receive low priority. China is the largest producer of tobacco, accounting for one-third of global tobacco production, and the four countries ranking after China account for another one-third, meaning that the top five countries account for two-thirds of global tobacco production (Table 3.1). These countries export tobacco as well as consume it domestically. Malawi and Zimbabwe are not big producers in terms of absolute tobacco production, but the percentage of arable land devoted to tobacco cultivation is large and they are highly dependent on cigarette exports in terms of trade balance. On the contrary, in Japan, there is little export revenue from tobacco since the percentage of arable land devoted to tobacco cultivation is small and almost all of the tobacco produced domestically is consumed domestically. However, the share of imported leaf tobacco used as raw material in domestic tobacco production is increasing.

The global trade volume of cigarettes increased rapidly from the mid-1980s, reaching a peak in the mid-1990s and decreasing thereafter (FAO 2003a). Concerning cigarette exports, the percentage of the global total accounted for by the EU and US is 40% and 21%, respectively (FAO 2003a). Regarding the imports, the EU and Japan account for 36% and 13% of global total, respectively, while the US accounts for only 2% (FAO 2003a). Japan has been the largest importer of US tobacco, in January 2003 accounting for 21% of the total export quantity of leaf tobacco and 68% of the total export quantity of cigarettes (USDA 2003). Most countries in the EU except Germany and Belgium have rarely imported tobacco leaf and cigarettes from the US but many countries outside the EU, especially some Arabic countries, are increasingly importing US cigarettes. The current situation of tobacco trade between Japan and the US is the result of the Japan-US negotiations that started in the 1970s. The price of Japanese tobacco leaf, determined by the Leaf Tobacco Deliberative Council, an advisory committee to the president of Japan Tobacco Inc. (JT), is the most expensive in the world (Table 3.2) (JT 2001a). About 40% of tobacco leaf used for manufacturing in Japan is domestically produced and the high cost of materials thus leads to high manufacturing cost of cigarettes.

In the US, production of tobacco leaf is protected by production quotas and the Tobacco Price Support Program, set by the Department of Agriculture. Tobacco leaf is traded in the market above the support price determined by the Secretary of Agriculture, and any unsold tobacco is then purchased in a

stabilization transaction financed by the Commodity Credit Corporation. For leaf tobacco growers, the program is beneficial in that the trade price is guaranteed. Against this, however, some analyses have shown that the high price of tobacco leaf is an obstacle to the expansion of production and exports (Zhang and Husten 1998). Likewise, Japanese tobacco growers are protected by high prices. This contributes to higher costs of cigarettes and influences the ability to compete in the international marketplace unless effective cost reduction processes are applied.

The situation between JT and the growers is delicate and conflicted. Although expensive, JT is required by the Tobacco Industry Law to purchase all domestically produced leaf tobacco. However, it has acknowledged the potential harm it suffers from the policies that protect growers (JT 2001a). Nevertheless, as in the US, JT and the growers cooperate in the exertion of political influence against tobacco control.

Table 3.2 International Comparison of Leaf Tobacco Prices (Unit: dollars/kg)

		1985	1990	1995	2000
Oriental tobacco	Japan	7.95	13.69	20.88	17.82
	USA	3.79	3.68	3.96	3.95
	Brazil	0.3	1.41	1.75	1.21
	Malawi	1.38	2.3	1.85	1.36
	Zimbabwe	1.68	2.62	2.12	1.69
Burley tobacco	Japan	6.63	11.7	18.58	16.53
	USA	3.51	3.86	4.13	4.3
	Malawi	1.06	1.84	1.48	1.02
	Brazil	–	1.34	1.68	1.1
Exchange rate (yen/dollar)		221.68	141.52	96.34	110.45

Source: JT 2001a

Due to the major global reorganization of the tobacco industry, global production of tobacco is increasingly dominated by a few companies. Excluding China, which accounts for nearly one-third of global cigarette manufacturing, Altria (formerly Philip Morris, PM), British American Tobacco (BAT) and Japan Tobacco (JT) are the three multinational tobacco companies dominating the global market (Table 3.3) (JT 2001b). Altria has the largest sales volume and the biggest share of cigarettes in the world, with Marlboro as its main brand, while BAT has the largest sales volume outside the US and the largest channels in most countries (Mackay and Eriksen 2002). To ensure its survival against this industry concentration, JT acquired RJR International in 1999 to become the third largest multinational tobacco company, providing it with a number of additional flagship brands (Winston, Camel and Salem) to complement Mild Seven. It is inevitable that JT will have to rely on its RJR brands in countries where use of 'Mild' as a descriptor is prohibited under the FCTC unless it develops novel brands for the world.

Table 3.3 Reorganization of Major Tobacco Companies around 1999 (100 million pieces)

Before reorganization		After reorganization	
PM (US)	9,445	PM (US)*	9,445
BAT (UK)	7,120	BAT + Rothmans (UK)	9,290
RJR/RJRI (US)	3,210	JT + RJRI (Japan)	4,768
JT (Japan)	2,723	Reemstma (Germany)	1,190
Rothmans (UK)	2,170	RJR (US)**	1,168
Reemstma (Germany)	1,190	Seita+Tabacalcra ***	1,120
KT & G (Korea)	990	KT & G (Korea)	990
Seita (France)	600		
Tabacalcra (Spain)	520		

* Changed company name to Altria
** Joint-venture with BAT in the US
*** Changed company name to Altadis

Source: JT 2001b

3.3.4 Economic determinants of tobacco consumption

In terms of total volume, global consumption of tobacco is on the increase, but consumption per capita peaked in the 1990s and has been decreasing since. In developing countries in particular, consumption is driven by population growth and the increase in adult populations (the aging of society). Besides demographic background, a second factor affecting tobacco consumption is income, which increased by a global average of 3% yearly from 1970 to 2000. In particular, while growth was 3% in advanced countries, in developing countries and in China it was 4% and 8%, respectively. The income elasticity of demand for tobacco varies from 0.2 to 0.8, and is higher in developing countries and lower in advanced countries, indicating that as income per capita increases, income elasticity decreases (Zhang 2000).

Other determinants of tobacco consumption include tobacco prices, customs, taxation, marketing and smoking regulations. Among these, tobacco price is the most important. Price elasticity of demand for tobacco is -0.9 in developing countries and -0.2 in advanced countries, and the larger the per capita income, the smaller the price elasticity (Zhang et al. 2000). A breakdown of tobacco prices show that the cost of tobacco leaf represents only a very small percentage of the total, with tobacco tax accounting for the biggest part. Given that tobacco tax is an important source of revenue, pricing policy through increases in tobacco tax is the most effective option in terms of public policy. This is because the price elasticity

of demand varies among people of different income brackets - price elasticity is small in upper-income groups (-0.2 to -0.3) but large in low-income groups (-0.7 to-0.8). Price increases impact higher-income groups (increasing tax revenue) and induce lower-income groups to reduce their smoking.

Japan's retail tobacco prices are the lowest in the world, both in terms of 'Big Mac' parity pricing in local currencies and in terms of the minutes of labor required to buy cigarettes (Table 3.4) and while the cigarette price in terms of labor minutes increased in many countries between 1991 and 2000, it decreased in Japan (Guindon et al. 2002). Guindon et al. (2002) have used this international price comparison to show that there is ample room in many countries for price policy through increases in tobacco taxes, and that Japan is a typical case.

Table 3.4 Minutes of Labor Required to Buy Cigarettes in Selected Countries

Country	City	Minutes	Annual change 1991-2000 (%)
Japan	Tokyo	8.9	−0.14
Switzerland	Geneve	12.5	5.43
Germany	Frankfurt	17.3	1.14
USA	New York	17.6	4.9
Canada	Toronto	20.7	−0.88
Republic of Korea	Seoul	26.6	9.24
Australia	Sydney	28.4	8.77
UK	London	39.7	5.46
Poland	Warsaw	55.7	−
Indonesia	Jakarta	61.7	−
China	Shanghai	61.8	−
Hungary	Budapest	71.4	−
India	Mumbai	102.5	−1.38
Kenya	Nairobi	157.6	3.09

Note: Marlboro or nearest equivalent international brand. Price divided by the weighted net hourly wage in 12 occupations
Source: Data extracted from (Guindon et al. 2002)

3.3.5 Economic losses from tobacco consumption

The tobacco industry has often responded to calls for tobacco control by emphasizing the economic benefits of tobacco and exaggerating its own economic loss. It never mentions the economic loss to society its products cause. Long-term consumption of tobacco results in various diseases and disorders, causing excess medical costs. Furthermore, it incurs significant indirect costs due to deaths and diseases. Particularly in the UK, US and Canada, where the tobacco boom started earlier and the burden from tobacco-related diseases has already increased, numerous studies on the economic loss from excess mortality and morbidity have been conducted since the 1970s, when medical cost increases became an issue. Given the differences in medical care systems, simple comparisons of medical costs among countries are meaningless. However, there is no doubt that excess medical costs have been incurred, and in amounts that are not negligible for each country.

In addition, indirect costs have amounted to several times the direct medical cost, although actual figures depend on the assumptions made in calculation. Given this, tobacco consumption will only lead to deficits in the future, in spite of significant revenue from tobacco currently.

3.3.6 Conclusion

When the former Ministry of Health and Welfare in Japan advocated the Health Japan 21 Program and started to investigate the FCTC in Japan, it withdrew numerical targets for drastic tobacco control, which were strongly opposed by lawmakers with a so-called vested interest in the tobacco industry as described in elsewhere in this report.

However, the risk of suits against JT, in which JT is the plaintiff (the government is a joint defendant in Japan), is increasing year by year both at home and abroad. Also, since triggered by the FCTC, the international responsibility of the government in owning multinational corporations has been recognized, leading to a sharp change in the Ministry of Finance's behavior. Namely, after passing through a phase in which the Council on Welfare and Science and the Fiscal System Council had different views on tobacco consumption restraints, the Japanese government subsequently accepted and finally ratified the FCTC on consumption restraints. It can be assumed that such a sharp change in the short term reflects a change in recognition within the government that is large enough to counter the opposition of the tobacco industry. Further broadly based analysis of the economic aspects of the tobacco industry and tobacco consumption will contribute to the data needs of sound tobacco policy as national policy.

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Chapter 4 TOBACCO CONTROL POLICES AND PROGRAMMES

4.1 Comprehensive Tobacco Control: a Global View

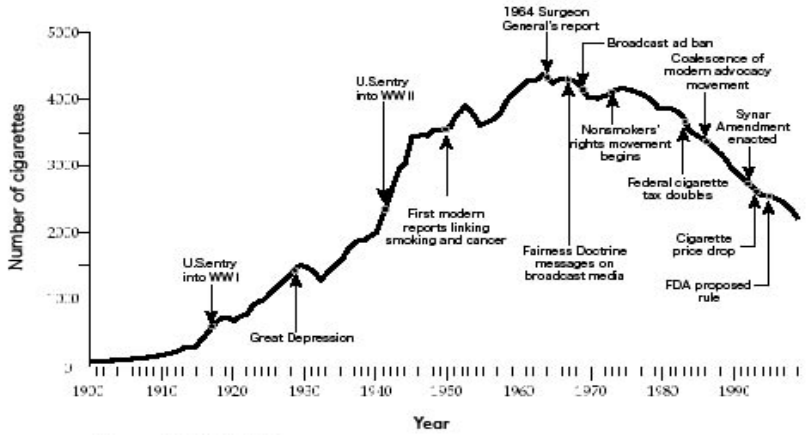
4.1.1 Introduction to comprehensive tobacco control

Achieving effective comprehensive tobacco control has proved to be a long and difficult journey. In what might be viewed as a proverbial policy-level 'journey of a thousand miles,' the beginning steps are often small, but deliberate. As the steps become progressively larger and experience grows, the policy development process may become increasingly complex, intersecting with multiple sectors of society and affecting public places, workplaces, and homes. Tobacco control efforts in some countries now span five decades, giving evidence that smoking, both active and passive, can be reduced, and that comprehensive approaches are needed. In the current context, countries initiating tobacco control programs can build on the experiences of other countries, transferring sound tobacco control policy and program principles across national boundaries and cultures.

The journeys of a number of countries that have been successful in developing progressive and effective domestic tobacco control programs at the national level have not been smooth and cohesive throughout their course. In the case of the United States, for example, the 50-year journey has been a series of successess and failures. It began in the early 1950's with the publication of the first studies linking smoking with increased risk for lung cancer and other diseases; continued into the 1960's and 70's with arguments over tobacco control science, politics and economics; and culminated with a leap forward in the 1990's with the development of comprehensive approaches to tobacco control and successful litigation against the tobacco industry (Figure 4.1). The multi-decade course of tobacco control in the United States, the United Kingdom, and other

western countries does not imply that an equally arduous course is necessary in other countries, including Japan. In fact, it is anticipated that 'lessons learned' over the decades in those countries that have successfully begun to control tobacco use may facilitate far more rapid progress elsewhere.

Figure 4.1 Trends in per capita Cigarette Consumption: United States 1900-1997



Source: USDHHS 2000

The collective tobacco control experience of most countries of the world has been reflected in discussions over the last several years related to the development and adoption by the World Health Assembly in May 2003 of the World Health Organization (WHO)'s Framework Convention on Tobacco Control (FCTC). The provisions of the FCTC serve as a logical backdrop for discussing tobacco control program options in Japan. The collective experience reflected in the FCTC discussions shows that significant investment in the national tobacco control infrastructure is required to develop and implement an effective tobacco control program. For example, in the United States, the Centers for Disease Control and Prevention (CDC) has developed 'order of magnitude' estimates of what it takes to do the job 'right' (i.e., provide sufficient program and human resources). Characterized as “Best Practices for Comprehensive Tobacco Control Programs,” the estimates are presented below in relation to nine program components that are considered critical to success; beyond these elements, an appropriate level of taxation and enforced regulations are needed:

- Community programs
- Chronic disease programs (e.g., heart disease prevention, cancer registries) to reduce the burden of tobacco-related disease
- School programs

- Enforcement of existing policies
- Statewide programs
- Counter-marketing;
- Cessation programs;
- Surveillance and evaluation; and,
- Administration and management.

"CDC estimates that the annual costs to implement all of the recommended program components range from $7 to $20 per person in small states (populations under 3 million) and from $5 to $16 per person in large states (population over 7 million). Total recommended program costs for the average state would range between $31 million (lower estimate) and $83 million (upper estimate) each year, translating to an annual total of $1.6 billion to $4.2 billion for comprehensive tobacco control programs nationwide (US Department of Health and Human Services (USDHHS) 1999)."

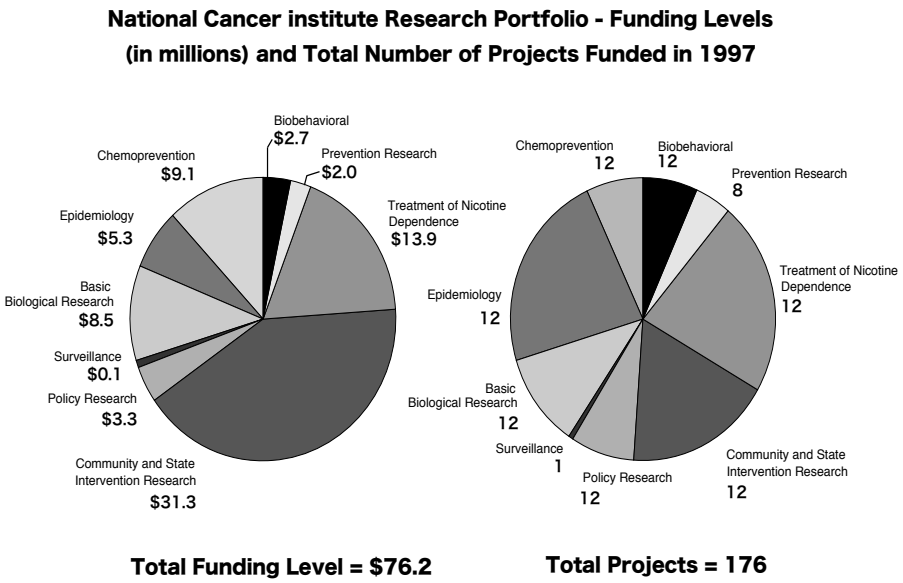
While few states in the US match up to these 'best practice' guidelines, tobacco control funding increased dramatically in the U.S. until 2001, resulting in reductions in tobacco use. For example, between 1992 and 1998, total *per capita* funding for tobacco control in the United States increased from about $7 to $40 (Consumer Price Index [CPI] adjusted to 1992 dollars); and total funding for tobacco control increased from US$90+ million to more than US$183 million (CPI adjusted to 1992 dollars).

At the national level, the CDC's Office of Smoking and Health (OSH) has a current annual budget of about US$100 million and directly employs more than 100 people. Among other activities, the OSH supports programs to prevent and control tobacco use in all 50 states; funds nine national networks to promote tobacco use prevention and control in selected priority populations; and provides grants to 21 states for coordinated school health programs. In the United States, the OSH takes broad-based national leadership that aims to coordinate federal, state, and local government agencies in reducing tobacco use. In addition, this leadership also focuses on enhancing collaboration among professional and voluntary organizations and academic institutions in advancing a comprehensive approach to tobacco control.

Underlying these initiatives is also a substantial commitment at the national level to support tobacco control research. For example, in 1997, the tobacco-related research portfolio of the National Cancer Institute (NCI) stood at US$76.2 million. This investment represented 176 different tobacco-related projects categorized into broad research categories, including bio-behavior, prevention of nicotine use, treatment of nicotine use, state and community projects, policy, surveillance, basic biology and epidemiology (Figure 4.2). This research serves as the scientific foundation for tobacco control, along with the empiric evidence that comes from program evaluation. NCI characterizes the importance of research as follows:

"It was the unanimous and fundamental conclusion of the Tobacco Research Implementation Group that an unequivocal commitment of the NCI to a comprehensive but focused program of research on tobacco use can help to reverse the epidemic of tobacco-related cancers (NCI 1998)."

Figure 4.2 National Cancer Institute Research Portfolio (Tobacco Research Implementation Plan)



Clearly, national commitment and leadership is required to successfully drive tobacco control in any country. While a level of commitment comparable to that made in the United States cannot be duplicated everywhere, this country's programs exemplify the needed broad-based approach. However, even the level of investment made by the United States is disproportionately small when compared to the contribution of tobacco use to the total cancer burden and to the smoking-caused burden of disease more generally. For example, in the United States, tobacco related cancers comprise 30% of all cancer deaths, while only 3% of the cancer research funding is spent on tobacco control-related research (NCI 1998). Expenditures for research remain small in relation to the size of the problem and in 2002, National Institutes for Health spent less than 1% of its budget on research on prevention and cessation issues (Schroeder 2004).

4.1.2 Current responses to the tobacco epidemic

4.1.2.1 Consumption, prevalence and health impacts

Overall annual *per capita* cigarette consumption has decreased in a number of countries (Table 4.1). However, countries that have implemented comprehensive tobacco control measures can demonstrate greater decreases. Experiences in many countries document that consumption can be reduced and that the smoking-attributed burden of disease will then decline. One indicator is the smoking-attributed number of deaths in men (or women) aged 35-69 years old, an age group in which smoking has substantial impact on morbidity and mortality from chronic diseases. For example, smoking-attributed numbers of deaths per year among males aged 35-69 are decreasing in the United States (from 157,000 in 1975 to 136,000 in 2000 (WHO/TFI 2001)) where the implementation of comprehensive tobacco control measures has been carried out over a sufficient period of time (20-30 years) to have had a measurable impact. Given this characteristic of the progression of the tobacco epidemic and the growing body of evidence unequivocally linking the use of tobacco to premature death and increasing disease burden, many countries and areas (e.g., Australia, Hong Kong and Thailand in the Asia-Pacific region) are committed to implementing comprehensive tobacco control programs.

In countries that have neither committed to nor implemented comprehensive tobacco control measures (e.g., Japan and China, with the exception of Hong Kong), *per capita* cigarette consumption has either increased or remained stable (Table 4.1). Based on patterns of rising consumption in countries where data on 'smoking-attributed numbers of deaths per year' are not available (e.g., China), it can be assumed with certainty that progression of the tobacco epidemic will repeat the well-documented North American and European experiences. For example, in Japan, the smoking-attributed number of deaths per year in males aged 36-39 increased from 18,000 in 1975 to an estimated 31,000 in 1995 (Hirayama 1981).

Table 4.1 Annual per capita Cigarette Consumption in Selected Countries, 3-year Moving Average

Country {area}	Year			
	1980	1990	1995	1998
Australia	106.5	88.5	73	63.6
China	161.8	264.3	255.5	246.6
Germany	98	88.2	82.2	72.2
Hong Kong, China	79.2	---	41.8	30.7
Japan	**123.5**	**112.2**	**109.6**	**96**
Malaysia	145.2	113.1	79.7	72.5

4.1.2.2 Policy development and the implementation of comprehensive tobacco control programs

On May 21, 2003, the 192 members of the WHO unanimously adopted the Framework Convention on Tobacco Control (FCTC) aimed at curbing tobacco-related deaths and disease (FCTC 2003). This is the first international treaty negotiated under the auspices of the WHO. The Convention requires countries to impose restrictions on tobacco advertising, sponsorship and promotion, establish new labeling and clean indoor air controls and strengthen legislation to clamp down on tobacco smuggling.

In the context of the FCTC, the Parties to the Convention, including Japan, agree with the objective of implementing "… tobacco control measures … to reduce continually and substantially the prevalence of tobacco use and exposure to tobacco smoke." Also, consistent with the Guiding Principles of the Convention, the Parties recognize the following specifically, in addition to other provisions of the FCTC:

- That price and tax measures are effective and important in reducing consumption.
- The need to provide for protection from exposure to tobacco smoke in indoor workplaces and public places, public transport, and other public places, "as appropriate."
- The need to regulate the packaging and labeling of tobacco products to ensure that these products are not promoted by any means that are "false, misleading, deceptive or likely to create an erroneous impression about its health effects, hazards or emissions …;" to include health warnings describing the harmful effects of tobacco use; and to provide information on the relevant constituents and emissions.
- The importance of education, communication, training and public awareness to effective tobacco control.
- That a comprehensive ban on advertising, promotion and sponsorship would reduce the consumption of tobacco products.
- The need to take effective action to promote cessation of tobacco use and adequate treatment for tobacco dependence.
- The need to "prohibit the sales of tobacco products to persons under the age set by domestic law, national law or eighteen." (e.g., by ensuring that tobacco vending machines are not accessible to minors and do not promote the sale of tobacco products to minors, and by prohibiting the distribution of free tobacco products to the public, especially minors.) The need to develop and promote tobacco control-related research, surveillance and the exchange of information among all interested parties (FCTC 2003).

Table 4.2 FCTC Provisions

Tobacco Control Issue	FCTC Article (s)*	Provisions**
Tax	**Article 6:** *Price and tax measures to reduce the demand for tobacco*	Recognizes price and tax measures as effective and important means of reducing consumption, especially among young people.
		States may implementing tax and price policies and prohibit or restrict sales and/or importations by international travelers of tax- and duty-free tobacco products.
Tobacco Smoke Exposure (Secondhand Smoke)	**Article 4(a):** *Guiding Principles*	Recognizes need to take measures to protect all persons from exposure to tobacco smoke.
	Article 5(b): *General Obligations*	Parties shall adopt and implement effective measures and cooperate with other Parties in preventing and reducing exposure to tobacco smoke.
	Article 8: *Protection from exposure to tobacco smoke*	Recognizes that scientific evidence has unequivocally established that exposure to tobacco smoke causes death, disease and disability.
		Parties shall adopt and implement and actively promote the adoption and implementation of measures providing for protection from exposure to tobacco smoke in indoor workplaces, public transport, indoor public places and other public places.
	Article 12 (a): *Education, communication, training and public awareness*	Parties shall adopt and implement effective measures to promote broad access to effective and comprehensive education and public awareness programs on the health risks of exposure to tobacco smoke.
	(**Article 14 (1)(a):** *Demand reduction measures concerning tobacco dependence and cessation*)	Parties shall develop and disseminate appropriate, comprehensive and integrated guidelines based on scientific evidence and best practices and shall take effective measures to promote cessation of tobacco use
Ingredient Regulation/ Disclosure	**Article 9:** *Regulation of the contents of tobacco products*	Parties shall adopt and implement effective measures for testing, measuring, and regulating tobacco products.
	Article 10: *Regulation of tobacco product disclosures*	Manufactures and producers shall disclose to governmental authorities information about the contents and emissions of tobacco products and disclose to the public information about the toxic constituents of the tobacco products and the emissions that they may produce
Packaging and Labeling	**Article 11:** *Packaging and Labeling of tobacco products*	Parties shall implement effective measures to ensure that product packaging does not promote a tobacco product by any means that are false, misleading, deceptive or likely to create an erroneous impression about its characteristics, health effects, hazards or emissions, including any term, descriptor, trademark, figurative or any other sign that directly or indirectly create the false impression that a particular tobacco product is less harmful than other tobacco products. These may include terms such as "low tar", "light", or "mild."
		Ensure health warnings are on each unit packet and package of tobacco products and that they are clear, large, visible and legible, at least 30% of the principle display areas and may include pictures or pictograms.
Advertising/Promotion	**Article 13:** *Tobacco Advertising, promotion and sponsorship*	Parties shall, in accordance with its constitution, undertake a comprehensive ban on all tobacco advertising, promotion and sponsorship.
	Article 16: *Sales to and by minors*	Parties not in a position to undertake a comprehensive ban due to constitutional limits shall apply restrictions on all advertising, promotion, and sponsorship.
		At a minimum, Parties shall prohibit all forms of promotion that are false, misleading or deceptive or likely to create and erroneous impression about its characteristics, health effects, hazards or emission; require health warnings on all messages that accompany advertising, restrict direct or indirect incentives that encourage the purchase of tobacco products; require disclosure of expenditures by industry; undertake a comprehensive ban (or restrict) advertising, promotion and sponsorship on radio, television, print media and other media such as the internet within a period of five years; and prohibit the sponsorship of international events, activities, and/or participants therein.
Cessation	**Article 4 (b):** *Guiding Principles*	Recognizes need to take measures to promote and support cessation.
	Article 14: *Demand reduction measures concerning tobacco dependence and cessation*	Parties shall develop and disseminate integrated guidelines based on scientific evidence and best practices and shall take effective measures to promote cessation and adequate treatment for tobacco dependence.
		Parties shall endeavor to promote programs at educational institutions, health care facilities, workplaces and sporting environments; include diagnosis and treatment in national health and education programs; collaborate with each other to facilitate accessibility and affordability of treatment, including pharmaceutical products.
Youth Access	**Article 4:** *Guiding Principles*)	Recognizes need to prevent initiation.
	Article 16: *Sales to and by minors*	Parties may require prominent indicators at the point of sale about the prohibition of sales to minors; ban sales on store shelves; prohibit the manufacture and sale of sweets, snacks, toys or any other object which may appeal to minors; ensure vending machines are not accessible to minors and do not promote the sale of tobacco to minors.
		Parties shall prohibit the distribution of free tobacco products.
		Parties shall endeavor to prohibit the sale of individual or small packets of cigarettes.
Liability	**Article 4:** *Guiding Principles*	Issues related to liability are an important part of comprehensive tobacco control.
	Article 19: *Liability*	Parties shall deal with criminal and civil liability, including compensation where appropriate
		Parties shall share scientific evidence and legal information, and assist in legal proceedings relating to civil and criminal liability.

Note: Although the cited articles do not always explicitly mention the issue noted in column one, the issue is embedded in the provision of the Articles.

Table 4.2 summarizes the specific provisions of the Framework Convention. Table 4.3 illustrates the extent to which selected countries have incorporated comprehensive tobacco control measures that are responsive to these provisions in their overall efforts to control the tobacco epidemic. The following general guidance was used by the authors of this chapter in deciding on the 'Yes,' 'No' or 'Partial' categorizations (Global Initiatives 2003, WHO/TFI 2001, WHO/WPRO 2000).

- 'Yes' – provision is mandated by legislation and/or regulation; AND, it is being implemented in an on-going, aggressive manner.
- 'No' – provision not mandated by legislation and/or regulation
- 'Partial' – some aspects of provision are mandated by legislation and/or regulation; some aspects are not mandated; AND/OR, the provision is not being implemented in an on-going, aggressive manner.

Table 4.3 Qualitative Assessment of the Implementation of Selected Comprehensive Tobacco Control Measures Reflected in the Framework Convention on Tobacco Control

Country	Measure							
	Price/Tax	Secondhand Smoke	Labels/Warnings	Advocacy/Education/Awareness	Ads/Sponsorship	Quit Help	Youth Access	Research
Australia	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes
China	Partial	Partial	Partial	Partial	Partial	No	No	Partial
Germany	No	No	Yes	No	Yes	No	Partial	Partial
Hong Kong, China	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Japan	No	No	Yes	No	No	No	No	Partial
Malaysia	No	Partial	Yes	No	Yes	Yes	Yes	No
Republic of Korea	Partial	Partial	Yes	Yes	Yes	Yes	Yes	Partial
South Africa	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Switzerland	No	No	Yes	No	Partial	No	Yes	Partial
Thailand	Yes	Yes	Yes	No	Yes	No	Yes	No
United States of America	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Principal sources: WHO/TFI Country Profiles; Country Profiles on Tobacco or Health 2000, WHO/Western Pacific Region; Campaign for Tobacco Free Kids, selected Country Case Studies

Note 1: In deciding on the 'Yes,' 'No,' or 'Partial' categorizations in the table, the following general guidance was used:
'Yes' - provision is mandated by legislation and/or regulation; AND, it is being implemented in an on-going, aggressive manner.
'No' - provision not mandated by legislation and/or regulation
'Partial' - some aspects of provision are mandated legislation and/or regulation; some aspects are not mandated; AND/OR, the provision is not being implemented in an on-going, aggressive manner.

Note 2: A discussion of selected measures that have proven effective in reducing tobacco use, including country-specific examples, follows in Section 3.5. While different countries have followed differing courses to a degree, the collective experience makes clear that the application of a comprehensive set of control measures is the most effective way to reduce tobacco consumption and protect the health and welfare of society. In considering the tobacco control measures that may prove most effective in Japan, consideration needs to be given to the status of the tobacco control epidemic, the context set by the tobacco industry, and the potential partners in tobacco control.

A discussion of selected measures that have proven effective in reducing tobacco use, including country-specific examples, follows in Section 4.1.3. While different countries have followed differing courses to a degree, the collective experience makes clear that the application of a comprehensive set of control measures is the most effective way to reduce tobacco consumption and protect the health and welfare of society. In considering the tobacco control measures that may prove most effective in Japan, consideration needs to be given in the country specifically to the status of the tobacco control epidemic, the context set by the tobacco industry, and the potential partners in tobacco control. In addition, special opportunities sometimes present themselves and an organized tobacco

control coalition is needed to take advantage of these situations. For example, in the Republic of Korea, a recent world-class sporting event offered an occasion to promote national tobacco control efforts.

Dynamic Korea: *Korea Scores With Tobacco Control* - Korea Times, 2002/06/02

"Football is not the only reason that the world will be eyeing the Republic of Korea from May 31. The country's success in an entirely different field will also be drawing attention. May 31 was also World No Tobacco Day, and for health officials in this field, South Korea is now the country to watch. Not only is it one of the co-hosts for the first official tobacco-free World Cup, it is also home to some recent very successful anti-tobacco efforts.

A survey published this week found that by the end of 2002, the number of male smokers will have dropped by a stunning 21% since May 2001, according to a survey by Gallup and the Korean Association of Smoking and Health (KASH). Few countries have seen such dramatic drops in smoking. By comparison, Japan's smoking rate among men has only decreased very slowly, while the United States took more than three decades to achieve a drop of 20% in its adult smoking rate… … South Korea has made a good start to a strong tobacco control campaign. Next January, smoking will be completely prohibited inside major government buildings, medical facilities and schools. Its World Cup anti-tobacco efforts are also here to stay – outdoor sports facilities with more than 1000 seats will ban smoking. Additional cigarette vending machines in subway stations and other public facilities will also be prohibited. In 2000, President Kim Dae-Jung made the Presidential house smoke-free and has been continuously giving crucial support to tobacco control.

The government is not alone in supporting tobacco control. So too are institutions and individuals. Of the country's top 100 companies, 79 have no-smoking campaigns in place, and nearly one in four (23 companies) have made their buildings smoke-free. A few companies were even offering special incentives for employees who give up smoking. Of course, all this has been helped by strong anti-smoking non-government organizations. KASH is well established, but there are also some new and dynamic players, such as the People's Coalition for a Smoke-Free Korea, which comprises some passionate and dedicated activists…."

4.1.3 Selected measures that reduce tobacco use

4.1.3.1 The need for a comprehensive approach

A wide variety of approaches, techniques, and strategies have been used to control tobacco use. Over the last decades, tobacco control approaches have evolved from solely focusing on changing the behavior of individual smokers, one at a time, towards changing the environment that surrounds smokers. Environmental change is accomplished through public and private policy initiatives; its purpose is to shift the social norms concerning tobacco use from 'accepting' to 'not accepting.' In the accepting environment, the public perceives tobacco use as a personal decision or choice made by adults. This perception can be shifted to be 'not accepting,' recognizing that smoking is an addiction fostered by the tobacco industry, often beginning in childhood, and a behavior that harms others, especially women and children. Making tobacco use the exception rather than the social norm has been a major thrust of tobacco control in countries such

as the United States, Canada, Australia, and Thailand.

Promoting change in societal perceptions of norms is essential to tobacco control since smoking initiation, maintenance, and cessation are strongly influenced by the social environment. However, social norms cannot be changed without addressing many factors, including the political, economic, and cultural conditions that enable and legitimatize tobacco use. In most situations, individuals conform and adapt to the social norms and behaviors of the majority. When individuals find that their actions are not consistent with those of the general public, then societal pressure can be used to change individual behavior (NCI 1991). Tobacco use will be reduced in a social environment that provides clear, consistent, and persistent messages that smoking is not socially acceptable. A comprehensive approach to tobacco control is needed for this purpose.

Such an approach incorporates actions to:

- Make cigarettes more costly to purchase
- Restrict or ban smoking in public
- Reduce public exposure to the relentless advertising of the tobacco industry
- Limit the access of children to tobacco, especially through vending machines

Critical components of such a comprehensive approach include:

- Increased taxation of tobacco products, especially cigarettes
- Information and media campaigns
- Restrictions on public and indoor smoking
- Advertising and promotional restrictions
- Cessation support initiatives
- Youth access regulations

In the United States, for example, where comprehensive tobacco control measures have been implemented, these efforts have altered the social acceptability of smoking, and contributed to substantial reductions in smoking prevalence and cigarette consumption. Comprehensive tobacco control programs have been implemented at federal, state, and local government levels and, as a result, the overall prevalence of smoking in the United States has decreased from 47% in 1965 to approximately 22% in 1999 (NCI 2003).

4.1.3.2 Price and tax increases

Increasing cigarette excise taxes is one of the most important tobacco control strategies available. Numerous studies have shown that increasing the price of cigarettes;

- Encourages some people to reduce the amount they smoke
- Encourages others to quit all together
- Prevents young people from starting to smoke
- Cessation support initiatives
- Reduces the number of former smokers who relapse back to smoking

A key tenet of economics is that the demand for a product decreases as the price increases (Jha and Chaloupka 1999). Even though cigarettes are an addictive product, this economic principle holds for tobacco use, and smokers purchase fewer cigarettes when cigarette prices increase. The poor and the young are most sensitive to price increases and generally for every 10% increase in the real price of cigarettes, adult smoking is reduced by about 3-5% and youth smoking by about 7%. The reductions are even greater in low- to middle-income countries where increasing the price of a pack of cigarettes by 10% reduces demand by around 8%. In the United States, the report, "Taking Action to Reduce Tobacco Use," from the Institute of Medicine concluded that the "single most direct and reliable method to reduce tobacco consumption is to increase the price of tobacco products, thus encouraging cessation and reducing the level of initiation of tobacco use (Jha and Chaloupka 1999)."

In South Africa:

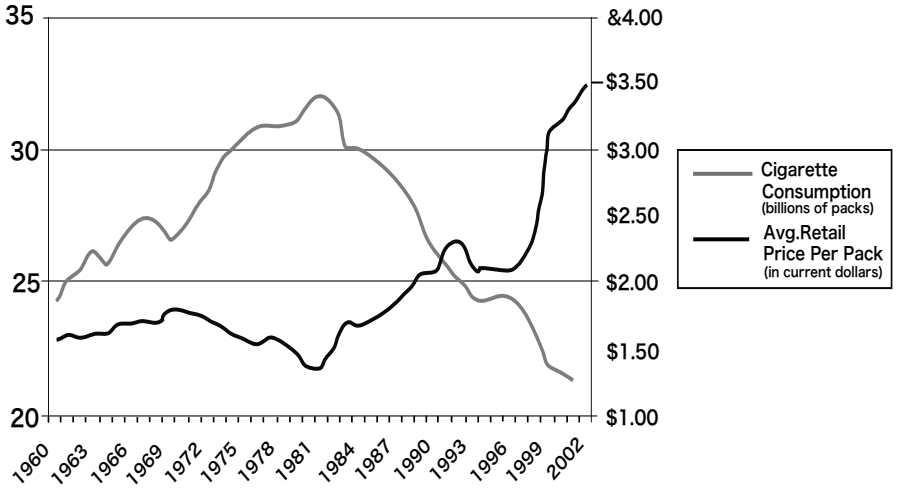
The Ministry of Finance increased tobacco taxes for the specific purpose of protecting the health of the people. Between 1994 and 1999, real tobacco excise taxes rose 149%, increasing real cigarette prices by 81%. The Government's tax revenues doubled, while consumption decreased by 21%.

Figure 4.3 illustrates the impact of higher cigarette tax rates on smoking consumption in the U.S. Many other countries have data that confirm the relationship between increasing cigarette taxes and lower consumption rates.

Canada's experience demonstrates both the beneficial effect of increasing taxes and the negative consequence of subsequently lowering cigarette prices (Figure 4.4) (Canadian Cancer Soc. 1999; WHO/WPRO 2000). From 1979 to 1991, the real price of a pack of cigarettes in Canada increased from $2.09 to $5.42 and smoking among 15 to 19 year olds fell from 42% to 16%.

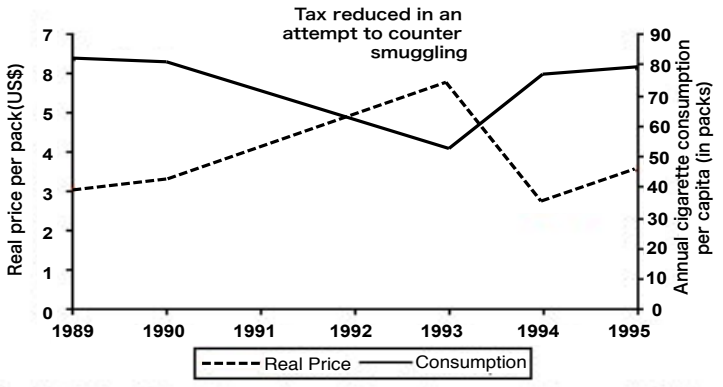
However, the Canadian government became concerned that the tax increase was responsible for an increase in smuggling of lower cost cigarettes from the United States. Interestingly, the tobacco industry also expressed concern about the increase in smuggling activity. In order to reduce the tax avoidance that was occurring because of the smuggling, Canada decreased the tax rate on cigarettes. This led to an almost immediate increase in youth smoking rates, the first such increase in youth smoking recorded in fifteen years (Canadian Cancer Society 1999).

Figure 4.3 Changes in US Consumption by Changes in the Price of Cigarettes



Source: Website of Campaign for Tobacco Free Kids. Raising cigarette prices reduces consumption, especially amongst kids (and the Cigarette Companies know it). http://tobaccofreekids.org/research/factsheets/pdf/0146.pdf

Figure 4.4 Cigarette Price and Consumption in Canada



Source: Jha and Chaloupka 1999

In countries deriving significant revenue from cigarette taxes, governments are often concerned that lower government revenues will result from higher taxes.

However, economic research in both low- and high-income countries has demonstrated that there is no reduction in government revenues when taxes are raised. Even with a substantial reduction in demand following a price increase, revenues from cigarette sales continue to increase in the short-term because the increase in taxes brings more money per pack, offsetting the reduction in sales (Jha and Chaloupka 1999).

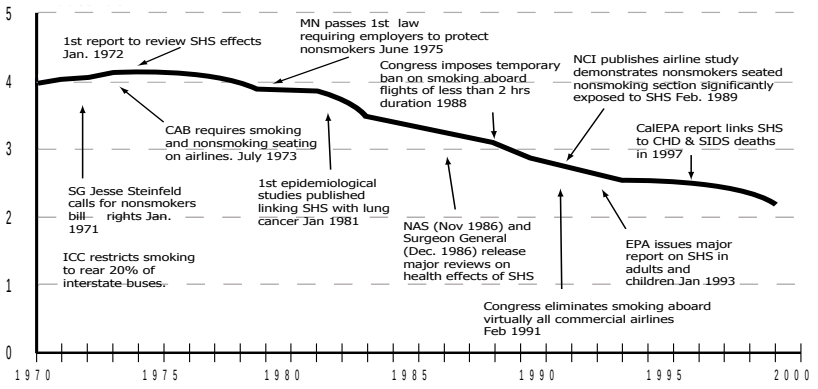
The earmarking of tobacco taxes for tobacco control-related activities, with the stipulation that tax revenues will be used for specific programs or projects rather than being placed in the general revenue stream, has significantly

enhanced tobacco control programs in many locations (e.g., the state of California in the United States and a number of countries such as Canada, Poland, Finland and Thailand). Even if only a small percentage of the tobacco excise tax increase is used for health promotion and tobacco control programs, there are substantial benefits to public health (Stephens et al. 2001).

Because of the efficacy of tax increases for reducing smoking, the tobacco industry aggressively opposes this type of legislation. To overcome the reluctance of governments to increase taxes, particularly in the face of powerful opposition from the tobacco industry, experience shows that concerted effort is needed to give all of the relevant stakeholders an understanding of the economic consequences and public health benefits of increasing taxes (Jha and Chaloupka 1999).

4.1.3.3 Secondhand smoke restrictions

Figure 4.5 History of Efforts to Protect Nonsmokers in the US from Secondhand Smoke: Change in Smoking Consumption by Years and Events



Secondhand smoke (SHS) causes acute and chronic diseases in nonsmokers, including infants, children, and adults (NCI 1999; National Institute for Occupational Safety and Health 1991; USDHHS 1986; US Environmental Protection Agency (EPA) 1992; WHO 1999). Regulations directed at SHS have the objective of reducing the involuntary exposure of nonsmokers to SHS with the attendant risks to health. One indirect consequence of SHS regulation is the creation of an environment that encourages smokers to reduce their consumption or to quit. Changing the social norms as they relate to SHS exposure and creating smoke-free areas has proved to be an important tobacco control strategy. Social norms around SHS exposure changed slowly in the US and some other countries initially, but the pace of change accelerated as the smoking minority shrank in proportion to the nonsmoker majority. Simply enacting policies and laws does not

change social norms, however. Experience shows that the public must be educated as to the dangers associated with SHS exposure; policies need to be enacted for limiting SHS exposure; and the policies need to be fully implemented and enforced. As learned over several decades in the US, achieving sufficient reduction of SHS exposure requires sustained effort and substantial time and such reduction cannot be accomplished without both public and private actions. Figure 4.5 presents data from the United States showing some seminal events that have occurred in the 30-year effort to implement policies and programs to protect non-smokers from secondhand smoke exposure.

Every country needs a comprehensive approach to tobacco control that includes both public and private steps to reduce the population's exposure to SHS. A growing number of countries have implemented restrictions on smoking in public places. This is generally accomplished by government action at the local, state, and national level. The locations most commonly made 'smoke-free' by legislative action include:

1. **Hospitals, childcare centers, schools and universities.**
2. **Public entertainment venues, such as sports stadiums, theaters, concert halls and museums.**
3. **Public transportation, including buses, taxicabs, and airplanes.**
4. **Restaurants, bars, retail stores, and shopping malls.**
5. **Offices and other workplaces.**

In Norway:

In April 2003, the Norwegian Parliament enacted legislation completely banning smoking in restaurants, cafes, bars, pubs, discos and other hospitality businesses that serve food or drinks for consumption on their premises.

Making some highly visible public venues smoke-free may have special symbolic importance. For example, significant progress has been made recently in the 'smoke-free' staging of major sporting events. Particularly noteworthy were the 2000 Olympics in Australia, the 2002 World Cup held jointly in the Republic of Korea and Japan, and the 2002 Winter Olympics held in the United States. The success of these smoke-free events destroys the proposition that tobacco sponsorship of sporting events is irreplaceable and that restricting smoking will adversely affect attendance.

Smoke-free workplaces facilitate reduction of smoking and cessation by workers. In countries such as the United States, Canada, Finland, and Australia, the number of both public and private workplaces implementing smoke-free regulations has increased greatly. In the United States, for example, the percentage of workers covered by totally smoke-free regulations has increased from just 3% in 1986 to 68.9% in 1999 with comparatively little resistance

(Shopland et al. 2001). Many studies have shown that restricting smoking in public places increases the likelihood that smokers in these settings will either quit smoking or reduce their consumption (Borland et al. 1990; Sorensen et al. 1991; Woodruff et al. 1993; Stillman et al. 2003). Studies have shown that totally smoke-free workplace policies have a greater effect in reducing smoking than less restrictive smoke-free policies allowing smoking in some areas. Internal research conducted at Philip Morris also reached similar conclusions in 1992: "Less restrictive workplace policies, such as smoking only in designated areas, have much less impact on quitting rates than totally smoke-free workplaces and very little impact on consumption (Heironimus 1992)."

A recent systematic review of the literature and meta-analysis was conducted to determine the quantity of effects of smoke-free workplaces on smoking employees as compared with the effects achieved through tax increases (Woodruff et al. 1993). Totally smoke-free workplace policies were associated with a drop in absolute prevalence of 3.8% (95% confidence interval 2.8%-4.7%) and a decrease in consumption of 3.1 (2.4-3.8) cigarettes/day per continuing smoker (Fichtenberg and Glantz 2002). In this same example, the combined effects of stopping smoking (lower prevalence) and lower consumption per continuing smoker yielded a total reduction of 1.3 cigarettes/day per employee (smokers and nonsmokers) (range 0.2–1.8), which corresponds to a 29% relative reduction (range: 11%–53%) (Fichtenberg and Glantz 2002). To achieve similar reductions in consumption, the tax on a pack of cigarette would have to increase from $0.76 to $3.05 in the US, and from £3.44 to £6.59 in the UK. The authors concluded that "if all workplaces became smoke-free, consumption *per capita* in the entire population would drop by 4.5% in the United States and 7.6% in the United Kingdom, costing the tobacco industry $1.7 billion and £310 million annually in lost sales. To achieve similar reductions tax per pack would have to increase $1.11 and £4.26 (Heironimus 1992). In addition, prohibiting smoking in the workplace reduces cleaning, maintenance, and repair costs of buildings; reduces the number of fires; lowers insurance costs; and leads to higher productivity among non-smokers and an overall healthier workforce (11th World Conference on Tobacco or Health 2000).

In Canada, a recent study has demonstrated that restrictive municipal laws limiting public smoking are positively related to increased numbers of non-smokers and a decrease in the numbers of cigarettes consumed by continuing smokers (Stephens et al. 2001). Research conducted in California found that smokers in communities that had more restrictive smoke-free worksite legislation quit smoking at a higher rate than in communities with no legislation restricting smoking (26.4% vs. 19.1%, respectively). A review of 19 studies from the United States and Australia found that worksites were "probably the most significant sites where smoking restrictions cause smokers to reduce their smoking consumption

(Chapman et al. 1999)."

Few population studies have been conducted to determine the overall impact of comprehensive tobacco control approaches that include smoke-free policies. However, recent data from the National Cancer Institute's American Stop Smoking Intervention Study (ASSIST), one of the largest tobacco control studies ever undertaken by the United States government, demonstrate that restrictive state-level clean indoor air policies and increased taxation decrease the prevalence of smoking and lower consumption levels.

ASSIST was a large-scale study conducted by the National Cancer Institute to determine the effect of comprehensive tobacco control on the entire population and environment of 17 states in the United States. Its goal was to change the social, cultural, economic, and environmental factors that influence smoking behavior. This was accomplished primarily through interventions in four policy areas: (1) promoting smoke-free environments, (2) countering tobacco advertising and promotion, (3) limiting tobacco access and availability, and (4) increasing tobacco price through new excise taxes. Of particular interest is the finding that the states included in this project had lower prevalence rates at the end of the project. In addition, states with the highest taxes and the most restrictive secondhand smoke legislation had the lowest smoking prevalence and consumption rates over time. It is estimated that if all states had implemented ASSIST, the reduction in smoking prevalence would have translated into approximately 278,700 fewer smokers nationwide. ASSIST demonstrates that investing in comprehensive tobacco control and promoting changes in tobacco control policies, such as secondhand smoke legislation, are effective strategies for reducing tobacco use (Stillman et al. 2003).

The tobacco industry regards the creation of smoke-free public and private places as a major threat to its business. Data from an industry-funded study predicted a 74% increase in quitting rates (e.g., from 2.5% to 4.4%) if smoking is banned in all workplaces. It also regarded such a ban as leading to a substantial loss in industry revenues, an important reason for the industry's opposition to legislation expanding smoke-free coverage (Heironimus 1992).

One tactic of the tobacco industry is to maintain the social acceptability of smoking through industry and corporate action. In this regard, one of the tobacco industry's action strategies is promoting the idea of 'accommodation'which plays on the 'right of the individual to make his or her own choice.' This strategy overlooks the fact that, in most cases (physical barriers notwithstanding), secondhand smoke ignores the rights of the individuals who choose not to smoke, i.e., the non-smokers who comprise the majority of society in all countries, including Japan.

4.1.3.4 Warning labels

Many countries now require some minimal warning labels on cigarette packs and advertisements. However, warning labels can only affect smoking behavior if they are properly designed to account for factors that influence smokers' behavior and minimize the appeal of the product. In many countries, health warning labels do not influence tobacco use significantly because their wording is weak and their placement and appearance make them inconspicuous (Krugman et al. 1999).

Numerous studies have determined the elements needed to have effective warning labels. Findings include the following:

1. Warning labels should occupy a minimum of 25% of the top of the front and back of the package *[note: FCTC requires 30% or more]*.
2. Labels should be in black and white or other sharply contrasting colors.
3. Type style and size should be specified to avoid industry efforts to undermine the impact of the warnings.
4. Messages should be unequivocal, simple, and stark.
5. Messages should convey the nature and magnitude of the risks of smoking.
6. Pictorial warnings are particularly appropriate for countries where smokers ignore standard warnings or where literacy rates are low.
7. Warning labels should be applied to all tobacco products, not just cigarettes.
8. Warning labels should include rotating messages, including messages such as:
    a. Smoking kills.
    b. Smoking causes heart disease.
    c. Smoking causes 85% of all lung cancer deaths.
    d. Smoking harms your baby.
    e. Quitting smoking now could save your life.
    f. Tobacco smoke can harm those around you.

Australia instituted product labeling in January 1995 to inform smokers of the long-term health effects of tobacco use. The Australian system includes six black and white, rotating messages that must cover 25% of the front of cigarette packs. One side of the pack lists all the toxic components, while the other side includes health warnings and related information that take up 33% of that panel (Chapman et al. 1999). Australia was the first nation to require that “quit information” be printed on every pack. A study in Australia found that a doubling in quit attempts was associated with the change in warning labels and cigarette

packaging (Borland 1997).

Canada, Brazil, and New Zealand have adopted large graphic health warnings. Canada recently proposed enlarging the health labels from 30% of the package face to 60%. (Figure 4.6) Studies in Canada and Australia found that the introduction of more graphic warning labels increased motivation to quit along with some increased awareness and concern about the health effects of smoking (Mahood 1995; Martens 2002). Another study from Canada found that cigarette package warnings were motivational for about half of the smokers who were thinking about quitting (Jha et al. 2000).

Figure 4.6 An Example of a Health Warning in Canadia

Source: Website of tobacco information by the Health Canada (www.infotobacco.com)

Thailand's Tobacco Products Control Act is based on the Canadian experience. Under this Act, cigarette packages carry prominent black-and-white health warnings on the front of the package. In addition, the message, "Smoking causes impotence" is included in their list of required warnings. South Africa has also adopted product-labeling regulations based on the Australian labeling model. Initial reports from South Africa indicated a 15% decrease in cigarette consumption three years after implementation of the new health warnings. Surveys showed that 58% of smokers were motivated by cigarette warning labels to quit or reduce their consumption (Public Citizen Health Research Group 1998). Beginning in January 2003, all tobacco products in the United Kingdom will carry new, stark health warnings on the back and front of the pack. The new health warnings will cover 30% of the front surface and 40% of the back of the pack. A thick black border will add an additional 10% to the area given over to the warning labels (The Tobacco Products (Manufacture, Presentation and Sale) Regulations 2002).

The evidence is clear that the use of warning labels and other types of information campaigns can have a significant impact on tobacco use. The effect of strong warning labels may be greatest in countries where tobacco control efforts

have been minimal, and in low-income countries where the population has had little exposure to information on the addictive nature of tobacco and its many adverse effects on health.

4.1.3.5 Information and mass media campaigns

Information campaigns may include the publication of official reports, such as the reports of the United States Surgeon General on smoking and health; targeting of specific audiences with selected information; distribution of self-help materials; public service announcements; and large-scale mass media initiatives. Such information and media initiatives are usually the first tobacco control efforts undertaken as a national program is developed and implemented. They are particularly effective in the early stages of a country's tobacco epidemic (NCI 1991). Comprehensive reports on the health impacts of tobacco (such as the United States Surgeon General's Report) are foundational to answering the challenges of the tobacco industry in some countries suggesting that the exact degree and nature of the health risks have not been established scientifically.

Public information campaigns can reach millions of people at a time. In many countries, governments have been an active force in disseminating information on the health consequences of smoking. Historically, much of this effort focused on strategies for changing individual behavior to raise the awareness of the population about the health effects of smoking and to encourage quitting. More recently, however, large-scale mass media campaigns have been used to counter the tobacco industry's advertising campaigns, such as the industry's eight billion US dollar expenditure in 2002 to promote its products (FTC 2003).

In many countries, governments have played a major role in disseminating information on the health consequences of smoking. Governments have invested in surveillance efforts to track the epidemic and have made these data available to the public as well as policy makers. Government reports such as the Surgeon General Reports from the United States Centers for Disease Control and Prevention, the Monograph series from the United States National Cancer Institute, and others have provided valuable information that has been scrutinized and approved by governmental agencies. Twice, the International Agency for Research on Cancer (IARC) of the World Health Organization has reviewed the evidence on smoking and cancer, first in 1986 (IARC 1986) and more recently in 2002 (IARC 2004).

On a number of occasions, developed countries have released major reports on smoking that have been widely disseminated and received intense media coverage. Many of these official reports detail the health consequences of active smoking and the dangers of exposure to secondhand smoke. These reports and the associated informational campaigns are particularly powerful if done or

endorsed by the government. They can demonstrate a clear policy commitment by government to effective, comprehensive tobacco control. In so doing, they have the effect of overcoming scientific ambiguity about the adverse health impacts of tobacco use and unequivocally establish the need for an aggressive approach to tobacco control. These so-called "informational shock campaigns" have been studied in Finland, Switzerland, Turkey, the United States, the United Kingdom and South Africa (Jha and Chaloupka 1999). These studies indicate that the impact of such campaigns is greatest where general awareness concerning the health risks of smoking is low or in the early stages of the development of tobacco control efforts.

Smoking Kills—A White Paper on Tobacco in the UK (The Stationery Office 1998)

In 1998, the Secretaries of State and the Secretaries of Health for Britain, Scotland, Northern Ireland, and Wales presented a White Paper on Tobacco to Parliament. The White Paper entitled, "Smoking Kills" set out detailed proposals by the government to reduce smoking rates by increasing cessation and reducing initiation, especially amongst youth. Among the committed tobacco control measures were included a proposal to increase tax and enact a wide ban on tobacco advertising and sponsorship. Most noteworthy, the Government proposed to couple the advertising ban with a 50 million publicity campaign aimed at increasing awareness and changing behaviors and attitudes. "Smoking Kills" not only successfully highlighted the newly proposed government initiatives but also served to legitimize the importance of tobacco control in the public's perception

Mass media campaigns are usually implemented as part of a comprehensive tobacco control program and are more effective when carried out in the context of a multi-strategy approach. The mass media provide an important mechanism for influencing social norms and ultimately promoting smoking cessation. Mass media campaigns can be implemented at the national level or targeted to specific regions, locations, or audiences. These campaigns can help accomplish the following:

1. Educate the public about the severity of the risks of smoking, the susceptibility of every smoker to adverse health consequences, and the health benefits of quitting
2. Educate the public about the health risks of exposure to secondhand smoke
3. Alert citizens and policy makers to the benefits of supportive tobacco control policy initiatives, including advertising restrictions, and restricted smoking in public places and workplaces
4. Address misinformation spread by the tobacco industry
5. Counter the economic and political influence of the tobacco industry
6. Reinforce the view that smoking is not an acceptable social norm.

Studies in North America, Australia, Europe, and Israel have demonstrated the effectiveness of providing negative messages about smoking (Jha and Chaloupka 1999). These negative message campaigns implemented by governments and health promotion organizations have consistently been found to reduce overall cigarette consumption, as in Turkey and Finland for example (Jha and Chaloupka 1999). Evidence suggests that media campaigns are most effective at eliciting smoking cessation when smoking has become perceived as unacceptable. The media have a strong influence on the attitudes and perceptions of a society and can be very effective at focusing the public's attention on specific topics (Dearing and Rogers 1996). In the United States, media approaches have been used to stimulate positive attitudinal and behavioral changes that have ultimately contributed to reductions in prevalence and consumption rates in the general population.

Mass media campaigns need to be of a certain scope and duration in order to reach the target audiences and to deliver the needed messages for tobacco control (Hopkins et al. 2001). Longer-term campaigns that are combined with other tobacco control program efforts can increase cessation attempts and lower smoking rates. In the United States, the state of California has implemented one of the largest media-based anti-smoking campaigns, with expenditures of about US$26 million per year. Evaluations found a higher rate of quit attempts and increased amounts of successful quitting in California after the media campaign was implemented (Burns et al. 2000). A study of the California campaign in 1993 estimated that every 10% increase in media campaign expenditures reduced cigarette sales by 0.5% (Hu et al. 1995). This translates into a reduction of 7.7 packs *per capita* or about 10% of the average sales (packs *per capita*) at the beginning of the campaign.

4.1.3.6 Advertising and promotion restrictions

Tobacco advertising and promotional activities create and stimulate the desire to use tobacco products. Restricting or eliminating tobacco advertising and promotion can increase the inclination to initiate smoking and decrease the motivation to maintain tobacco use. Advertising and promotion bans are most effective if they are comprehensive and cover all types of media, including restrictions on the use of brand names, images, and logos. Data from a study of 22 countries on the effectiveness of advertising bans found that comprehensive bans on cigarette advertising and promotion can reduce smoking, but limited bans or partial bans have little or no effect. The study concluded that, if the most comprehensive advertising restrictions were in place, cigarette consumption would fall by more than 6% in high-income countries (Jha and Chaloupka 1999).

The strongest evidence to date of the significant effect on tobacco

- **In Poland, the Tobacco Control Law includes a complete ban on all tobacco advertising and promotion.**
- **Norway's 1973 Tobacco Control Act, as amended, unconditionally bans all forms of tobacco advertising and prohibits the free distribution of tobacco products.**
- **In Canada, the advertising of tobacco products is prohibited except for product information and brand-preference advertising that is not lifestyle advertising, misleading or appealing to persons under 18.**
- **In 1999, the South African Parliament strengthened the 1993 legislation, effective in 2001. The new legislation prohibited all tobacco advertising, promotion and sponsorship.**

consumption that restricting promotional activities can have comes from a study commissioned by the government of New Zealand of trends in 33 countries from 1970 to 1986. The countries studied (24 free-market economies and 9 centrally-planned East European economies) provide over 400 calendar years of observation of different tobacco prices, personal incomes, and advertising restrictions, including tobacco advertising bans. The methodology of this study was rigorous and examined adult tobacco consumption, accounting for income and tobacco price effects as well as health education effects. The overall finding of this study was that ". . . the greater a government's degree of control over tobacco promotion, the greater the annual average fall in tobacco consumption and in the rate of decrease of smoking among young people." Other findings of this study include the following:

- "Total advertising bans for health reasons are, on average, accompanied by falls in tobacco consumption four times faster than in partial ban countries.
- In countries where tobacco has been promoted virtually unrestricted in all media, consumption has markedly increased (+1.7% per year).
- In countries where advertising has been totally banned or severely restricted, the percentage of young people who smoke has decreased more rapidly than in countries where tobacco promotion has been less restricted (New Zealand Toxic Substances Board 1989)."

Canada and New Zealand have been able to implement restrictive regulations to limit tobacco advertising, while the United States has not been able to accomplish similar restrictions at the federal level due to Constitutional restrictions. Countries without constitutional restrictions, such as Thailand, have been more successful in limiting and banning cigarette advertising.

The adverse impact on children is another critical reason to ban or restrict tobacco advertising. Growing evidence shows that the industry directs much of its advertising efforts toward markets with growth or potential growth, including youth markets. Children are greatly influenced by this advertising and remember the graphic images and advertising slogans. Studies have also shown

that children are highly influenced by advertising and most often buy the most heavily advertised brands (USDHHS 1994). The fact that children have greater recall for cigarette messages than for well-known cultural icons is an indirect measure of the power of the industry's marketing campaigns (Fischer et al. 1991). While the tobacco industry argues that it is not recruiting new smokers with its massive advertising and promotional campaigns, and that the campaigns are only to encourage dedicated smokers to remain loyal to their chosen brands, studies of brands such as Camel, with its cartoon characters that were appealing to children, found a significant increase in the percentage of the youth market (Fischer et al. 1991).

4.1.3.7 Cessation

Tobacco use and dependence represent a serious public health problem that must be addressed if the epidemic of tobacco-related disease and death is to be reduced. All tobacco products contain nicotine, which is responsible for the addiction of smokers (USDHHS 1989). Tobacco dependence is classified as a mental and behavioral disorder (F17.2) according to the WHO International Classification of Diseases, ICD-10 (WHO 1992). Experts in the field of substance abuse consider tobacco dependence to have both biological and social components and to be as strong or stronger than dependence on substances such as heroin or cocaine (USDHHS 1990). These factors make quitting and staying quit very difficult (USDHHS 1989). In addition to these factors, tobacco dependence is facilitated by the tobacco industry, which exerts enormous economic, political, social, and regulatory pressure to promote its products.

Smoking cessation has immediate and substantial health benefits, and substantially reduces the risk of most smoking-related diseases. One year after quitting, the risk of coronary heart disease (CHD) decreases by 50%, and within 15 years, the relative risk of dying from CHD for an ex-smoker approaches that of a lifetime non-smoker. The relative risks of developing lung cancer, chronic obstructive lung diseases, and stroke also decrease, but more slowly. Ten to fourteen years after smoking cessation, the risk of mortality from cancer overall can decrease to a level near that of never smokers, depending on the past pattern of tobacco use (NCI 1997). Smoking cessation has a beneficial effect on pulmonary function, particularly in younger subjects, and the rate of decline among former smokers returns to that of never-smokers (USDHHS 1990). To achieve successful cessation of smoking on a very large scale requires more than simple 'cessation programs.' Treatment of tobacco dependence needs to involve a range of techniques, including counseling, telephone and internet support, and appropriate pharmaceutical aids which aim to help people to stop using tobacco and avoid subsequent relapses if successful (NCI 2000). Countries have

had varying experiences in applying these techniques and providing support in different environments - e.g. in health care systems, workplaces, and at the population level.

Behavioral counseling and pharmacotherapy for tobacco dependence can contribute substantially to improved health by enabling tobacco cessation. A wide range of nicotine replacement products are currently in use, including 2 mg and 4 mg gum, patch, lozenge, nasal spray, and oral inhaler, as well as bupropion (Fiore et al. 2000). There are also various types of behavioral treatments including self-help materials, brief interventions, and cessation clinics. Cessation treatment can be delivered by health care professionals, over a telephone 'quit line' and by using a computer and web-based interactive programs (Gilpin et al. 1993; NCI 2000; Ockene et al. 1994; Zhu et al. 1996). Even among persons who may eventually quit smoking on their own without any type of intervention or treatment, encouraging cessation earlier in a person's smoking history could reduce the overall burden of disease, which is strongly related to the duration of tobacco use.

Although treatment can help a smoker quit, it is often difficult for the addicted smoker to quit. There are a number of reasons why treatment is less appealing to the smoker than the continued use of tobacco products, beyond the addicting properties of tobacco products. Tobacco products are designed to be appealing and the tobacco industry makes efforts to ensure that these products are easy to purchase at a cost that will not limit consumption. However, treatment medications are required to have demonstrated safety and effectiveness and they are intentionally not designed to be appealing so as to avoid overuse. The sale of treatment medications in most countries is highly regulated with limited access, usually through prescription, while tobacco products often are not regulated and are extremely easy to access. In some countries, including the US, nicotine replacement therapy is sold as an over-the-counter medication, without prescription, but this route of access is still heavily regulated. Similarly, behavioral therapy is often not conveniently available or is not easy to access; requires trained personnel and is labor intensive; and has been found to appeal only to certain groups of smokers (Henningfield 2002).

There are numerous reviews of effective cessation treatments. These include the United States Public Health Service Clinical Practice Guideline, London's Royal College of Physicians Report, and the Society for Research on Nicotine and Tobacco's Treatobacco.net website project (Fiore et al. 2000; Royal College of Physicians of London 1992; WHO/SRNT 2003). The reviews have shown the efficacy of pharmacotherapy, which can almost double the probability of achieving long-term abstinence from smoking. Behavioral treatment is also effective and when combined with pharmacotherapy can lead to substantially increased success with cessation.

The literature also encourages all healthcare personnel and clinicians to advise and counsel their patients to quit smoking (Ockene 1987). Healthcare professionals can serve a critical role in reducing the serious consequences of the tobacco epidemic. As key opinion leaders, experience indicates that all health professionals, including doctors, dentists, nurses, and pharmacists, should be encouraged to be non-smokers and offer smoking cessation counseling as a standard practice.

As shown by substantial evidence, tobacco cessation treatment should be one component of comprehensive tobacco control efforts that include increasing taxes on tobacco, restricting public smoking educating the public about the dangers of tobacco and benefits of cessation, and restricting tobacco product advertising and marketing. Societal factors are critical to promoting non-smoking as a cultural norm. Policies to control tobacco use must be seen as the driving force for cessation efforts, treatment utilization, and support for abstinence from tobacco use (NCI 1991).

4.1.3.8 Youth access

Reducing youth access to tobacco products is a key component of a comprehensive tobacco control program. Reducing the demand by youth for tobacco products is also important. But even more important is restricting the supply and easy access to these highly addictive products by children. Minimum age laws can help restrict youth access to tobacco products and they are currently in effect in many countries around the world. However, to be effective these laws need to be strictly enforced and merchants must be required to demand proof of age for any customer who appears to be underage. Strictly enforcing youth access laws sends a message to the public that tobacco control is a serious matter.

However, when laws restricting children's access to tobacco products are not enforced, then youth purchase cigarettes from all available sources (USDHHS 1994). Studies have found that making it more difficult and expensive for children to buy cigarettes reduces youth smoking (Stead and Lancaster 2000). In the US, a survey conducted in 1998 reported that 90% of children 15 to 16 years of age could purchase cigarettes easily or very easily (Johnston et al. 1998). In the UK a 1996 survey found 25% of all secondary school children tried to purchase cigarettes in the previous year with only 38% being refused (Jarvis 1997). In many countries, such as Japan, vending machines provide extremely easy access to cigarettes leading to more difficulty in controlling youth smoking rates. Banning vending machines is more effective to reduce access by children than fitting them with locks or limiting the hours of access by children (Forster et al. 1992).

Actually enforcing laws prohibiting sales of cigarettes to children can reduce youth smoking rates. However, voluntary programs asking retailers not

to sell cigarettes to children, such as those programs promoted by cigarette companies, are not effective (DiFranza and Brown 1992). It seems that aggressively enforcing youth access polices and taking a comprehensive approach to this issue can lead to significant reductions in youth smoking. Studies have demonstrated that interventions to teach retailers how not to sell to underage customers can lead to decreases in the number of outlets selling tobacco to youth (Stead and Lancaster 2000). However, there needs to be compliance with the policies for these results to be seen. Some studies have indicated that compliance rates must be over 80% to see meaningful effects in both reduced sales and changes in youth behavior (Rigotti et al. 1997). In addition the effectiveness and feasibility of retailer interventions depends on attitudes and resources in countries to tackle this difficult problem (Stead and Lancaster 2000).

In many countries, cigarettes are sold in 'kiddie' packages (small packs of cigarettes with less than 20 cigarettes) or by street vendors by the 'stick.' These small packs or loose individual cigarettes appeal to children because they are easier to purchase since the cost is lower. In addition, individual cigarettes do not contain warning labels and are easier to conceal. Legislation to prohibit the sale of single sticks or "kiddie packs" is a necessary policy initiative to prevent and reduce the use of tobacco products by youth.

In the United States, youth access-related laws and their enforcement have been strengthened in the last decade, significantly reducing the rate of illegal sales and building community awareness of and support for tobacco control. While recent research conducted in the United States calls into question whether laws governing sales to minors can actually reduce youth smoking rates, these laws remain an obvious reflection of societal norms concerning the use of tobacco by young people (Rigotti et al. 1997; Forster et al. 1998).

Another approach:

"In 2002, legislation in the province of Saskatchewan [Canada] was enacted prohibiting the visible display of tobacco product packages in any store where minors have access. This groundbreaking measure, preceded only by Iceland, was strongly opposed by the tobacco industry. The legislation curbs an important form of promotional activity. The province of Manitoba subsequently adopted similar legislation to become law on 1 January 2004."

4.1.3.9 Tobacco litigation

Tobacco litigation is now proving to be a useful and productive strategy, after far more limited success previously. This strategy has transformed the tobacco control landscape in the United States. However, even though the Tobacco Industry has lost some major cases, they still manage to win a large share of cases brought against them (Sugarman 2002). Other countries are now beginning to employ this tobacco control strategy. Tobacco litigation is not a new strategy and

it has not always been successful or easy, even in the United States. From 1954 to 1996 the tobacco industry was uniformly successful in not paying any settlements and employed tactics that made cases extremely expensive and time consuming to pursue. Individual smokers brought these early cases against the tobacco industry. The tobacco industry offered in its defense that smokers had made a personal decision to smoke despite the mandated health warnings on cigarette packs since 1966. Smokers were blamed for their poor judgment and lifestyle. However, beginning in the 1990s, litigation in the United States moved forward on other bases, including class action cases, third party reimbursement actions and secondhand smoke issues (Daynard et al. 2000).

As a result of successful litigation, the tobacco industry has been forced to pay large settlements of approximately 10 billion dollars per year to reimburse States for healthcare expenditures resulting from tobacco use. The largest settlement to date in the United States occurred on November 23, 1998, amounting to more than US$200 billion. The Attorneys General and other representatives of 46 states, Puerto Rico, the US Virgin Islands, American Samoa, the Northern Mariana Islands, Guam and the District of Columbia signed an agreement (the Master Settlement Agreement) with the five largest tobacco manufacturers (Brown & Williamson Tobacco Corporation, Lorillard Tobacco Company, Philip Morris Incorporated, R.J. Reynolds Tobacco Company, Commonwealth Tobacco, and Liggett & Myers). This ended a four-year legal battle between the States and the industry that began in began in 1994 when Mississippi became the first state to file suit. Four states (Florida, Minnesota, Mississippi and Texas) had previously settled with tobacco manufacturers for $40 billion (National Association of Attorneys General (NAAG) 2003).

This Master Settlement Agreement resulted from the states taking action to recover their Medicaid costs for treating diseases attributed to smoking. In addition, the state law suits forced the tobacco companies to release millions of pages of their internal documents disclosing fully some of their secret strategies and covert operations. However, while the states were able to recover substantial ammounts from the tobacco industry, theys were not required to use the funds for tobacco control or other health-related programs.

Unlike the United States, Japan does not have a 40-year history of tobacco product-related illness litigation. The decision rendered in the Tokyo District Court in October 2003, denied all plaintiffs' claims in Japan's first significant lawsuit for tobacco-related illness (Levin 2004). Decisions like this were handed down for many years in the US before the recent wave of tobacco litigation, which has led to some sucesses.

A brief overview of the Master Settlement Agreement (NAAG 2003)

Public health/youth access restrictions

Prohibits youth targeting in advertising, marketing and promotions by:

- Banning cartoon characters in advertising
- Restricting brand-name sponsorships of events with significant youth audiences
- Banning outdoor advertising
- Banning youth access to free samples
- Setting minimum cigarette package size at 20 (sunsets 12/31/01)
- Creates a National Foundation ($250 million over the next 10 years) and a Public Education Fund ($1.45 billion between 2000-2003)

Changing corporate culture

- Requires the industry to make a commitment to reducing youth access
- Disband tobacco trade associations
- Restricts industry lobbying
- Opens industry records and research to the public

Enforcement

- Provides court jurisdiction for implementation and enforcement
- Establishes a state enforcement fund ($50 million one-time payment)

Attorney fees (funded separately from the $206 billion in payments to states)

- Requires the industry to reimburse states for attorney fees (reimbursement will be based on the market rate in each state)
- Requires the industry to pay for outside counsel hired by the states
- The settlement agreements does not effect contracts states have with outside counsel, but permits states to seek reimbursement from the settlement if the state has paid the fees of an outside counsel and the outside counsel fails to pursue either a liquidated fee agreement or arbitration, through the settlement
- Outside counsel can either negotiate a liquidated fee agreement or go through arbitration
- The liquidated fee agreements will be paid from a $1.25 billion pool over a four-year period
- The industry will pay whatever the arbiters award, but payments will be subject to a $500 million per year cash flow cap

Financial Provisions

- States will receive over $206 billion over 25 years
- Up-front payments - $12.742 billion
- Annual Payments, beginning April 15, 2000 - $183.177 billion through 2025

- Strategic Contribution Fund, 2008-2017 - $8.61 billion
- National Foundation ($250 million over the next 10 years)
- Public Education Fund (at least $1.45 billion 2000-2003)
- State Enforcement Fund ($50 million, one-time payment)
- National Association of Attorneys General ($1.5 billion over the next 10 years)

Other litigation

In 1999, two large jury verdicts against Philip Morris by individual smokers led to large punitive damage awards, as well as compensatory damages (Henley v. Philip Morris Inc. 1999; Joann Williams-Branch v. Philip Morris 1999). The tobacco industry documents proved valuable in securing these awards. A class action suit on behalf of injured or deceased smokers (Engle v. RJ Reynolds Tobacco 1999) was also successful initially because of the industry documents. In the Engle case it has been said that "when the documents have been introduced, jurors see the defendants as greedy, callous, deceptive, and manipulative an rule for the plaintiffs, often awarding punitive damages to boot (Daynard 2000)." However, not all of these cases have been successful and juries continue to side with the industry against individual claims by smokers (Tobacco Control Resource Center 2003). Other countries have been using litigation involving private individual cases as well as class action and reimbursement cases. Individual suits against the tobacco industry have been filed in some other countries including Argentina, Ireland, Israel, Finland, France, Japan, Norway, Thailand, and Turkey.

Third-party reimbursement cases that are modeled after the successful state Medicaid reimbursement cases continue to be filed. Even Native American tribes are suing the tobacco industry for funds to treat the high incidence of disease found in this population. The US Federal Government has sued the tobacco industry to recover costs associated with Medicare, veterans, and military health programs and to penalize the industry for profits that wer made using illegal strategies. This lawsuit seeks to "disgorge profits the industry has received as a result of its violation of the Racketeer Influenced and Corrupt Organizations Act" (US Department of Justice v. Philip Morris 1999).

In a recent verdict, an Illinois Circuit Court judge found Philip Morris USA liable in a class-action consumer fraud lawsuit and ordered the company to pay $10.1 billion for failing to inform consumers that its "light" cigarettes were not less harmful than full-tar cigarettes.

A major element of the ruling was that Philip Morris, a unit of Altria, knew that light and low-tar cigarettes were actually more harmful than their regular counterparts because of increased ventilation in the reduced-tar product, which allows more toxic smoke to be inhaled by consumers. A report issued by the National Cancer Institute in November 2001 concluded that the tobacco industry

for decades has deceptively marketed light cigarettes as reducing smokers' health risks despite knowing from their own research that these cigarettes were no safer than regular brands (NCI 2001). Based on internal tobacco industry documents, the report found that the tobacco companies intentionally manipulated the design of their light cigarettes to produce less tar when tested by government testing machines, but not when smoked by actual smokers who changed their smoking habits to maintain nicotine levels. Philip Morris was to pay $3 billion in punitive damages to the State of Illinois and $7.1 billion in compensatory damages to smokers of light cigarettes. Philip Morris was also ordered to pay $1.78 billion in lawyers' fees. In order to appeal the verdict, Philip Morris said it would have to post a $12 billion bond. This is the first light, or low-tar, cigarette case to reach trial. It is also one of the few class-action lawsuits to be certified against a tobacco company. In this case, the class consists of 1.1 million Illinois smokers who bought Marlboro or Cambridge Light cigarettes from 1971 to February 2001 (Day 2003).

4.1.3.10 Research

In summarizing the South African experience, Dr Yussuf Saloojee, Director of the National Council Against Smoking, ascribed the country's success to the bold leadership of the Health Minister and then-President Mandela, and identified several other contributing factors, including
Production of sound epidemiological and economic data on tobacco use in South Africa by the Medical Research Council and the School of Economics of the University of Cape Town.

Research is not an end in itself; it needs to be conducted in a timely manner and focus on priority issues. It needs to address the important questions asked by relevant stakeholders and, at the same time, begin to lay the foundation for answering key questions that are likely to be asked in the future. Tobacco control-related research needs to be relevant to the policy context; it needs to support and drive public health policy development and implementation.

The scope of tobacco control research is broad and ranges from molecular studies of addiction pathways to epidemiological studies of cancer incidence, psychological studies of the impacts of tobacco advertising, and policy-related studies on the most effective legislative approaches to reducing tobacco use. Controlling tobacco use is complex and involves genetic, bio-behavioral, social, political, economic and cultural factors. Research to address this problem must span the entire continuum and be trans-disciplinary in nature. Tobacco control research involves building:

1. The research infrastructure to pursue observational, intervention, and policy research of local importance, and
2. Capacity within the country for conducting epidemiological, behavioral, and policy research; and for providing related prevention, treatment, communications,

and health services.

In Canada:

Research on Canada's experience with tobacco, such as smoking rates and costs of tobacco use, was essential in informing the public and Parliamentarians.

The collection and synthesis of data, the interpretation of outcomes, and the dissemination of information from existing studies are also part of the research continuum. Each country needs basic information about the health consequences of tobacco use on its citizens and tools for tracking the course of the epidemic. Careful monitoring and surveillance is necessary to provide this accurate and up-to-date information. Information is also required to determine the impact of the tobacco epidemic on important population target groups and to provide the necessary data to influence policy makers to make evidence-based decisions to promote the health of the population. Implementation and program management measures should also be developed to track tobacco program efforts. These data will help assess program effectiveness and determine if the programs have been efficient. Local evidence needs to be used in combination with, and build linkages to, the voluminous external evidence on causality and associations of tobacco use with disease already reached by expert groups and governments throughout the world. In addition, economic data on the costs associated with tobacco use and the economic effects of tobacco control interventions are essential to policymakers contemplating comprehensive legislation. Legislative research also becomes increasingly important as individual countries have success in combating the tobacco industry through legal and regulatory approaches.

4.1.4 Implementing comprehensive tobacco control

4.1.4.1 Partnerships

A strong international partnership drove the development of the Framework Convention on Tobacco Control (FCTC). This partnership included a wide range of multi-lateral, bi-lateral and non-governmental organizations (e.g., the Framework Convention Alliance). In collaboration with its Member States, the World Health Organization (WHO) established a network of regional and national focal points to coordinate participation in the FCTC development process. A consensus was forged out of this complex process that was, at times, both tedious and painful. This is the first time that a global treaty has focused on a health issue and this is the first time that low-, medium- and high-income countries have united to develop a collective response to chronic diseases. The FCTC establishes a logical scientific, technical and policy framework for controlling the tobacco epidemic but also shows a model of how diverse groups can work together on a complex and difficult issue. National governments need to create and nurture partnerships involving the public, non-governmental organizations and local

government in developing and implementing comprehensive tobacco control plans. Each country needs a network of individuals and organizations that share information and expertise and work in a coordinated fashion to implement tobacco control. Since tobacco control is a highly multidisciplinary field, it requires a wide range of individuals engaged in tobacco control activities, including researchers, public health professionals, economists, lawyers, advocates, political scientists, business people and politicians. Coalitions have been an effective tool used to bring together these diverse groups and individuals. It is crucial that there are mechanisms that facilitate communication between the different groups and individuals so they can work synergistically toward common objectives.

In many cases, the FCTC process has already built networking capacity and multi-sector cooperation at the national level. Multiple countries established formal inter-ministerial committees to prepare for the FCTC negotiations. These committees gave different ministries (health, finance, customs, agriculture, etc.) the opportunity, often for the first time, to discuss and address the domestic burden of tobacco. Now that the negotiations are complete these committees need to continue to meet. If not already present, a government office dedicated to tobacco control must be created in order to facilitate the implementation of legislation in accordance with FCTC obligations. National tobacco control networks should also include nongovernmental organizations and professional societies dedicated to controlling tobacco use. Throughout the FCTC negotiations, the Framework Convention Alliance (a network of individual NGOs, organizations, and existing coalitions/alliances working at national, regional and international levels to support the development of a strong FCTC) demonstrated the effectiveness of NGOs working together in encouraging policymakers to remain committed to the overarching public health objectives of tobacco control.

Importantly, every country needs local tobacco control champions or individuals. These individuals could come from a wide variety of organizations and interest groups but must have a demonstrated interest in tobacco control. These individuals should be capable of mobilizing public opinion and be knowledgeable about how to support policy change in culturally appropriate ways. These 'tobacco control champions' are a critical element of national capacity. Efforts to identify new motivated individuals and keep them engaged demands a systematic approach to health leadership development and a long-term commitment and investment from tobacco control partners with resources and experience.

4.1.4.2 Practical approaches to comprehensive tobacco control

Policy, legislation and an action plan comprise the broad elements of a comprehensive approach to tobacco control. Policy reflects the political mandate

to control tobacco use; legislation provides the legal framework to support tobacco control; and the action plan serves as the pragmatic roadmap for actually doing tobacco control. While countries may differ somewhat in how they address these elements, they cannot be ignored if the tobacco epidemic is to be controlled in an effective and timely manner. The WHO has emphasized that policy and legislative approaches for both health promotion and health protection are essential components of any national effort to control tobacco use (USDHHS 2000). In light of this, what does an effective approach to comprehensive tobacco control look like in practice?

> "Review of past studies on the political process of smoking control legislation distilled several common factors contributing to success: strong coalitions, commitment of medical communities, executive branch influence, sympathetic political will (leadership), international networks, issue framing and media involvement" (Sato 1999).

The state of California has had the largest and most comprehensive tobacco control program in the US. In November 1988, the Tobacco Tax and Health Promotion Act (Proposition 99) was passed by California voters, mandating the development and implementation of the California Tobacco Control Program. The 1999 fiscal year budget in California for the tobacco control program was $126.8 million ($3.90 *per capita*) for tobacco control efforts funded by the Department of Health Services and the Department of Education. California adopted the framework developed by the National Cancer Institute for the ASSIST program (USDHHS 2000), which focused on changing social norms. The goal of this approach is to "indirectly influence current and potential future tobacco users by creating a social milieu and legal climate in which tobacco becomes les desirable, less acceptable, and less accessible (State of California 1998)." The four broad priority areas which were adopted for program planning and funding were: 1) protecting people from exposure to SHS, 2) revealing and countering tobacco industry influence, 3) reducing young people's access to tobacco products, and 4) providing cessation services (State of California 1998). The California program has developed a very strong media campaign, which receives about 22% of their funding (State of California TCS 2003a). The media campaign focuses primarily on changing the public opinion concerning smoking and raising public awareness of the tobacco industry's efforts to manipulate and deceive the public concerning the dangers of smoking and exposure to SHS. The California program also places considerable emphasis on developing a broad statewide infrastructure that reaches into communities across the State (State of California TCS 2003b). The program also funds the Tobacco-Related Disease Research Program (TRDRP). The mission of TRDRP is to "support research that focuses on the prevention, causes, and treatment of tobacco-related disease and the reduction of the human and economic costs of tobacco use in California." Since the inception of the research program, $305,013,863 has been expended to fund 944 grants to 77 institutions in the State of California (Tobacco-Related Disease Research Program 2003). In addition,

ongoing surveillance and evaluation is funded to assess the program performance and impact. Since the passage of Proposition 99 in 1988, the adult smoking prevalence in California has declined significantly from 22.8% in 1988 to 17.4% in 2001. Since 1988, *per capita* cigarette consumption in California has declined by 60%. During the same period, per capita cigarette consumption in the entire nation (including California) declined by 34% (State of California TCS 2003b).

THE CALIFORNIA SMOKEFREE INDOOR WORKPLACE LAW

Starting in 1990 with the City of Lodi, an accelerating proliferation of city and county clean indoor air ordinances swept across California in response to Program and local coalition activities. Community after community raised the issue and experienced what the Program's media campaign termed "the invasion of the tobacco people." These struggles were highly educational, the process proved healthy for local tobacco control and capacity building, and in 1994 a state law was passed prohibiting smoking in most California workplaces. At that point, when California communities were receptive, the Program began to emphasize the effective implementation of the new law and to promote other local policies that would close the loopholes in the state law.

One notable exception to California's 1994 Smokefree Indoor Workplace Law was a two-year postponement of the smokefree requirement for bars and gaming clubs. This was particularly objectionable because it permitted smoking in the bars of restaurant-bar combinations. After one single-year extension was enacted by the state legislature and subsequent efforts by the anti-tobacco constituency to fight off numerous attempts to pass yet another extension, the bars and gaming clubs exception expired on January 1, 1998, and smoking in California bars became illegal.

The challenge then became to implement the new smokefree bar law, and to avert a damaging reversal that could weaken the entire Smokefree Indoor Workplace Law. The Tobacco Control Program emphasized education of the public and the bar-restaurant industry. Ads showed bartenders and waitresses asking for protection from secondhand smoke where they work. Local programs made educational visits to bars. Packets of information and local training sessions were provided to both bar owners and local code enforcers across the state. Despite a multi-million dollar tobacco industry public relations campaign to provoke bar owners to resist and disobey the law, the antitobacco constituency succeeded in thwarting efforts in the legislature to revoke the law during its difficult first year. Recent opinion polls show that the law is widely supported by the general public.

Both Thailand and Poland share a common tobacco control history: a history in which multinational tobacco companies successfully penetrated the country but were ultimately defeated by tobacco control advocates through the enactment of comprehensive legislation. Common denominators in the political process included: solidarity amongst local coalitions, strong and vocal health agency allies, political champions, support from international tobacco control agencies, and media advocacy. The stories of both countries show how rapidly progress can be made.

The "Thai Cigarette Case" became world renowned as a defeat in trade but a victory in health. In 1989, the United States Trade Office, under Section 301 of its 1974 trade act, accused Thailand of unfairly restricting imports of US cigarettes and cigarette advertising. Major multinational tobacco companies (Philip Morris, RJ Reynolds, and BAT through the US subsidiary Brown and Williamson) petitioned the US trade representative (USTR) to invoke trade sanctions against Thailand unless the country complied with the following demands: allow import of foreign cigarettes, reduce tariffs, repeal laws banning

advertising, and expand distribution. Similar trade threats by the USTR were made in Japan, Korea, and Taiwan. All these three countries capitulated and were forced to allow tobacco advertising. It seemed unlikely that a small developing country such as Thailand would be able to counter US trade threats.

The US demands were seen as neocolonialistic and triggered strong vocal protests by health groups in both Thailand and US. The case was widely covered in the national and international media as a form of US aggression. In response to the adverse publicity, the USTR referred the investigation to the General Agreement on Tariffs and Trade (GATT), the Geneva-based international trade resolution panel. Prior to a GATT ruling, Thailand quickly acted to pass a comprehensive tobacco control bill that required a total ban on advertising and promotion, prominent health warnings, restrictions on public smoking, and a multimillion dollar tobacco control program. Thailand also petitioned GATT to allow WHO to testify on the health effects of tobacco and other possible adverse effects of opening previously closed markets.

Thailand eventually lost the case and was forced to allow cigarette imports. However, GATT, referencing WHO recommendations, went on to delineate nondiscriminatory policies that would allow countries to protect the health of their populations without bans on cigarette imports. Such measures allowed under GATT included: ad valorem taxes, advertising bans, price restrictions, ingredient disclosures, strong warning labels, and even a ban on brand names and imagery. GATT's reference to these measures undercut multinational companies' ability to rapidly penetrate the market and gain new customers. GATT's ruling represents one of the most important achievements for international tobacco control in the last decade. It is a clear message from the world's trade body that developing nations have the right to protect health by keeping their cigarette markets noncompetitive.

Lessons learned from Poland's struggle with multinational tobacco companies are similar: enacting comprehensive legislation proved key to controlling industry abuses and reducing consumption. The democratization of Poland in the late 1980s led to the privatization of the tobacco industry. By the 1990s, 90 percent of the tobacco industry belonged to multinationals who saw Poland's large number of heavy smokers as a prize market. The takeover of the Polish tobacco companies by the multinationals, the use of state-of-the-art marketing techniques, and the increased productivity, all suggested increased consumption rates to come in a country that already had very high rates of smoking and of smoking-caused disease. However, the emerging civil society and independent mass media brought new opportunities for tobacco control. Health advocates, acting in coordination with international tobacco control agencies, used the media to widely disseminate information on the health crisis of the nation and pointed to cigarette use as one of the leading causes of cancer and mortality.

POLAND'S TOBACCO CONTROL LEGISLATION:

- Protects the right of non-smokers to live in a smoke-free environment
- Promotes a tobacco-free life style
- Creates legal and economic conditions to encourage reduction in tobacco use
  Informs the public about the adverse effects of smoking and the levels of harmful substances through messages on tobacco packages and in advertisements in magazines for adults
- Decreases the maximum levels of harmful substances in tobacco products
- Provides treatment and rehabilitation of tobacco-dependent persons in public health facilities free of charge
- Prohibits smoking in health and educational institutions and other public buildings, with specific authorization for local government to restrict smoking in additional places
- Prohibits the sale of tobacco products to minors, including sales through vending machines and in packages of fewer than 20 cigarettes
- Prohibits production and marketing of smokeless tobacco
- Prohibits advertising and promotion of tobacco products on television and radio, in cinemas, newspapers, magazines for children and teenagers, in educational and cultural institutions, and in sports facilities
- Requires on each package of cigarettes two different warnings on the adverse effects of tobacco and on levels of tar and nicotine contents, with the messages covering 30% of each side of the cigarette pack
- Provides penalties of imprisonment and fines for violating the law

In 1995, Poland passed the Law for the Protection of Public Health against the Effects of Tobacco Use by an overwhelming 90% of the vote. Poland's tobacco control legislation is today considered one of the most comprehensive. WHO has called Poland's tobacco control program "an example to the rest of the world." The box below provides a brief list of some of Poland's legislative components. Reduced consumption and gains in health have already been seen.

These case studies demonstrate that changes can occur when a comprehensive and concerted effort is taken to reduce tobacco use. The lessons learned from these case studies and efforts in many other countries is that in order to reduce the serious and devastating health and social consequences related to smoking and tobacco use, countries must establish comprehensive tobacco control programs. Nothing else will successfully compete against the multinational tobacco companies' intense advertising and marketing, their strong political influence and the powerful addictive drug that they sell.

These comprehensive programs need to have political support and funding to achieve their goals. Programs must be sustainable because it takes time to change social norms concerning tobacco use. While some short-term changes in attitudes concerning smoking and tobacco use may occur in a population, it takes many years to actually perceive behavior and cultural changes. Stopgap or partial measures may help address some short term issues but are not the answer and cannot help countries in ending the epidemic. It is important to understand that without concerted and coordinated actions, the necessary decrease in death and

disease will not be possible. While we have discussed many different elements and approaches to tobacco control in this chapter, the overarching principle is that for tobacco control to be effective countries need to develop their own vibrant tobacco control community capable of offering effective program and policy options and influencing the public awareness. Funding for tobacco control programs must be sufficient and under-funded efforts have little effect against the tremendous resources of the tobacco industry. The most effective approach to controlling tobacco use is to establish a well-funded and sustained comprehensive program that employs a variety of approaches. While employing one or two approaches is useful, a more powerful effect can be achieved when components are combined and a synergistic effect is created. Individual countries can determine the components of the program that best reflects their societal structure and culture. Using local and international research, countries can determine how to best construct a comprehensive effort that can attack tobacco use from a systematic approach.

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4.2 Tobacco Control in Japan

4.2.1 Intervention program development in Japan

4.2.1.1 Background

There are few published studies evaluating the effects of smoking cessation intervention and behavioral research programs in Japan. While smoking cessation programs have been implemented at schools, worksites and community settings for decades, most have been small demonstration projects that do not incorporate appropriate research designs and are not grounded in behavioral science and theory.

Table 4.4 summarizes tobacco intervention studies presented at the Japanese Society of Public Health Annual Meeting of 2001 and 2002, the biggest scientific meeting on public health in Japan. Among 12 studies, only one used a random sampling method to choose an intervention group. Five studies compared the intervention group with other groups, but only three used comparable control groups. In terms of intervention itself, only three studies employed a theory or model to build the intervention program. Although abstracts do not always include all information required, the table illustrates that intervention studies in Japan are still generally immature in design.

Historically, public health activities in Japan have been planned and implemented mostly by the public sector, primarily the national and local governments and their branches. Program evaluation is rarely a requirement because of budget limitations and thus programs and practice are not informed by research or science.

Table 4.4 Summary of Intervention Studies on Smoking Cessation and Prevention Presented at the Japanese Society of Public Health Annual Meetings of 2001 and 2002 (Listed from Abstract Books, 2 years, No Overlapping)

Name Abstract No. Year	Setting	Target	Number of Targets	Sampling Method	Control Group	Intervention Method and Theory	Outcome (Quitting rate)
K. Suzuki 02M10-3 2001	School	Elementary (6th grade) & junior high school (1st-3rd grade) students	Elementary: 108, Junior high: 404	Convenient sampling	Comparison with previous research in 2000	No description	Increased knowledge of smoking and positive attitude to the prevention of passive smoking
M. Kise 02P2-22 37377	School	5th grade students in two elementary schools	139 students out of total 228	Convenient sampling	218 out of 228 students in two other schools	Lectures (45 min_3)	Targets developed a more negative image of smoking than controls
S. Tarayama 02P2-29 13 Sep - 19 Dec 2001	Community	Residents who want to quit smoking	Male: 10, Female: 4	No description	None	Lecture, counseling, NRT, e-mail & telephone tutorials, meeting with participants	71.4% (3 months later)
K. Morishita 02P2-44 No description	Community	Participants in a quit smoking contest	244 people	Convenient sampling	None	No description (3 months)	42.2% (M:46.5%, F:12.9%); 26.3% (20-29 years of age), 58.5% (over 70)
Y. Harima 02P2-53 Jan-Feb 2002	School	High school students	158 students	Convenient sampling	None	Posting educational materials about Tobacco in school's restrooms	Slightly decrease in attitude toward future smoking
A. Suziki 02P3-89 2001	Community	Pregnant women	No description	No description	None	Lectures in prenatal classes	No description
Y. Takahashi 01 2-19 1998	Internet	Participants in a stop smoking program, who used NRT	88 participants	Convenient sampling	None	NRT and/or e-mail counseling	61% (6 months later), 56% (1 year later); No difference by NRT use
M. Nakamura 01 2-25 No description	Health check-ups at work place, community and clinic	People receiving a health check-up	1189 people	Random	1125 people	Optimum intervention to each stage: precontemplation, contemplation, and preparation. Follow-up for 3 months. Transtheoretical model	6 months: 3.1% (intervention group), 1.7% (control group). Contemplation stage; 3.2% (intervention), 1.7% (control). Preparation stage; 11.5% (intervention), 4.8% (control).
H. Miyasawa 01P2-92 No description	School	Female college students attending stress management classes	109 students	No description	Another 109 students taking a class on smoking hazards	Lecture (90 min) and selective work: excises (39 people), craft (35) and perfume (35).	Significantly reduced smoking rate in the stress management class, especially in the exercise group
C. Takahashi 01P2-93 2000	Community & work place	People who are interested in quitting	29 people (contemplation stage: 13, preparation stage: 16)	No description	None	Lecture and 6 telephone tutorials during the session. Follow-up telephone tutorials 1 and 3 months later. Transtheoretical model	3 months: 28% (overall), 56% (preparation stage), 60% (contemplation stage)
T. Onishi 01P2-94 1999-2001	School	Junior high school students	230 students	Convenient sampling	1) senior students. 2) a preliminary study	1. Knowledge, 2. Role playing for rejection, 3. Advertising literacy, 4. Anti-smoking ads production. Life skill	1) 50% reduction in the number of students intending to smoke at the age of 20. 2) Increased number of students intending to reject the offer of tobacco from friends or seniors
S. Ninomiya 01P2-102 2000	Community	People at a stage of contemplation and preparation who are interested in quitting	19 people	Convenient sampling	None	Quit smoking sessions and tutorials by public health nurses. Transtheoretical model	0.316

In addition, public health workers do not possess the knowledge and skills to plan, implement and evaluate behavioral research programs. Japan has only one School of Public Health, which has been under the Ministry of Health, Labor and Welfare since 1938. Thus, there are limited educational opportunities for public health workers to obtain the necessary training or experience in this area of research. In the clinical setting, only very recently have nurses and physicians considered smoking an important health issue. The smoking rate among nurses exceeds that of the general female population while that among male physicians is lower than in the general male population but nevertheless much higher than in other developed countries.

The mass media in Japan have ignored the problems of smoking for many years. The lack of attention to this serious health issue may reflect the large revenue received from the tobacco industry for cigarette advertising.

Only relatively recently have large studies with appropriate theory-based designs been carried out and reported in Japan. Some of these are discussed in the following sections.

4.2.1.2 Intervention for different groups

School settings

This section describes educational programs for smoking prevention conducted in school settings from elementary school to university, including professional schools (excluding medical and nursing schools). School-based prevention research is, however, limited. These programs do not seem to be informed by research from other developed countries where large-scale smoking prevention programs have been conducted. However, some recent studies have begun to use quasi-experimental designs to evaluate the effectiveness of various types of programs for high school and elementary studies. Smoking prevention self-learning materials have been developed and studies have tested their effectiveness.

Takahashi et al. (1995) developed smoking prevention self-learning materials for junior high school students featuring a role-playing game system. This program focusses not only on the health hazards of smoking but also on dependence and the social impact of smoking behavior. A quasi-experimental intervention study was conducted to evaluate the effectiveness of this program. A junior high school of 500 students was assigned as the intervention school and another of 477 students as the control. Knowledge of smoking and its health implications were significantly increased in the intervention group at two months after the program. Attitudes towards smoking became negative in some subgroups of the intervention group. However, there was no difference in current smoking status or the intention to future smoking between the two groups.

Nishioka et al. (1996) conducted a quasi-experimental intervention study at elementary schools in 1992 and 1993. An intervention group consisting of 106 fifth graders underwent a series of smoking prevention sessions, and a control group in the same grade was selected from another school in the same city. The study found a remarkable effect on knowledge of the health hazards of smoking and toxic substances in smoke. No effect was shown on intention to smoke at age 20 or self-efficacy in refusing tobacco use. The effect on current smoking was not clear.

Kawabata et al. (1999) studied the relationship between self-esteem and smoking behavior among Japanese early adolescents as part of a three-year longitudinal intervention program on smoking prevention in the school setting. Baseline data were reported in 1999.

In 2002, the Education Committee of Wakayama Prefecture introduced a smoke-free school policy that prohibits all tobacco use anywhere within public schools, including the school grounds around the buildings. The purpose of this policy was to protect children from exposure to secondhand smoke and

to discourage them from smoking by showing teachers as non-smoking role models. Several education committees, including those of Inuyama City (Aichi Prefecture), Kuwana City (Mie Prefecture), Kasai City (Hyogo Prefecture) and Saga City (Saga Prefecture) have followed Wakayama Prefecture's initiative, and many municipalities and even individual schools plan to adopt the policy. Short- and long-term evaluation studies are required, including sustainability and impact on smoking rate among students and teachers.

Occupational settings

Developed countries such as the US have had decades of experience in developing, implementing and evaluating smoking cessation programs and the creation of smoke-free worksites. Japanese researchers could benefit from the knowledge obtained from these previously conducted and well-evaluated programs so as not to redo already established links between smoking cessation programs and positive outcomes (Moher et al. 2004). A few Japanese studies have found that smoking cessation programs at work have helped smokers to quit smoking.

Muto et al. (1998) conducted a six-month smoking cessation program called 'Smoke Busters' at a chemical company. The abstinence rate of 35 participants was 22.9% at one year after the intervention, which was higher than the 5.7% of the age-, sex- and job category-matched control group.

Shimizu et al. (1999) conducted a randomized intervention study in the Omihachiman City Office in 1993. Participants (n=53), volunteers from among current smokers in the city office, were randomly divided into intervention and control groups. The intervention group received intensive education for five months, including two group lectures and three individual counseling sessions. After the five-month intervention, smoking cessation rate in the intervention group (19.2%) was higher than that in the control group (7.4%), although not significantly so.

Kadowaki et al. (2000) conducted a randomized controlled intervention study at a radiator factory. All male smokers were randomly allocated to the intervention group (n=132) and the control group (n=131). After the five-month program of individual counseling by the participating medical doctor, cessation rate was 12.9% in the intervention group and 3.1% in the control group. Among those who succeeded in quitting, 48.6% maintained cessation at 18 month after the program's end.

Of more interest are research studies that evaluate the effects of smoke-free policies and their impact on Japanese workers. One such project conducted by Mizoue et al. (2000) reported the effect of workplace smoking restrictions on smoking behavior among workers in city government offices. A 12% lower prevalence of smoking and a 17% higher proportion of ex-smokers were found in workplaces with strict, no-smoking policies which banned smoking in the

workplace as compared to worksites with less restrictive policies and which allowed smoking in private offices and meeting rooms or established no-smoking hours. Moderate policies, such as work area smoking bans with designated smoking areas inside the workroom, had little impact on smoking behavior. This type of research is important for Japan and demonstrates how smoke-free polices can be implemented and are effective in encouraging cessation.

Community settings

Smoking cessation programs are frequently offered to smokers in the community by municipal or prefectural public health centers all over Japan. However, most are very small trials without any theoretical framework, and although some are appropriately evaluated and the results presented at academic meetings, few are ever published.

Health care settings

Higashi et al. (1995) conducted a randomized control trial to evaluate the effectiveness of a smoking cessation program at the annual physical checkup. The intervention group (426 men and 42 women) received a 2-minute smoking cessation guidance session with behavioral goal setting and a leaflet on how to quit, followed by an encouragement card one month after the initial intervention and a small gift for successful quitting at the 6-month follow-up. Quitting rate was 7.3% at 6 months and 10.1% at 12 months in the intervention group, but 4.4% and 5.3%, respectively, in the control. The difference at 12 months was statistically significant.

Terazawa et al. (2001) conducted a controlled intervention trial to evaluate the effectiveness of a new cessation program developed by Nakamura et al. (1995), which consisted of a single brief individual counseling session and four follow-up telephone calls. Two hundred and twenty-eight smokers visiting a company health center for an annual health checkup were randomly divided into two groups, 117 to the intervention group and 111 to the control. Smoking status questionnaires were administered before the counseling session to assess their stage in the change toward smoking cessation. Nurses who had completed training courses for the program then provided a series of stage-matched cessation counseling sessions to the intervention group. During these sessions, carbon monoxide in expired air and nicotine metabolites in urine were measured to enhance self-perception of smoking. Only those clients who set a quit date during their counseling session received follow-up telephone calls. The cross-sectional smoking cessation rates at 6 months and 1 year of follow-up were 6.2 times higher in the intervention group than in the control group. The continuous cessation rate at 1 year of follow-up was 7.6 times higher in the intervention group

Some physicians provide smoking cessation programs through the

Internet. No peer-reviewed articles on the effectiveness of on-line programs have been published.

Health care professionals

Smoking rates for health professionals remain high in Japan. A survey carried out among 2nd and 5th year medical students found the smoking prevalence was 25.1% in men and 8.8% in women in the 2nd year and 43.1% and 9.3%, respectively, in the 5th year. While these rates were lower than those in the general population, they are nevertheless high (Kawakami 2000). Awareness of the harmful effects of smoking and intention to perform smoking interventions were found to be quite low among Japanese medical students (Kawakami 2000). While the medical students surveyed knew that smoking caused lung cancer (97%), smokers were more likely to think smoking is not harmful. Knowledge of other smoking-related diseases was generally less than 50% and many of the medical students indicated that they had learned of the deleterious effects of smoking from places other than their medical classes.

Smoking rates among Japanese physicians were found to be 27.1% for men and 6.8% for women, about half the age-adjusted prevalence among the general Japanese population (Ohida et al. 2001). The rate for male physicians is high when compared to other developed countries such as the United States (3%) and United Kingdom (4%). The prevalence of smoking among female nurses in Japan was 18.6%, which was higher than the age-adjusted prevalence for the general female population. Only 15% of the nurses surveyed supported banning smoking in the hospital where they worked, whereas 81.6% supported restrictions on smoking (Ohida et al. 1999). Education for health care professionals is needed to provide understanding why tobacco control policies, such as establishing smoke-free hospitals and workplaces, would be beneficial. Smoking cessation programs geared exclusively for physicians and nurses is also recommended. Physicians and nurses are important role models and should be encouraging smoking cessation and tobacco control.

Mass media

The first anti-smoking advertisement in Japan was broadcast by the WHO Collaborating Center at the National Cancer Center in 1994 by a cable television network for a short period. Unfortunately, the audience was small and no evaluation study was conducted.

Hokkaido Television Broadcasting Co., Ltd. (HTB) started a campaign against smoking called "Delicious Clean Air Campaign: Come on 10,000 Quitters!" on a daily evening TV program, "Yugata Don! Don! (Evening Go! Go!)," on May 31, 2002. HTB is a commercial TV company that covers Hokkaido Prefecture in the northern part of Japan. The campaign included a series of everyday short

TV programs on various tobacco-related topics, presentation of smoke-free restaurants, the Quit Smoking Ashram and the "10,000 Quitters' Declaration." The campaign continued for 12 months, or more than 70 broadcasts. This was Japan's first long TV campaign against smoking.

4.2.1.3 Legislative intervention

New waves of smoke-free initiatives have been made in recent years, some of which are described below. Many are quite remarkable, often from local authorities and even very small towns in a few cases. In the last decade, the national government has promoted decentralization in various policy areas. Each local government has to seriously think of its identity with regard to policy development. In community health, all prefectures and many municipalities have developed a local version of the year 2000's "Healthy Japan 21" plan. Most of these local health plans have set tobacco as a priority target. Overall, experience shows that decentralization in health planning and administration is a supporting factor in the development of smoke-free initiatives by local authorities.

Ordinance to remove street-front cigarette vending machines

In 2001, an ordinance prohibiting the placement of vending machines for cigarettes, alcohol and adult magazines with street-frontage was promulgated by Fukaura Town in Aomori Prefecture. The ordinance mainly targeted cigarette vending machines, given that fewer than 10 alcohol and magazine vending machines were involved. The mayor and town council took this step, the first legislative action to control cigarette vending machines in Japan, to discourage the purchasing of cigarettes by minors.

Although Fukaura Town is a small municipality of 9,000 residents and the number of targeted vending machines was less than 40, the ordinance led to a nationwide dispute. The town officials also proposed subsidies for cigarette retailers to move cigarette vending machines from outside to indoors. During the 180-day transition period, town officials visited each cigarette retailer to encourage compliance. However, retailer opposition to the ordinance and to the town officials themselves was organized and nation-wide, involving national and local cigarette retailer associations, and at the end of the transition period only 8 of 36 cigarette vending machines had been relocated or removed.

Ordinance to prohibit smoking in designated street areas

On Oct. 1, 2002, Chiyoda Ward, one of the 23 special administration wards which together make up metropolitan Tokyo, and which includes the nation's busiest political and business areas, introduced an anti-smoking ordinance that prohibits smoking and discarding cigarette butts in designated areas, mainly

busy streets near railway stations (Figures 4.7, and 4.8). After a one-month respite period, officials started charging offenders a 2,000 yen ($19; $1=105 yen) fine. This is Japan's first non-smoking rule that carries a non-penal fine.

Figure 4.7 Streetside Signs Describing a Local Government's Non-smoking Regulation

Location: Ichigaya Station, Chiyoda Ward, Tokyo, 2003

Figure 4.8 Signs on the Sidewalk

Location: Ichigaya Station, Chiyoda Ward, Tokyo, 2003

Ward officials patrol designated non-smoking areas as teams of 6 or 7 members to avert trouble over the imposition of the fine. The patrollers are trained to show their ID first, then point out the violation to the offender and ask them whether they are aware smoking is banned on the street. At the end of November, one month after the initiation of the penalty, 749 people had been

fined, an average of 24 smokers a day. The number of discarded butts around Ichigaya Station, one of the designated areas, dramatically decreased following the enactment of the ordinance, from approximately 1,000 at the end of September 2002 to 38 one month later.

The mayor, who is himself a smoker, said that he believes it is no longer possible to rely on people to voluntarily keep the street butt-free. The ward has since expanded the designated non-smoking areas to several other stations.

As of April 30th 2003, for the first six months of full implementation, 2,892 people had been fined, of whom approximately 70% paid on the spot. Some offenders paid later by bank transfer. The delinquency rate was 17% of all offenders.

Many local governments are now interested in this non-smoking ordinance and some have expressed plans to introduce it.

Health Promotion Law

The national government introduced the Health Promotion Law in May, 2003 (enacted in 2002), which includes a provision on the responsibility of administrators for the prevention of passive smoking in public spaces. Although the act has no provision for penalties for offenders, all private railway companies except Japan Railway in the metropolitan area promptly adopted a smoke-free policy in all stations. Most city and prefecture offices followed suite.

Some restaurants posted signs saying "Because of the enactment of the Health Promotion Law, we have made this restaurant smoke-free. Thank you." Although there are no data on the number of restaurants and shops that have adopted a smoke-free policy since May 2003, awareness of passive smoking and smoke-free policies among Japanese have no doubt increased.

Warning labels on cigarette packs

Officials of the Ministry of Finance have announced that Japanese tobacco companies will be required to include more explicit health warnings on cigarette packaging by July 2005. The revisions - the first in 14 years - would bring Japan's regulations closer to the WHO's guidelines on cigarette packaging, set in May of 2003. Current labeling only says that cigarettes can damage one's health and warns against excessive smoking. Eight new warning labels will more directly address the risks of lung cancer, heart disease and stroke. The new warnings will also focus on the hazards to pregnant women and children and the nature of nicotine addiction. However, even these new warning labels are weak in comparison with those of countries such as Canada, Brazil and Thailand with their explicit language and graphic pictures covering most of the cigarette package. The eight new Japanese warnings still include vague language and do not have any graphic images. For example, the wording on one of the Japanese warnings says,

"Smoking is one cause of lung cancer for you. The risk of dying from lung cancer is epidemiologically estimated as about two to four times higher for smokers than for nonsmokers. (Details are shown at the website of the Ministry of Health, Labor and Welfare; http://www.mhlw.go.jp/…) " This is an improvement from the current Japanese labels, which state, "Be careful not to smoke too much as doing so may harm your health." The following statement was made by Dr. Eitaka Tsuboi of the Japan Medical Association concerning the new warning labels which they consider to be too weak: "Smokers need to be informed of the real risks of smoking, with information on specific diseases. Strongly worded rotating warnings are most effective." (Tobacco Under the Microscope 2002).

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4.2.2 Tobacco control policy development in Japan

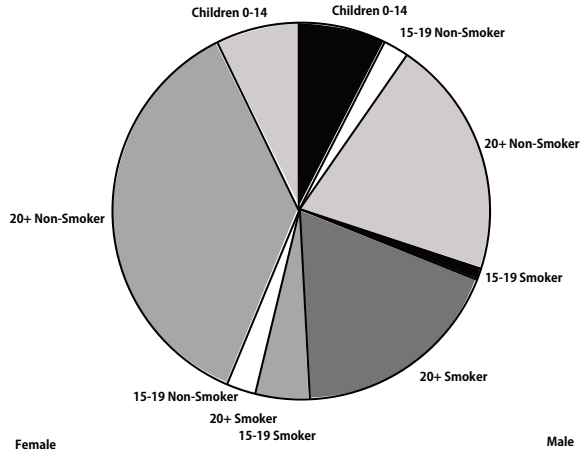
4.2.2.1 Background

Japan faces a unique and difficult policy dilemma in relation to tobacco control program development: the Government is responsible for the health and welfare of Japanese society; and the Government also owns a controlling interest in Japan Tobacco. In the short term, the revenue generated from tobacco use is significant; in the long term, rising public health costs associated with tobacco use will be enormous, overshadowing the short-term benefits of tobacco sales.

To add to the complexity, the Finance Ministry holds a nearly 50% share of Japan Tobacco, Inc. (hereafter JT), and, upon retirement, top officials of the Ministry of Finance often assume high level positions in JT. In short, the Government officials responsible for overseeing JT and those responsible for operating JT have a shared interst in maintianing and maximizing profits of JT. From a public health perspective, this is an 'unhealthy' situation. Because of the jurisdiction of the Ministry of Finance in tobacco-related matters, the Ministry of Health, Labor and Welfare could do little to restrict smoking for health promotion reasons until enactment of the 2003 Health Promotion Law. In fact, the Ministry has not had either a department nor staffs with expertise in dealing with tobacco products.

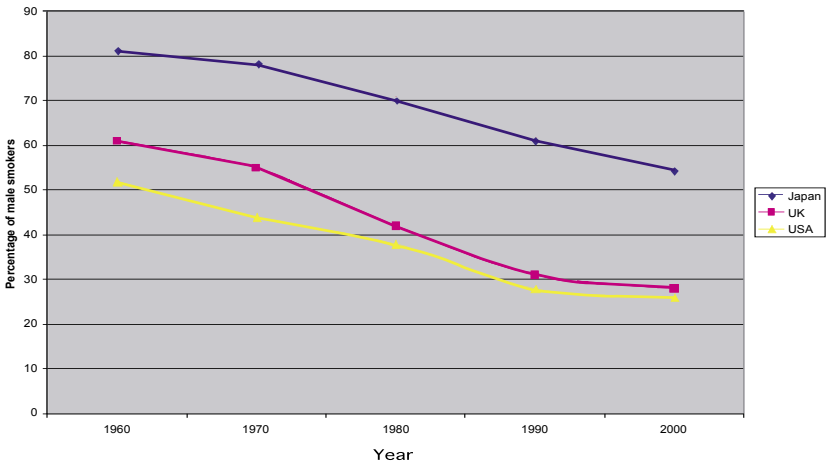
Japan has one of the highest smoking rates among industrialized nations. The Japanese society, to which JT is responsible, however, has a majority of nonsmokers, including approximately 28% who smoke and about 72% who do not smoke(Figure 4.9)(National Institute of Population and Social Security Research 2003; Shafey et al 2003).

Figure 4.9 Prevalence Distribution of Smoking Status by Age Groups and by Gender, Japan 1999-2000



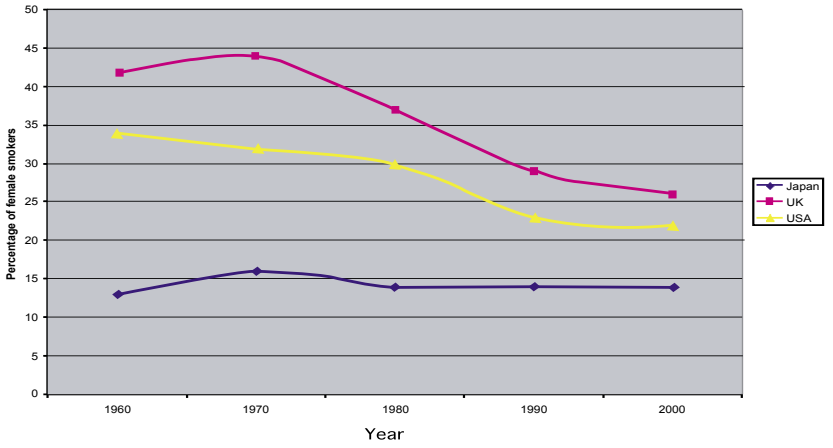
Source: Data compiled from (National Institute of Population and Social Security Research 2003),and (Shafey et al. 2003).

Figure 4.10 Smoking Trends in Men in Japan, the UK and USA



Source: WHO Nations Database

Figure 4.11 Smoking Trends in Women in Japan, the UK and USA



Source: WHO Nations Database

Figures 4.10 and 4.11 compare the smoking rate for men and women in Japan, the United Kingdom and the United States. The smoking rate for men is about 57.5% in Japan as compared to approximately 24% of men in the US (San Francisco Department of Public Health 1999; US Department of Commerce 2001). The overall smoking rate for women in Japan is more than 13%. However, a 1999 case study in Japan found "a disturbing increase in smoking rates among young people (particularly young women)."Between 1986 and 1996, smoking rates among Japanese women in their 20s rose from 15% to 20%. Youth smoking rates have also been rising at an alarming rate. From 1990 to 1996, smoking among 17-year-old boys went from 26% to 40%, while smoking among 17-year-old girls tripled from 5% to 15%" (San Francisco Department of Public Health 1999).

JT, the third-largest multi-national tobacco company, has expressed their corporate values in a mission statement. Among other things, it states that:

> **"We respect the views of society on tobacco, and are ethical and responsible in our activities…."(JT 2003).**

Yet, Japan has had only limited tobacco control activities at the natinal level and the close ties of JT to the government appear to have long been an inpediment to tobacco control.

The particular context for tobacco control in Japan today sets an urgent need for the development and implementation of an effective tobacco control policy. The health, welfare and rights of the 72% of society that does not smoke need to be protected and the 28% of society that does smoke, particularly those that have become addicted to tobacco, also need to be motivated and helped to quit. These needs can only be met by a comprehensive policy enhancement and control program development approach that includes elements to change the social environment as well as cessation approaches to help smokers quit. This policy enhancement and control program development process needs to be accomplished within a reasonable timeframe, consistent with all of the provisions of the WHO Framework Convention on Tobacco Control.

4.2.2.2 The FCTC and Japan

Since 1999, Japan, along with other Member States of the World Health Organization (WHO), has fully participated in the process of developing the WHO's Framework Convention on Tobacco Control (FCTC), an international treaty for controlling the global tobacco epidemic. The Ministry of Health, Labour and Welfare and the Ministry of Finance arrived at opposing views regarding the FCTC during the deliberations. These opposing views centered on the FCTC targets and overall objectives. The Ministry of Health, Labour and Welfare wanted to focus on ways to reduce tobacco consumption to promote health. The Ministry of Finance, on the other hand, asserted that the government should merely provide information that enables individuals to decide for themselves whether or not to smoke, and that no measures should be taken to reduce consumption of tobacco products or to ban them (Hanai 2003).

The final version of the FCTC was endorsed by all the WHO Member States, including Japan, at the World Health Assembly in May 2003. The FCTC now serves as a comprehensive framework for tobacco control policy development, enhancement, and implementation. The task that now lies before the Member States of the World Health Organization is to ratify this Convention individually and provide for its timely and effective implementation in their various spheres of national and international influence.

4.2.2.3 Country preparedness for the FCTC

The WHO's Western Pacific Regional Action Plan on Tobacco or Health for 2000-2004, endorsed by Member States, including Japan, at the 50th session of the Regional Committee in September 1999, emphasizes a comprehensive, multi-sector, strategic approach to tobacco control. The Plan provides a framework for the development of national plans of action to control the tobacco epidemic. As part of its on-going collaboration with Member States, the WHO Western Pacific Region includes in its Tobacco Free Initiative database [http://tfi.wpro.who.int] an assessment of each country's status in relation to "Preparedness for the FCTC (WHO/TFI 2000)." This assessment, initially made in 2000, focuses on factors that were considered critical to the adoption of the FCTC by the World Health Assembly, and factors that are now considered critical to the ratification and subsequent implementation of the FCTC by the Member States. These factors are:

- Participation in other International Health-related Treaties
- National Plan of Action for Tobacco Control
- National Coordinating Body for Tobacco Control
- NGO's for Tobacco Control
- Independent Media

Table 4.5 Qualitative Rating of the Preparedness of Selected Countries for the Framework Convention on Tobacco Control

Country	Factor					
	Participation in international health	National plan of action	National coordinating body	NGOs	Independent media	Overall ranking
Australia	1	1	1	1	1	5
China	1	0	1	0	0	2
Hong Kong China	0	1	1	1	1	4
Japan	0	0.5	0.5	1	0	2
Malaysia	0	0	1	1	0	2
Republic of Korea	0.5	0	1	1	0	2.5

Source: WHO Western Pacific Region Tobacco-Free Initiative database 2003

Table 4.5 presents Western Pacific countries rated using an 'orchid' - the Regional symbol for the Tobacco Free Initiative - scale. In relation to each factor, full orchids are given for being well-prepared; half-orchids are given for being partially prepared, with some work still required; orchids are not given if substantial effort is still required. The overall assessment of a country's preparedness is based on the following:

4 – 5 Orchids: National infrastructure for tobacco control is well established and may serve as a resource for other countries in the Region.

2 –3 Orchids: Some national infrastructure for tobacco control is in place, but other factors

(political, economic, etc.) may hinder support for the FCTC or national experience in tobacco control is relatively new. Advocacy needed to convince key decision-makers to decide in favor of the FCTC.

0 – 1 Orchid: National infrastructure for tobacco control minimal.

Concerted effort is needed to generate awareness and support for the FCTC and to establish national capacity to address the tobacco epidemic.

In relation to these criteria, the current WHO Western Pacific Region Tobacco-Free Initiative country-specific database [http://tfi.wpro.who.int] indicates the following for Japan:

"The Government's majority share in the tobacco industry is a significant factor to consider when assessing Japan's likelihood to vote for the FCTC. Encouraging developments include the designation of a national coordinating body for tobacco control and the adoption of the National Plan of Action on Tobacco or Health in 1995. A number of NGOs have been active in education and advocacy to control tobacco use. As the Japanese population ages, the rising costs, both direct and indirect, due to chronic illness and disability from smoking may persuade the Government to strengthen tobacco control efforts (WHO/TFI 2000)."

4.2.2.4 Japanese tobacco control infrastructure and efforts

Table 4.6 Analysis of Infrastructure for Tobacco Control in Japan

Infrastructure	Current Status	Activities and Goals
National Government	Lack of national resources (funding and staff) for tobacco control. Total per capita funding is less than 1 yen.	Increase funding and staff for tobacco control to approach funding for other health priority areas such as AIDS which is 100 yen per capita.
	2000- Healthy Japan 21st includes tobacco control as one of nine priority areas; however, no implementation plan exists.	Ministry of Health, Labor and Welfare should develop action and implementation plan. Direct goals to reduce consumption, prevalence and youth smoking should be included replacing ambiguous language in current document.
	No coordinating body, agency or department focuses on tobacco control.	Creation of an Office on Smoking or Health in government or affiliated organization like "National Institute for Public Health.
	2003- Health Promotion Law includes language concerning smoking surveillance and smoking restrictions in public places	Incentives to develop programs and materials to inform and educate the public.
Local Government	Limited national subsidies for local tobacco control. This situation is worsening as national subsides are shrinking.	Allocate local tax increases for tobacco control. Educate local financial officials on the economic benefits associated with tobacco control.
	2001- Local Healthy Japan 21st includes tobacco control as one of nine priority areas; however, no implementation plan exists. However, some local governments have taken the initiative to launch tobacco control programs and have passes local youth acce	Develop an action and implementation plan. Include direct goals to reduce consumption; include prevalence and youth smoking in place of ambiguous language in current document.All local governments will exercise own initiatives and pass local ordinances.
NGOs	NGO Council on Tobacco Control functions as advocacy body. Associations include Heart, Cancer, Cancer Research and Health and Fitness, Public Health.	Council needs to take more direct action and assert more influence over the policy arena. In addition, help increase funding for tobacco control.
	Grassroots organizations focus mostly on local efforts, lobbying government, suing the tobacco industry and educating the public.	Improve cooperation and collaboration in working toward tobacco control. Act in a coordinated fashion and increase efforts in policy and media advocacy.
Other Organizations	Medical associations, nursing association and academic bodies are taking initiatives for tobacco control.	Improve cooperation and collaboration in working toward tobacco control. Act in a coordinated fashion.
Media/Advocacy	Major media sources influenced by Tobacco Industry through advertisements and sponsorship, limiting the availability of information for the public.	Ban tobacco advertising and sponsorship and encourage free and accurate dissemination of news related to tobacco issues
Research/Academic Instituttions	Research budget on tobacco increasing but for limited research groups and research agenda.	Increase total budget on tobacco control research and review allocation of existing research budget.
	Randomized trials are rare. Policy evaluation study is poor.	Encourage multidisciplinary studies. Strengthen evaluation studies on policy and programs on tobacco.
	Tobacco industry funded resaearch is prevail.	Encourage disclosure of conflicts of interest and move on tobacco free research budget.

Table 4.7. Brief Review of Tobacco Control Policy a in Japan

Policy	Current Status	Outcome/Impact	Activities and Goals
Price and Tax	1998- 20 yen increase to compensate for National Railway debt	Increase not allocated for health or for infrastructure for tobacco control	Taxes should be increased at both the local and federal level to 100 yen or to a level that would be consistent with that of other developed nations.
	2001- Minister of Finance admitted that tax increase would save lives.	Important statement	Current tobacco tax revenues are $20,000,000,000 while the budget for tobacco control is only 1 cent per capita.
	2002- Failed attempt to raise tax by 40 yen	Opposed by JT.	
	2003- Increase of 20 yen for General Fund	JT and other multi-national tobacco companies collected millions of signatures against tax increase. JT developed a systematic procedure to oppose tobacco control. Increase not for health or for infrastructure for tobacco control.	Increasing the per capita expenditure to $1.00 per capita. Funds could also be used to compensate farmers to grow alternative crops.
Second hand smoke	2002- Clean Outdoor Ordinance passed in Chiyoda Ward of Tokyo. Bans smoking in designated outdoor public places.	Huge media attention. Helping to change social norm and reduce acceptability of smoking in public places. Very well accepted by residents and visitors. JT established smoking trailers to accommodate smoking.	Other local governments should pass similar ordinances since it has now been demonstrated as feasible.
	2003- Health Promotion Law, Article restricting smoking in public places.	Private railroad companies in metropolitan area made all stations smoke-free (n=730). Many local government buildings made smoke-free. Public schools made smoke-free. Other areas beginning to be made smoke-free. No enforcement included in law.	Implementing and evaluating smoke-free policies in hospitals, worksites and other public places. Provide public information campaign concerning health dangers of smoking around children.
Warning Labels	2003- Finance System Council revised the warning labels for Japan to be consistent with FCTC.	Increase in number of different health warning messages from 1 to 8. Messages now include warning about specific diseases and conditions including lung cancer, heart disease, stroke, emphysema, addiction, pregnancy outcomes, passive smoking, and smoking by minors	Make language more explicit about the health dangers. Make language more explicit about the health dangers of second hand smoke. Provide cessation information including benefits of cessations and techniques on how to quit.
Advertisement	2003-Tobacco Institute of Japan revised the voluntary code to be more consistent with international code of other tobacco industries.	Attempt to escape from further governmental regulation.	Establish links between voluntary policies and international tobacco industry strategy. Establish the fact that voluntary advertising policies do not protect the public.
	2003- Finance System Council plans to strengthen advertising restrictions to be consistent with FCTC.	Product placement and smoking in movies on TV, and in comics has been increasing as tobacco industry shifts focus of advertising campaigns.	
Youth Access	1900- Act prohibiting minors from smoking and prohibiting sales to minors.	Vending machines also function as billboards since they include extensive advertising. Major source of youth access.	Reduce youth access to tobacco products.
	Tobacco industry voluntary restriction on dispensing cigarettes from vending machines from 11 PM to 5 AM. However convenience stores can sell. Retail licenses to sell tobacco are increasing. ~ 630,000 vending machines across Japan; ~1 vending for each 27 citizens	JT developed Age ID card and machines that will only dispense with this card. JT lobbied Government to accept this type of youth access restriction. JT also owns a major vending machine company.	An important step would be banning vending machines or restricting placement of machines to avoid areas where children would have unsupervised access. Requiring purchases of tobacco to be limited to face-to-face transactions would prevent vending machine sales
Interventions-Prevention and Cessation	Small scale intervention programs are available, very few of them with good study design.	Total effectiveness and efficacy of the program may be poor.	Well-designed effective intervention program should be developed.
	School based prevention program is poorly utilized but under development by the Ministry of Education project.	With increasing number of tobacco free schools, hospitals and workplaces, needs for prevention and cessation are increasing.	Tobacco free schools and hospitals 100%. Workplace smoking restriction is also encourage.
	Cessation support system is getting popular. Cessation guideline project is started by the Ministry of Health, Labour and Welfre.	Cessation support is more widely available. Medical fee for cessation support should be covered by the health insurance.	Effective cessation support program should be available. Increase different pathways toward tobacco free. Increase short intervention by health professionals to increase motivation to quit.

National government

There is currently very little infrastructure or effort focused on tobacco control at the national level in Japan (Tables 4.6 and 4.7). There is no department or agency that has tobacco control as a primary area of interest. There is no full-time staff devoted to this issue. Funding for tobacco control is minimal, at less than one (1) yen *per capita*. Japan's lukewarm attitude toward controlling tobacco use can be traced to the government's administrative structure for tobacco products. In stark contrast with other developed countries where serious efforts to restrict tobacco use are being made under the leadership of their health, welfare, labor and education ministries, Japanese law governing the tobacco industry gives the Finance Ministry the authority to decide and approve the pricing, advertising, and warnings associated with tobacco products, as well as the authority to set the standards for installing cigarette vending machines (Hanai 2003).

In 2000, Japan released a report, "Healthy Japan 21st Century" that included tobacco as a priority area. Subsequently, however, no implementation plan has been developed and no funding has been provided to control tobacco use. At the same time, JT has grown considerably with profits continuing to increase, particularly as a consequence of marketing to citizens of other Asian nations.

There are other factors that are impediments to tobacco control in Japan. One critical barrier is the ubiquity of cigarette vending machines. Vending machine are easy to access and represent one of the biggest obstacles to discouraging minors from smoking. There are about 620,000 vending machines in Japan - nearly three times as many as there were a quarter of a century ago when anti-smoking campaigns started (Hanai 2003).

The Health Promotion Law, enacted in 2002 and enforced in 2003, represents an important starting oint for tobacco-free policies in Japan. This law requests the administrators of public facilities to 'make effort' to reduce or eliminate the hazard from passive smoking. It applies to schools, gymnasium, hospitals, theaters, halls, exhibition halls, department stores, offices, governmental buildings and restaurants and other locations. While there is no penalty or fine, smoke-free policies are being widely adopted by the public and private sectors.

Japan did enact a sales tax increase on cigarettes in July 2003. However, none of these funds were earmarked for tobacco control and Japan Tobacco reported a 30% increase in sales prior to the tax increase as smokers rushed to purchase cigarettes before the tax was implemented (Uranaka 2003). It is important to note that even with this increase in the tax rate, cigarettes in Japan are cheaper than in most other developed countries (Mackay and Eriksen 2002).

Japan lags far behind other developed countries in its tobacco control efforts. "Advertising of tobacco products has increased since imports were liberalized, and can now been seen in every railroad car; nonsmoking is designated in less than 1 percent of taxicabs; only half of private corporations and restaurants

have banned smoking or instituted smoking and nonsmoking areas; and the price of a pack of cigarettes in Japan is the lowest among the Group of Seven nations, at about a quarter of the price in New York." (Hanai 2003). The Ministry of Finance has held discussions on issuing a directive to ban tobacco advertising on television, radio, the Internet, and magazines for minors as well as eliminating the giving away of free tobacco samples on the street. In addition, such a ban would also eliminate advertising on buses and trains. Currently the industry is asked to voluntarily refrain from advertising their products. However, experience in other countries indicates that voluntary bans are ineffective and the FCTC calls for legislation to restrict advertising.

Currently the Japanese health warnings on cigarettes are extremely weak and likely to be ineffective. For the last fourteen years the warnings have been vague, stating only that, "Since smoking might injure your health, let's be careful not to smoke too much." The Ministry of Finance has recently announced plans to change the warning labels to include more specific messages. These would be stronger messages about the health effects of smoking, including the fact that cigarettes cause lung cancer, heart disease, stroke and emphysema. However, numerous countries have already moved from small print warning labels to pictorial warning labels that also take up the majority of the surface of a cigarette pack (Moffett 2003).

Local government

In recent years, local governments have played a leading role in protecting Japanese society from the adverse effects of secondhand smoke, establishing no smoking areas in public places such as city halls and parks and on public transport (e.g., all Japanese domestic flights are non-smoking). Chiyoda Ward was the first local government in Japan to enact a smoke-free outdoor ordinance in 2002. Details of this ordinance are provided elsewhere (Section 4.2.1). Many other local governments are following this initiative to enact similar ordinances.

The seating areas of major league baseball stadiums in Yokohama and Kobe were designated non-smoking in 2000; and, more recently, the local venues for the 2002 World Cup (hosted by Japan and the Republic of Korea) were declared smoke-free.

Local governments have also taken the lead on a number of tobacco-related issues, including cigarette butt littering, controls on outdoor vending machines and aggressive health promotion campaigns.

Over the last decade, hundreds of municipalities in Japan have enacted cigarette butt littering ordinances (Levin 2004). While these ordinances have little direct impact on tobacco use, they indicate the willingness of local governments to become involved in tobacco control-related issues. They do, however, attract

media attention and indirectly provide encouragement for addressing more substantive and contentious issues. Also in an effort to circumvent the law, Japan Tobacco has instituted mobile smoking lounges equipped with music so smokers have a place to smoke (Uranaka 2003). Mayor Takayoshi Hirasawa of Tukaura Village, Aomori Prefecture, announced plans in late 2000 to propose an ordinance to his council prohibiting outdoor vending machines. Although only a few vending machines were involved, the proposal drew strong opposition from the tobacco industry because of its precedent-setting implications.

NGOs

Non-governmental organizations in Japan have been campaigning against tobacco since the 1970s. In 1987, the year that the Ministry of Health and Welfare officially recognized tobacco use as hazardous to health, the "Women's Action on Smoking" was formed; An NGO Council on Tobacco or Health was established in 1991; and the Japan Medical and Dental Association for Tobacco Control was established in 1992.

There are many anti-tobacco organizations in Japan focusing on various aspects of tobacco control such as smoke-free environments; education regarding the harm caused by tobacco use; and advocacy to control tobacco use. Japan's largest nationwide anti-tobacco organization, *Nihon Kin-en Yuai Kai*, has a membership of over 45,000 individuals. Another non-governmental organization, *Nihon Kin-en Kyokai*, has about 10,000 members (Levin 2004). The challenge for these organizations is to come together to form a stable support base focused on effecting the timely ratification and implementation of the Framework Convention on Tobacco Control in Japan. Their contribution could include:

- **Promoting the implementation of effective evidence-based national tobacco control measures**
- **Encouraging greater cooperation among the people and organizations engaged in tobacco control work**
- **Facilitating the transfer of information in culturally relevant terms and the sharing of experience and knowledge**
- **Strengthening national and local tobacco control movements**

The history of tobacco control suggests that the most effective way forward lies through the development of significant partnerships and alliance building involving a wide range of relevant stakeholders. The complexity of the tobacco control situation in Japan, particularly the Government's direct involvement in the industry, makes this a compelling task. General public support will be important in ratifying the Framework Convention on Tobacco Control (FCTC); and local government cooperation will be critical to its effective

implementation. Collaboration with non-governmental organizations at both the national and local levels will be essential if advocacy initiatives are to succeed. And, cooperation with and among international partners will be advantageous in helping ensure the timely development of a comprehensive, balanced national plan of action for tobacco control.

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4.3 Comparative Analysis of Tobacco Control Policy and Programs

4.3.1 Role of the government

Japan lags behind other developed countries when it comes to tobacco control efforts. When viewed in this international comparative context, Japan has extremely weak tobacco control measures. In contrast with other developed countries, where serious efforts to restrict tobacco use are being made under the leadership of their health, welfare, labor and education ministries, Japanese law governing the tobacco industry gives the Finance Ministry the authority to decide and approve the pricing, advertising, and warnings associated with tobacco products, as well as the authority to set the standards for installing cigarette vending machines. Moreover, many of Japan's limitations on tobacco product advertising, including TV and radio broadcast restrictions, and most recently, restrictions on large-format urban billboards, have come out of the non-binding tobacco industry self-regulation action and not binding governmental policy although the Tobacco Industry Law requires such self-regulation.

The Japanese Parliament (Diet) formally recognizes through legislation that tobacco is good business for the economy and good business for the government, making Japan uniquely different from other developed countries such as the US and UK. The Diet's perspective on tobacco is based on a nearly 100-year history of national government ownership of Japan's tobacco conglomerate, first as a wholly owned monopoly enterprise, and more recently, from a majority ownership position in Japan Tobacco Inc. (JT), a vast multi-national private corporation that retains a legal monopoly over tobacco manufacturing in Japan. However, since the Japan Anti-Tobacco League was established in the Diet, gathering over 90 active parliamentarians, political debate over tobacco or health

has dramatically changed.

Recently the pace of tobacco control activities in Japan has dramatically increased. Japan increased the tax on cigarettes in July 2003. Even though this was a very modest increase, JT vigorously opposed it. Evidence from other countries has demonstrated the value of tax hikes in reducing tobacco consumption (Jha and Chaloupka 1999). This tax increase created substantial media attention, including favorable editorial writing. Local governments in Japan have recently begun to take a more proactive role in developing and implementing tobacco control policies such as implementing local plans of Healthy Japan 21 and establishing no-smoking areas in public places such as city halls and parks and on public transportation. This is consistent with activity in other countries like the US that have demonstrated the efficacy of local policy initiatives as an effective strategy to accomplish tobacco control goals, especially where the tobacco industry has considerable political clout at the national level of government.

4.3.2 Infrastructure for tobacco control

Despite the recent increase in tobacco control activities, tobacco control policy development in Japan is very minimal when compared to other developed countries. One reason for such minimal action is a lack of the financial investment necessary to develop capacity or infrastructure for advancing meaningful tobacco control efforts at the national level. The Life-Style Diseases Prevention Section at the Ministry of Health, Labor and Welfare is now serving as the focal point for tobacco control efforts, but there is no governmental department or agency in Japan that is specifically appointed to this role and have regulatory authority over tobacco issues. Currently, there is no full-time staff devoted to gathering information, planning and policy development, or consultation for tobacco control. Japan has only one School of Public Health, thus allowing limited educational opportunities for public health workers to obtain the necessary training or experience in this area of research and practice.

Funding for tobacco control is minimal at less than one (1) yen *per capita*. Japan's lukewarm attitude toward controlling tobacco use can be traced to the government's administrative structure for tobacco products. In the US, in contrast, at the national level, the CDC's Office of Smoking and Health (OSH) is well funded and directly employs more than 100 people. Its structure and activities are described in detail elsewhere (Chapter 6.1.1). The contrast with the situation in Japan is stark.

While there are many anti-tobacco organizations in Japan focusing on various aspects of tobacco control such as smoke-free environments, education regarding the harm caused by tobacco use, and advocacy to control tobacco

use, the challenge remains to form strong coalitions that can work together as a collective force to combat the strong political support for the tobacco industry in Japan. Therefore, following the lessons learned from tobacco control in other countries demonstrates that the most effective steps forward lie in the development of significant partnerships and alliance-building which involves a wide range of relevant stakeholders. Also, almost 20 academic and professional associations such as the Japan Medical Association, Japan Nursing Association, Japan Lung Cancer Society and Japan Cancer Society officially stated their tobacco-free policies and encourage their members to be tobacco-free as well as to educate the public and their patients. These activities were never seen in the past and they would definitely change the social norm in Japanese society and stimulate other organizations to promote concerted actions against tobacco.

4.3.3 Tobacco control policy and programs

In many countries, governments have played a major role in disseminating information on the health consequences of smoking. They have invested in surveillance efforts to track the epidemic and made these data available to the public as well as policy makers. National surveys on smoking behaviors have been periodically conducted in the US and government reports, such as the Surgeon General Reports from the United States CDC, the Monograph series from the United States National Cancer Institute, and other publications have provided valuable information on tobacco control. The information is carefully reviewed and approved by the governmental agencies supporting the report. In Japan, there have been three editions of reports on Smoking and Health edited by the Ministry of Health but efforts on accumulating and evaluation of scientific evidence for such governmental reports need to be more encouraged in Japan.

The mass media has played an important role in tobacco control efforts in many countries. Until very recently, the mass media in Japan almost completely ignored the smoking problem. One reason for the lack of attention to this serious health issue was related to the large revenue the broadcasting companies received from the tobacco industry for cigarette advertising or sponsorship. However, in the past two years, there has been a noticeable trend toward more significant coverage of tobacco control in the media along with the recent increase in the number of tobacco control policies in society.

While there has been some progress in Japan, it is important to note that the social acceptability of smoking still remains high as highlighted by a recent decision rendered in the Tokyo District Court. The court denied all plaintiffs' claims in Japan's first significant lawsuit for tobacco-related illnesses. The court decision recognized some of the health-related harm associated with cigarette smoking. However, the Court's recognition of tobacco-related harms for these

plaintiffs was only that smoking caused an 'increased risk' for lung cancer and other illnesses, "but other causes could have been responsible for the plaintiffs' cancers."

The court stated that tobacco smoking is addictive, but only mildly so, such that one can easily quit by the exercise of individual will. Specifically: "Smokers tend to lose their ability to freely determine their will, but with a strong will and effort, one can quit." The Court expressly noted that the addictiveness of tobacco is less severe than the addictiveness of alcohol or of illegal drugs. The Court seemed to accept JT's posture with regards to addictiveness and ignored or misused epidemiological evidence. A comparison needs to be made from this court decision and the public statements of Philip Morris, which has publicly acknowledged that tobacco is the cause of disease and is highly addictive (Philip Morris USA).

4.3.4 Conclusion: the FCTC as a golden opportunity for tobacco control policy

Tobacco control achievements have been varied among countries. In particular, countries in which the political power of the tobacco industry is strong enough to influence governmental decision-making processes and in which tobacco-related disease epidemic is still in the beginning stage have lost opportunities to strengthen tobacco control. Japan is among such cases, as pointed elsewhere in this report. The Ministry of Health once attempted to reduce tobacco use for Healthy Japan 21, the national health strategy for 2010, but its efforts collapsed under aggressive political pressure by the tobacco industry.

However, the FCTC's potential as a positive force for long-term changes in Japan cannot be underestimated because the FCTC gives the world a fundamental basis to renew tobacco control policy with the globally shared and explicit goal to reduce tobacco use and exposure. To this end, many countries, especially Japan, could initiate serious political debate on structural changes in tobacco control policy linked to industry management. The requirements of the FCTC are comprehensive and intensive.

Thus, during the course of preparation for the FCTC, many deficiencies in the current policy could have been and should have been corected. Concerted efforts were in fact made by different ministries toward the shared objectives required by the FCTC. With sufficient numerical goals for domestic policy achievement as well as thorough monitoring and evaluation of implementation, real achievement in the health of the nation will inevitably be successful.

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Chapter 5 RECOMMENDATIONS

RECOMMENDATIONS

5.1 Preamble

This report, “Tobacco Free ＊ Japan: Recommendations for Tobacco Control Policy”, was written to provide a perspective on the state of the tobacco epidemic in Japan and to offer recommendations for controlling the epidemic. The report addresses the current and future burden of disease caused by smoking in Japan, efforts to control the epidemic to date, and a listing of steps that might be taken in the future to control the epidemic. The report places the tobacco epidemic in Japan within the broader context of experience in many other countries that have faced and responded to this same threat to public health. The report comes at a particularly critical time for Japan, in advance of its anticipated signing of the Framework Convention on Tobacco Control (FCTC) over the next months, a global treaty that commits participating countries to implement tobacco control programs. As Japan moves forward to act on the FCTC’s tobacco control and research provisions, the recommendations made in “Tobacco Free * Japan” should prove useful as a starting point for innovative policy development.

This report was prepared by a team of authors from Japan and the United States with the intent of providing an evidence-based foundation for these policies. The report systematically brings together evidence relevant to tobacco control in Japan, covering the patterns of smoking in Japan, the health effects of smoking in Japan, policy measures taken in Japan to date, and the tobacco industry in Japan and the implications of its close relationship with the Japanese government. Lessons have been learned in other countries that can be useful to Japan; to identify these “lessons learned”, relevant international information is also reviewed with comparison to the current situation in Japan. The report concludes with a set of policy recommendations that are set in the context of the principles set forth in the FCTC, principles that Japan accepts in its ratification of this landmark treaty.

Japan is at a critical point in the country’s epidemic of tobacco use that

began 50 years previously. A half of its men are smokers and the number of cigarettes that they smoke has increased sharply across the 1960s and 1970s, placing them at high risk for the many diseases caused by smoking. Fortunately, smoking is uncommon among Japanese women with only about 15% currently smoking. Unfortunately, smoking is increasing among young women, who have been targeted by the multinational tobacco corporations including our own as elsewhere. A dual strategy based in cessation for the addicted smokers, largely male, and in prevention for youths, both boys and girls, is urgently needed. This report's recommendations offer a starting point for developing and implementing a stronger tobacco control effort in Japan.

The smoking of manufactured cigarettes has now been the dominant form of tobacco use for over a century and mortality statistics from many countries chart the resulting epidemics of heart disease, lung disease, and cancer. Lung cancer, for example, was a rare disease at the start of the twentieth century and is now the leading cause of cancer death in the United States. Epidemiological and other research has established smoking as a cause of an ever-lengthening list of diseases; its adverse effects begin before birth and extend across the full lifespan. The risks for most of these diseases increase with the number of cigarettes smoked and the length of smoking and decreases after quitting. The type of cigarette smoked, e.g., 'light' vs 'regular', does not have a strong effect on the risk of smoking.

This report summarizes the major studies in Japan on active and passive smoking and health, comprising over several hundred papers coming from many individual epidemiological studies, including case-control, cohort, and some cross-sectional investigations. These studies, not surprisingly, show that smoking increases risk for many diseases in Japan as elsewhere in the world. There are a lesser number of studies from Japan on passive smoking, but these studies have been a critical component of the broader base of evidence on passive smoking and disease, particularly for lung cancer.

The evidence from studies in Japan is convincing in showing associations of active smoking with the many diseases already causally linked to smoking. The relative risks are quite comparable for some diseases, compared to those in other countries: coronary heart disease and some cancers. The various forms of chronic lung disease caused by smoking have received little investigation in Japan. Similarly, adverse reproductive effects of smoking in Japan have not been extensively investigated, perhaps reflecting the low prevalence of smoking among women. The observed risks for lung cancer are notably lower than risks in studies carried out at the same time in the United States and Europe, even though

comparable risks were found for laryngeal cancer, bladder cancer and stomach cancer. Research on mechanisms, while not a topic of this review, has not indicated a basis for considering that differing mechanisms of pathogenesis would come into play in Japanese compared with other smokers.

The studies reviewed in this report lead to a conclusion that active smoking causes the same diseases and other adverse health effects in Japan as elsewhere in the world. Because of the high rates of smoking among Japanese men, passive smoking is highly prevalent in Japan's homes and workplaces, as well as in other key places. Women and children, constituting a non-smoking majority of the country, are unable to avoid exposure and are at risk for the adverse consequences and diseases caused by passive smoking.

Over the half-century that has passed since the first definitive studies were published linking smoking to lung cancer and other diseases, substantial progress has been made in some countries in curbing the epidemic of tobacco use. There have been many "lessons learned" from these countries that offer strategies to be considered for use in Japan. Experience in many countries shows that strategies for preventing and controlling tobacco use need to be comprehensive, target youth smoking, promote cessation by addicted smokers, and reduce passive smoking. The array of strategies should include laws that restrict access of minors and control smoking in public places and workplaces, and limit advertising and promotion, and taxes on cigarettes should be set sufficiently high, as higher taxes reduce smoking by youths and promote cessation, without loss of revenue to governments for the short-term. Deceptive marketing of products with labels such as "light" should also be controlled. Each country needs to put surveillance in place for patterns of smoking and for the health consequences of smoking. Of course, an infrastructure is needed for these activities and every country should have a national focal point for tobacco control.

This report documents only limited efforts to date for controlling the epidemic of tobacco use in Japan. At the national level, there is presently no office charged specifically with tobacco control, the tax rate on cigarettes is low, minors have ready access to cigarettes, particularly through vending machines, and protection of nonsmokers from passive smoking is inadequate. Most importantly, cigarette smoking remains as an accepted activity that is interwoven into life in Japan, a situation parallel to that in the United States and many other countries decades ago.

The slow pace of tobacco control in Japan can be attributed to a substantial extent to the inseparability of the tobacco industry and the government, which

retains the major control over the Japanese tobacco industry. Government revenues from the Japanese tobacco industry are substantial and the industry's scope and reach has been expanded through internationalization. Absent a strong anti-tobacco focal point, either within or outside of the government, the influence of the tobacco industry together with many powerful political allies is largely unopposed at present.

5.2 General Recommendations

This report offers a comprehensive series of recommendations for consideration and potentially for implementation. Of course, targets for tobacco control will change over time, and ongoing surveillance and redirection of efforts to address the most critical areas will be needed. Of the many areas to be addressed in the list that follows, we consider that priority should be given to several, based on both their urgency and the potential for immediate impact. Some are within the domain of the Ministry of Finance and others, the Ministry of Health, Labour and Welfare. (1) As an initial step, an office for tobacco control should be established within the national government, securing the initiative by the Ministry of Health, Labour and Welfare. (2) The level of taxation of tobacco should be increased and greater consideration given to taxation as one of the key approaches to tobacco control. (3) Secondhand smoke control should be strengthened using the Health Promotion Law. (4) The government should recognize the need for a radical reform of Tobacco Business Law for an effective implementation of FCTC, whose enforcement would be in a stark contradiction to the current provision of this Law. (5) Finally, given the large numbers of male smokers, at high risk for tobacco-caused disease and death, steps should be taken to promote cessation, which would have immediate health benefits.

The authors of this report consider that Japan is at a critical and pivotal moment in the course of its tobacco epidemic. The majority of its men are addicted smokers who will inevitably face premature onset of chronic, crippling, and fatal diseases, and its nonsmoking women are a target for aggressive marketing by the Japanese tobacco industry, majority controlled by the government, and other multinational corporations. The Framework Convention on Tobacco Control (FCTC), a needed platform for addressing a global epidemic, commits Japan to a series of measures related to tobacco control. Recognizing the significant health and economic burden imposed by tobacco on its citizens and acknowledging the policy requirements of the FCTC, the Japanese government should move to implement an effective national tobacco control policy, using the most appropriate tobacco control measures drawn from the scientific evidence reviewed by this report.

Tobacco growing, production, and marketing are a substantial component of the Japanese economy and the government receives substantial tobacco tax revenues. The implementation of tobacco control should not be slowed by economic considerations and having a national tobacco control policy does not involve either banning tobacco products or eliminating the tobacco industry immediately. It does imply, however, a transformation of tobacco use from being viewed as socially accepted to being seen as dangerous and even fatal, for smokers and non-smokers. As tobacco is the only legally available consumer product that kills through normal use, tobacco should be regulated accordingly so as to reduce its risks and many negative health consequences to the fullest extent possible.

This report extensively documents the tight linkage of the tobacco industry to the government and the substantial revenues that come to the government from tobacco sales. This unique relationship in Japan has placed financial considerations above the public's health and engendered concern that tobacco control will have adverse economic consequences. For the short-term, experience in other countries suggests that governments do not lose revenue when tobacco taxes are raised, and cigarettes are priced too cheaply in Japan at present. Any costing of tobacco control needs to also take into consideration the expenditures for care of smoking-caused diseases, the loss of productivity from these diseases, and the shortening of the lives of smokers. Every country should be seeking to optimize the health of its citizens and not to harm them. The authors of this report view the health and lives of the Japanese as the most important resource of the country and we sincerely endorse tobacco control policies that acknowledge the need to protect and advance the public's health.

The authors of this report encourage the Japanese government and society and particularly its leaders to have a Tobacco Free Japan as a national goal. To that end, policy recommendations follow below.

5.3 Policy Recommendations

5.3.1 With regard to the FCTC

The FCTC offers a critically needed set of provisions for implementing a national tobacco control program. Failure to sign, ratify, and abide by the FCTC would signal a globally unacceptable stance by Japan, particularly given the multinational nature of the Japanese tobacco industry. We call for:

- Ratification of the FCTC and implementation of effective tobacco control measures following its provisions.

- Prompt signing and ratification of the FCTC followed by immediate and thorough implementation of effective tobacco control measures following its provisions.

- In this regard, we further call for:

- Strengthening of current national laws, which are inadequate for achieving the goals of the FCTC, protecting present and future generations from tobacco use, and from exposure to tobacco smoke.

- Implementing of changes quickly following ratification of the FCTC.

- Establishing an appropriate and coordinated administrative system to overcome the weaknesses of the present, fragmented situation around tobacco control within the government.

- Acknowledging explicitly that active and passive smoking cause disease and premature mortality.

- Ensuring the compliance of the tobacco industry in Japan with FCTC-based norms in the international context, with regard to, for example, advertising restrictions and measures to prevent cross-border smuggling of tobacco products.

5.3.2 With regard to Infrastructure

These countries that have been most successful in controlling tobacco use have established infrastructure that includes a national office, ongoing information gathering, and resources for program implementation and evaluation. We call for:

- The immediate establishment of a national center for tobacco control to serve as the focal point for information gathering, planning and policy development, and consultation.

- Provision of an adequate budget for tobacco control, moving from the present level of 1 yen per capita to 100 yen per capita. These funds should be drawn from the tax on tobacco, a model that has proved effective in other countries.

- Many sub-national governmental levels in Japan have taken positive steps toward effective tobacco control initiatives in recent years. Such activity should be recognized, encouraged, and more widely achieved throughout Japan. In no case should national measures serve as a pre-emptive floor barring more

comprehensive and aggressive efforts at the prefectural and local governmental levels.

- Professionals in tobacco control are needed for Japan. Steps should be taken to foster their development.

- Continued development of coordinated NGO networks concerned with tobacco control.

5.3.3 Pricing and Tax Policy

Appropriate pricing of cigarettes helps to keep youths from smoking and promotes cessation by some smokers. Comparison of cigarette prices in Japan to other developed countries indicates that Japan's prices are among the lowest. An increase in tax would benefit public health, provide a source for funding tobacco control, and not reduce government revenues for the short-term. We call for:

- An increase in the price of tobacco by progressively increasing taxation to reach the levels in those countries with successful tobacco control. Given the low prices of cigarettes in Japan today, the initial increase should be at least 100 yen per pack or more.

- Some of the resulting tax revenue should be directed towards tobacco control programs and research as well assisting tobacco farmers in moving towards other crops or sources of revenue.

- Measures should be taken for prevention of tax avoidance such as by cross-border smuggling.

5.3.4 Secondhand Smoke Exposure

Secondhand smoke exposure causes substantial morbidity and mortality. Nonsmoking Japanese are heavily exposed to secondhand smoke in public and private places. These exposures can be readily controlled. We call for:

- Strengthening and enforcement of the existing Health Promotion Law, which has provisions related to secondhand smoke. A goal should be smokefree public places and workplaces.

- Implementation and enforcement of Health Promotion Law and local clean air ordinances.

- Implementation and enforcement of clean indoor air standards under labor and occupational safety laws and regulations.

- Reviewing the smoking restriction standards of Ministry of Health, Labour and Welfare with consideration of exposures to include carcinogens.

- Health education and other campaigns to reduce secondhand smoke exposure in homes and private passenger cars.

- Health professional organizations should educate their members concerning the consequences of secondhand smoke exposure and target susceptible groups,e.g., children with asthma.

5.3.5 Ingredient Regulation and Disclosure

During the processing of tobacco and the manufacturing of tobacco, a variety of chemicals and additives are used. Some of these may have negative health implications. We call for:

- Reviewing the existing testing method, that is currently based on the Tobacco Business Law.

- Disclosure of harmful ingredients/components

- Regulation of all harmful ingredients/components

- Disclosure of raw materials and additives

- Regulation of raw materials and additives

5.3.6 Packaging and Labeling

Sales of cigarettes in quantities smaller than 20 per pack can facilitate access of minors. Package warning labels that provide unambiguous and graphic warnings have proved to be more effective than small labels which do not explicitly describe the risks of smoking.

Especially in Japan, the use of brand names including words such as “mild” or “light” is particularly prominent, likely misleading smokers with implied health messages.

- Cigarette packages should be manufactured and sold only with units of 20, as smaller packages facilitate access of minors.

- Package warning labels should cover more than 30% of the surface of packages, being gradually increased to 50% or more.

- The warning labels should have both clear text in an appropriate point-size and color and compelling graphic images, instead of the current text-only labels, with test marketing and scientific evaluation of the means used to discourage smoking as effectively as possible.

- The warning labels should be placed on the top of the surface of packages with prominent bold frames.

- The use of brand names that imply a lower level of risk should be prohibited.

5.3.7 Advertising and Promotion

The tobacco industry spends large amounts of money on advertising and promotion with the explicit goal of expanding market share for particular companies and their brands, and the unstated goal of expanding the market for their products. These activities take diverse forms and have proved difficult to control in many countries. We call for:

- Limitation of advertising and promotion to point of sale, except those locations that are easily accessible by minors.

- Advertisement and promotion ban in any media accessible to minors, including television, printed publications and the Internet.

- Prohibition of indirect advertisement, titled events, promotional goods or services, and commercial goods or services with brand names or logos.

- Regulation of smoking scenes and bans of compensated product placement in TV dramas and movies accessible to minors.

5.3.8 Cessation

For all smokers, regardless of age, cessation is of proven benefit for reducing risk for developing disease and avoiding premature mortality. In fact, prevention of smoking by youth will have little immediate impact on the burden

of smoking-caused disease, while cessation by middle-aged and older smokers has immediate impact. Comprehensive tobacco control programs are directed at both cessation and prevention. We call for:

- Programs to increase the identification of smoking as a health problem for smokers and awareness of the addicting nature of nicotine, and education of health professionals in facilitation of cessation.

- Campaigns to promote smoking cessation by Japan's smokers, particularly men.

- Further development of facilities and services for cessation through governmental and workplace providers.

- Coverage of cessation services by medical insurance plans.

- Campaigns to encourage private employers to promote smoking cessation among their workforce, in light of both costs savings and workforce health benefits

5.3.9 Youth Access

The continued smoking by the youth of Japan is unfortunate and the report's authors are particularly dismayed by the rise of smoking in young girls. Remarkably, smoking by teenagers and young adults remains acceptable. Even young smokers have evidence of damage from their smoking and earlier age of starting to smoke brings greater risks for many of the smoking ニ caused diseases. We call for:

- Enforcement of face-to-face retailing of cigarettes with strict age identification in concert with elimination of all tobacco product vending machines in the Japanese society.

- Strict enforcement of Tobacco Business Law and Act for Minors on Preventing Smoking regarding prohibiting sales to minors.

- Use of new, evidence-based prevention approaches coming from research in Japan.

- Encouragement of local governments to enact ordinances to prevent youth smoking.

5.3.10 Liability and Policy Development Processes

In some countries, litigation has been useful as tobacco control measure. In the United States, there has been extensive litigation leading to several victories, the Master Settlement Agreement, and access to millions of tobacco industry documents. Each country has its own legal system and approaches from other countries may not be immediately transferable to Japan. We call for:

- Exploration of the potential for litigation to serve as a tobacco control approach for Japan focusing on both liability issues and industry document discovery.

- Implement steps to prevent document destruction, tampering, or hiding (such as to overseas offices) with criminal penalties imposed on violators. Ensure whistleblower protection laws are implemented in all workplace settings.

- Increased transparency in decision-making process on tobacco control policy in the government.

- No involvement of the tobacco industry or its affiliates in decision-making process except at occasions of public hearings and/or written official documents.

- Full disclosure of conflicts of interests at any level of tobacco control including policy development, researches and advocacy and so on.

5.3.11 Actions Needed Now

This chapter offers a lengthy list of recommendations, some readily implemented and others requiring substantial resources and a longer timeframe. We urge that immediate priority be given to the following:

- Youth access to cigarettes and other tobacco products needs immediate and strict restriction. Without tight control and preferably elimination of vending machines, youths will continue to have ready access to cigarettes, regardless of regulation of in-store sales.

- A tobacco tax increase should be immediately implemented. Substantial evidence indicates that government revenues will not fall for the short-term and that smoking will be reduced proportionately to the tax increase. We urge that a portion of any tax increase be committed to supporting tobacco control.

- At present, Japan does not have a focal point within the government for tobacco control, a gap that needs to be addressed immediately. An adequately staffed and positioned office should be established within the government; the development of a national tobacco control plan should be a first charge.

5.4 Research Recommendations

5.4.1 With regard to Infrastructure

Research in support of tobacco control in Japan is hindered by lack of an overall plan, limited funding, and inadequate capacity. Consequently, the evidence base for tobacco control is inadequate. Thus, we call for:

- A national coordinating body for research on tobacco among governmental organizations to be established and provided with sufficient staffs and financial resources (or with an authority for resource appropriation).

- Basic surveillance for monitoring and evaluation of the consequences of tobacco control measures. Some key indicators include smoking prevalence and consumption, second hand smoke exposure, willingness to quit, and support for particular policies. The existing, ongoing surveys such as the National Health and Nutrition Survey, the National Health and Welfare Survey, or the National Survey on Smoking and Health should be utilized to generate data to meet such policy requirements.

- Education and training of researchers on tobacco.

- The government's research budget for tobacco control to exceed the amount provided by the tobacco industry.

- Establishment of up-to-date information resources, such as a reference database.

5.4.2 Role of scientific researchers and their professional organaization

Effective tobacco control requires the active engagement of professional scientific organizations, health professionals, scientific researchers, and other leaders. In the past, such engagement has been considered inappropriate for academia, but in the past few years more than a dozen health professional organizations have published a tobacco free declaration. Some are taking concerted actions. Thus, we call for:

- Individual scientific researchers and their organizations to take more initiative on tobacco control.

- Scientific organizations to make official commitments or declarations on tobacco control and to have all meetings smoke-free.

- Disclosure and discussion of conflicts of interests related to tobacco industry funding.

- Continuous and concerted efforts to share information and to enhance mutual understanding, with a goal of launching a multidisciplinary tobacco control assembly.

5.4.3 Research Agenda

As discussed in this report, studies on tobacco in Japan are limited and narrowly shaped, compared to the full-range of research areas relevant to tobacco control. Some, as genetic susceptibility and addiction, have been emphasized in tobacco industry research. Progress on tobacco control in Japan might be accelerated by comparative research that would facilitate the use of approaches already tested in other countries. Such research should address not only the health risks of smoking but tobacco control approaches. Thus, we urge:

- Epidemiological studies on tobacco and health in Japan, which are needed to document that actual risks to the population.

- Intervention studies to complement the observational epidemiological studies, as few having been carried out to date.

- Evaluation of existing intervention programs for their effectiveness and efficacy in reducing tobacco use.

- Wide implementation of intervention programs with proved effectiveness and efficacy.

- Government support of work on addiction.

- Further work on Japanese tobacco products and the characteristics of their smoke.

- Research involving other disciplines, including economics, risk communication,

pubic policy and social marketing.

- Continuous efforts to translate scientific language into more general language for decision makers and the public to fully understand the scientific evidence.

- Simulation studies and decision models to predict future gain or losses, from successful or failed tobacco control, to visualize and foresee what should be theoptimum policy options in Japan.

5.5 Closing Comments

The authors of this report, an international team of medical, public health, and other scientists, stepped forward to write this report because of a shared expectation that the report would advance public health nationally and even globally. With the recent internationalization of the Japanese tobacco industry, Japan's actions on tobacco control have not only national but global implications. While this report has addressed national tobacco control only, we urge an open discussion of the propriety of government ownership of a company that makes and markets a lethal product. The potential for short-term profits needs to be carefully weighed against the world's diminishing tolerance for the tobacco industry and the possibility for long-term adverse consequences arising from global liability for disease and death.

The Japanese tobacco industry has now become one of the world's largest players on the international scene of tobacco marketing. Unfortunately, like other multinational tobacco corporations, its targeted markets will inevitably include the developing nations where smoking is increasing. We question whether the government of one of the world's most advanced nations should be the major controller of the tobacco industry that exports such a deadly product. At the least, an open discussion of this issue should take place.

In the United States, the 1964 report of the Surgeon General stands as a landmark and defined the clear beginning of a national tobacco control agenda. The authors of this report are hopeful that it may some day have the same significance for Japan and that further reports, coming from a new national center, will sustain a movement that is just beginning.

POSTSCRIPT

Postscript A:
Tobacco Industrial Policy and Tobacco Control Policy in Japan

1 Introduction

National tobacco policy in Japan runs in competing directions, along a strong line of legislatively established industrial policy promoted primarily through Japan's Ministry of Finance and a weaker line of mostly administrative tobacco control policy promoted primarily by its Ministry of Health, Labour and Welfare (Ministry of Health). This chapter looks separately at the two vectors in a historical overview of an unbalanced tug-of-war, beginning with tobacco industrial promotion policy and followed with tobacco control policy.

The final section considers the future of tobacco policy in Japan with reference to the Framework Convention on Tobacco Control (hereafter FCTC). This section hypothesizes that Japan's domestic circumstances with regards to tobacco control seem primed for significant improvement, but expresses concern that Japan will follow the United States in unkindly exporting the enormous public health burden of its tobacco industry to economically weaker and more vulnerable nations of the world.

2 Tobacco industrial policy

Historically, industrial promotion policy has been the primary governmental force with regards to tobacco in Japan. The 1984 Tobacco Industry Law reflects this most clearly. It seeks for the nation "the sound development of the national economy and..... stable fiscal revenues" by advancing "the sound development of our nation's tobacco industry." Simply put, the Japanese Parliament (Diet) has formally recognized that tobacco is good business for the

economy and good business for the government.

The Diet's perspective on tobacco correlates to a nearly 100-year history of national government ownership of Japan's tobacco business, first as a wholly owned monopoly enterprise, and more recently, from a majority ownership position in Japan Tobacco, Inc. (hereafter JT), a vast multi-national private corporation that retains a legal monopoly over tobacco manufacturing in Japan.

2.1 Monopoly days: The Ministry of Finance's tobacco business

Full government monopoly ownership of the tobacco industry in Japan dates to 1904. Ostensibly to preserve lucrative tax revenues in a wartime economy, but also to preclude further market entry by James Buchanan Duke's powerful American Tobacco Company (Kluger 1996), the government transformed a lesser monopoly on leaf tobacco sales into a complete monopoly on both leaf sales and manufacturing owned and operated directly by the nation's Ministry of Finance.

Japan's tobacco industry grew strong under monopoly protection and government control. Following Allied Occupation guidance in 1949, the Ministry of Finance transferred its tobacco business from an internal division to a newly formed public corporation, the Japan Tobacco and Salt Public Corporation (JTSPC), an organizational appendage of the Ministry of Finance. This public corporation grew substantially as a business enterprise while remaining fully subordinate to Ministry of Finance control. Senior Ministry of Finance officials routinely "descended from heaven" to cozy but dominant JTSPC executive positions, while mid-level Ministry of Finance officials supervised JTSPC operations under a close watch.

In the subsequent decades of Japan's rapid economic expansion, JTSPC's sales grew smoothly. As documented elsewhere in this volume, male smoking prevalence, already established at high levels during the wartime and post-war period, remained steady while *per capita* consumption rapidly increased (reflecting consumers' improved spending power). In the meanwhile, the protected market environment supported peripheral economies, including a sizable tobacco leaf agricultural sector, an industry-held wholesale establishment, and a widely disbursed retail distribution network.

In the early 1980s, a variety of factors converged to push the Japanese government to again restructure its tobacco business. Foreign governments, particularly the US Reagan administration on behalf of its tobacco giants Philip Morris and R.J. Reynolds Tobacco, put pressure on Japan in trade negotiations to end the monopoly protection regime (Kluger 1996; Sugarman 2001). Contemporaneous domestic pressures included broad-reaching efforts to

accomplish national administrative reform and concerns over contentious labor/management relations in all three of Japan's major public monopolies: telephone system, long-distance rail, and tobacco. A scheme for 'privatization' of tobacco in Japan moved forward, reaching fruition in the 1985 Tobacco Industry Law described above.

The privatized regime maintained an unmistakable tobacco industrial promotion posture. While legislative records makes clear that this was to appease an extremely powerful agricultural sector, industry documents dating back to the 1970s and 1980s also show an emerging awareness among tobacco industry players of market counter-pressures from consumers, activists, and other public officials about the health consequences of tobacco use (JTSPC 1979; R.J. Reynolds Tobacco 1979). This was presumably another likely factor towards establishing a protective oversight framework. Thus, even in the mid-1980's, when governments of many economically developed nations were moving towards tobacco control efforts (Kagan and Vogel 1993), the newly established legislative scheme for tobacco business in Japan retained industry oversight in the hands of the business-friendly Ministry of Finance and an industry-dominated government advisory council.

2.2 Budget rules: tobacco industrial policy in the post-privatization era (1985 to present)

Tobacco industrial policy in the post-privatization era is accomplished directly, through Ministry of Finance guidance and support, and indirectly through the Ministry's budgetary power.

Taking advantage of the protective legislative regime, the Ministry of Finance, the industry-dominated government advisory council, and Ministry of Finance agents inside JT have already reshaped the formerly flaccid domestic government enterprise to a vast global multi-national corporation now standing at number three on the world stage of international tobacco companies (JT 2003). These same players have worked to preserve the industry's position through business-favorable domestic tax and cigarette pricing determinations (Jha 1999; Chaloupka 2001; Watanabe 2003).

The Ministry of Finance's successful deployment of institutional dominance through its control over the annual fiscal budget process seems even more important. When the budgetary axe swings over lesser agency heads, all players understand the dangers of seeking funding for measures likely to be unpopular with Ministry of Finance budget directors. This enables a wordless annihilation of much meaningful tobacco control program development at the national governmental level, reflected in miniscule tobacco control budgets for decades. Although the reality is admittedly more complicated than presented here

(particularly with regard to the role of intervening legislators (McCubbins and Noble 1995)), overall, Ministry of Finance ownership of tobacco in Japan subtly achieves tobacco industrial promotion by precluding funding for governmental tobacco control initiatives that would otherwise impair the industry's advantages.

2.3 Who owns Japan Tobacco? The debate over further privatization

Both JT and the Ministry of Finance have long wished to accomplish the business of privatization, unfinished because of agricultural interest groups' self-protection in the early 1980s. The Japan Tobacco Incorporation Law requires the Minister of Finance to retain at least two-thirds of JT's stock "for the time being" and at least one-half of JT's stock 'in perpetuity.' Accordingly, the Minister of Finance's holdings are precisely 64.5% of JT's publicly traded stock (Table A.1).

Table A.1 Privatization of Japan's Tobacco Monopoly, 1985 to present

Date	Event	Government ownership	Comments
April, 1985	JT established	**100%**	Japan Tobacco & Salt Public Corporation abolished
October, 1994	First public stock offering	**81.9%**	Poor market interest resulted in less than full subscription for offering
June, 1996	Second public stock offering	**66.7%**	Sale intended for October 1994 completed
April, 2000	Presidency of Katsuhiko Honda announced	0% *(proposed)*	Honda indicates wish for privatization
December, 2000	JT seeks privatization	0% *(proposed)*	Company task force announced
January, 2001	MOF Minister Miyazawa asks for formal report on privatization	50% *(proposed)*	Sale expected in 2002
December, 2001	MOF panel report recommends sale to 50% level	50% *(authorized)*	Sale expected in 2002
July, Dec, 2002	Sale to 50% postponed twice	**66.7%** *(as of 1 June, 2003)*	Owing to market conditions
2003	2.2% sold	**64.5%** *(as of 1 April, 2004)*	
April, 2004	Sale to 50% announced	50% *(planned)*	Sale expected by June 2004

JT officials seek full privatization with no retained government share. While this aspiration coincides generally with the government's announced plans to reduce its share in the other two former state monopolies, NTT and Japan Railway, government plans remain focused on an intermediate divestment of JT stock down to a 50% share. In December 2002, the Ministry of Finance's Policy Review Commission approved divestment to the 50% level (Fiscal System Council 2002a). Two successively scheduled sales were cancelled owing to financial market circumstances and the sale is presently on indefinite hold with a target for early 2004 (Nikkei Weekly 2003).

The foremost political interests at stake in the debate are unrelated to tobacco control. These reflect a persistent and significant divide among pro-tobacco interest groups, most notably between JT (and its Ministry of Finance friends) and tobacco agriculture (and its Ministry of Agriculture friends) in a

relatively even balance of powers (Fiscal System Council 2002a).

Many tobacco control activists in Japan view the government's ownership of JT as an affront to the moral dignity of the nation and actively seek a complete separation of powers between the industry and the government. These proponents generally regard divestment as a necessary step for meaningful tobacco control to succeed in Japan (Hanai 2003). On the other hand, at least one observer has suggested that pragmatically, privatization of JT to date has worked against the interests of tobacco control in Japan (Sato 2000). Others have waged a similar debate with regards to privatization of government monopolies elsewhere (11th World Conference on Tobacco or Health 2000)

This author views further divestment as distinctly counter-productive to tobacco control interests. Rather, tobacco industry ownership should be transferred to the Ministry of Health under a Tobacco Products Control Law for Japan. Health could then develop a meaningful, compassionate, and comprehensive tobacco control regime, while restraining though direct ownership controls the nation's principal tobacco enterprise. Moreover, the precautionary principle should apply here; the government stake is like a railroad right-of-way that, once abandoned, will be nearly impossible to restore.

3 Tobacco control policy

In contrast to industrial promotion policy, tobacco control policy has a shorter and shallower history. Meaningful tobacco control policy was virtually nonexistent before and after the swift demise of an initial effort taken by Japan's Ministry of Health in 1964. This void can be attributed to explicit Ministry of Finance intervention in 1964 and a subsequent chilling effect that continued successfully for nearly thirty years. During that time, the Ministry of Finance put forward minimal steps in response to external pressures, but little more action was evident.

More recently, the tides have changed somewhat. After the Ministry of Health began to take a weak hold on tobacco control in 1987, its initiative grew incrementally (measured relative to pre-1987 circumstances) through the 1990s. However, aggressive Ministry of Health action was quashed in the spring of 2000 when the tobacco industry and the Ministry of Finance won a major policy battle in a drawn-out public confrontation over the future of tobacco control in Japan. As of this writing, the Ministry of Health seems to be trying again, now supported by the first national legislation addressing tobacco control, the Health Promotion Law of 2002, and with the potential of further backing if Japan ratifies and abides by the global FCTC.

As documented elsewhere in this volume, national tobacco control measures in Japan remain extremely weak when viewed in an international

comparative context. Local measures have been more diverse and, at times, have shown greater success. Space does not permit a complete elaboration of local initiatives in Japan, but it is important to recognize the many positive developments now occirring, including some modest tobacco control information campaigns, enforced restrictions on tobacco smoking in public places (including crowded outdoor areas in some major urban centers in Tokyo and elsewhere), and one ground-breaking rural locale that has banned outdoor cigarette vending machines (Levin 2001). Many recent local efforts are the fruits of the Healthy Japan 21 initiative (described in more detail below), carrying the weight for a barred nationwide program. While disparate local measures seem unlikely to effectively reduce the public health consequences of tobacco use in Japan on their own, they serve an important role in framing public discussions and consciousness and paving the way towards more comprehensive national reforms.

Finally, it should be briefly noted that non-binding tobacco industry 'self-regulation' has been a historically significant source of informal tobacco control policy for Japan. This remains true. Again, space does not permit a complete discussion of this complicated issue, whereby modest and meagerly steps often serve as the only game in town, forestalling more aggressive and effective governmental action (Jacobson and Zapawa 2001). Most of Japan's few limitations on tobacco product advertising, including TV and radio broadcast restrictions, and most recently, restrictions on large-format urban billboards, have come out of the 'self-regulation' regime (Table A.2).

Table A.2 Voluntary Advertising Restraints as Claimed by the Tobacco Industry, 1985-2003

Date	Industry self-imposed restriction
Apr.85	Television commercials between 6 p.m. and 9 p.m. Advertisements in women's magazines and magazines with 50% of readers underage Advertisements using celebrities and models popular with minors (Note: only pertained to broadcast advertising; this kind of advertising persists in print media and billboards)
Aug.87	Advertisements using images of smoking women
Jan.89	Television commercials from 5 a.m. to 8 p.m.
Oct.95	Radio commercials on weekends Outdoor billboards within 100 meters of the front entrance of elementary, junior and senior high schools
Apr.98	All television and radio cigarette product commercials (Note: does not include 'manner campaigns' and corporate image promotions, which are still broadcast regularly on Japanese television)
Jun.02	Advertising in magazines with more than 25% of readers underage Outdoor billboards larger than 35 square meters

Source: Asahi Shimbun, July 9, 2003; notes by Levin, July 2003

3.1 Finance runs the show: tobacco control policy through 1987

3.1.1 Complete Ministry of Finance control through 1964

Until 1964, the Ministry of Finance was the only player in tobacco control in Japan. At least two changes seem to have been carried out through behind-the-scenes informal administrative guidance from the Ministry to JTSPC in the late 1950s. The most significant turn was JTSPC's development and promotion of filter cigarettes. Filter cigarettes, which were virtually unavailable in Japan in 1960, rose to capture over 90 percent of the market by 1970 and 98 percent of the market by 1980. In 1957, JTSPC also commenced internal research into the effects of tobacco upon health, though unlike US counterparts' research, the unpublished results of this research remain out of the public's purview.

In fairness, Japan's circumstances at this time were not dramatically different from tobacco control policy elsewhere around the world. Moreover, it should be noted that Ministry of Finance involvement in these initiatives is only presumed from knowledge of how Japanese government agencies operated at the time (Johnson 1982; Young 1984), and has not been confirmed via publicly available documents.

3.1.2 Lost turning point: the quashed 1964 public health engagement

US Surgeon General Luther Terry's 1964 report on Smoking and Health was a clarion call to action for senior public health officials in Japan. Just two weeks after the report's release, the Ministry of Health's Pediatrics Section Chief issued a directive to all prefectural governors and to mayors of major cities urging stronger efforts for the prevention of underage smoking to promote pediatric health. Two days later, the Ministry's Public Health Section Chief assembled a committee of nine medical specialists to evaluate the US report. This committee reported back within only a week, and while hedging somewhat their observations about local circumstances in Japan, the specialists' conclusions were nonetheless grave: **"[I]t can be inferred from the instant report that in the long term, juvenile commencement of smoking and heavy smoking consumption will become major causes of lung cancer mortality [in Japan] above present levels."**

Based upon the latter report, the same Public Health Section Chief, on February 6, 1964, issued MOH's second directive on smoking and health to all prefectural governors and the mayors of major cities declaring it to be "clear that long-term and heavy tobacco consumption by adults detrimentally affect health" and stating a desire that measures be taken to widely disseminate information and guidance to the public concerning the health harms caused by smoking.

In what must be the greatest lost opportunity ever for public health in

Japan, these Ministry of Health officials and their peers instantaneously shifted from urgent action to perfect silence and the Ministry took no further official public action on smoking and health for 24 years. Hearsay reports allege (and reasonable logic accepts) that this was due to immediate and intense Ministry of Finance pressure at the highest levels. Other governmental and political interests may have been involved as well, including the agricultural and trade ministries and their public constituencies.

Certainly, the "what-if" game brings sad epidemiological results to consider where tobacco related mortality would be today in Japan if the Ministry of Health had been able to continue vigorously pursuing tobacco control policies from 1964.

3.1.3 1964 -1987: Finance's unrivaled dominance and minimal regulation

Despite that Japanese ministries are known for claiming extraordinarily broad-reaching jurisdictional reach in comparison with their US counterparts (Johnson 1982; Haley 1989), the Ministry of Health's null stake in tobacco control was confirmed publicly in 1971 when the Minister of Health testified in the Diet that tobacco was beyond his ministry's jurisdiction. In fact, even the World Health Organization's 1970 important recommendation on tobacco or health, officially delivered to the Minister of Health, was merely forwarded to the Minister of Finance with no other public action.

In subsequent years, the Ministry of Health issued only three notices of rather limited scope. A 1978 notice directed administrators of national hospitals and clinics (only a very few of Japan's many hospitals) to restrict smoking in those facilities to designated smoking areas. A 1980 request asked prefectural governors, mayors of major cities, and Tokyo ward chiefs, to strengthen their efforts to provide public education about the health effects of tobacco smoking. And a 1984 request asked prefectural governors to ask public medical service providers under the governors' jurisdiction to consider smoking restrictions or improved ventilation in hospital and clinic waiting areas, particularly in facilities where patients with respiratory ailments or and infants might be gathered.

Meanwhile, in the late 1960s, JTSPC took two small steps that may also be presumed to have come from Ministry of Finance policy guidance. From April 1967, JTSPC made public tar and nicotine levels of its cigarette brands and initiated its first 'self-regulation' program concerning tobacco advertising and promotion in November 1969.

Ultimately the Ministry of Finance was somewhat active in only one instance in this time period. Two weeks after officially receiving the 1970 WHO recommendation from the Minister of Health, the Ministry of Finance submitted an inquiry to the Monopoly Industries Government Advisory Council asking for

advice on appropriate measures concerning smoking and health. The Advisory Council's report came back with predictably tame recommendations, particularly finding that a health warning on tobacco packages was not advisable. However, outside pressure from opposition members of the Diet and newspaper editorial pages pushed the Ministry of Finance to take slightly more aggressive measures. On April 20, 1972, the Ministry of Finance issued formal instructions to JTSPC to follow the report's recommendations regarding tar and nicotine disclosure and, going further, to place a modest warning on cigarette packaging: "For health reasons, let's be careful not to smoke too much."

Apart from this, the Ministry of Finance's construction of a post-1964 tobacco control policy vacuum through 1987 was nearly perfect. Throughout this time, Finance took the minimum measures sufficient to prove that some action was taken while fundamentally preserving its primary interest of promoting the tobacco industry. Tobacco control initiatives by other government agencies were essentially nil.

3.2 Rivalry emerges, Health vs. Finance: 1987-2001

3.2.1 Health's first steps get some results

Japan's Ministry of Health returned to public engagement in tobacco control in conjunction with the Sixth World Conference on Smoking and Health in Tokyo in 1987. Since Japan would be on the world's stage with little to show in terms of governmental tobacco control efforts, Ministry of Health officials hastily prepared a white paper on smoking and health that was released just one month ahead of the conference. This was the first government document in Japan to unambiguously recognize links between tobacco and various health harms. The report extensively documented adverse public health effects concerning tobacco use, but concrete suggestions for tobacco policy reform were allegedly removed prior to publication.

The 1987 White Paper spurred reform by the Ministry of Finance, unquestionably modest (or perhaps, minimalist) in scope, but nonetheless the highest level of tobacco control seen in Japan to date. In 1988, Finance's Tobacco Industry Government Advisory Council set up a sub-committee to consider tobacco and health issues. This Council's May 1989 report proposed strengthened warnings and tar and nicotine levels on tobacco packages and invited industry 'self-regulation' concerning tobacco television advertising and outdoor tobacco vending machines' late night operations. Proposed changes arrived gradually over the next seven years. Tobacco package warnings were revised to the warning presently in use ("As smoking might injure your health, let's be careful not to smoke too much") almost two years later. Television advertising for cigarettes

moved back from an 8:54 pm starting time to 9:54 in August 1990, and to 10:54 pm in April 1991 (keeping the important late night news closing slot until April 1998). Finally, in 1996, Japan's tobacco vendors' industry association agreed to turn off outdoor vending machines from 11 pm to 5 am after April 1996 in a measure ostensibly to prevent youth access to tobacco purchases. (Levin 2000).

Regardless of its modest success with the 1987 White Paper, the Ministry of Health once again opted for a quiet role after 1987, coordinating annual pronouncements with WHO's World No-Smoking Day and little more. Tobacco was erased from the draft text of a 1989 report on national health promotion and the 1993 revised edition of the White Paper on Smoking and Health followed the first edition's model by omitting any policy recommendations.

3.2.2 Tobacco Action Plan Working Group, 1995

Things started to change from October 1994 in conjunction with the temporary absence from power of the Liberal Democratic Party, which had been the ruling political party since 1955. Not surprisingly, this was a time for making changes in countless areas of public policy. The Ministry of Health's move came when the Director General of the Health Service Bureau established a Tobacco Action Plan Working Group to consider national policy direction regarding tobacco and health. In contrast to Finance's Tobacco Industry Government Advisory Council, Health's Working Group members were balanced to include cancer specialists and representatives from consumer and anti-smoking groups as well as tobacco industry representatives and their allies.

After several highly contentious meetings, the Working Group's March 1995 report was major news. The report urged action in three broad areas: (1) comprehensive prevention of underage smoking, (2) creation for non-smokers of an environment supporting the removal or reduction of passive smoke exposure, and (3) providing support for current smokers who desire to quit or cut back consumption. (The report's conclusions also included an acknowledgment of the beneficial attributes of smoking.) The report proposed approximately twenty specific policy initiatives aimed towards fostering the three goals identified above.

Hindsight in 2003 reveals limited accomplishment of the optimistic goals articulated in the 1995 Working Group Report, although positive momentum has been constant with regards to environmental tobacco smoke exposure in public places. But the symbolic value of the 1995 Working Group's action should not be overlooked. The Ministry of Health's interest and achievement in tobacco control has ebbed and flowed since, but the basic jurisdictional fact that Japan's Ministry of Health will be engaged in tobacco control policy no longer seems in doubt (Kessler 2001).

3.2.3 The battle over Healthy Japan 21

In November 1996, despite the fact that the Liberal Democratic Party had returned to power, tobacco control remained on the Ministry of Health's agenda owing to then Prime Minister Ryutaro Hashimoto's appointment of Jun'ichiro Koizumi to the Health portfolio.

Koizumi strongly supported and encouraged tobacco control efforts at the Ministry. Most notably, Koizumi intervened in favor of tobacco control in the preparation of an important official White Paper on Health published in 1997 that unequivocally indicated tobacco as an addictive product that is harmful to the user and harmful to others. This powerful language, anathema to the Ministry of Finance's outlook, arguably represented Health's first direct challenge to Finance's hegemony on tobacco policy.

The next round was a setback for tobacco control. In February 1998, Koizumi established the Ministry's 21st Century Tobacco Policy Deliberation Committee with a balance of Health- and Finance-approved supporters similar to the makeup of the 1995 Working Group. Tobacco industry supporters successfully maneuvered this Committee to wind down its activities in August 1998 with an inconclusive report presenting conflicting views for future tobacco policy. Although little forward motion was achieved, a key lesson appears to have been learned here. Subsequent Ministry of Health committees have not since provided courtesy seating to tobacco industry supporters likely to disrupt or derail tobacco control initiatives.

Koizumi lost his position as Minister of Health in July 1998, but his replacement, Sohei Miyashita was also a strong supporter of tobacco control. Under Miyashita's lead, the Ministry of Health supported three major tobacco control initiatives: sending a tobacco control expert to the October 1999 FCTC Working Group meeting in Geneva, supporting a November 1999 WHO International Conference on Women and Children's Tobacco Use in Kobe (Samet and Yoon 2001), and including tobacco control as a part of 'Healthy Japan 21' (hereafter HJ21), the Ministry's newest overall public health initiative.

HJ21 was a major health promotion initiative under the aegis of the Ministry's Council on Public Health, one of Health's foremost advisory bodies. The HJ21 Working Group's tobacco sub-group was the first panel established under Ministry of Health authority to operate without including at least a minority of Finance's delegates. In August 1999, the tobacco sub-group, working free of Finance's influence, announced draft plans to halve the percentage of Japanese who smoke and the total number of cigarettes consumed annually in the country by the year 2010. These hard-hitting numerical-based targets immediately became the focal point for an all-out political battle waged by all interests connected with

the tobacco industry in Japan.

First, a new Director-General of the Ministry's Health Services bureau in September 1999 was appointed. Miyashita's replacement as the Minister of Health followed shortly thereafter. The new Minister, Yuya Niwa, would not defend the draft as the new Health Services administrator took it apart. In November 1999, just after the WHO conference in Kobe (the timing here is unlikely to have been a coincidence), the Liberal Democratic Party's crucially influential Policy Research Council sent a resolution to the Ministry of Health opposing numerical targets in the Healthy Japan 21 program with regards to tobacco.

In February 2000, the HJ21 Working Group, under pressure to preserve the HJ21 overall program threatened by pro-tobacco interests, eliminated the numerical targets pertaining to tobacco. The HJ21 Program was inaugurated with only weak hortative aspirations including 'dissemination of knowledge,' "making a thorough distinction between where people can and cannot smoke," and "promoting programs to help people stop smoking to the point where they can receive assistance anywhere."

In July 2000, Prime Minister Mori appointed a top leader of tobacco industry supporters in the LDP, Yuji Tsushima, as the Minister of Health, to annihilate any lingering tobacco control sentiments within the Ministry's ranks. By August 2000, the Ministry's Office of Smoking and Health had no staff and tobacco control was a part-time job for two low-level non-professional staffers in the Ministry's Public Health section.

Although the next section suggests that things may at last be changing, HJ21 represented another major lost opportunity in Japan. Moreover, the loss reveals the entrenched and powerful status of the tobacco industry's voice in public policy at least as recently as 2000. This is not surprising. The Liberal Democrats are famed for their strong ties to agricultural interests and have a long history of protectionism in favor of those interests. Moreover, a number of other powerful interests seem inclined to push the Liberal Democratic Party towards a pro-tobacco industry perspective. The party has long-standing and close ties in the central Tokyo area with the Ministry of Finance bureaucracy, with powerful pan-industry business organizations such as the Keidanren that include JT among their members, and presumably with the senior executives of JT itself. Second, the party is responsive to media and advertising industry interests, most notably Japan's big five major media companies and with the world's largest advertising combine. Given the enormous sums spent by the tobacco industry on advertising and promotion in Japan, the media and advertising world shares a pro-tobacco perspective that is certain to be reflected in its political 'wish lists.' Finally, the greatest political interest favoring the tobacco industry likely comes from the collective voices of over 300,000 tobacco retailers. Tobacco retail includes both

major business players (e.g. the convenience store chains) and a multitude of 'mom-and-pop' tobacconists present in every electoral district. Not only elected officials from tobacco growing regions or party leaders with elite ties to the Tokyo business community, but rather virtually every LDP parliamentarian has reason to acquiesce to pro-tobacco interests.

3.3 Has the tide turned? Tobacco control policy in Japan today

Since the summer of 2001, there has been an unprecedented (for Japan) series of major tobacco control policy-related events in Japan. To this observer, it seems that meaningful policy initiatives are accomplishing real changes in the tobacco environment in Japan. At least within the domestic arena and without regarding JT's multinational growth outside Japan, the tide may have turned (Table A.3).

Table A.3 Major Tobacco Policy Events, 2001-2003

Date	Event	Comments
Summer 2001	Minors Smoking Prohibition Law revision	Penalties strengthened; substantial media attention
Mar.02	Parliamentarian's Tobacco Control League established	Announced on March 7, 2002 with 64 members; by December 2002, over 90 parliamentarians had signed on
Summer 2002	Health Promotion Law of 2002	Art. 25 provides for nationwide protection from tobacco smoke pollution
Oct.02	Fiscal System Council Interim Report on Smoking And Health	Generally industry defensive but recommends baseline tobacco control policies including revision of package and advertising warnings;
Dec.02	Health Sciences Council Report on Future Measures for Smoking	Recommends substantial tobacco control policy changes for Japan
Mar.03	Tax increase approved	¥20 per pack, effective July 1, 2003
1.May.03	Health Promotion Law takes effect	Substantial nationwide media attention; countless large and small positive changes towards clean indoor air
21.May.03	FCTC unanimously approved in Geneva	Government of Japan agrees in early May to vote to approve treaty (though no commitment to join as signer); substantial nationwide media attention
1.Jul.03	Tax increase takes effect	Roughly 8% price increase on cigarettes nationwide

3.3.1 Acts of parliament: the revised Minors' Smoking Prohibition Law and the Health Promotion Law

In September 2001, the Japanese Diet revised Japan's 100-year old Minors' Smoking Prohibition Law to strengthen the penalties imposed on merchants who sell to minors where the retailers know the buyer to be purchasing for their own use. It is easy to imagine that the practical result of the 'knowing' clause makes the law text profoundly self-limiting, but further limitations curtail Japan's youth-oriented tobacco control regime as well. The law has no official compliance assessment or enforcement system and the ubiquity of free-standing tobacco vending machines throughout Japan allows youth free access to tobacco

without having to face a merchant. Nevertheless, at a minimum, the legislative revision brought the issue of youth smoking into the public arena and arguably confirmed a degree of public support for policies to reduce youth smoking rates. It was a small first step heralding further reforms to come.

Far more significant legislative action came one year later with the enactment of the Health Promotion Law of 2003. This law, the outcome of the Healthy Japan 21 project, enacted a wide-ranging list of health promotion measures primarily addressing lifestyle-related health promotion initiatives. Buried inside the law, Article 25 established Japan's first nationwide statutory provision addressing protection from tobacco smoke pollution:

> **"Prevention from Passive Smoking Exposure: Persons who manage schools, gymnasiums, hospitals, theatres, public assembly halls, gallery spaces, department stores, offices, government buildings, restaurants and bars, and other facilities used by numerous people should try to take whatever steps are necessary to prevent passive smoking exposure (i.e. being forced to breath other persons' tobacco smoke in indoor or functionally equivalent spaces) for the users of such facilities."**

A new force on the tobacco policy political scene, the Japan Parliamentarians' Tobacco Control League, facilitated this remarkable enactment, emerging from the ashes of the Healthy Japan 21 numerical quota defeat. The non-partisan League, established on March 7, 2002, gathered 64 Diet members from all of the major political parties. Its opening meeting achieved substantial media coverage (Watanabe 2002). Moreover, a host of additional Diet members continued to sign on later, significantly exceeding its founders' expectations. By December 2002, over 90 parliamentarians or roughly 12% of the total membership had gone on the record endorsing the idea of a tobacco control legislative agenda for Japan (Watanabe 2003).

The merely hortative language of Health Promotion Law Article 25 may appear inadequate, but this kind of phrasing is relatively common in Japanese legislative texts aiming towards achieving difficult and controversial social changes (Levin 1997). Contemporaneous guidelines on tobacco smoke pollution issued by the Ministry of Health took a more aggressive stance, indicating, for example, disfavor of open air separation of smokers from non-smokers and/or air cleaning devices as ineffective. Moreover, as noted below, even within weeks after the law took formal effect, its accomplishments have been substantial.

3.3.2 Dueling councils: Finance and Health face off

Following the enactment of the Health Promotion Law, and with work

on the FCTC moving forward in Geneva, the spotlight shifted from the legislative to the administrative arena. Throughout 2002, two separate government advisory councils of experts were at work in competing efforts to design tobacco policy for Japan under a future global FCTC regime.

Finance's team, under the auspices of the powerful Fiscal System Council, took the front position by publishing its interim findings in October 2002. The report's findings and recommendations were primarily industry-defensive. The report's overall posture was that non-youth related tobacco control policy should only be aimed towards informed consent (and accordingly, smoking then becomes the individual consumer's responsibility), that reducing tobacco consumption or prohibition are inappropriate policy goals, and that notwithstanding global movement towards the FCTC, policies should be independently developed by nations in accordance with their own values and political systems. Nevertheless, the report gave in to external pressures in at least two key areas – acknowledging that smoking has been epidemiologically proven as a disease risk factor, and agreeing to revise (details to be worked out later- and the devil is in the details) Japan's tobacco package and advertising warnings to stricter requirements in compliance with the anticipated FCTC. On the other hand, the report was replete with defensive positions, including that tobacco is an 'item of preference' for consumers, refusing significant restrictions on marketing practices such as with regards to 'light' and 'mild' tobacco products, and essentially keeping vending machines on the landscape in Japan, albeit with some restrictions on the location of machines and an expectation that age-verification technology will eliminate youth access problems by 2008.

It is fair to describe the Health Science Council's Report on Future Measures for Smoking in Japan, issued December 25, 2002, as the polar opposite of the Fiscal System Council's report. This report proffered ample evidence-based findings on tobacco health harms to smokers and non-smokers, and addressed addictiveness. The report included what was perhaps the broadest-to-date economic assessment on the costs of tobacco use for Japan, including for example recognition of implications for labor productivity associated with increased mortality. The Health Science Council proposed a broad set of counter-measures for Japan's future, consonant with the FCTC and the best interests of public health. Most dramatic was a call to reduce youth smoking to zero and promotion of smoking cessation programs nationwide.

Obviously, the two dueling reports were speaking to their respective constituencies. However, the ramifications are more significant than a staged shouting match. First, both reports explicitly targeted policymakers in the Japanese Government involved with the FCTC intergovernmental negotiations. (Arguably, both were influential. The Japanese Government assiduously worked on behalf of JT to weaken the FCTC text during intergovernmental negotiations.

On the other hand and contrary to many expectations, the Government voted with the unanimous body of the World Health Assembly to approve the final text of the FCTC in May 2003). Second, because Finance's limited concessions are certain to be achieved, this will at least revise Japan's modest package warning in place since 1991: "As smoking might injure your health, let's be careful not to smoke too much." Finally, it is clear that independent tobacco control initiatives are now permanently established as part of the policy framework for Japan. In light of the history reported in this chapter, this represents a true sea change.

3.3.3 From a snowball to an avalanche: tobacco control policy in 2003

In 2003, the pace of tobacco control activity continued to grow, with the majority of events reflecting forward progress.

In January, the Japanese parliament followed a ruling party proposal for a modest tax increase on cigarettes, the first tax increase explicitly justified in the name of reducing tobacco consumption. While the roughly ¥20 per package increase was less than had been initially hoped for by public health advocates, a massive public relations campaign launched by tobacco industry forces in late 2002 to avoid any increase was also unsuccessful. This was a tobacco control victory. Given the substantial body of evidence showing the value of tax hikes towards accomplishing reductions in tobacco consumption, one hopes for further increases to come (Chaloupka et al. 2001).

Tobacco control drew substantial media attention, including favorable editorial writing, in 2003 associated with the tax increase decision, the March FCTC intergovernmental negotiations, the May FCTC enactment, the May 1 implementation of the Health Promotion Law Article 25, and the implementation of the ¥20 per package tax increase on July 1. Among these events, Article 25 has had the most significant short-term impact on the environment in Japan and the Act's potential as a positive force for long-term change in Japan cannot be underestimated.

The list of smoking restrictions and other tobacco control items reported in the media in connection with Article 25 is too long to particularize and, in fact, inadequate since the media has likely only revealed the tip of the iceberg. Major reports focused on the eight private railways in the Tokyo area removing their vestigial designated smoking areas, a number of local and prefectural governmental buildings banning all indoor smoking, schools and universities completely removing smoking from their campuses, and even a new line on Japan's famed 'Bullet Train' that will have no designated smoking cars from its inception. Moreover, countless other changes are observable though not reported in the media. All across Japan in public and privately-owned facilities, non-smoking areas have been set up where none existed before, and formerly

designated smoking areas have been reduced or eliminated creating wholly smoke-free spaces. Unblocking a dam of pent-up hopes and expectations, Article 25 has served as an energized catalyst giving legitimacy and authority to clean air advocates in Japan.

4 Conclusion – Japan's Future with the FCTC

Understanding of Japan's past governmental practices in the international arena takes on greater importance with the development of the FCTC. Evidence shows that Japan's treaty negotiations have been 'largely defensive in nature'when faced with developing international law obligations that run counter to domestic practices and interests (Warsaw 1998). This phrasing captures Japan's methodology in the FCTC intergovernmental negotiations (The Daily Yomiuri 2003) where Japan took the bottom prize among all national and international participants in the FCTC negotiations as most frequent recipient of the Framework Convention Alliance's reproachful Dirty Ashtray Award (Framework Convention Alliance 2003).

Warszawa's study of Japan's follow-up on the Convention for the Elimination of Discrimination Against Women (CEDAW) is revealing. To avoid embarrassment, Japan voted for the CEDAW Convention in the UN General Assembly and was one of the few nations in the world to ratify the Convention with no reservations (Warsaw 1998). In subsequent practice however, Japan has been willing to buck international pressure in the implementation of its obligations under CEDAW. After making superficial amendments to its domestic laws to apparently put the nation in compliance with international obligations, many observers argue that meaningful gender policy change in Japan has not been forthcoming (Knapp 1999; Kawakawa 1999).

Given this data, it is at least a fair conjecture that questions of Japan7s ratification of the treaty and its future implementation of the FCTC will follow similar paths, i.e. Japan will ratify the FCTC, but its realization of the its goals and obligations will proceed slowly.

On the other hand, domestic trends over the past two years have shown an unmistakable trend towards more significant tobacco control policies. It seems highly possible that within Japan, effective tobacco control policies will continue to be developed and implemented, and positive results will follow. This author observed in the past that a conscientious effort to reduce Japan's high tobacco consumption would have high prospects for success (Levin 1997). This remains true. With the growing strength of the Parliamentarians' League for Tobacco Control and apparent popular satisfaction with changes coming through under the Health Promotion Law, there may at last be room for optimism that Japan will soon turn the corner on the inequitable and tragic burden of tobacco-related

disease at home.

Concern lingers with Japan's involvement in the global tobacco epidemic through its multinational business proxy JT. This behavior may leave Japan in an unfortunate rogue status (together with the United States and Great Britain) as responsible for countless deaths of non-Japanese people around the world. Yet, for example, none of the three significant advisory reports sponsored by the government in recent years addressed international issues relating to Japan's global tobacco industry (Fiscal System Council 2002a, b; Health Sciences Council 2002). Accordingly, policy makers in Japan may wish to consider further the international implications of their tobacco control policies together with their domestic policy advances.

Notes

1. Much of the history set out here is drawn from Levin (1997), which is extensively footnoted with research references. For historical matters through 1996, citations are omitted and readers are invited to find further information in that article

2. In 2001, the Japanese government carried out a massive reorganization of nearly all national government agencies. Nearly all existing agencies were reshaped, merged, divested, and renamed (in official English, Japanese, or both). For example, the former Ministry of Finance (Okurasho) became the Ministry of Finance (Zaimusho), with various functions divested to new agencies. The former Ministry of Health and Welfare (Koseisho) merged with the former Ministry of Labor to become the Ministry of Health, Labor, and Welfare (Kosei-Rodosho). Nevertheless, these agencies' core functions were not significantly changed with regards to tobacco policy. Accordingly, for simplicity and clarity, this chapter uses the current names throughout, regardless of reference to current or prior entities.

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Postscript : B
The Tobacco Industry and its Activities in Japan

1 Introduction

Through litigation in the United States and other avenues, tobacco industry's internal documents have become accessible to the public and have been the focus of research. These documents provide a picture of the industry's plans, activities, and efforts to thwart tobacco control.[1] In order to obtain background and additional information for the issues discussed in the chapters of this report, we reviewed industry documents for mention of Japan Tobacco Inc. The documents described here reflect the interaction of Japan Tobacco Inc. with other tobacco multinationals.

This appendix provides an overview of the tobacco industry activities in Japan and how they have interfered with the development of effective tobacco control policy measures.

2 Methods

An Internet-based search on tobacco industry documents related to Japan was carried out. These documents have been made publicly available on the Internet after the November 1998 Master Settlement Agreement between US based tobacco companies and 46 US states and the territories. Although Japan Tobacco International USA became a participating manufacturer in February of 1999, it was not one of the Original Participating Manufacturers;[2] therefore it is not required to maintain a website with internal documents that result from legal disclosure procedures. However, documents from Japan Tobacco Inc. are available on other companies' website.

The search, mainly in the UCSF Legacy Tobacco Industry Documents Library (http://legacy.library.ucsf.edu/), with supplementation from industry-maintained sites such as Philip Morris (www.pmdocs.com), was conducted during the months of May and June 2003 using Japan* as the main keyword, but limited by date to documents written in 1998-2002. Supplemental searches using earlier dates were conducted to follow-up on keywords identified through the initial search. Earlier documents were also used when historical context for events was needed. In addition, refined searches were used to pursue some topics more in depth. For example, Japan & ETS & Consultant* was one of the additional searches conducted.

Data were also obtained from some publicly available information in media outlets and the tobacco companies' own websites.

3 Major Findings

3.1 The Japanese Tobacco Market

Japan Tobacco Inc.

The Japanese tobacco market is dominated by Japan Tobacco (JT). JT is part of the Japan Tobacco Inc. (JT Inc.), which also owns Japan Tobacco International (JTI). In addition to tobacco, Japan Tobacco Inc. owns pharmaceutical and food businesses, as well as other business such as real state and agriculture[3] but the major revenue generating business for the company is the domestic and international sales of tobacco products.[4] In the fiscal year ended March 2003, JT Inc. announced a decrease in domestic sales of tobacco, but a "strong performance" by its international tobacco business, with a net sales increase of JPY 27.3 billion to JPY 691.3 billion.[4]

The Japan Tobacco Inc.'s domestic tobacco business, Japan Tobacco, has 75% of the market share in Japan.[5] Japan's main brands are Mild Seven, Cabin, Caster, Seven Stars and Peace, with Mild Seven being Japan's leading cigarette. Solely owned by the Japanese government for decades, as Japan Tobacco and Salt, in 1985 it became a public company. However, the government still owns 2/3 of the company shares. (Foreign companies, mainly Philip Morris and British American Tobacco, have the rest of the market share.)

In 2002, JT Inc. issued its new global wide mission as a "promise to deliver 'irreplaceable delight' which means pleasurable surprises, something surpass your expectations, joy to all our stakeholders and to be an 'irreplaceable company'."[6] In fact, although many tobacco companies have become more

upfront about admitting the harmful health effects of smoking, JT Inc. continues to release vague statements on the issue, emphasizing that "cigarettes give a refreshment to your life".[7]

Japan Tobacco International (JTI) was part of Japan Tobacco's expansion process, which catapulted when in 1999 Japan Tobacco bought the international operations of R.J Reynolds Inc. JTI is now the third largest multinational tobacco company in the world, behind Philip Morris and British American Tobacco, and manufactures "three of the world's top five cigarette brands - Camel, Mild Seven and Winston - and one of the world's leading menthol brands, Salem."[8] JTI is based in Switzerland.

Of interest are JTI's official statements on several smoking and health issues and a declared intention to focus on the development of reduced harm tobacco products. JTI's website emphasizes smoking as an adult decision, but unlike JT Inc.'s website tobacco page, at least JTI acknowledges that public health authorities have determined that smoking carries risks. It further states that "These risks distinguish tobacco from most consumer goods and they place upon us a real burden of responsibility. It's a responsibility we expect to be held accountable for, together with governments and the rest of society."[9] Both JT and JTI claim that cigarettes are an "item of personal preference (Shikohin in Japanese)".

Although publicly stating that it is open to debate on the issue of smoking and health, JTI fails to fully agree with health hazards of smoking, and usually takes the position that

> Public health authorities have determined that smoking is a cause of, or an important risk factor for, certain diseases, including lung cancer, heart disease and chronic obstructive pulmonary disease (COPD). They inform the public accordingly; we support their efforts to do so, and we believe that people should take these conclusions into account when deciding whether or not to smoke... Notwithstanding the gaps in scientific knowledge, we have long recognized the real risks associated with smoking. This recognition has driven much of our product development research and our desire to develop an appropriate regulatory framework for tobacco. It is also the basis of our commitment to stop minors from smoking and our willingness to embrace sensible and practical restrictions on marketing our brands... different societies feel very differently about smoking. In many cases this means extremely tough regulation. We have

> the right to express our point of view but we ultimately respect the judgment of each individual society. We do not believe that there is a single, global "solution" to the tobacco controversy.[9]

On the issue of exposure to second hand smoke, which will be discussed later in this appendix, JTI states that "smoking is annoying to many non-smokers. If people want to smoke they need to show more courtesy to non-smokers. We advocate appropriate separation of smokers and non-smokers. We accept that the burden of responsibility lies with smokers rather than non-smokers."[9]

On a 2000 media report JT Inc. President, Masaru Mizuno, is quoted as saying:

> ····The Japanese tobacco market is mamoth···· There are absolutely no restrictions on distribution and marketing···· In Japan, the industry self-regulatory advertising rules render it impossible to advertise specific brands of cigarettes on TV or radio. But the rules are even more stringent in Europe and America.[10]

The Japan Tobacco Inc. website does not include positions on smoking and health issues in its domestic tobacco business page. It does include the following:

> Raising awareness about smoking manners via the "Smokin' Clean" campaign.
> For more a favorable relationship between tobacco and society, [sic] JT has been running its Smokin' Clean campaign for more than 20 years since 1974. Through the campaign, we ask all smokers not to discard their cigarette butts in public places, to be careful considerate to nonsmokers and to be careful to prevent fires. While we're aggressively taking on dissemination and improvement of smoking etiquette by spreading these messages through ads on TV, newspapers and public transportation, we are also conducting clean-up campaigns around the nation throughout the year. We sponsor the installation of smoking stands in train stations, downtown areas and sightseeing spots as part of the campaign to "put the cigarette butts properly into the ashtray or smoking stand." We make and offer portable ashtrays in collaboration with the nation's beautification organization and tourism association. We also engage in the joint development of train air-conditioning and ventilation systems using JT's

> advanced technologies, in an effort to seek solutions enabling smokers and nonsmokers to coexist. [5]

As exemplified by JT Inc.'s decades-long program, restrictions of public smoking in Japan are based on reduction of litter and the risk of burning others with a lit cigarette, relying on Japanese's society emphasis on manners and tolerance. Public smoking restrictions have seldom, to date, been based on the health effects of exposure to tobacco smoke. Another interesting source of information is competitors' profile reports found in the Philip Morris files discussing JT. Some are extensive and detailed accounts of the business operation, structure, and business strategies of the Japanese company.[11]

Philip Morris International (PMI)

PMI's presence in Japan increased in the mid-1980s, after the market was liberalized to foreign companies. At the time, PMI maintained a licensing arrangement with JT for Marlboro manufacturing, but established, in 1985, a Japanese subsidiary, Philip Morris Kabushiki Kaisha (PMKK).[12] A 1987 document discusses the Japanese tobacco market and strategies to maximize PM's access to it. It notes how, despite the privatization, JT has control of all steps of cigarette production and distribution; therefore, establishing good working relationships with JT is an essential step for PM's entry in the market. [13]

A 1999 PMI presentation discusses how the company's presence in the Japanese market is a "story of foresight, perseverance, commitment to our trademarks, effective lobbying, and some luck."[14] This presentation describes PM's history in Japan, how it overcame existing barriers in order to achieve a growing share of the market, including how PM took advantage of the US Government Marketing, Advertisement and Distribution Agreement with Japan:

> ····Together with other U.S. cigarette exporters, we began lobbying the U.S. government to take up our case. They agreed to do this. In 1983 the government signed a historic Marketing, Advertising and Distribution agreement with the Japanese. Duties were reduced from 90% to 35% and later to 20%. We [PMI] acquired the right to advertise in all media and expanded our distribution from 14,000 to approximately 30,000 outlets out of a potential market of about 200,000 outlets. All along we persevered with our marketing efforts... The 20% duty [on imported cigarettes] remained the problem [to further growth and lower the price of PM brands]... In 1985, Philip Morris began

> pressing the U.S. government to investigate Japanese trade practices in the cigarette market under Section 301 of the Trade Practices Act. After eighteen months of negotiations an agreement was reached that provided total suspension of tariffs on imported cigarettes effective April 1, 1987 ... In 1987 our volume more than doubled... Today cigarettes are the leading U.S. export to Japan. And PMI has two-thirds of that business····[14]

A 2000 PMI presentation[15] on the Japan region provides important information about PMI in Japan and the importance of the country as a cigarette market and for PM's profits. In 1996 PMKK was PMI's biggest contributor. PMKK has approximately 20% share of market and it keeps gaining. PM has five core brands in Japan: Parliament, Virginia Slims, Lark, Philip Morris and Marlboro. All brands have "lights" variant as well as a growing share for Marlboro menthol. This presentation discusses the negative impact of a 1997 tax increase, coupled with a softer economy, on the cigarette market, and how in March 1998, PMI rolled back the 10 yen price increase, seeing an immediate response, "illustrating the growing price sensitivity of Japanese consumers." The presentation also describes as a main event the "decision to voluntarily eliminate electronic media", effective April 1998, and how it led to the reinvention of media campaigns, mainly for Lark and Philip Morris. In addition, Virginia Slims is described as "the best known cigarette for women in this market and a terrific growth brand for PMKK····".[15]

This 2000 presentation also discusses the introduction of the December 1998 tobacco tax. It states:

> As we became aware that this tax increase was going to take place, one of our biggest concerns was how it would affect our Lark brand recently revived by the 10 Yen roll-back. Based on careful analysis, including possible competitive reactions, we agreed with New York management to absorb the 20-yen tax increase on the Lark brand and favor the continued long-term growth of the business····[15]

As discussed below, Lark's success is part of the Japanese market trend to choose "light" cigarettes.

The presentation also addresses policy issues:

> As a strong number two in the Japanese market we must also take an increasing role in industry issues. There are currently

> four major areas in which we are active both independently and as part of the Tobacco Institute of Japan. Underage smoking prevention, littering, packaging recycling and cigarette excise taxation····Littering prevention is an important part of our "good smoking" manner campaign····With the Japanese government facing huge budgetary pressure a further [tax] increase was proposed [in 1999]. The efforts of the industry and the opposition of smokers defeated this proposal before it was formally discussed in the parliamentary budget session···· Japanese society has in the past dealt with cigarette industry issues in a reasonable manner and helped by our efforts this should continue to be the case in the future····[15]

In a 1995 overview of the Japanese market PM stresses the importance of strengthening both alliances within the industry to oppose tobacco control measures. [16] The overview also discusses the need for PMKK to strengthen its own lobbying power and "develop further relationship with government officials and politicians" in order to continue to gain share of market in the country. [16] Another strategy suggested is for PMKK to develop "continuous public relations programs to become an important member of Japanese society." [16] In fact, similar to its activities in other parts of the world, PMKK supported several philanthropic endeavors, such as the publication of a book to celebrate the 10th anniversary of the Japan Art Association [17] and it support for young, emerging artists, among other philanthropic endeavors. [18]

The Tobacco Institute of Japan (TIOJ)

The Tobacco Institute of Japan (TIOJ) is an industry group and works to protect the industry's interests in the country. It is also a testing laboratory which in 1989 was authorized by the Minister of Finance to measure tar and nicotine content and to verify values stated in packs of cigarettes sold in Japan. The laboratory used a measuring system that was different from the ISO/FTC system. TIOJ also conducts yearly "experts meetings" for comparison of data between manufacturing companies and to discuss results of companies' collaborative studies, allowing several tobacco companies to exchange information on testing technology, testing methods and testing laboratory accreditation, etc. Some of the companies participating in these meetings include: Japan Tobacco Inc., BAT, Philip Morris, RJ Reynolds, Chinese State Tobacco Monopoly Administration, Godfrey Philips India, India Tobacco Company. The meetings also included presentations about new products and discussion about methods to measure tar and nicotine in new, "low" tar and nicotine products.[19-25] There is evidence that in

2000 or 2001 it changed and started to use ISO smoking methodology.[26, 27]

TIOJ assesses all new products according to existing "smoking methods" . The documents suggest that when PM introduced a new product for which no measuring method existed, as the product wasn't commercially available anywhere else in the world (most likely Oasis, described below), there was a need to modify existing methods used by TIOJ before the product could be launched in the market. (The new product was a cigarette that was inserted in a lighter and maintained a constant heating source.)[26]

In 1998 TIOJ led the initiative to ban tobacco advertising on TV, radio or any electronic media, as part of its efforts to enhance the industry's youth smoking prevention programs. [28]

Communications between companies

At least as early as 1986, JT met with scientists from US tobacco companies to discuss possible collaboration on second hand smoke-related projects. A December 1986 meeting report written by a RJR scientist also demonstrates that there were concerns among JT scientist about the possibility that the US would "meddle in Japanese matters".[29] There was also some concern at the time about US participation in TIOJ, since at the time Japan Tobacco Inc. could still

> **discuss the benefits of smoking to their press but the U.S. industry prefers not to make such statements. JTI [Japan Tobacco Inc.] believes that they must continue to make such benefits statements to counter the increasing anti-smoking activities. They [JT Inc.] are concerned that the foreign industry does not understand this position. During the next 12-18 months, JTI must strengthen its public affairs skill particularly in response to medical claims**‥‥[29]

There are several exchanges of correspondence between PM and JT, as well as internal PM communications, where the joint discussions about regulatory issues are brought up.[30-32] In a letter, presumably by a PM executive to Mr. Honda, then Senior Executive Vice President of Japan Tobacco Inc. (he became CEO in April 2000), the areas in which the companies could work together were listed as:

- Youth smoking Prevention
- Sensible marketing restrictions designed to address youth smoking and consistent with the position that we are a responsible industry marketing to

adults who choose to smoke.
• Consistent positions on health warnings.
• Accommodation programs and support of courtesy (smoking manners) campaigns.
• Cooperation on litigation, both in terms of claims brought in U.S. courts and claims brought in individual international markets
• The level and structure of excise taxes with particular emphasis on retaining or converting these taxes to a fully specific structure in all international markets.[33]

In a 1999 letter from PM Vice President for Corporate Affairs, Steven Parrish, to Mr. Fujishiro, Managing Director of JT Inc., Parrish states:

> **As I mentioned at our meeting, we hope that we can continue to share ideas and work together with JT on issues of common concern to us both. We share your strong belief that there are global issues on which we must work together to develop strategies that always respect the historical and cultural differences of individual societies.**[34]

Some of the common concerns mentioned were the World Health Organization (WHO) and litigation as well as youth smoking prevention efforts.[34, 35] JT has been successful, so far, in court cases brought against it in Japan.[36]

With the acquisition of the international brands of RJR, JT became a big player in the international arena; hence it is not surprising that Philip Morris and JT had initiated discussions at the corporate affairs level on how to protect the industry's interests by presenting a somewhat united front. As discussed below, JT acquisition was at approximately the same time that the WHO started the negotiation process of the Framework Convention on Tobacco Control (FCTC). The FCTC seemed to have brought the industry together to discuss many of their common concerns and strategies. There was also an increased concern about litigation, which the industry perceived as being fueled by WHO. A 1999 presentation discusses the development of a cooperation model between JT-PM similar to the one developed between PM and other companies, such as BAT. The "litigation cooperation" proposal included a "joint witness development program" and a "joint litigation prevention" program.[35]

Some correspondence in Philip Morris files indicates that prior to an April 2000 interview, both companies exchanged their position statements, where JT maintained its position that "statistical association do not prove causation" and that it will continue with its "smoking manners" (i.e. courtesy) campaign (while

PM was making more open admission about the causal links between smoking and lung cancer).[37, 38]

3.2 Low Tar ("Lights") Products

It is currently widely accepted by the scientific community that "lights" cigarettes are not less harmful to health than regular cigarettes and that the tobacco industry for decades promoted these cigarettes as a "healthier" choice for smokers who could not quit. The denomination of a cigarette as "light" or "mild" is based on a machine reading of tar and nicotine yields when the cigarette is smoked by the machine and it does not reflect the actual human intake of these or any other substances.[39-42]

There are official and non-official reports that JT opposes any proposal to ban cigarette descriptors such as "lights" and "mild", since it would affect its best selling national and international brand, Mild Seven.[43-45] There is also evidence that the low tar and nicotine (LTN) is a growing trend in the Japanese market. Industry documents discuss proposals to reduce the tar readings in several brands – although these focus on reducing the machine-measured readings, not the human intake of such substances.[46] Another apparent growing market segment was the menthol market, specifically "menthol lights".[15, 47-50]

A 1999 media article, published by Asahi Shimbun,[51] circulated among BAT employees addressed the rising incidence of lung cancer in Japan and provided an overview of the LTN segment in the country while suggesting that the false reassurances provided by marketing strategies of such cigarettes might be related to the rising incidence of adenocarcinomas of the lung:

> The low-tar cigarette, as defined by Japan Tobacco Inc., contains 6 milligrams or less of tar. The product also contains less nicotine. Early low tar products were first marketed by foreign cigarette manufacturers around 1985 as a way of penetrating the Japanese market. The product's share of domestic sales – a mere 2 percent in 1988 – soared to ····42.8 percent in fiscal 1997 ···· A spokesman for the Japan's Tobacco publicity department commented that, although the possibility that smoking was a risk to one's health could not be dismissed, the link between smoking and cancer had yet to be scientifically resolved. "therefore, we are not ready to comment on the tar content," he concluded.[51]

A 1999 presentation by Japan Tobacco at a Tobacco Symposium in Hong Kong[52] titled "Making Mild Cigarettes Popular with Smokers: How has Japan Tobacco been so successful in promoting mild cigarette brands in its domestic and neighboring markets?"[53] provides insight on marketing strategies and the growing "mild" trend in the country. It starts by defining a "mild cigarette" as a

> cigarette with "delicacy of aroma and taste, soft touch in the mouth, smooth to throat, and low irritation". We use expressions "mild" and "Light" as different meanings. As you recognize, the concept of "mild" is without any direct relation to the tar and nicotine contents. That is, "mild" has a wider and deeper meaning beyond simply having low tar/low nicotine.···· [If mild and lights] are compared in the form of water, "Mild" is mineral water and "Light" is a sparkling water.[53]

This presentation started with a section on the history of tobacco in Japan, followed by the success of Mild Seven, which was launched in 1977 and has, since 1978, remained the most popular brand in the country. This presentation is a good example of circling around the main issue, which is seen in other JT statements, because it never really explained the strategy behind the success of Mild Seven. Despite earlier statement that the "mild" concept was not related to tar and nicotine contents, Mild Seven is in the LTN category. The presentation explained that:

> The concept of Mild Seven brand is based on "Delicacy of taste and smoothness"····The direct appeal to the concept of "mild" has perfectly matched the trend of taste towards 'mild' that has been realized by the industry···· Mild Seven took the initiative in naming 'mild' in Japan ... To our pleasure, since the success of Mild Seven, 'mild' become [sic] widely used for products of other categories, for example, soft drinks···· products with 1 mg tar content occupy 11% [share of market in 1998], making 45% of the market share when combined with products 1 mg to 6 mg tar content. Comparing these data with data of other countries, you can recognize Japan is the advanced market of low tar/low nicotine content. This is not simply due to preference to low tar/ low nicotine contents, but also the taste for "mild" always exists as an undercurrent. I believe that this, mild concept, interacts with preference to "low tar/low nicotine contents", creating such a particularity of the Japanese market···· [53]

A 1999 JT company profile report prepared for PMI[11] states that

> For its main tobacco business, JT has been promoting its overall marketing strategy of introducing a "sub-brand" which branches out from its premier brands like Mild Seven. Additionally, JT has also been proceeding with its expansion of low tar products targeted for health-conscientious smokers and female smokers. The latter segment has been increasing as a percentage of the total smoking population in Japan.[11]

PMKK has been countering this JT strategy with Lark, which is repeatedly cited by the company as a success story. By maintaining prices low, even after tax increases, PM was able to increase Lark's share of market.[15, 54] There is some evidence that as part of the marketing of Lark to the Japanese and Asia markets was to have the product, with the Japanese ads, be distributed in Duty Free shops at airports in the United States West Coast.[55, 56]

Oasis

A 2000 PMI presentation discusses the introduction of a new product, Oasis, in the Japanese market:

> Reflecting the importance of the Japanese market and the willingness of Japanese consumers to try new products, Japan was selected as the first international test market for the Accord concept also being tested in Richmond area in the United States. In Japan we call the cigarette Oasis, due to very high brand awareness of Accord as a car, and the concept of digital smoking. Oasis was introduced in January 1999····Media coverage of the introduction was high and generally positive. Consumer response also exceeded our expectations····[15]

Oasis is one of the industry's attempts to develop reduced harm products and it is being tested in Japan as an alternative smoking product (it is called Accord in the United States).[57] Oasis is described as "reduced risk" cigarette that "in addition to eliminating side stream smoke, ash and creating virtually no lingering odor, the technology in the electrically heated Accord and Oasis significantly reduces biological activity and a number of specific smoke constituents such as carbon monoxide and many of the constituents identified by the public health

community as known or potential carcinogens."[57]

It is important to note that to date, these new products developed by the tobacco industry, such as Oasis, have not been widely and unequivocally recognized as being reduced risk tobacco products.

There are several documents discussing the development and marketing of Oasis.[27, 58-61] A 1999 e-mail demonstrates some of the issues being considered for the claims that would accompany Oasis advertisement:

> As we claimed in the case of E4 (JP) advertisement, we are going to claim that
> 1) ambient smoke associated with smoking Oasis with new improved Digital Lighter (3i) is XX% less than those with most popular Japanese cigarettes.
> 2) Odor associated with smoking Oasis with new improved Digital Lighter (3i) is very low and almost low as blank room.
>
> Therefore, for advertisement purpose, we need either of the following data sets:
> a) Scientific study of 3i (JP) vs. major Japanese cigarettes (as we did for E4(JP))
> OR
> b) Scientific study or evidence that amount of ambient smoke and odor from E4 and 3i(JP) is identical or the same.
>
> As far as I can explain the fact to FTC, it's OK for us. But I guess having evidence a) should be a lot easier for us to convince FTC.[58]

(The E4 was one of the lighter models used for the Oasis system, and there is evidence that in 2001 it was replaced by a different model.[27, 62])

There is evidence that after the launch of Oasis in Japan, PM was planning, in 2001, to fund a "molecular epidemiology study for Oasis".[63, 64] The study goal was to "confirm harm reduction for Oasis smokers in Japan".[63] There is also some evidence that research was conducted, and presented at an Asian Toxicology meeting (ASIATOX), on the constituents and biological activities of smoke from Accord/Oasis.[65, 66]

The industry's efforts at developing reduced risks products, exemplified by the test marketing of Oasis in Japan and of similar products in the United States, are perceived by many in the public health community as another industry attempt to circumvent more meaningful regulatory measures. This industry effort

has been described as a parallel to earlier industry efforts to promote "safer" products, such as the introduction of filter tips and later the low tar, low nicotine products. Although the industry has been aggressively pursuing harm reduction technology, it remains to be determined whether or not these new products will have an impact in reducing health risks from tobacco use at the individual and population level, and the debate continues among health care professionals and researchers about the best way to research these products in order to guide policy development.[42, 67-70]

3 .3 Science and Research

As it has done everywhere else,[71-76] in Japan the tobacco industry has also been involved in conducting and sponsoring research. In addition to evidence of conducting marketing research as well as smoking prevalence surveys, [16, 77] there is evidence of the industry's involvement in the development of research that could affect tobacco control activities.

As described by Hong & Bero,[78] the industry mounted an aggressive strategy to counter the now historical 1981 study by Japanese researcher, Takeshi Hirayama. Hirayama's study[79] concluded that non-smoking wives of heavy smokers had twice as much risk of developing lung cancer than non-smoking wives of non-smokers. His study broke new scientific ground and had regulatory implications for clean indoor policies. Hong & Bero described how the industry became involved in financing a study to refute Hirayama's while at the same time keeping its involvement secret. Hong & Bero quoted several internal industry documents discussing how the industry planned to hide its involvement in the "Japanese spousal study". For example, they quote the following 1991 letter:

> ····**Dr Chris Proctor [from BAT] might supervise this work but his presence should be low key and not appear in any of the publications, particularly since this is a Japanese study**····[80]

The Industry's "Japanese Spousal study" was published under the authorship of P.N Lee, a tobacco industry consultant, with acknowledgement of a Japanese colleague and vague acknowledgement of the tobacco industry funding.[81] In fact, this desire for keeping the tobacco industry's involvement secret is a frequent industry strategy to maintain scientific credibility of its scientific representatives. The industry acknowledges that in many parts of the world, a scientist's link with the tobacco industry could undermine the credibility the research findings.[76]

PM's Worldwide Scientific Affairs (WSA) Strategic Plan for 2000, when discussing the issue of scientific credibility, states that "... It is clear that tobacco industry scientist have virtually no scientific credibility in most venues..."[82] In fact, in the WSA strategic plan for 2000, the mission statement was to "generate credible scientific information on tobacco, cigarette smoke, and smoking, which guides Philip Morris decisions."[82] The plan then addresses internal and external factors associated with this lack of credibility in the media and within the scientific community, as well as the regional differences that exist in regards to the acceptability of scientists' link with the tobacco industry. In regards to the lack of credibility within the scientific community, the plan states that

> Despite this lack of credibility, particularly for biomedical scientists, there are enormous regional differences. Scientific credibility with respect to industry scientists is extremely low in the US, in the EU region, and in Australia; relatively low in EE and CEMA; reasonably high in Latin America and Asia; and quite high in Japan... The reasons for this difference are certainly not difficult to guess. With the exception of Japan, regional differences are most likely accounted for by the availability of research funds. In Asia and Latin America research funds are quite limited, and it is easy to find scientists willing to work with the tobacco industry···· The fact that tobacco industry scientists continue to have considerable credibility can be attributed to three factors. First of all, any "doctor", even one who works for the tobacco industry, is a highly educated individual and consequently receives considerable credit within the scientific community. Secondly, the acknowledged technical excellence of Japan Tobacco ensures credibility for these scientists and, by association, tobacco scientists. Lastly, the environment in Japan still remains friendly toward smoking. It should be noted that these three reasons also apply to certain other countries in the Asian region, but perhaps to a lesser degree because of the lack of a domestic industry with the same degree of competence and influence that Japan tobacco [sic] possesses.[82]

The WSA is in charge of the company's research efforts worldwide, but it is also apparent that research and scientific affairs were not the only objective of the WSA. Other WSA objectives included hiring academic consultants and giving grants, and it had several plans for research in Japan and in the region. For example, the WSA's 2000 Plan for the AJA [Asia-Japan-Australia] region[83]

included, among other objectives, to contribute "to the active dialog with external scientific community." This attempt to be involved with the "external scientific community" is not unique to Japan and it fits with WSA's broader goal of gaining scientific credibility.[76, 84, 85] To meet this objective, several activities were carried out: PMKK WSA Japan employee, Dr. Kohji Takada, served as an invited part-time lecturer at Keio University; he also served as an officer in several scientific societies of which he was a member, such as the Japanese Pharmacology Society, Japanese Society of Neuropsychopharmacology, Japanese Young Researchers' Society of Neuropsychopharmacology, among others; and he was a peer reviewer in several Japanese Pharmacology journals.[83, 86]

Additionally, the WSA 2000 Plan for the AJA region includes not only the conduct of research, but also support of "accommodation programs" such as Courtesy of Choice (a tobacco industry strategy to maintain the social acceptability of smoking,[87, 88] described below), including the identification of consultants to assist in the industry's effort to "accommodate" smokers and non-smokers.[83] The activities developed by the WSA also included "support for regional litigation with scientific information" in Japan, [83] as well as support for the "long-term objectives" of the business.[89]

The mission of WSA AJA was summarized as

> **Provide, as scientific/technical resource, initiative and support primarily in the areas of ETS and Product Integrity in the Asia, Australia and Japan regions to accomplish the Philip Morris International goals.[90]**

Several documents from PM's WSA AJA illustrate the range of "scientific activities" developed by the company, as well as the array of scientific expertise of its employees. From a 1998 plan, it seems that the group had expertise in areas ranging from neuro-biology to engineering. The group was involved with the industry's accommodation program, ventilation projects, neurochemistry of nicotine, hiring consultants, and joint industry activities such as ARTIST (discussed below), among other areas.[91-101] As elsewhere, scientists with WSA AJA attended policy meetings, such as the meeting of the "21st century Tobacco Countermeasure Deliberation Council",[102] discussed below; and had discussions about "ventilation and indoor air issues with Japan Tobacco", and about the industry's accommodation program; [92, 93, 103] and attended scientific meetings. [100, 102] The industry developed its own scientific meetings as well as participated in outside meetings. This involvement with meetings was part of the industry's effort in monitoring all scientific and regulatory developments related to tobacco use.[104,

[105] There is also evidence that WSA AJA staff was a member of the Environmental Management Committee in Japan, as well as the Asian region committee.[106]

The documents describing the accountabilities of PMKK WSA staff, Takada, and his activities (including dissemination of smoking and health news from Japan to the rest of the company) provide another example of the utilization of science to advance the industry's policy goals. In addition to participation in industry-wide groups, Takada's tasks included the development of relationships with local and regional scientists; participation in scientific meetings and membership in scientific societies; publication of articles with "independent" scientists, and monitoring of scientific development, including in the area of Indoor Air Quality.[105, 107-109] Membership in scientific societies was described by Takada as important to obtain the latest information in areas critical for WSA in subjects that included epidemiology ("including ETS"), toxicology and carcinogenesis.[110] Participation in scientific meetings and societies gave industry scientists an opportunity to approach outside scientists for gathering of information.[111-115]

Takada's tasks also included the development of positions on issues such as addiction and compensation.[105]

Several documents summarize different research proposals funded by the WSA in Japan. The studies addressed nicotinic receptors; [116] the combined effects of nicotine and ethanol, which was considered an "emerging issue";[117, 118] and animal studies of the effects of exposure to tobacco smoke. [119]

There is evidence that Japan Tobacco was part of industry's strategies to monitor and infiltrate scientific meetings on tobacco and health, notably the 6th World Conference on Tobacco Or Health, which took place in Japan.[120] There is also evidence that JT perceived the World Conference "not to be a scientific conference but more of a political meeting to encourage prohibition of smoking" and that it had consider strategies to deal with the Conference as well as plans of conduction its own "ETS symposium" prior to the conference and to send industry scientist "not to attend but for the purpose of challenging scientific nonsense" .[29] In August of 2000, in response to the release of WHO's report Tobacco Company Strategies to Undermine Tobacco Control Activities at the World Health Organization, [120] where those allegations of infiltration of the World Conference were made, JT denied "paying any scientists whatsoever to attend or present papers at this conference."[121]

Smoking Research Foundation (SRF)

Similar to the US Council for Tobacco Research, [84] JT created the Smoking Research Foundation in 1986. The prospectus for the creation of the Foundation states that

> Scientific studies on smoking were initiated in Japan by Japan Tobacco & Salt Public Corporation, which in 1957 entrusted the project to selected research groups. After years of development, these groups today have become Japan's largest medical research body in the field... The reorganization of Japan Tobacco & Salt Public Corporation into Japan Tobacco Inc., effected on April 1, 1985, has given us the opportunity to establish a new foundation to further expand the research previously conducted... Based on these goals and viewpoints we have decided to establish the Smoking Research Foundation (provisional name), which with the support of numerous and diverse sectors of society will subsidize and assist the research groups in scientific researches on smoking.[122]

The list of committee members that assisted in establishing the Foundation is a mix of tobacco industry, health, academia and other business sectors.[122]

The Foundation's annual report for 1997 states that the "main objective of the SRF is to clarify the relationship between smoking and human health through scientific investigation covering a wide range of areas".[123] The areas indeed include: carcinogenesis, genetics, cardiovascular and respiratory diseases, pharmacology, passive smoking, epidemiology, and others.[123, 124] There is evidence that by 1997/1998, Philip Morris was an active participant of the Foundation activities.[125] The Foundation website contains a list of hundreds of studies funded by the industry in the past decade as well as currently-funded studies.[126]

It 1997 the Foundation constitution was revised, and by then, its objective was to

> contribute to the nation's policy-making on tobacco business, by promoting and entrusting the scientific research on smoking etc. as well as collecting related materials and information.[127]

Although it is clear that the Foundation was created and is funded by the tobacco industry, the Foundation English language website describes it as:

> an independent non-profit organization established in 1986. The Foundation aims to support financially a wide range of high quality scientific research projects on smoking and health, and to collect information about smoking related matters. The researches supported by the Smoking Research Foundation are strictly scientific and are planned and performed by researchers mainly at universities. The results of the researches are published in an annual research report of the Smoking Research Foundation and also in scientific research journals in Japan and abroad.[126]

3.4 Joint industry Efforts

The Japanese tobacco industry has been involved in several industry wide initiatives and groups. For example, JT and JTI participate in CORESTA, its task forces, technical groups and research efforts.[128-131] CORESTA is the Cooperation Centre for Scientific Research Relative to Tobacco, an industry wide group that develops scientific research in several aspects of tobacco and cigarette, from leaf to cigarette ingredients and smoke emissions. CORESTA's research often guides regulatory and standard setting procedures both at the national and international level. For example, CORESTA, and thus indirectly, the tobacco industry, developed and approved several of the standards and measures associated with tobacco and tobacco products adopted by the International Organization for Standardization (ISO).[40] For JT, participation in those organizations provides another avenue for input into scientific and regulatory affairs related to the tobacco industry that affect JT's business domestically and internationally. JT is also a member of the trade/information groups Tobacco Merchants Association and the Tobacco Manufacturers Association.[132-134] In addition, representatives from Japan Tobacco contributed funds and attended meetings of the now closed Center for Indoor Air Research.[135-138] (CIAR – which was created to fund research that would benefit the industry's interests, mainly by denying the scientific evidence about health effects of exposure to secondhand smoke; promoting ventilation technology; influencing the development of indoor air quality standards; all measures to support the industry's goal of maintaining the social acceptability of smoking and preventing the creation of smoke free environments.[76, 139-141])

Two specific joint industry projects in the region: ARTIST and the JT-PM Joint Asian Consultant Program[107, 142, 143] are discussed below, but other ventilation and indoor air quality projects also exist.[103] These joint efforts were used to disseminate research findings on topics related to smoking and health, as well as to develop strategies to address industry concerns with tobacco control activities

in the region.[144]

Asian Region Tobacco Industry Science Team (ARTIST)

A January 1999 document describes ARTIST as a non-profit organization, with membership open to "all scientists and other technically competent individuals employed by tobacco companies located in, or whose affiliates operate in, the Asia-Pacific region."[145] Japan Tobacco and Japan Tobacco International are members. ARTIST's purpose is:

> 1) To contribute to the quality of scientific research on topics related to tobacco, tobacco smoke and smoking in the Asia-Pacific region····
> 2) To support the introduction of technologies for the accommodation of both smoking and non-smoking individuals in an environment where they can comfortably coexist····[45]

Also relevant are the restrictions on ARTIST:

under no circumstances shall it[ARTIST]:

> 1) make any statements (either public or nonpublic) regarding the health risks associated with, or any other consequences of, using any tobacco product;
> 2) fund or conduct (either directly or indirectly) any research relating to smoking and health;
> 3) fund or conduct (either directly or indirectly) any research relating to the marketing or development of new tobacco products····[145]

Although the stated overall objective of ARTIST was to support the development of a regional scientific network, one of the objectives of ARTIST's first meeting was to "discuss the legal and regulatory issues involving [ARTIST's] scientists."[146] Since 1996, ARTIST's members have met twice a year and the minutes from these meeting provide some insight into the activities developed by this group.[146-151]

At the ARTIST meetings there were presentations on research conducted by industry scientists, and by guest speakers, on topics that included indoor air pollution and risk assessment methodology. There were also updates and overviews of current Indoor Air Quality situation and regulation in the region. As

described below, the tobacco industry had an aggressive strategy to counter claims about the health effects of secondhand smoke and to oppose smokefree policies. ARTIST's scientific endeavors contributed to this industry's overall strategy. For example, at the October 1999 Kyoto meeting[148] there was a presentation on "Current situation of Indoor Air Pollution in Japan"; a presentation by JT on the development of "various ventilation systems in public places to attempt a suitable improvement of smoking environment····"; a presentation by PM Asia on "Technological Options for Accommodation", with description of case studies; and a presentation by PMI on "ETS and Childhood Disease". In addition, the meeting had reports on emerging issues in the region. At the time, in Japan, the emerging issues mentioned was "Healthy Japan 21, analysis of cigarette-smoke constituents, and ETS-related questionnaire by Ministry of Health and Welfare; WHO Conference in Kobe····" [148] (The 1999 Kobe meeting was a WHO-sponsored conference on women and tobacco.)

Another summary of an ARTIST meeting provide some evidence of the difference in positioning that JTI takes when compared with some of the other tobacco companies. At the November 2000 Hong Kong meeting, JTI representative presented on "Conflicts of 'Advice'"

> **Conflicting advice and opinions concerning many key S&H issues by various governmental, public health, and advocacy organizations were exemplified. Question was raised as to which advice is right, in the face of such conflicting opinion from public health authorities and regulators concerning low yield products, tar ceilings, and addiction, etc.**[151]

There is also evidence that ARTIST members were encouraged to publish their research in peer-reviewed journals. [94]

Second hand smoke and the JT-PM Joint Asian Consultant Program

For decades the tobacco industry has been developing worldwide strategies to oppose the growing evidence on and public awareness of the harmful effects of second hand smoke and the policy measures that promote clean indoor air.[71, 152-154] These strategies encompass the development of "accommodation" campaigns, where the industry communicates that smokers and non-smoker can share the same environment if there is tolerance and courtesy towards each other.[155] One such international campaign, developed and funded by the tobacco industry and used in Japan, is the Courtesy of Choice program[152] in hospitality venues – which is based on the separation of areas for smokers and non-smokers, with no

accountability for protection against the health effects of second hand smoke.[152] The industry also promotes ventilation solutions. Despite the current lack of ventilation technology that would remove all toxic substances contained in tobacco smoke, the industry promotes ventilation technology and indoor air quality standards that would remove some of the odor, but not all of the risk, from areas where smoking is allowed.[156, 157]

In Japan, the emphasis has been on courtesy, i.e. "smokers especially, but non-smokers too, should be courteous towards each other ... Simple courtesy can go a long way to resolve friction and disputes that might arise regarding smoking." [155] JT's promotion of "smoking manners" has encouraged the installation of ventilation and smoke removal systems, although there has been no evidence to date that these systems reduce the harmful smoke components from the air. Acceptance of courtesy as the best way to handle second hand smoke provides fertile grounds for the tobacco industry to oppose effective clean indoor air policies.[16]

The 1996/1997 plan for the Asia, Japan and Australia region[90] states that

> ETS as an issue has not yet been "fully developed" in the minds of policy makers, and the Region's Corporate Affairs management has initiated programs to:
>
> (1) maintain or improve the social acceptability of smoking in Asia;
> (2) ensure the reasonable and rational outcome of regulatory and quasi-regulatory initiatives;
> (3) promote the accommodation of smokers and nonsmokers through voluntary self-regulation by the affected parties and/or reasonable government initiatives;
> (4) communicate our views to, and put the issues into perspective with, opinion leaders and the public, and position PM as a reasonable partner in the decision making-process.[90]

In 1997, JT and PM Asia Inc. (PMAI) entered into an agreement to

> encourage scientific research activities concerning environmental tobacco smoke (ETS), indoor air quality (IAQ) issues and other emerging scientific issues regarding tobacco and smoking by scientists located in the region comprised

> by Japan, Korea, Taiwan, China, Hong Kong, the Philippines, Malaysia, Indonesia, Singapore, Thailand, Vietnam and Australia (hereinafter called Territory).[158]

This agreement was similar to other consultancies arranged by tobacco companies in other parts of the world as part of its ETS Consultants Project.[159, 160] Based on the agreement, JT and PMAI would support external scientists in conducting and publishing research on ETS and IAQ, as well as sponsoring symposia on these topics. In addition the companies agreed to monitor all developments in these areas and to share information that could be important to both companies, while maintaining the freedom to conduct individual projects as well.[158]

There is evidence that prior to this agreement the industry was already collaborating in an ETS consultant program in order to counter the perceived US influence in the region and to prevent expansion of the non-smokers' rights movement beyond the US.[90, 161-163] For example, for 1996, the estimated cost of some of the activities in the region was US$ 54,500, to be split between PM and JT. Japan Tobacco and the Smoking Research Foundation have been funding studies on the effects of passive smoking since the 1980s, and JT have been an active participant in industry-wide scientific and public affairs efforts to maintain the social acceptability of public smoking.[29, 124, 164-166]

In 1995 a lawsuit was brought against JT by eight non-smokers who claimed a variety illnesses and discomfort due to exposure to secondhand smoke and requested compensation for their suffering as well as an end to the manufacturing and distribution of cigarettes by JT, or alternatively, that no cigarettes with more than 0.4 mg of nicotine be manufactured and distributed, and that JT include stronger warning labels about the health effects and addictiveness of cigarettes.[167] The March 15, 1999 ruling by a Nagoya District Court found in favor of JT.[167] The ruling acknowledged the discomfort suffered by the plaintiffs due to passive smoking and, to some extent, the harmful effects of smoking but failed to fully acknowledge the health effects of exposure to secondhand smoke. In fact, the ruling cited the industry's defense that the IARC study did not find a significant relationship between ETS and lung cancer [168] and other industry's defenses. It stated

> As mentioned above, in the current circumstances, smoking has not been necessarily detected as a carcinogen of lung cancer, respiratory diseases and other diseases and, therefore, the influence of passive smoking on health is positioned as a

> **research subject for the future.**[167]

The 1999 ruling also discussed the high level of social acceptability of smoking in Japan, as a matter of individual choice, but recognized that many non-smokers experience discomfort from other people's smoke.[167] It stated:

> **It is natural for non-smokers to wish to evade passive smoking ····The acts of the Defendant of manufacturing, distribution and import of cigarettes are the sources of indirect smoking, from the context that smoking would not exist should the there be no such act of the Defendant····[However] the acts of the Defendant are merely of an indirect nature. Indirect smoking by non-smokers is a result brought by the act of smoking by smokers. Therefore, the first step shall be taken by smokers, giving consideration to non-smokers····**[167]

Nonetheless, towards the end, the ruling acknowledged that other countries have been taking measures to protect the health of non-smokers, based on scientific evidence, and suggested that JT place a voluntary warning about secondhand smoke in the cigarette packs it produces.[167] There is no evidence to date that JT will implement this suggestion.

Japan Tobacco and Japanese scientists have been involved with PM in plans to frame research showing the harmful effects of secondhand smoke as junk science, most notably, in the industry's risk assessment definition efforts, previously described.[72, 74, 169] For example, Japan was part of the industry effort, partly supported by CIAR, to involve Asia in countering the IARC study on second-hand smoke and lung cancer,[74, 170] and Japan Tobacco was requested to indicate the name of Japanese scientists to participate in the industry-sponsored 1997 Guangzhou, China "International Workshop on Risk Assessment and Good Epidemiological Practices".[171, 172] Japanese scientists did participate in the meeting, although it is not clear if there was any additional involvement between these scientists and the industry. [173]

The JT-PM Consultant Program[142, 174] was similar to the worldwide ETS Consultant program[154] in that it monitored regulatory and scientific developments in the area of exposure to secondhand smoke, and had industry consultants and employees involved in scientific meetings presentations, as well as publishing industry-financed studies.[175] Part of the program objectives was to "contribute to the quality of research, scientific/technical publications and conferences, the unbiased use of scientific findings by regulators, and the development of scientific

resources in the region." [174] We found no evidence in the documents that the program has ended.

In addition to participation in the JT-PM Consultant Program, the industry monitored the development of "draft standards to assess workplace ETS exposure" ,[104] and PM held discussions with both JT and the TIOJ about ventilation and accommodation, again, as part of the industry's worldwide strategy to oppose clean indoor air policies.[176, 177] One of the PM's WSA planned projects for the region was to "contribute to the activities of the core [indoor air measurement] group".[178] As explained in the plan's summary, the objective for WSA is "to recommend a minimum set of constituents that needs to be measured for IAQ assessment and ventilation technology evaluation; to produce a manual/handbook for measurement protocols and methods; and to identify resources external to WSA suitable for carrying out such measurements." [178]

And as described above, Philip Morris' WSA was involvement in the development of science and policies regarding accommodation, indoor air quality and ventilation requirements.[91, 103] For example, one of the proposed WSA AJA projects for 1998 was "Technology for accommodation solutions" with the objective of supporting "accommodation initiatives with technical expertise" such as expertise ion ventilation and filtration, as well as assistance with the Courtesy of Choice program.[92, 93] In Japan, it seems that the main concern was to address "indoor odor problems." [92] Another WSA AJA project was to participate in the establishment of an "Asian Center of Excellence for Exposure Assessment of Indoor Air Constituents" in Korea, which would support a "regional resource to carry out high quality exposure assessments.[179] Apparently, PM purchased equipment and was planning to conduct several personal monitoring studies in the region, including Japan, and to publish the results of such studies in peer-reviewed journals.[179, 180] We were unable to determine whether or not these studies have been completed and published.

In addition, we found a 1995 proposal to conduct an "ETS personal monitor studies in Asia and Japan", apparently written by Nicholas Farrell of the Hazleton laboratory in the UK (which has worked for the industry on other projects). This is a study similar to other personal monitoring studies funded by the industry,[181] in which subjects would carry air collection pumps throughout their daily activities and supposedly measure exposure to ETS constituents. The proposal states that the advantages of funding such an expensive study (US$ 1 million for three Asian cities plus 4 cities in Japan) were that in addition to providing the industry with data to counter WHO scientific and policy recommendations, the results of such studies gather enormous media attention, and may lead to an impact on

ETS-related policies that is favorable to the industry. The proposal claims to be "an attempt to accommodate both business and scientific needs."[182]

Another WSA AJA activity was to sponsor an ASEAN scientific scholarship program to "develop scientific and technical expertise on indoor air quality in the region and promote good science"[183] where university students would spend time learning about indoor air quality issues enhancing the "research potential in the area of indoor air quality".[183] The "needs" listed by WSA AJA for the 1998 plan, for Japan included:

> **Support activities in line with the trend of the Japanese society towards 'separate smoking' including installation of Thomex [sic] air-cleaning device in several domestic airport lounges.**[184]

Tornex is a Japanese company that manufactures ventilation systems claimed by the company to allow smokers and non-smokers to share the same area creating a "mutual satisfactory environment for both parties; non-smoker and smoker can share the same space under the condition that the former is not trouble with smoke and latter is allowed to smoke without worrying about complaints from the former." [185] It includes an "artificial tornado forming technology" [185] alleged to remove all tobacco smoke from the environment. Tornex products are installed in "more than 33,000 places all over Japan, such as Airport, Train Station, Hospital, Government Office, City Hall, Baseball Stadium, Factory, even Restaurant and Cafe." [185] There are a few references in the documents of industry-funded research to evaluate the performance of Tornex products, in an apparent collaboration between the tobacco companies and Tornex.[186, 187]

External scientific consultants were contracted to perform "high quality research", monitor "local developments" and address "smoking & health or indoor environment issues".[98] Consultants in the region, including Japan, as well as other external scientists, were in frequent contact with WSA scientists. [98] Japan was also listed along with China, in a 1998 WSA plans, as one of the priorities countries for the organization of scientific symposia "related to the indoor environment or smoking or health" where both internal and external scientists would present on topics such as lung cancer and ETS. [101]

There is some indication that in 1999 Philip Morris Asia considered funding several research proposals by Hong Kong consultant, and Hong Kong University of Science and Technology professor, Christopher Chao,[188] to, for example, assess the "performance of air purification units installed in three airports in Japan" at a cost of HK$120,000[189] and to assess the performance of a "standalone air purification

unit manufactured by a Japanese company" at a cost of HK$40,000.[190] We were unable to determine if this study is being carried out.

3.5 Tobacco Control

A year 2000 article in the trade journal Tobacco Reporter discusses the Japanese tobacco market, and states that despite some problems related to a growing anti-smoking activism, a slow economy and an increase in taxes, it is still one of the largest markets in the world. The article highlighted the Japanese consumer receptivity to new products and how, as a developed country, Japan has imposed relatively few restrictions on "tobacco advertising. Instead, the industry adheres to a voluntary advertising code established by the Tobacco Institute of Japan" and that society's attitude towards smoking remains "tolerant". The article credited a managing director of the TIOJ as stating that the "Japanese anti-smoking movement is largely inspired by the World Health Organization."[191]

Most of the restrictions in place regarding tobacco marketing and advertising are based on voluntary agreements by the tobacco industry and not legislative or regulatory action by the government.[192] In addition, it seems that as recent as April of 2000, the Japanese Ministry of Health and Welfare (MOHW) had not acknowledged "tobacco dependence" as a disease, which makes it easier for tobacco industry to maintain that nicotine is not an addictive substance.[193]

In 1994, in response to a 1989 WHO resolution to strengthen tobacco control, the MOHW created a Study Group to consider and develop a recommendation to the Ministry on a Tobacco Action Plan for Japan. This group was formed by representatives of medical groups, media, academia, labor and tobacco industry representatives. [16, 194] The final report of the group acknowledges the relationship between tobacco and several diseases, and recommends that

> Smoking countermeasures must take into account these fundamental understandings [about tobacco use] and put forward three basic thrusts – "smoking prevention", "segregation of smokers from non-smokers" and anti-smoking support and smoking in moderation measures" from the point of view of thoroughly eliminating smoking among minors, creating an environment which eliminates and reduces the effects of passive smoking on non-smokers and at the same time promoting non-smoking support for those who do not wish to smoke and smoking in moderation for those who wish to continue smoking.[194]

When detailing how these "smoking countermeasures" should be developed and implemented, it is clear that the industry had an important role in the study group. The measures emphasize voluntary self-regulation to "reduce the overall volume" of tobacco advertising; school-based programs to educate minors; "[self-] regulation of the operating hours" of vending machines "while taking into consideration the situation of retail stores." The countermeasures to "segregate" smoking are heavily focused on accommodation of smokers and non-smokers, ventilation systems and recommended to be voluntary. The recommendations to "help smokers cut down" essentially recommend that "steps must be taken to support anti-smoking counseling", including cessation education for health care professionals, and that information about smoking and health should be provided to smokers that wish to continue to smoke. [16, 194-196]

The White Paper and Healthy Japan 21

Annually since 1956 Japan's Ministry of Health and Welfare releases a "White Paper" describing issues that the Ministry will address and the actions it will take in any given year. Apparently, 1997 marked the first time the Ministry gave more than cursory attention to the issue of smoking and health, mentioning for the first time passive smoking and nicotine addiction. The "Tobacco White Paper" is a document prepared by the Public Health Council and published by the MOHW. This document addresses tobacco and public health issues for the country, normally proposing voluntary measures. In 1998, the portion of the document on smoking was reduced in scope. PMKK's employee Takada background summary on the "White Paper" states:

> **It is also noted that "measures to eradicate or reduce the effects of passive smoking" which appeared in the 1997 edition was described as "creation of an environment that eliminates or reduces the harm of passive smoking" in the 1998 edition.[197] [emphasis by Takada]**

A third edition of the "Tobacco White Paper" was planned for 1998, "summarizing domestic and foreign scientific information on the issue of tobacco and health, as well as information on tobacco countermeasures in other countries" .[197] In 1998, recognizing a growing body of knowledge about tobacco and health, and an increase in tobacco use among young people in Japan, the MOHW determined that "the need has arisen ... for appropriate responses [i.e. tobacco control] including deliberation on management measures." [197] Thus, the MOHW created in February 1998 the "21st Century Tobacco Countermeasure Deliberation

Council", with the objective of deliberating "full-scale countermeasures against tobacco which contains harmful and dependence producing substances from the standpoint of risk assessment and risk management."[197] Tobacco industry representatives were members of the Council.[198] A summary of one of the Council meetings provides an insight of the level of discussions. The Council members seemed to be divided on how to proceed with the discussion, with some claiming that if they were a committee to develop tobacco countermeasures, the assumption was that either it had been already established that tobacco is harmful to health and/or that it was decided that regulatory measures should be approved before more research into cause-effect relationship was conducted.[199] Tobacco industry representatives opposed the Council approaching its work from the premise that tobacco was harmful. Y. Ohkawa, from Japan Tobacco, is quoted as saying:

> At present, there is general negativity towards tobacco in society, but I would like to see fair discussion here ···· Tobacco is an item of choice for adults, and whether to smoke or not should be left to the judgment of the individual. While tobacco may possibly pose bodily risks, its effects regarding overall health, including the psychological aspects, have yet to be elucidated. Concerning passive smoking, it undoubtedly irritates the eyes and nose, but its relationship to cancer is an issue for the future. Of course, the problems of smoking by minors and smoker's manner are serious, and we should aim for a society in which nonsmokers and smokers can coexist····[199]

The final report of the Council, released in August 1998,[200] shows that at a minimum the industry managed to prevent a more assertive report. The final report is merely a summary of the deliberations that took place over the course of several meetings. A few excerpts of the report are highlighted:

> ···· As for effects on the health of smokers themselves, it was pointed out that the incidence of many diseases ... is higher than for non-smokers, and that the negative effects are brought to bear on the health of nonsmokers in proximity. However, opinions were also presented expressing doubt regarding epidemiological cause-and-effect relationship between tobacco and disease especially on the effects of passive smoking... The opinion was voiced that tobacco is an item of individual preference having a long history as well as certain cultural facets; therefore it would not be proper for the government to interfere without following legal procedures····[200]

The summary then addressed some of the main areas the Council agreed to discuss, given that it was not an "appropriate venue" to discuss smoking and health. The areas they focused on were smoking prevention, mainly among minors, and included measures that broadly would address tobacco advertisement and vending machines; retail sales and role of society; separation of smokers and nonsmokers, including smokers manners education and ventilation standards; provision of information to consumers, including labeling and packaging. (Vending machines are increasingly a source of cigarette sales, and some studies demonstrate that a large percentage of underage smokers use vending machines to buy cigarettes. The industry has stated that as a voluntary measure to assist with youth smoking prevention it would work to lock machines at night.[13, 201, 202])

It is clear from the Council's summary that the tobacco industry's position against taxation, regulation and indoor smoking bans were included on the final document as well. Thus, other than a general agreement on the need for smoking prevention among minors, based on the fact that minors are not as competent as adults to make an informed choice about smoking, there wasn't any additional agreement on tobacco control measures that have proven to be effective elsewhere.[200]

A complicating factor in Japan is that warning labels are determined by the Tobacco Business Law, under the authority of the Ministry of Finance. (The main objective of this 1984 law is to "promote the sound development of the Japanese tobacco industry, thereby securing stable national revenues."[202]) Any company could go above and beyond the existing vague warning, but none are required to do so.[200]

The Council's summary concludes by saying:

> There was a great deal of spirited debate in this deliberation council from the standpoint of promoting tobacco countermeasures, as well as from the standpoint of proceeding with caution. Regarding future issues to be examined by the Ministry of Health and Welfare, it was suggested that the nature of tobacco administration from the standpoint of health problems, and the preparation of a legal framework separate from the Tobacco Business Law for dealing with tobacco on the basis of public health, be taken up as quickly as possible. In addition, this deliberation council was not able to discuss sufficiently a number of concrete issues, which cannot be

> addressed by the Ministry of Health and Welfare alone. These include, for example, handling of the tobacco problem in school education; surveys of air pollution caused by tobacco indoors and outdoors, and methodology of such surveys; labeling and price; components of cigarettes; problems stemming from activities of multinational companies that employ a double standard; etc.[200]

The 1999 version of the White Paper has an assessment of the then existing measures to counter tobacco, and emphasized that to date, the tobacco control measures takes were primarily aimed at "disseminating the correct knowledge about smoking and health" in a voluntary basis and in agreement with the tobacco industry.[203-205] The "three pillars" of these measures were listed as" prevention of smoking, separate smoking from non-smoking areas, and support for smoking cessation, which is similar to the 1995 Action Plan recommendations previously discussed. The paper does acknowledge the increase of smoking among youth, especially women, and that other countries have effectively taken more aggressive tobacco countermeasures, and states that "tobacco countermeasures to be taken in the future" [203] are:

From the standpoint also of preventing life-style related diseases, the Ministry of Health and Welfare positions tobacco measures as one of the important challenges in the field of public health, and will conduct a fact-finding survey on smoking and health issue (in fiscal 1998 and 1999), compile a report on the latest domestic and external scientific findings concerning tobacco and health (fiscal 1998), conduct analysis of tobacco smoke constituents (fiscal 1999), and consolidate the information dissemination system in tobacco and health (fiscal 1999), among other activities.[203]

The report also included a call for "stepped up collaboration and cooperation with WHO" particularly in the area of tobacco and in cooperating with the WHO-sponsored Kobe conference on women and tobacco,[203] but did not include any measurable tobacco control objective.

According to a newspaper account circulated among PM executives, the "fact finding survey" described in the 1999 White Paper was scheduled to start in January 1999 and the plan was to survey 20,000 people about their smoking status, attitude and beliefs about second hand smoke and addiction.[206]

To date, Japanese health warning labels on cigarettes packs, required by 1990 legislation, state "since smoking can damage your health, be careful not to

smoke excessively". [207] In addition, in 1989, the industry voluntarily agreed to include an additional notice on all packs that could be translated as "please mind your smoking manners." [207] There has been several media reports about the warning labels and other tobacco control issues in Japan, but these accounts seem to be dominated by the conflict between the Ministry of Finance and the Ministry of Health, Labour and Welfare.[208, 209]

Healthy Japan 21

Healthy Japan 21 was a MOHW 10-year health promotion plan. In a draft released in 1999 it proposed that domestic tobacco consumption and smoking rates be cut by half in 10 years. It was the first time that the MOHW set a numerical target to address tobacco in Japan. The draft also had several other tobacco control measures, such as educational campaigns and public smoking bans. The release of the draft received wide media coverage in the country and reportedly drew immediate opposition from the tobacco industry, which submitted comments to the MOHW. According to media reports, JT and others stated that setting numerical target values means that the government controls people's taste and choices." [210]

From a series of exchanges between PM's Japan employee and PMI, it is clear that the industry had several internal discussions and input in the development of "Health Japan 21".[211-214] For example, a draft report of PM's Worldwide Regulatory Affairs (WRA), states that

> WRA advised PMKK with respect to a proposed TIOJ response to a draft interim report on tobacco control issued by the Tobacco Subcommittee of a Ministry of Health and Welfare initiative known as "Health Japan 21". The draft interim report addresses a number of tobacco control issues, including consumer information, reduction of adult smoking incidence, and prevention of youth smoking, ETS and smoking cessation.[215]

A February 2000 memo indicates that the industry succeeded in modifying the goals of the 10-year plan:

> TIOJ informed PMKK today of the targets of the section of a "Healthy Japan 21" plan concerning smoking, decided at the last (6th) meeting of the "Healthy Japan 21 Planning Committee"····
> These were:
> □ dissemination of sufficient information on health effects of

smoking

□ elimination of smoking by minors

□ through segregation of smoking at public places and workplaces, and dissemination of information regarding smoke segregation methods with high quality

□ provision of supporting programs to those who want to quit or cut down on smoking at every cities, towns and villages

This, numerical targets concerning smoking, i.e. "halve the adults' smoking incidence" and "halve the cigarette consumption per capita", were withheld.[216]

Thus, it seems that the tobacco industry was successful in convincing the MOHW to "drop" its numerical targets related to decreasing smoking prevalence and cigarette consumption.[217] Media reports stated that the industry's opposition was supported by a "special Liberal Democratic Party committee on the tobacco and salt industries" who submitted a resolution to the MOHW with arguments almost identical to those of the tobacco industry, i.e. that the government attempt to set a numerical target was a violation of :adults freedom of choice." [218]

The Framework Convention on Tobacco Control (FCTC)

The tobacco companies did not welcome the development and, in late May of 2003, the approval of the FCTC. As the FCTC negotiations started, in 1999, tobacco companies, including Japan Tobacco International (JTI), attempted to influence the process in order to minimize the restrictions that the FCTC could impose on the sales and marketing of tobacco products. There was covert and overt industry participation, and the WHO/FCTC was a topic of high importance, one that PM perceived as in need of joint efforts from the part of the industry.[219, 220]

In fact, there is evidence that in 1999/2000, BAT, PMI and JTI attempted to develop a joint project that would create an industry-wide self-regulatory system, therefore preempting the need for the FCTC, while at the same time giving the perception that the industry was open to dialogue with WHO and willing to accept some of WHO's demands.[221-224] Apparently, however, the three companies could not agree with most of the terms and voluntary restrictions that such scheme would impose, and it seems that the only product of this effort was the joint industry voluntary marketing code, discussed below.

In the Fall of 2000, the WHO conducted public hearings on the FCTC

and JT's submission reflects some of the positions that the company would take throughout the process. Overall, the industry stated that there was no need for an international treaty on tobacco, and written submissions to the WHO, including that of JT, are available on WHO's website. [225, 226] Additional comments submitted by JT to WHO emphasized smoking as an adult choice and harm reduction approaches. It stated that smokers should be informed, but not encouraged, to quit, arguing that whether or not to continue to smoke should be a matter of free choice; and it supported accommodation of smokers and non-smokers based on "mutual consideration", among other suggestions for what believed were interventions that "might have a measurable and sustained impact on tobacco use." [227] A Philip Morris account of the oral statements made at the WHO hearings summarizes Japan Tobacco's position as follows:

- [JT] Said the "openly acknowledge" the health risks of smoking and that JT is "willing to shoulder its responsibility".
- Asserted that tobacco is already highly regulated, and that additional regulation is warranted to further publicize the health risks, disclose product contents. Reasonably restrict marketing, YSP [Youth Smoking Prevention], reduce the "annoyance of ETS", address smuggling ("We don't benefit" from it), and develop reduced-risk products.
- Cooperation, not confrontation, is needed to make progress
- Said they are opposed to ad bans, raising taxes, abolition of descriptors and "one size fits all" approaches, as well as demonization of "Big Tobacco"
- National governments know what's best for each country on tobacco regulation.
- Argues that the idea that putting the big companies out of business would benefit the public health is "ivory tower", that the result would be no control over either the product or the revenue derived from it.
- Public health authorities have concluded that smoking causes disease, and JT believes that this conclusion is a mandate for the company to develop reduced risks products.
- When asked whether JT accepted the consensus that smoking causes diseases, sated that "JT agrees" with the public health community. Was asked how they intend to compensate smokers who become ill from smoking;

> replied that it is not JT's responsibility to compensate smokers, and that JT believes that its role in this regard is to help develop reduced-risks products.[225]

A JTI account of the hearings concluded that

> In our view, the most significant outcome of the public hearings is likely to be that WHO will now claim that it has heard from all organizations with an interest in the **FCTC, including the tobacco industry. However, while we welcomed the opportunity to express our views, we do not believe that the public hearings constituted genuine consultation.**[46]

JTI's hearing account also discussed Philip Morris International "change in position" in regards to several smoking and health issues, as demonstrated by changes in its website. This account also reports on the 1st Intergovernmental Negotiating Body meeting (INB), which were the formal meetings in the development of the FCTC, and how the companies, including JTI, would continue to try to gather information from the diverse delegations involved in the negotiations of the FCTC. [46]

The public relations firm Mongoven, Biscoe & Duchen, Inc. (MBD) had been working for Philip Morris in several attempts of PM to derail tobacco control, including infiltration in advocacy groups, and more recently, by advising on strategies to influence the FCTC.[228] In a 1999 memo to PM's Matt Winokur, Jack Mongoven discusses the Japanese position in regards to the FCTC and summarizes Japan's conflicting position when it comes to significant tobacco control measures:

> **According to activist-oriented newspapers, Japan has accepted the [WHO's] invitation to express support for the [FCTC]···· Japan's acquiescence sets the stage for conflict between Japan' s Health Ministry and its Finance Ministry... [WHO] is organizing a conference on tobacco for November, in Kobe ["Avoiding the Tobacco Epidemic in Women and Youth"]····The conference will probably not generate considerable anti-tobacco activism, but it will introduce the justifications and concepts of the FCTC to the Japanese people ... The conference will have modest goals and it will probably receive considerable media attention in Japan, if for no other reason than for its novelty. The real issue, according to observers, remains the potential revenue loss to the**

> treasury – estimated at $20 to $22 billion – which can probably trump any demands made by the Health Ministry. The Health Ministry's job (and by extension WHO's job) will be to provide the Finance Ministry with compelling data that shows a long-term financial benefit to the ratification of the FCTC and to halving the number of smokers in Japan.[229]

A 2001 JTI document states that some of JTI's objectives are to:

- Provide intelligence on developments in the FCTC/WHO process
- Inform Governments/WHO delegates to ensure they are aware of JTI's arguments
- Co-operate as appropriate with competitors to maximize the effort
- Campaign to raise wider issues in the media and influencer circles (threat of transnational governments to sovereignty etc)
- Build reputation as an open (on risks) and transparent (on ingredients) company.[230]

This 2001 JTI document then summarizes all of WHO's FCTC-related activities for the first 6 months of 2001, including the release of "monographs and press releases which both demonise the tobacco industry and actively support radical anti tobacco measures."[230] The document concludes by saying that

> Most of our [JTI] efforts during the past 6 months have been focused on monitoring the development of the FCTC and provide feedback to the various markets and functions. The release of the next FCTC draft will lead to a re-definition of JTI's arguments and a deeper involvement of the markets and functions in order to I) ensure that national governments are fully aware of them and II) raise wider issues within the local media and influencer circles.[230]

In March 2002, it came to light that Japan Tobacco had paid £4,500 per month to Roger Scruton, a self-proclaimed philosopher and a conservative British journalist, to mount a campaign to discredit the WHO and the FCTC. For years, Mr. Scruton has had several articles and reports condemning WHO for focusing on tobacco instead of AIDS and other communicable diseases. For the JTI public relations campaign, the intent was to have Scruton publish specific articles on the

FCTC in all major international newspapers. It became apparent that Mr. Scruton has received a salary from JTI for years, but failed to disclose these financial ties to the several papers that published his columns, including the Wall Street Journal and the Financial Times.[231, 232]

Media reports account that JT's main objection to the FCTC was related to the proposed ban on descriptors such as "lights" and "mild" – mainly because of the threat against its best selling brand Mild Seven. The final text of the FCTC bans misleading language on cigarette descriptor, but it is not specific about banning terms like "mild", which are provided as an example of terms that could be misinterpreted, and the government of Japan approved the FCTC. It remains to be seen if it will sign and ratify the treaty.[233] After months of fighting the European Union's directive banning such descriptors, alleging that the term Mild was used as part of the brand name, and it refers to taste and not to nicotine or tar content, JT Inc. announced that it would stop selling Mild Seven and Mild Seven Lights in Europe. [234]

Voluntary marketing Code and Other Youth Initiatives

For decades, the tobacco industry worldwide, including the tobacco industry in Japan, has been developing voluntary marketing codes in which the industry announces restrictions in the medium and form that it will use to market its products.[160, 235-237] And for decades these codes have been ineffective in curbing smoking rates. In fact, the messages of industry youth campaigns stay clearly away from health effects of smoking and emphasize smoking as an adult decision; the voluntary marketing codes contain loopholes that allow promotions that are appealing to young adults, making it seemingly more appealing to young people to smoke. [238]

In 2001, as a response to the growing threat of the FCTC, the tobacco industry issued a joint voluntary marketing code, signed by BAT, JTI and PMI and a few other companies. How this code was developed seemed to have been a complex negotiation process among the three large companies. Although not all documents related to the code are available, there are enough drafts to suggest that the main goal of the industry was to maintain the "right to communicate with adult smokers" under the industry's own terms, and reiterate the smoking is an "informed adult choice".[239-241] This 2001 JTI presentation stated:

Objectives of marketing standards

- **Demonstrate responsibility and alignment with society**

- Restricting youth access to tobacco marketing
- Ensuring that adults are appropriately informed about the risks of smoking
- Accepting principle of restrictions given nature of product
- Seek and allow for inclusion of tobacco family [239]

[emphasis in original]

It is clear that this industry as a group was taking a preemptive measure in order to avoid marketing policies aimed at banning tobacco advertisement, promotion and sponsorship. The "International Tobacco Products Marketing Standards", with its adult only focus, falls short of any meaningful tobacco control measure. In fact, a tobacco stock analyst, Bonnie Herzog, in 2001 referred to the international code as public relations efforts, stating that

> [We] believe that the multinational's strategy is proactive and is a way to improve their image... One would think that the elimination of certain marketing practices would effectively decrease advertising spending and hence increase margins, however we believe the modest amount multinationals actually spend in these types of practices [that would be eliminated with the international code] will be redirected into other types of marketing promotions, i.e. point of sale activity.[242]

In addition to the "code", PM and JTI have been sponsoring youth smoking prevention TV spots which are aired on MTV worldwide. BAT, which was one of the original sponsors, withdrew from the program, as criticisms grew that these campaigns were no more than public relation efforts. In fact, studies have indeed shown that the industry's Youth Smoking Prevention programs are ineffective and counterproductive for tobacco control efforts.[238]

A June 1999 PMKK presentation summarizes the industry's "Youth Prevention Initiatives in Japan",[243] which is run by the TIOJ. Similarly to other ineffective youth campaign in the world, the Japan campaign focuses on retailer education and distribution of material (posters, brochures, etc). The difference is that in Japan it is not the sales of cigarette to minors that is illegal, by smoking by those younger than 20 years of age is against the law. The industry campaign is an attempt to show it is concerned with responsible marketing and educating cigarette sales personnel about the existing law. The industry initiative also has a high school component with the distribution and placement of posters reminding high school students to follow the rules and that smoking is prohibited. In

1999 the industry was seeking government endorsement to "enhance campaign credibility." Such support would be sought from the Ministries of Education, Health, and Youth Affairs, to name a few.[243] The theme of the 1999-2000 posters, both for high schools and retailer distribution focused on the rule (law). For example, a poster with a young man in a skateboard was translated as saying "Having rules makes things more fun. Smoking is prohibited to anyone under 20 years old. It's the rule."[243] Thus, it is clear that the industry is focusing on the adult appeal of smoking in its "prevention" campaign.

The last page of this presentation, however, provides an insight of how differently PMKK and JT handle their corporate affairs. PMKK announced that it intended to add the following warning on packs and cartons: "Underage Smoking Prohibited" [243] (This language is similar to PM's language in other parts of the world.[160]) According to this 1999 presentation, JT "showed strong opposition" to PM's proposal,[243] for the following reasons:

It seems that any decision on the warning was delayed until after the release of the white paper. The presentation further comments that "JT, BAT, RJR all believe the industry should act together."[243]

4 Limitations

This appendix is meant to be an overview of the activities of the tobacco industry in Japan. The search was limited to documents that were available on the Internet, thereby excluding the millions of pages of industry documents maintained by British American Tobacco in its Guildford, UK depository. Another limitation is that mainly documents dated from the late-1990s and beyond were selected for analysis. In addition, only documents addressing the topics discussed here were reviewed, and the search ended in June of 2003. That excluded thousands of Japan-related documents that are available on the Internet but were not included either because of date or relevance to the overview presented here. Furthermore, hundreds of documents have been posted on the Internet since the end of the search for this appendix. A more in-depth analysis of all tobacco industry documents related to Japan that are currently publicly available is recommended for a more comprehensive discussion of the tobacco industry activities in Japan.

5 Conclusion

Japan Tobacco thoroughly dominates the tobacco sector in Japan, creating unique tobacco control challenges in that country. Industry documents reveal that,

on the domestic and global scene, Japan Tobacco International operates much like its main rivals, BAT and PMI, focusing on the maintenance of marketing freedoms, the opposition to taxation and the promotion of the social acceptability of smoking. All three leading multinational companies market to youth, deny smoking's health risks to whatever extent allowed by their lawyers and pursue bigger sales and a greater market share both in Japan and worldwide.

Domestically, however, JT does not have to lobby government in quite the same fashion as the competition: It is the government! Although the company is no longer wholly owned by the government, it is still a hybrid of a private company and a public institution. In all countries, the Health and Finance Ministries show a tendency towards policy conflict over tobacco. In reality, the goals of greater public health and stronger finances should be complementary when it comes to tobacco, given the high societal costs imposed by smoking but, from a political, short term agenda perspective, the long-term view of tobacco control can be obscured by immediate concerns, particularly with regard to possible reductions of tax revenues. In Japan, where consensus, courtesy and tolerance are highly valued, and where cigarette warning labels and restrictions on marketing and smoking in public places are among the weakest in the world, the industry has historically had virtual carte blanche. Even strong scientific evidence can be ignored, as the documents show, when there is a cultural bias in favor of the industry's views and the status quo. The political limitations may in part explain the inability, to date, of the Ministry of Health and Welfare to implement scientifically-sound tobacco control measures.

JT executives sit on key government committees, a ventilation company has entered into a partnership with JT, and there is evidence of strong resistance to changes in tobacco policy that go beyond voluntary self-enforced measures. The social climate in Japan is slowly changing, but there remains a wide acceptability of public smoking. The most successful measures to restrict public smoking, in fact, are not based in health, but in the desire to reduce littering and fire hazards. The tobacco industry has taken advantage in the cultural believe that values tolerance and courtesy to oppose effective public health measures promoting clean indoor air and to promotes its "accommodation" of smokers and non-smoking programs, including promotion of ventilation "solutions".

The industry has also found that the academic community in Japan remains very tolerant of working with the industry and has been funding prestigious Japanese institutions and researchers for decades. Such practice, according to industry reports, is not perceived as a conflict of interest in Japan in the same way that it has been increasingly being denounced in Western countries.

Clearly, tobacco control advocates in Japan face daunting challenges, but several groups are active and have achieved some measurable success. The domestic market is shrinking, thanks in part to advocates' efforts, to higher taxes that were imposed in response to changes in the global economy, and to a global downward trend in consumption in the developed world. This again presents a challenge as JT will naturally control an even larger fraction of the shrinking market and will seek to expand its global reach in order to grow and respond to stockholder expectations. In fact, Japan Tobacco has a legislative mandate to be profitable.

With the passage of the FCTC and the growth of JTI, Japan's domestic policies and role in the international tobacco control community will likely receive more focus. The political limitations of the government highlight the need for organized efforts by the non-government organizations involved in tobacco control in Japan. The battles ahead will not be easy, but the revelations provided by the documents reviewed here will arm Japanese advocates and their worldwide colleagues with the best possible tools to help them strategize and determine the best ways to challenge Japan Tobacco and make inroads with policy makers. The Japanese government will need to be lobbied effectively in order to see that its interests and those of the Japanese people are better served by responding to the dictates of sound health and scientific policy and not to the vested, established interests of Big Tobacco.

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APPENDIX

Appendix: A
Details of Individual Studies on Smoking on Cancer in Japan

1 Cancer in a single site

1.1 Head and neck cancer

On examination of oral and pharyngeal cancers, Hirayama reported that the relative risk (RR) of developing cancer of the mouth or pharynx was 2.19 for smokers and 3.04 for drinkers (Hirayama 1982). In his book (Hirayama 1990), relative risk (90% CI) for oral cancer was 2.17 (1.20-3.91) for cigarette smoking and 2.83 (1.86-4.32) for alcohol consumption. Respective values for the pharynx were 2.09 (0.79-5.55) and 2.87 (1.66-4.97).

A multivariate analysis by Takezaki based on case-control studies reported that the relative risk (95% CI) of oral cancer was 2.3 (1.6-3.4) for smoking, 1.9 (1.4-2.6) for drinking and 0.6 (0.4-0.8) for consumption of salty food (Takezaki et al. 1996). With respect to smoking, the results of these two cohort and case-control studies were in good accordance.

A relationship between smoking and cancer of the maxillary sinus was reported by Fukuda (Fukuda et al. 1987). Based on a case-control study, current or past smokers had a relative risk of 3.0 ($p<0.05$) for men and 1.6 (NS) for women after adjustment for disease history, education, occupation and domestic heating systems. Due to the rarity of cases, only a limited number of reports was available.

1.2 Esophageal cancer

Hirayama investigated the relationship between daily cigarette smoking

and esophageal cancer (Hirayama 1990). The relative risk (90% CI) for esophageal cancer was 2.24 (1.72-2.91) for male smokers and 1.75 (1.21-2.51) for women. The relative risk values were comparable between men and women.

The results were stratified according to the number of cigarettes smoked per day. Men smoking 1-9 cigarettes per day had a relative risk of 1.62 (1.09-2.41). This increased to 2.04 (1.54-2.71) for 10-19 cigarettes and 2.69 (2.05-3.53) for 20 or more. Respective values in women were 1.74 (1.04-2.91) and 2.45 (1.53-3.93). These findings provide strong evidence of a correlation between esophageal cancer risk and the number of cigarettes smoked in both male and female smokers.

An additional multivariate study examined the relative risk for esophageal cancer after considering risk-enhancing factors such as hot tea and alcohol, as well as risk-reducing factors such as green or yellow vegetables, gender, age and area of residence (prefecture) (Kinjo et al. 1998). Adjusted relative risk was 1.0, 1.5 (0.8-2.8), 1.8 (1.3-2.5) and 1.9 (1.4-2.7) for non-smokers, ex-smokers, light smokers (1-14 cigarettes/day) and heavy smokers (15 or more cigarettes/ day), respectively. The contribution of smoking to esophageal cancer relative risk was decreased after further adjustment for risk-enhancing and -reducing factors in a second multivariate analysis model. It should be noted that the combination of daily alcohol, tobacco use and hot tea consumption elevated the relative risk to 5.7 (3.7-8.9).

A case-control study by Nakachi reported that the relative risk of cigarette smoking was 2.4 (1.397-3.00) for men and 2.3 (1.023-5.174) for women (Nakachi et al. 1988). A combination of alcohol use and cigarette smoking increased these values to 5.7 (0.2555-125.936) in men and 2.0 (0.512-7.945) in women. With the combination of hot beverage consumption and cigarette smoking, relative risk for esophageal cancers was 3.1 (0.967-9.885) in men and 2.5 (0.887-6.919) in women. The authors noted that when heavy smoking was accompanied by excessive intake of rice the relative risk was very high, at 19.2 (3.412-108.618). In contrast, alcohol consumption accompanied by excessive rice intake showed a lower but still high relative risk of 13.8 ($p<0.01$). The authors suggest that high rice intake is associated with a decrease in the consumption of risk-reducing nutrients. The contribution of cigarette smoking to esophageal cancer relative risk is correlated with risk-enhancing factors such as alcohol drinking, hot beverage consumption and salty food intake, as well as with risk-reducing factors such as raw vegetables, fruits, seaweed, and meat intake.

A subsequent study by Takezaki investigated 284 cases and 11,936 controls matched for age, year and season of visit, drinking pattern and consumption of raw vegetables (Takezaki et al. 2000). Adjusted relative risk was 1.0, 1.6 (0.9-2.8) and 3.5 (2.1-5.8) for never-smokers, ex-smokers and current smokers, respectively. Consideration of the number of cigarettes smoked per day

yielded a relative risk of 3.1 (1.8-5.5) for individuals smoking 1-19 cigarettes/day and 3.5 (2.1-5.9) for smokers of 20 or more. The length of time an individual had smoked was also considered. Individuals smoking between 1 and 29 years had a relative risk of 2.2 (1.1-4.4), compared to 3.6 (2.1-6.0) for those smoking more than 30 years. The authors examined the correlation between age of first cigarette and risk for esophageal cancer. Smokers who started smoking at less than 20 years of age had a relative risk of 3.9 (2.2-6.9) compared to 3.3 (1.9-5.5) for those who started at 20 or older. Finally, the interval since the last cigarette was also examined. Former smokers with 1-9 smoke-free years had a relative risk of 2.3 (1.3-4.2) as compared to 1.3 (0.7-2.3) for those with 10 or more smoke-free years.

1.3 Stomach cancer

Whole stomach

Case-control studies have identified a consistent association between stomach cancer and smoking (Kono et al. 1988, Unakami et al. 1989, Kato et al. 1990, Hoshiyama and Sasaba 1992a, Inoue et al. 1994). The odds ratio (OR) for current or former smokers developing stomach cancer were around 2. The ratio was slightly higher among men than women, probably due to the difference between them in the overall proportion of smokers. A dose-dependent relationship was observed when analysis was done for the total amount of cigarettes smoked. The odds ratio for ex-smokers was equal to or lower than that for current smokers with low total cigarette dosage (Kato et al. 1990, Hoshiyama and Sasaba 1992a, Inoue et al. 1994). A dose-response relationship among ex-smokers was not observed (Inoue et al. 1994).

In a case-referent study by Inoue, an examination of smoking and stomach cancer revealed an odds ratio around 2, with a higher value observed in men (Inoue et al. 1999). This was consistent with the results of the case-control studies. A slightly stronger association was seen among the younger stratum (<60 years old) than in the older group in both men and women. A dose-response relationship was also observed, especially among men. The risk for former smokers was between that of never-smokers and current smokers. Age at the start of smoking as divided at 20-year intervals did not substantially change risk among smokers, except among the younger stratum (<60 years old), for whom the association between age at initiation and stomach cancer was stronger than for the older group.

Cohort studies (Hirayama 1984, Kato et al. 1992b, Sasazuki et al. 2002) report a relative risk of stomach cancer for current smokers of 1.5-2.29 and for ex-smokers of 1.6 and 2.61. With regard to the amount smoked, a dose-dependent relationship was not apparent for either age at the start of smoking or the number of packs smoked per year (Sasazuki et al. 2002).

By subsite, histology and cancer cell behavior

The association between smoking and the appearance of cancer at different subsites of the stomach was examined. Analysis of the cardia, middle and antrum showed a higher correlation with the cardia (Inoue et al. 1994, Sasazuki et al. 2002). Examination of histologic type, namely intestinal type and diffuse type, did not reveal a strong association between smoking and these specific subsites, although a slightly stronger relationship was seen with intestinal-type cancer and smoking in women (Kato et al. 1990). Sasazuki examined the behavior of histologic-type tumors in distal portions and reported that the differentiated type in in this areas was strongly associated with smoking (Sasazuki et al. 2002).

1.4 Colorectal cancer and adenoma

Among four case-control studies examining an association between colorectal cancer and smoking, one study showed a significantly increased risk of colorectal cancer among heavy smokers. An individual currently smoking 31 or more cigarettes per day had a 2.4-fold increased risk (95% CI 1.3-7.5) of cancer after adjustment for gender, age, BMI and alcohol consumption (Yamada et al. 1997). However, when colorectal cancer was examined by subsite, three case-control studies found no positive association for colon cancer among male smokers (Tajima and Tominaga 1985; Inoue et al. 1995), female smokers (Inoue et al. 1995), or male and female smokers combined (Hoshiyama et al. 1993). Among these studies, one found a significant inverse association between current smoking and colon cancer (Hoshiyama et al. 1993). In contrast, of three case-control studies, one found a significant positive relationship between male and female smokers (including former smokers) and rectal cancer (Inoue et al. 1995), with odds ratios of 1.9 (95% CI 1.1-3.2) for men and 1.7 (95% CI 1.0-3.1) for women. Another study found an insignificant positive relationship (Hoshiyama et al. 1993) between current smoking (men and women combined) and rectal cancer. No cohort studies are available.

Five case-control studies have reported an association between colorectal adenoma and cigarette smoking. For men currently smoking, colorectal adenoma was significantly associated in a dose-dependant manner in two studies (Todoroki et al. 1995; Inoue et al. 2000). Current and former smokers using 800 or more cigarettes per year were at a significantly increased risk (OR = 3.5-4.1). Nagata did not find an association between colorectal adenoma and current smoking, but heavy smokers (men smoking 30 years or more) had a significantly increased risk of colorectal adenoma (Nagata et al. 1999). By subsite, sigmoid colon adenoma was positively and dose-dependently associated with smoking (Honjo et al. 1992; Honjo et al. 1995). Nagata found that current smoking had a positive and

significant association with proximal colon adenoma, but not with distal colon adenoma (Nagata et al. 1999). No association was found between rectal adenoma and current smoking in two case-control studies (Honjo et al. 1995; Nagata et al. 1999). One case-control study found a significantly increased risk of colorectal adenoma (OR = 2.2) among female smokers and former smokers as compared to nonsmokers (Nagata et al. 1999).

An increased risk of sigmoid colon adenoma was seen in men with a history of smoking in one of three case-control studies (Honjo et al. 1992). However, two studies found no association between former smoking and colorectal adenoma (Nagata et al. 1999, Inoue et al. 2000) or adenoma at any subsite (Nagata et al. 1999).

Current cigarette smoking was also significantly and dose-dependently associated with an increased risk of colorectal carcinoma in situ (Yamada et al. 1997). No significant relationship was observed between colorectal carcinoma in situ and a past history of smoking (Yamada et al. 1997).

1.5 Liver cancer

A clear association has been shown between smoking and liver cancer (Tanaka et al. 1988, Tanaka et al. 1990, Tsukuma et al. 1990, Tanaka et al. 1992, Yamaguchi 1993, Tanaka et al. 1995, Mukaiya et al. 1998). In a study which took account of hepatitis virus B and C status, Tsukuma reported an odds ratio after adjustment for viral status of 2.30 (95% CI 0.90-5.86) for the development of liver cancer (Tsukuma et al. 1990). In view of the association of blood transfusion with viral hepatitis, especially type C, Tanaka adjusted for a positive history of transfusion (Tanaka et al. 1992; Tanaka et al. 1995). An odds ratio of 1.3-1.4 was seen for men smoking more than 11.0 packs of cigarettes per year and 1.9 (95% CI 0.90-5.86) for a positive history of smoking in women.

In a number of follow-up studies(Oshima et al. 1984, Inaba et al. 1989, Hiyama et al. 1990, Inaba et al. 1990, Tsukuma et al. 1993, Chiba et al. 1996, Tanaka et al. 1998, Mori et al. 2000), smoking was again reported to be associated with liver cancer. In a study of HBsAg-positive blood donors, and after adjustment for alcohol consumption, Oshima reported an odds ratio of 6.3 for heavy smokers (30 or more cigarettes per day) (Oshima et al. 1984). Hiyama reported similar results in a study of subjects with alcolholism. Heavy smokers (more than 30 cigarettes per day) had an odds ratio of 5.8 (95% CI 1.0-34.2) (Hiyama et al. 1990).

In a study of patients with chronic liver disease and liver cirrhosis, Inaba reported that smoking was associated with death from liver cancer (Inaba et al. 1989, 1990). After adjustment for hepatitis virus types B and C and stage of liver disease, Tsukuma reported a rate ratio of 2.30 (95% CI 0.90-5.86) for current smokers (Tsukuma et al. 1993). For hepatitis virus type C-positive patients

with chronic hepatitis, Chiba reported a rate ratio of 2.46 (95% CI 1.11-5.49) for smokers with a pack-year index of more than 400 (Chiba et al. 1996). Mori reported hazard ratios of 3.75 (95% CI 1.62-8.68) for individuals with a positive history of smoking after adjustment for status of both virus types (Mori et al. 2000). They also reported a significant additive interaction between smoking and a high titer for hepatitis C virus antibody ($p<0.05$). Interestingly, Tanaka reported that drinking and smoking were not significantly correlated with an elevated risk of liver cancer after taking into account the status of both virus types (Tanaka et al. 1998).

No cohort studies have been reported linking liver cancer with viral status as determined by serology (Shibata et al. 1986, Hirayama 1989a, Shibata et al. 1990, Goodman et al. 1995, Mizoue et al. 2000). However, Hirayama reported that the risk for daily cigarette smokers of liver cirrhosis developing into liver cancer was 2.67 (95% CI 1.49-4.79) (Hirayama 1989a).

Discrepancies are seen when examining the association between smoking and liver cancer. One factor may be hepatitis virus status. Since clinical laboratory tests for hepatitis C virus were not available until 1989, few studies report hepatitis C viral status. Several studies instead used a history of blood transfusion or chronic liver disease. After chronic liver disease associated with hepatitis virus is taken into account, a clear correlation is seen between smoking and liver cancer.

1.6 Pancreatic cancer

Three case-control studies and two cohort studies have examined the risk of pancreatic cancer among smokers in Japan. All reported an increased risk of cancer in current smokers compared with non-smokers. Ishii et al reported an increased risk among smokers using a Ridit score analysis (Ishii et al. 1973). In their report, the incidence of cigarette smoking was significantly higher in the pancreatic cancer group than in the control by Ridit score ($p<0.05$). In Hirayama, based on a prospective cohort study involving 265,118 participants, the age-adjusted increased risk was 1.56 (1.22-1.99) for men and 1.45 (1.00-1.92) for women (Hiayama 1989c). Three studies calculated the risk with stratification for the number of cigarette smoked per day. Mizuno reported in a multi-institutional case-control study (Mizuno et al. 1992) that the risk for smokers of more than 23 cigarette per day was 2.56 (0.93-7.04), although all smokers' risk was 2.80 (1.19-6.37). Goto reported a 4.67 (1.21-18.05)–fold higher risk for smokers of more than 10 cigarettes per day and a 6.50 (1.32-32.11)–fold higher risk for 20-year smokers (Goto et al. 1990). In the JACC study, one of the largest cohort studies in Japan, Lin reported a 3.3 (1.38-8.1)–fold higher risk of pancreatic cancer, with significance only for smokers of 40 or more cigarettes per day (Lin et

al. 2002).

1.7 Lung cancer

Current smoking and overall lung cancer risk

Substantial data are available concerning the relationship between smoking and lung cancer in Japanese men living in Japan. Three cohort studies (one of which included Japanese-American men residing in Hawaii) and five case-control studies have examined the overall lung cancer risk due to cigarette smoking. All these studies reported that cigarette smoking statistically increased the overall risk for lung cancer. In the three cohort studies the relative risk for men was 4.5-11.4 (all significant) (Chyou et al. 1993; Wakai et al. 2001; Sobue et al. 2002), while odds ratio in four of the case-control studies was 1.9-4.4 (all significant) (Esaki and Chang 1977; Shimizu et al. 1986; Sobue et al. 1994; Wakai et al. 1997). For women, one cohort study reported that the relative risk was significantly increased, to 4.2 (Sobue et al. 2002), and four case-control studies reported odds ratios of 2.8-4.4 (all significant) (Esaki and Chang 1977; Shimizu et al. 1986; Sobue et al. 1994; Wakai et al. 1997).

Current smoking and lung cancer by histology

Several studies examining lung cancer risk by histologic type showed that the magnitude of the association of smoking and lung cancer is determined by histologic type.

A strong correlation exists between smoking and squamous cell carcinoma. One cohort study reported that smoking significantly increased the risk of squamous cell carcinoma and small cell carcinoma for both men (RR = 12.7) and women (RR = 17.5) (Sobue et al. 2002). All six case-control studies found a strong correlation between smoking and squamous cell carcinoma in both men and women. In five case-control studies, the odds ratio of squamous cell carcinoma for men was 4.3 (includes current vs. never- and ex-smokers combined) (Shimizu et al. 1986) and 5.2-18.1 (Tsugane et al. 1987; Sobue et al. 1988; Shimizu et al. 1994; Sobue et al. 1994; Wakai et al. 1997). The odds ratio was 6.4-28.2 for women.

One cohort study (Sobue et al. 2002) reported an increased risk of adenocarcinoma among current smokers; the relative risk was significantly increased for men (RR = 2.8) and similarly but nonsignificantly increased for women (RR = 2.0). The relationship between smoking and adenocarcinoma was examined in seven case-control studies. A significant increase in odds ratio (1.9-5.0) for men was observed in five of these studies (Shimizu et al. 1986; Sobue et al. 1988; Suzuki et al. 1990; Sobue et al. 1994; Wakai et al. 1997). Two studies found no such positive association (Tsugane et al. 1987; Shimizu et al. 1994). For women, three of seven studies found a significant increase in risk (OR = 1.8-2.9)

(Shimizu et al. 1986; Sobue et al. 1988; Suzuki et al. 1990), but another three of the seven found no such association (Shimizu et al. 1994; Sobue et al. 1994; Wakai et al. 1997). One case-control study found a non-significant inverse association between smoking and adenocarcinoma of the lung (Tsugane et al. 1987).

A small number of studies have addressed the relationship between smoking and small cell or large cell carcinoma. A statistically significant increase in risk among current smokers was seen in two of three case-control studies. Results showed an odds ratio of 6.9-21.4 in men and 12.1-14.4 in women for small cell lung cancer and 3.8-4.1 for men and 3.7-3.8 for women for large cell lung cancer (Sobue et al. 1988; Sobue et al. 1994). One study examined the risk among current smokers as compared to nonsmokers and former smokers combined; the reported odds ratios were 3.9 (men, small cell lung cancer), 4.5 (women, small cell lung cancer), 3.4 (men, large cell lung cancer), and 4.0 (women, large cell lung cancer) (Shimizu et al. 1986).

Amount and duration of smoking (dose-dependency) and lung cancer

Dose-dependency has been examined in one cohort study and several case-control studies. The cohort study reported that the risk of overall lung cancer, squamous cell lung cancer (combined with small cell carcinoma) and adenocarcinoma was increased with increasing duration of smoking or the number of cigarettes smoked per day in men (Sobue et al. 2002). The gradual elevation of risk with increasing intensity of smoking was more evident for squamous cell carcinoma (plus small cell carcinoma) than adenocarcinoma. The relative risk of squamous cell carcinoma (plus small cell carcinoma) and adenocarcinoma for 60 or more packs/year as compared to nonsmokers was 15.2 (95% CI 5.0-46.9) and 3.0 (95% CI 1.3-7.0), respectively (Sobue et al. 2002). In the case-control studies, a correlation existed between the duration and quantity of cigarette smoking and the odds ratio in male smokers (Esaki and Chang 1977; Tsugane et al. 1987; Suzuki et al. 1990; Shimizu et al. 1994; Sobue et al. 1994; Wakai et al. 1997). Squamous cell carcinoma was more affected by smoking pattern than adenocarcinoma in these studies. For female smokers, one cohort study found that the relative risk for all lung cancer was 3.3 for 0-29 packs/year and 10.1 for 30 or more packs/year (Sobue et al. 2002).

Former smokers and overall lung cancer

The risk of overall lung cancer among ex-smokers was found to be higher than that for never-smokers, but less than or equal to that for current smokers. In two cohort studies, the risk for all cancers among former smokers was 2.2-3.1 (Chyou et al. 1993; Sobue et al. 2002) for men and 3.7 for women (Sobue et al. 2002). Two case-control studies found an increased risk for former smokers compared to nonsmokers (RR = 2.4-2.8 for men, 2.1-5.3 for women) (Sobue et al.

1994; Wakai et al. 1997).

One cohort study reported that the risk of squamous cell carcinoma among former smokers was significantly increased for men and women (RR = 5.1 for men and RR = 17.5 for women) (Sobue et al. 2002). A significant increase in squamous cell carcinoma was also observed for men and women in two case-control studies (Sobue et al. 1994; Wakai et al. 1997).

With respect to adenocarcinoma, in contrast, one cohort study found no elevation in the risk of adenocarcinoma in men (RR = 1.3) but a significant increase in women (RR = 4.3) (Sobue et al. 2002). Among three case-control studies, for men, one found a significant 3.2-fold increase in odds ratio (Suzuki et al. 1990), but two found no association (Sobue et al. 1994; Wakai et al. 1997). For women, one study found a significant 1.7-fold increase in odds ratio (Sobue et al. 1994), while two found no association (Suzuki et al. 1990; Wakai et al. 1997).

One case-control study examined the risk of small cell lung cancer and large cell lung cancer among former smokers as compared to never-smokers. The odds ratio of small cell cancer and large cell cancer was 9.2 (significant) and 2.6 (nonsignificant) for men and 4.7 (significant) and 4.1 (significant) for women, respectively (Sobue et al. 1994).

The risk of all lung cancers, squamous cell carcinoma, and adenocarcinoma among former smokers was decreased as the years since cessation increased (Sobue et al. 1994; Wakai et al. 1997; Wakai et al. 2001). After 15 or more years' cessation, the risk of lung cancer mortality among former smokers was the same as that among never-smokers (Wakai et al. 2001).

1.8 Breast cancer

Three case-control studies in Japan have examined smoking and the risk of breast cancer. Two reported no significant increase in risk for breast cancer among cigarette smokers (Tajima et al. 1990; Kikuchi et al. 1990). Tajima reported an increased risk (1.58 with a significance level of 0.10) for breast cancer from passive smoking (Tajima et al. 1990). Hirose examined breast cancer risks and smoking after stratification for menopausal status (pre- vs postmenopause) (Hirose et al. 1995) and concluded that current smoking increased the risk of breast cancer in premenopausal women

1.9 Cervical cancer

Four case-control studies have examined the relationship between cervical cancer and smoking. All four reported a significantly elevated risk of cervical cancer in smokers. In the report of Tajima, odds ratio was 2.58 for current smokers and 2.29 for passive smoking ($p<0.05$) (Tajima et al. 1990). Using data

from the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC) in Japan, Hirose reported a risk of 2.19 (1.78-2.69) for all smokers and 1.30 (1.07-1.59) for passive smokers. Adjustment was made for all variables which were statistically significant in the univariate analysis (Hirose et al. 1996). Hirose subseqently reported the risk of cervical cancer in a more detailed analysis (Hirose et al. 1998). In this report, the elevated risk for smokers was 2.31 (1.84-2.92) for all smokers and 1.42 (1.13-1.79) for passive smokers. Adjustments were made for age, marital status, age at first pregnancy and number of pregnancies. In an age-matched case-control study, Sasagawa reported an elevated risk for smokers of 2.50 (1.1-5.7) (Sasagawa et al. 1997).

1.10 Ovarian cancer

Only one report regarding the risk of cigarette smoking for ovarian cancer in women in Japan has been identified (Mori et al. 1996). This study was conducted using ovarian cancer cases from several hospitals in Northern Kyushu. Controls participated in an ovarian cancer mass screening program in the same area. Risk for ovarian cancer from smoking was 1.60 (95% CI 0.78-3.27).

1.11 Prostatic cancer

Two case-control studies are available regarding prostate cancer and smoking in Japan. Both concluded that smoking was not related to the risk of prostate cancer. Oishi reported that prostate cancer risk in current smokers was 1.36 (0.76-2.45) and 0.59 (0.34-1.03) for the two types of controls, benign prostatic hyperplasia patients and the general population, respectively (Oishi et al. 1989) . Oishi also reported that the prostate cancer risk in ex-smokers was 0.77 (0.44-1.35) and 1.41 (0.81-2.48) for the respective controls (Oishi et al. 1989). In the report by Furuya, the risk for prostate cancer in smokers was 0.99 (0.69-1.31) (Furuya et al. 1998).

1.12 Bladder cancer

Four case-control studies in Japan have examined the association between tobacco smoking and cancer of the bladder. All studies were frequency-matched for gender and age. Morrison evaluated the risk of cigarette smoking on bladder cancer in Boston, USA, Manchester, UK, and Nagoya, Japan (Morrison et al. 1984). In this report, the risk of cancer from smoking in Nagoya was reported as 1.7 (95% CI 1.1-2.9) for all male smokers. Risk according to the quantity of cigarettes smoked was also analyzed. Although a dose-response relationship seemed to exist, a trend analysis was not conducted. Ohno analyzed the risk of

smoking on bladder cancer with stratification by gender and age using the same data set as Morrison (Ohno et al. 1985). According to the report, the risk of bladder cancer from smoking was 1.89 (1.15-3.10) for men and 3.53 (1.72-7.32) for women. Higher risks were reported for elderly than middle aged subjects. Nishio reported the risk of smoking as 3.23 (1.94-5.70) for men and 3.21 (1.40-7.32) for women (Nisio et al. 1989). Nakata reported the risk as 2.40 (1.42-4.04) for men and women, with risk increasing commensurate with the number of cigarettes smoked and years of smoking (Nakata et al. 1995).

1.13 Hematopoietic malignancy and related disorders

Few studies have investigated the association of smoking and hematopoietic malignancies. Myelodysplastic syndrome (MDS, including refractory anemia), a poorly understood set of neoplastic hematopoietic disorders, was examined in one case-control study (Ido et al. 1996). The moderate yet insignificant associations between MDS incidence and smoking, with RRs of 1.4 and 2.7 for men and women, respectively, are difficult to reconcile with the mystery surrounding the pathogenesis of this disorder. Correlations between smoking and acute non-lymphocytic leukemia and acute leukemia were examined by Wakabayashi (Wakabayashi et al. 1994). The risk for acute non-lymphocytic leukemia was 1.8 with a 95% CI of 0.96-3.23. For acute leukemia the risk was 1.7 (95% CI 0.99-2.84). An association between the number of of cigarettes smoked and the incidence of acute leukemias, with RRs of 0.9, 1.6, 1.7, and 4.1 for persons reporting cigarette consumption of 0-10, 11-20, 21-30, and 31 or more cigarettes per day, respectively, increased the confidence ($p<0.05$) that smoking may contribute to the genesis of this malignancy, although the mechanism appears to be as elusive as in the case of MDS. A report from Matsuo showed no association between smoking and malignant lymphoma except for a slightly increased incidence in former smokers (Matsuo et al. 2001a).

2 Combined sites

2.1 Multiple/second primary, and upper aerodigestive tract cancer

The association of smoking with not only cancer having a single site of origin but also that having combined sites, namely second/multiple primary cancer (S/MPC) and upper aerodigestive tract cancers (UDTC), has also been evaluated. The idea of "field cancerization" is supported by these two (S/MPC, UDTC) conditions.

From case-control studies, smoking dose was associated with MPC for lung (Sugimura et al. 1987) but not stomach cancers (Hoshiyama and Sasaba 1992b). With regard to stomach, colorectum, liver, lung, breast and uterus, a high number of cigarettes smoked (30 or more per day) was significantly associated with MPC (Kato et al. 1985).

After a primary cancer in the mouth and meso- or hypopharynx, smokers using 20 or more cigarettes per day at diagnosis of the primary cancer had a greater than three-fold greater risk for a second occurrence (SPC) at any site. Moreover, if a second occurrence was limited to the oral cavity, pharynx, larynx or esophagus, the risk was elevated more than 10 times. Alcohol consumption magnified the risk (Kinoshita et al. 1997). A similar relationship between smoking and alcohol consumption, and SPC after head and neck cancer was also suggested (Nakamizo et al. 1993). For SPC following laryngeal cancer, the heaviest smokers were found among patients with SPC (Kobayashi et al. 1990), and the occurrence of SPC was more than two times higher than expected (Hiyama et al. 1992). As for SPC after stomach cancer, current smokers had an elevated risk (1.82: 1.02-3.26) whereas ex-smokers did not (0.95: 0.42-2.13) (Kinoshita et al. 2000). In a case-

control study of SPC after esophageal cancer, current smokers using 30 or more cigarettes per day, or 50 or more packs per year, had significantly higher risks (17.5: 3.2-94.7, 12.7: 2.1-19.5, respectively) (Morita et al. 1994). Regarding SPC after SCLC, interview with patients with a smoking history following diagnosis (or relatives of deceased patients) showed that smoking cessation within 6 months after the initiation of treatment was associated with a significant reduction in the risk of SPC compared to those who continued smoking (Kawahara et al. 1998).

Most studies of SPC have focussed on the upper aerodigestive tract (UADT). These sites are among the so-called "smoking-related cancer" sites. An association with smoking tended to be more apparent when SPC sites were limited to these UADT or "smoking-related cancer" sites.

2.2 Measures of burden of smoking-attributable cancer

A cohort study of the general population in the town of Hisayama showed that death from malignant neoplasms for individuals aged 40-54, 55-69, or both was correlated with smoking (Hirota et al. 1986). A cohort study of male physicians compared the risks for current smokers to those physicians who had quit and to never-smokers. The relative risk was 1.38 (1.07-1.77) for current smokers using 1-19 cigarettes/day and 1.99 (1.52-2.59) for 20 or more cigarettes/day. No significant association with alcohol consumption was observed (Kono et al. 1985, Kono et al. 1987).

A reanalysis of the six-prefecture cohort, from one of the largest cohort studies in Japan, evaluated smoking and cancer mortality. A linear relationship was noted for the relative risk of cancer of the oral cavity, esophagus, stomach, liver, pancreas, larynx, lung or bladder and daily cigarette usage in men. In women this positive correlation was observed between daily smoking and liver, pancreatic, lung and uterine cancer. Relative risk of smoking 10 cigarettes per day for all cancers as calculated for each 4-year period varied from 1.2 to 1.5 for men and from 1.3 to 1.5 for women. A higher relative risk with increasing age was seen for men. This tendency was apparent for lung cancer, where relative risk varied from 2.4 to 5.4 (Akiba and Hirayama 1990).

From a study using longitudinal information on smoking habit, the relative risk for all cancers was 1.6 (1.5-1.7) for current smokers and 1.2 (1.1-1.4) for ex-smokers. A relative risk significantly higher than 1.0 was observed in esophageal, stomach, liver, gallbladder, nasal cavity, lung, cervix uterine and bladder cancers for current smokers, and in esophageal, stomach, liver and lung cancers for ex-smokers. (Akiba 1994)

A recent large cohort study of mortality due to smoking indicated a relative risk of cancer death of 1.61 (1.20-2.15) for men and 1.83 (1.14-2.95) for women. The proportion of cancer deaths attributable to smoking was estimated to

be 25% for men and 4% for women (Hara et al. 2002).

Esophageal cancer was associated with smoking in 53.6% of cases studied by Yokoyama (Yokoyama et al. 2002), while more than 90% of cases were associated with significant alcohol consumption. An analysis of national mortality data using mortality rates among non-smoking and nondrinking women as baseline estimated an attributable risk of esophageal cancer death in men using both alcohol and cigarettes of 86.3%, and of buccal cavity and pharynx cancer deaths of 84.5% (Parrish et al. 1993).

Significant recent increases in the burden of smoking-associated morbidity/mortality in Japan were indicated from recent analyses of trends in smoking-associated mortality and premature death (expressed as years of life lost; YLL per 1,000) using data compiled for the period 1985 to 1995 (Shibuya 1999). Mortality from malignant neoplasms attributable to tobacco increased 29.4% for men (44.2/100,000 in 1985, increasing to 57.2/100,000 in 1995) and 17.2% for women (9.5/100,000 in 1985 and 11.2/100,000 in 1995). Tobacco -related premature death increased 43.7% for men (327.2 YLL in 1985 to 470.1 YLL in 1995) and 39.9% for women (65.9 YLL in 1985 to 92.3 YLL in 1995) (r=0.03, K=1 for age weight).

Using the numerical estimation methods of Hara (Hara et al. 2002) and data from Vital Statistics 2002, the annual burden of cancer deaths attributable to smoking in Japanese men and women is now approximately 46,000 (25% of 183,849) and 5,000 (4% of 120,437), respectively. Lung cancer deaths alone attributable to smoking total approximately 30,000 (68% of 43,895) and 3,000 (18% of 17,723) for men and women, respectively, in this instance using the relative risk estimation by Sobue (Sobue et al. 2002) on annual incidence data for 1998 from The Research Group for Population-based Cancer Registration (The Research Group for Population-based Cancer Registration in Japan 2003)

3 Factors which modify the effect of smoking on cancer

3.1 Lifestyle: alcohol intake, diet and environment/occupation

Alcohol intake

With regard to esophageal cancer in case-control studies by Hanaoka, there seemed to be no combined effect of smoking and alcohol drinking, and moreover, the risk of cancer for smokers was reduced toward null after adjustment for alcohol drinking (Hanaoka et al., 1994). However, a cancer screening study among active alcoholics comparing exposure of 50 or more pack-years with less than 50 pack-years showed that increased exposure was associated with a significantly increased incidence of esophageal cancer (2.8: 1.4-5.7), oropharyngeal cancer (5.1: 1.3-19.5) and multiple cancer (11.8: 2.3-60.7). Alcoholics with inactive ALDH2, stronger beverage choice, and 50 or more pack-years represented the majority of patients with multiple cancer diagnoses (5/8: 62.5%), a striking finding considering the much lower proportion of such heavy alcoholics among patients with esophageal cancer alone (2/28: 7.1%) (Yokoyama et al. 1996).

Prospective studies of Japanese-Americans residing in Hawaii demonstrated that combined smoking and alcohol drinking had a synergistic effect on the induction of multiple cancers (Kato et al. 1992a; Chyou et al. 1995).

Diet

Active smokers who drink alcohol on a daily basis and eat a meat-rich diet have a high risk for cancer at multiple sites. Supplementation of their diet with moderate quantities of green and yellow vegetables (GYV) reduced their risk of cancer by about 30% (RR 0.67) (Hirayama 1989b). Specific site cancers which were reduced in prevalence by dietary modification in such high risk individuals

included oral and pharyngeal cancer (RR 0.46), esophageal cancer (RR 0.77), stomach cancer (RR 0.59), liver cancer (RR 0.47), laryngeal cancer (RR 0.41), lung cancer (RR 0.71) and bladder cancer (RR 0.68).

While smoking cessation has cancer risk-reducing effects on its own, with incidence approaching normal (never-smoker) rates as the period of non-smoking lengthens, daily GYV consumption further reduces such risk. Lung cancer mortality rates in former smokers were reduced by dietary modification, from 95.3 per 100,000 to 29.7 per 100,000 person years (standardized mortality rates) for 1 to 4 years of cessation), and from 55.8 per 100,000 to 30.0 per 100,000 for 5 or more years of cessation. Moreover, daily GYV consumption appeared to reduce the risk for lung cancer attributable to passive smoking environments. Women whose husbands smoked 1-19 or 20 or more cigarettes daily and whose diets were deficient in GYV had age- and occupation-standardized lung cancer mortality rates 1.9 and 2.4 times, respectively, those of nonexposed, non-smoking women, but these were reduced to only 1.3 and 1.6, respectively, upon adoption of a GYV-rich diet. The overall benefit for passive smokers who maintained adequate GYV intake was statistically significant in this study, at an odds ratio of 0.71 (0.54-0.94) (Hirayama 1986).

The significant detrimental effect of a deficient diet was apparent in a case-control study of smoking-related lung cancer in which subjects had varying intakes of fruit and vegetables. Daily isocaloric consumption of fruit, raw vegetables, green vegetables, lettuce, or cabbage reduced the risk of lung cancer among current smokers when compared to smokers who maintained a simpler, starch-based diet. These effects were independent of both the age at which cigarette smoking started as well as the number of cigarettes smoked per day. Multivariate analysis suggested that the highest preventative effects were provided by fruit and raw vegetable intake among current smokers, and by fruit intake among former smokers (Gao et al. 1993).

Other lifestyle factors

Besides the beneficial effects of complex diets containing fruits and vegetables and detrimental effects of a high starch intake (high rice consumption) discussed above, several other elective habits can modify the smoking-related risk of cancer. In a case-control study of esophageal cancer in Japanese smokers, frequent sake drinking and salty food consumption increased the risk to a greater than additive extent, with each risk factor appearing independent over a wide range of intake levels (Sasaki et al. 1990). A case-control study of Caucasian and Japanese Hawaiians indicated that smokers with low daily fluid consumption had an elevated risk of bladder cancer (Wilkens et al. 1996).

As mentioned earlier, the association between smoking and cancers of the breast or female genital organs are marginal and difficult to interpret. The

differences between smoking-related risk reported for Eastern and Western women, with marginally increased risks for the latter, are difficult to reconcile. A marginally significant increase in breast cancer risk was found for Asian women with high progesterone receptor expression (p=0.063), which may in turn be an index of overall estrogen stimulation of a given tissue. Smoking status had little relation to the incidence of breast cancer in women grouped according to this index, or according to estrogen receptor status (Yoo et al. 1997). As mentioned earlier, several case-control studies have pointed to a significant association between cervical cancer and smoking. Because most cases of cervical carcinoma are dependent on the presence of sexually-transmissible human papilloma viruses, contracted from sexual partners and their extended contacts, and the clinical test for the infection was available only recently, it has been difficult for investigators have been reticent to dissociate the many social issues that surround smoking, drinking, sexual conduct and oral contraceptive use.

Environment and occupation

A case-control study of smoking as a modifier of the effects of respiratory asbestos exposure indicated a strong association, with an increasing incidence of lung cancers in smokers, especially of Kreyberg I-type lung cancer (Minowa et al. 1991). The study, stratified on the basis of asbestos fiber count in lung tissue, indicated that smokers were at an increased risk for cancer even at a relatively low asbestos lung burden, at which only a low incidence of cancer would have been expected among nonsmokers (Hiraoka et al. 1990).

Arsenic, implicated as a human carcinogen, synergizes with smoking habit to dramatically increase the risk of lung disease. A study of arsenic mine or refinery workers indicated a significant excess risk of respiratory cancers and lung cancer deaths among mine workers with a smoking history (Tsuda et al. 1990). The synergistic increase in lung cancer incidence in these worker populations, with little lung cancer seen among arsenic-exposed nonsmokers, may have also been evident in a historical cohort study of a community that consumed high levels of arsenic in contaminated well water (Tsuda et al. 1995). Among those persons who ingested well water with high total arsenic doses (1 or more ppm), crude mortality rates were substantially higher among smokers than nonsmokers. Of those who ingested lower total doses (0.05 or more ppm), 92% of those with a smoking habit were debilitated by what appeared to be a synergistic interaction between two exposures.

Ironworkers who also smoke did not show elevated risk from the additive effects of iron/silica dust. However, there are other workers with diseases that appear to reflect synergistic induction with smoking. These were workers who answered that they worked in areas other than mining, steel manufacture, building construction, road construction and ship building, and therefore presumably in

chemical plants (Yamaguchi et al. 1992). This synergy can only be speculated to involve an interaction between unknown, possibly related classes of occupational agents with the complex mixture of polycyclic hydrocarbons, arylamines, nitrosamines, carbon monoxide and soot that makes up tobacco smoke.

3.2 Genetic polymorphism of enzymes related to xenobiotic agent detoxification

Accumulating evidence points to the influence of genetic polymorphisms, i.e., variable activities or expression of specific proteins, in conferring an increased or decreased incidence of disease for a given level of chemical exposure. Recent studies have indicated that genetic variations within human populations may be responsible for heterogeneous susceptibility to smoking-related diseases, whether by differences in the metabolism of smoke-associated tars, or in the ability of smoke-exposed cells to repair, regenerate or die. Although advances in methodology continue to refine our understanding of smoking-associated pathogenesis, the focus of the following presentation is on evidence for differences in detoxification enzyme activity or cell growth regulation that relate to smoking-related problems of particular relevance to Japanese and other Asian populations.

Cytochrome P450 (CYP) [EC:1.14.14.1], CYP 1A1

This metabolic enzyme is a major determinant of the transformation of smoke-associated tars, variously referred to as polycyclic hydrocarbons (PCHs) or aryl hydrocarbons (AHs), into chemical species that can be eliminated from the body, but can also give rise to mutagenic chemical species. The aryl hydrocarbon hydroxylase (AHH) activities that are useful for measuring relative P450 1A1 protein abundance are found to increase when tissues are challenged with small doses of tar-like chemicals. This 'inducibility' is due to increased CYP 1A1 gene expression, and may differ between individuals with the different genotypes that constitute the polymorphism.

Low-dose smokers (less than 30,000 cigarettes consumed over a lifetime) with the CYP1A1*2C genotype were more likely to develop lung cancer than smokers with the CYP1A1*2A or CYP1A1*2B genotypes (Kawajiri et al. 1990; Nakachi et al. 1991). These excess cancers were typically poorly differentiated adenocarcinomas, rather than the squamous or small cell cancers typical of smoking-related lung cancer. The increased overall incidence of cancer among smokers with the CYP1A1*2C genotype relative to the CYP1A1*2A appeared to be independent of smoker dose over a considerable range (Nakachi et al. 1995).

The basal activity and inducibility of AHH activity associated with

CYP1A1 genes in response to cigarette smoking (Kiyohara et al. 1997) was associated with lung cancer risk, with high odds ratios associated with both high inducibility and low non-induced activity, even after normalizing to an equivalent number of cigarettes smoked per day. Individuals with the CYP1A1*2C genotype in particular showed high inducibility and high odds ratios for lung cancer incidence (Kiyohara et al. 1998). It is difficult to make firm conclusions from these results without considering other factors, including possible linkage disequilibrium with genetic loci for other metabolic detoxification activities. At the least, however, these results provide an enticing link between smoking-associated disease and induced AHH activity.

CYP 2E1

No interaction was observed between smoking and CYP2E1 polymorphism among Japanese Brazilians (Nishimoto et al. 2000).

CYP 2A6

In one study, the CYP2A6*4/*4 genotype, due to a homozygous deletion of the gene, was found to be unexpectedly absent from all squamous cell carcinomas (0/105) and small cell carcinomas (0/44) examined (Ariyoshi et al. 2002). The investigators found that individual smokers with this genotype tended to consume fewer cigarettes per day, making the CYP2A6*4/*4 genotype one of the first candidate genetic determinants with a potential effect on smoking behaviour.

N-acetyltransferases (NAT) [EC:2.3.1.5]

These enzymes conjugate amine functions on arylamine and other xenobiotic chemicals with acetyl moieties, enhancing elimination of these potential toxins from the body. Polymorphisms among these genes have been firmly associated with altered responses to therapeutic drugs and toxins.

Among oral squamous cell carcinomas, the odds ratio for tumor cells to express the high specific activity NAT1*10 genotype (Yang et al. 2000) rather than the more common low specific activity NAT1*4 or *3 genotypes did not differ between smoking and non-smoking patients (Katoh et al. 1998). In contrast, bladder cancers from smokers tended to be slow acetylator genotypes (homo-/heteroxygotes of NAT2*5, NAT2*6, NAT2*7, and NAT2*14) (Katoh et al. 1998), conferring a significantly higher odds ratio than that for bladder cancers of nonsmokers, which tended to carry rapid acetylator genotypes (homo-/heteroxygotes of NAT2*4 allele) (Inatomi et al. 1999).

Glutathione S-transferase (GST)[EC:2.5.1.18]

This enzyme is also associated with the modification of foreign chemicals

to facilitate their elimination from the body. However, its additional functions in the neutralization of highly reactive metabolites and free radicals and in maintaining redox potential may serve a more general role in recovery from toxic stress.

Smokers with a GSTM1 null (-) genotype tended to have a higher risk of developing lung cancer than smokers with functional GSTM1 alleles (Kihara et al. 1993). Lung cancers developing in smokers with the GSTM1 null genotype were Kreyberg I-type cancers, especially squamous cell carcinomas. Dose-response relationships, in terms of cigarettes smoked per day and the number of years of active smoking, were not prominent (Kihara et al. 1994). The overall distribution of GSTM1 genotype-associated lung cancers by age of incidence, gender, smoking status and predominant histological type was distinct (Kihara et al. 1995b). Smokers with the GSTM1 null genotype suffered from an increased incidence of non-laryngeal head and neck cancers (Kihara et al. 1997). Significant evidence for haploinsufficiency, and interactions with GSTP1 alleles in either homo/heterozygous variant genotypes (Kihara et al. 1999), support the putative relationship between reduced phase II enzyme activity and elevated DNA damage. The GSTP1 mutant genotype (exon 5) alone had no influence on the risk of lung cancer, irrespective of smoking status (Yamamura et al. 2000).

The GSTM1(-) genotype was more frequent among smokers with gastric adenocarcinoma (Katoh et al. 1996), and in male patients aged less than 70 years with squamous and small cell carcinomas of the lung (Kihara et al. 1995b).

The results to date support the hypothesis that mutations in both GSTM1 and GSTP1, resulting in null or reduced detoxification activity, are associated with an elevated risk of lung cancer. Further, evidence on GSTM1 polymorphism from the Japanese studies reviewed in this section suggest associations between null or reduced enzyme activity and cancer, especially in the upper aerodigestive tract.

Other enzymes

Certain toxic products of AHH action on tars can be further metabolized by NAD(P)H:quinone oxidoreductase 1 (NQO1). An assessment of smoking-related esophageal and lung cancer incidence indicated that persons with a NQO1-null genotype (T609T vs wild type C609T) had a higher risk (odds ratio) than other genotypes, although the results were only marginally significant (Hamajima et al. 2002).

Similarly, with regard to 8-oxoguanine DNA glycosylase (OGG1), a DNA repair enzyme with a polymorphism involving a moderate-activity Ser326Cys enzyme and a low-activity Ser326Ser form, little difference in risk of stomach or lung cancers was seen in individuals differing at this locus (Sugimura et al. 1999; Ito et al. 2002), nor for stomach cancer (Hanaoka et al. 2001).

Aldehyde dehydrogenase (ALDH) polymorphisms were associated

with a smoking-related increase in risk for colonic polyposis, with smokers (<400 cigarette-years) of the ALDH2 *1/*1 (low ALDH activity) genotype having a significantly higher risk. The possible relationship of alcohol drinking and smoking with polyp severity suggested a specific role for the enzyme in individuals with this genotype (Takeshita et al. 2000). In contrast, the ALDH2 1543 G to A substitution conferred no significant difference in risk of esophageal cancer (Matsuo et al. 2001b).

It is possible that some polymorphisms play a role in modifying other risk factors in smokers. With regard to myeloperoxidase (MPO), for example, current smokers with an A allele at the –463 G to A polymorphism had a lower risk of Helicobacter pylori infection (Hamajima et al. 2001b).

Combination of enzymes

(1) CYP and GST

As might be expected of metabolic systems for xenobiotic detoxification which consist of multiple enzymes acting in sequence, with the product of one enzyme serving as the substrate for the next, characteristic combinations of genotypes are reported to confer differences in the risk of smoking-related disease. For example, individuals with the CYP1A1*2C (Val/Val) and GSTM1(-) combination genotype were more prevalent within case populations than in their age-matched control populations (Nakachi et al. 1993; Kihara et al. 1995a). The increased risk of lung cancer with differences in these genotypes was especially evident among individuals with a low cumulative cigarette dose and a longer duration of non-smoking, with less difference in risk seen among heavy smokers (Nakachi et al. 1993). Among nonsmokers, this combination genotype was also more prevalent among lung cancer cases than matched controls (Kihara et al. 1995a), suggesting a general risk for lung cancer causation in individuals with low basal activities of both enzymes. Similar results indicating increased susceptibility at low cumulative cigarette dosage were evident among smokers with small cell carcinoma (Kihara et al. 1995a). An increased risk of oral cancer was also apparent in case-control studies of populations, with increased risk associated with individual low activity of either genotype or, more particularly, the combination genotype (Sato et al. 2000; Sato et al. 1999). Conflicting results were seen in two studies of esophageal carcinoma, with the combination genotype conferring either increased risk (Nimura et al. 1997) or no significant difference (Hori et al. 1997).

Analyses of esophageal squamous cell carcinoma tissue for AHH activity in microsome preparations demonstrated that AHH activity was substantially elevated in situ among smokers, especially among individuals with low alcohol consumption. Interestingly, no significant difference in the expression of common CYP1A1/2 proteins was evident in thse esophageal tissue preparations. In addition, neither protein expression nor GST enzyme activity varied according to

smoking or drinking habit, although individuals with the GSTM1 null genotype clearly had lower overall GST activity (Nakajima et al. 1996)

(2) NAT and GST or sulfotransferase

No significant association was apparent in an investigation of smoking-associated risk of colorectal cancer with individual isoforms of GST (M1, P1, and T1) and NAT (1 and 2) or their genotypic combinations (Yoshioka et al. 1999).

NAT and phenol sulfating sulfotransferase (SULT) are phase II detoxification enzymes which mediate chemical conjugations that facilitate elimination from the body. Because these enzymes may either compete for substrates, or substitute for individual deficiencies in the other, their composite activity may have relevance to smoke toxicity. The combination of a low specific activity sulfotransferase genotype (ST1A3*1/*1 homozygote) with a slow-acetylating NAT (NAT2 genotype) confers significant risk (very high odds ratio) for urothelial cancer, but such individuals appear to be at no more risk of smoking-associated bladder cancer than individuals with the single, NAT2 slow acetylating genotype (Ozawa et al. 2002).

(3) Other combinations

Single locus variability in NQO1, GST isoforms (T1, M1, and P1), CYPIA1 and OGG1 had no association with the smoking-associated risk of lung adenocarcinoma. However, the combination genotype of NQO1 (higher activity type, Pro/Pro) and GSTT1(-) was associated with a higher risk (odds ratio) for lung adenocarcinoma, both in comparison to other genotypic combinations and when compared to nonsmokers of the same genotypic combination (Sunaga et al. 2002).

Large, well-controlled investigations of smoking-associated oral disease among individuals with differing combinations of genotypes involving GST M1, GST T1, CYP1A1, CYP 2E1 and ALDH2 found that, after exclusion of individuals with the cancer-prone combination genotype GSTM1(-)/CYP1A1*2C, there was little difference among genotypes in risk for smoking-associated oral cancers (Katoh et al. 1999; Sato et al. 1999; Sato et al. 2000).

Genetic polymorphisms: other molecules

Polymorphism at the cyclin D1 locus, specifically at the RNA splice-associated codon 241, are associated with differences in the relative risk of transitional cell cancer of the urinary bladder. Smokers with the AA or AG genotypes at codon 241 were found to be at higher risk of high-grade urothelial cancer, with the magnitude of association with smoking increasing from GG to AG to AA (Wang et al. 2002).

Smokers with L-myc polymorphisms differed in risk of esophageal cancer. Individuals with the SS and LS genotypes, involving intron 2 of L-myc,

were at higher risk of esophageal cancer than smokers with the LL genotype. This risk was especially evident among smokers with high alcohol consumption (Kumimoto et al. 2001). While the incidence of lung cancer was also elevated among smokers with the L-myc SS and LS genotypes, the additive effect of alcohol consumption on smoking-associated lung cancer risk in these subjects was minimal (Kumimoto et al. 2002).

With regard to Helicobacter pylori infection, a major risk factor for gastric cancer, the influence of interleukin-1 (IL-1; a mediator of inflammation) polymorphisms on H. pylori infection status was also examined. In a study to examine the effect of lifestyle factors such as smoking on the prevalence of H. pylori infection, individuals with IL-1 beta C31T genotypes exhibited a higher prevalence of infection' moreover, current smoking strengthened the association between C31T genotypes and infection (Hamajima et al. 2001a). Although a biological mechanism for the interaction between smoking and inflammation has not been clearly elucidated, this result suggests a synergistic effect of smoking-associated tissue response and specific IL-1B genotype on inflammatory response.

4 “Molecular signatures” - smoking-related changes often observed during carcinogenesis

4.1 Mutations of cancer-associated genes

Most contemporary theories of carcinogenesis ascribe cancer ‘initiation ’ events to mutation of critical cancer-associated genes. Subsequent mutation, and cell selection for both genetic and epigenetic variation, lead to a cancer cell that carries its carcinogenic history within its genome in a partially decipherable list of point mutations and chromosomal translocations, generally near the critical cancer-associated genes. The following discussion presents recent evidence for common mutations that have been found within smoking-associated tumors.

p53

Somatic cell mutation of p53 is common among smoking-associated lung cancers (Kondo et al. 1996; Sekine et al. 1998), and for NSCLC lifetime cigarette consumption was closely related to p53 mutation (Suzuki et al. 1992), especially when cumulative cigarette dosage is high. Smoking-associated cancers of lung (NSCLC) and bladder frequently exhibit G to T transversions within coding sequences (Suzuki et al. 1992; Habuchi et al. 1993), whereas cancers arising among nonsmokers are less likely to carry such point mutation (Takeshima et al. 1993; Takagi et al. 1998). An association between somatic mutation and smoking has been most evident in younger (<65) individuals and among carriers of a germline p53 polymorphism known as Pro-allele (Murata et al. 1998).

Germline polymorphisms of p53, especially at codon 72 of exon 4, have been associated with differing risk of lung cancer development, although apparently unrelated to smoking in most cases (Murata et al. 1996). Further study has shown that individuals carrying the Pro-allele haplotype exhibited a higher

smoking-related mutation rate than Arg/Arg homozygotes (Murata et al. 1998).

K-ras

The demonstration of K-ras point mutation leading to a constitutively active oncogene has become a classic example of a mutational mechanism of carcinogenesis. In line with theories attributing smoke-related carcinogenesis to mutagenic byproducts of tar metabolism, genetic mutations of K-ras among cases of NSCLC were almost exclusively restricted to individuals who reported high-dosage smoking histories. Such mutations tended to be G to T transversions of codons 12 or 13 (Noda et al. 2001). In contrast, pancreatic cancer cases exhibiting this point mutation are less often associated with smoking status (Nagata et al. 1990).

4.2 Interactions between metabolic activation/detoxification enzymes and oncogenes

A synergistic interaction between p53 functions (eg. DNA damage surveillance) and xenobiotic metabolism was suggested by the association of an excess risk of lung cancer among individuals carrying germline p53 polymorphism (codon 72 of exon 4) as well as CYPIA1(*2B or C) and GSTM1(-) (Kawajiri et al. 1993). Smokers with CYPIA1*2B or*2C genotypes (Val/Val genotype or *2C genotype) were at higher risk of mutation of p53 or K-ras. Additional risk was conferred by the GSTM1(-) genotype in combination with CYPIA1 Val/Val or *2C genotypes (Kawajiri et al. 1996). The persistence or altered metabolism of certain components of smoke may increase the likelihood of metabolic activation to mutagenic products by alternative pathways and permit responses by cells and tissues to the nonmetabolized smoke constituents (eg. via AH receptor).

4.3 Genomic stability, chromatin structure and cell cycle regulation

Microsatellite instability (MSI) was slightly elevated in lymphocyte cultures of smokers with transitional cell carcinoma of the urinary tract (Uchida et al. 1996). In tumors and nontumorous lung tissues of patients with NSCLC, hypermethylation of D17S5 marker loci were more frequent among smokers (Eguchi et al. 1997).

The actions of smoke constituents on cell growth regulation, by way of the combined effects of genetic damage by mutagenic byproducts, chromatin structure modifications and altered activities of cell cycle-associated proteins, may prove to be considerably more complex than is given by theories of smoking-associated disease restricted to genetic mutation.

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Appendix (B)

1. About the database

Appendix: B1
About the database

Internationally Acclaimed Database Founded to Realize Evidenced-Based Policy

Results from epidemiological research contained in this report have been entered in a database managed by the Institute for Global Tobacco Control, and anyone interested can freely download data by accessing the homepage of Tobacco Free*Japan (www.tobaccofree.jp) for purposes such as developing new figures and tables or reanalysis. The attached evidence tables were developed using this same procedure. The homepage also contains a download manual and a users manual.

The database was originally developed by Dr. John Samet, coeditor of this project, for the purpose of preparing materials for court hearings for the lawsuit filed by the Minnesota State government and others against the tobacco industry in l994, requesting reimbursement of medical expenses for smoking-related damages (the lawsuit was later expanded nationwide). The database was then further developed jointly by the Institute for Global Tobacco Control and the Center for Disease Control and Prevention (CDC) to support the publication of the 2004 report Health Consequences of Smoking: a Report of the Surgeon General (http://www.cdc.gov/tobacco/sgr/sgr_2004/index.htm).

This is a landmark occasion to have a database of such international caliber established for the use of the Tobacco Free*Japan project before the Evidence-Based Policy is to be established and a full-fledged tobacco control policy is to be pursued in Japan after the ratification of the Framework Convention on Tobacco Control (FCTC). The integration of accurate and reliable data and information, when shared by all interested people, will facilitate the development of a national tobacco control policy and the promotion of research, inviting many people to be involved in dealing with public health.

Appendix (B)

2. Evidence tables

Tobacco-Free Japan Database

Evidence Tables

Abdominal Aortic Aneurysms

Author	Subjects	Study Type	Data				Comments
Goldberg, RJ et al; 1995	2,710	Cohort					Cerebrovascular disease outcome: Thromboembolic Stroke.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Blood Pressure, Body Mass Index, Gender, Heart Rate, Hematocrit, Physical Activity, Serum Cholesterol, Serum Glucose, Serum Triglycerides, Serum Uric Acid.
			0	1.00			
			1 - 19	2.54	1 - 6.45		
			20	3.38	1.68 - 6.78		
			21 - 80	3.56	1.7 - 7.45		
Ishikawa, S et al; 1999	2,514	Cohort	No Abstractable Data				"There were no significant differences between the groups in the frequency of smoking, diabetes mellitus, and coronary artery disease (Table 2)."

Absenteeism

Author	Subjects	Study Type	Data				Comments
Muto, T et al; 1992	21,924	Cross Sectional					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 10	0.81			
			11 - 20	1.05			
			> 20	1.19			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 10	1.25		< .05	
			11 - 20	1.32		< .01	
			> 20	1.48		< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 10	1.22			
			11 - 20	1.55		< .01	
			> 20	1.25			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 10	1.30		< .01	
			11 - 20	1.32		< .01	
			> 20	1.42		< .01	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 19	0.83			
			20 - 39	1.22			
			> 39	0.63			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 19	1.36		< .01	
			20 - 39	1.35		< .01	
			> 39	1.05			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 19	1.52		< .01	
			20 - 39	1.48		< .01	
			> 39	1.22			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			0	1.00			
			1 - 19	1.39		< .01	
			20 - 39	1.32		< .01	
			> 39	1.06			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.51			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	2.51			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.13			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.67			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	0.84			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	3.60		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.20			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	2.41		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Circulatory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.04			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.15			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.67		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.55		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.36		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.30		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.26		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.20			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.12			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.35		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Respiratory Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.36		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.28			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.73			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.67			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.51			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.31			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.25			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.65			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.51			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.27			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Gastrointestinal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.43		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	2.56			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	2.41		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	2.01			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	2.25		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.91			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.19			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.54			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.21			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.05			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Musculoskeletal Disease. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.51		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.62			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.52			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.20			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.35			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.43		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	0.63			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.99			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.38			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	0.77			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), Due to Accident of Poisoning. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.04			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.20			

Absenteeism

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.65		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.67		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.51		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.15			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.19		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.32		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.16			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Ex-Smoker	1.34		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-59), Gender (Male), All Causes. Adjusted for Age, Alcohol Consumption, Body Mass Index, Exercise, Job Title.
			Never Smoker	1.00			
			Current Smoker	1.35		< .01	

Aerodigestive Cancer

Author	Subjects	Study Type	Data				Comments
Kinoshita, Y et al; 2000		Cohort					Cancer = Second primary cancer. Aerodigestive cancer= cancer of the esophagus, liver, pancreas, larynx, lung, and bladder.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender, Stage, Type of Adjuvant Therapy.
			Never Smoker	1.00			
			Current Smoker	3.00	1.24 - 7.28		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender, Stage, Type of Adjuvant Therapy.
			Never Smoker	1.00			
			Ex-Smoker	1.04	0.32 - 3.39		

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
Akiba, S et al; 1998	Not Specified	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	0.92			
			15 - 24	0.79			
			> 24	0.92			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.12			
			15 - 24	1.09			
			> 24	1.17			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.29			
			15 - 24	1.20			
			> 24	1.22			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (70-79), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.40			
			15 - 24	1.36			
			> 24	1.26			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>79), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.19			
			15 - 24	1.24			
			> 24	1.05			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.09			
			15 - 24	1.13			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.51			
			15 - 24	1.49			
			> 24	1.38			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.41			
			15 - 24	1.26			
			> 24	1.63			

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (70-79), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.28			
			15 - 24	1.28			
			> 24	1.63			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>79), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.11			
			15 - 24	1.19			
			> 24	1.39			
Friedman, Gary D et al; 1979	4,289	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, CHD Risk, Education, Emotional Disturbance, Gender, Marital Status, Occupational Hazard, Serious Disease.
			Never Smoker	1.00			
			Current Smoker	2.10		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male). Adjusted for Age, Alcohol Consumption, CHD Risk, Education, Emotional Disturbance, Gender, Marital Status, Occupational Hazard, Serious Disease.
			Never Smoker	1.00			
			Current Smoker	2.10		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Female). Adjusted for Age, Alcohol Consumption, CHD Risk, Education, Emotional Disturbance, Gender, Marital Status, Occupational Hazard, Serious Disease.
			Never Smoker	1.00			
			Current Smoker	2.20		< .05	
Hara, M et al; 2002	41,484	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.05	0.85 - 1.29		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.02	0.82 - 1.28		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.50	0.82 - 2.73		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.27	0.65 - 2.48		

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	1.44	1.12 - 1.84		
			20 - 29	1.56	1.23 - 1.99		
			> 29	1.57	1.28 - 1.93		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	1.64	0.98 - 2.72		
			20 - 29	1.52	0.8 - 2.88		
			> 29	2.61	1.52 - 4.47		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	0.95	0.78 - 1.16		
			> 29	0.96	0.76 - 1.21		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	1.27	0.63 - 2.57		
			> 29	2.20	0.75 - 6.44		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.89	1.36 - 2.62		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.55	1.29 - 1.86		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	1.66	1.4 - 1.95		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.03	1.52 - 2.73		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Current Smoker	1.29	1.26 - 1.32		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.31	1.27 - 1.36		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.35	1.3 - 1.41		
			10 - 19	1.25	1.22 - 1.29		
			> 19	1.29	1.25 - 1.33		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.30	1.24 - 1.36		
			10 - 19	1.32	1.25 - 1.38		
			> 19	1.40	1.26 - 1.56		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.09			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.28			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.36			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.31	1.21 - 1.42		
			5 - 9	1.17	1.05 - 1.31		
			> 9	0.91	0.82 - 1.02		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.63	1.31 - 2.02		
			5 - 9	1.32	0.95 - 1.84		
			> 9	1.57	1.16 - 2.12		
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Non-Smoker	1.00			

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Current Smoker	1.28		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.34		< .05	
Ito, Y et al; 1997	2,353	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Ex-Smoker	0.90	0.5 - 1.59		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.68	0.36 - 1.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Ex-Smoker	2.14	0.48 - 12.05		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.71	0.21 - 2.43		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Ex-Smoker	0.98	0.57 - 1.68		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.63	0.36 - 1.1		
Izumi, Y et al; 2001	43,408	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Physical Activity, Physical Functioning Status.
			Never Smoker	1.00			
			Ever Smoker	1.47	1.18 - 1.83		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Physical Activity, Physical Functioning Status.
			Never Smoker	1.00			
			Ever Smoker	1.26	0.91 - 1.75		

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Physical Activity, Physical Functioning Status.
			0	1.00			
			< 20	1.24	0.93 - 1.67		
			> 20	1.48	1.18 - 1.85		
Kawaminami, K et al; 2003	10,546	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.19	0.98 - 1.45	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.45			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	1.31	1.1 - 1.56		
			21 - 40	1.52	1.23 - 1.89		
			> 40	1.58	1.04 - 2.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.75 - 1.59		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.24			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	1.27	1.02 - 1.58		
			21 - 40	1.98	1.05 - 3.74		
Morioka, S; 1996	1,308	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1989-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	1.40	0.94 - 2.08	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1990-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	1.60	1.04 - 2.44	< .05	

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1991-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	2.12	1.28 - 3.51	< .01	
Nakamura, K; 1985	294	Other	No Abstractable Data				Among male smokers including those who quit, significant excess of death was observed from "other form of heart disease" ($p<0.05$) and "other diseases of liver" ($p<0.01$).
Paffenbarger, RS et al; 1986	16,936	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			> 20	1.00			
			< 20	0.58			
			0	0.50			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.76	1.56 - 1.99	< .001	
Shibuya, K; 1999	265,000	Cohort	No Abstractable Data				Findings show a considerable increase in mortality due to tobacco in Japan.
Takezaki, T et al; 1999	7,662	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Non-Smoker	1.00			
			Ex-Smoker	2.15			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.27			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			Non-Smoker	1.00			
			Ex-Smoker	1.81			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.72			
Tomita, M et al; 1991	38,621	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Calendar Period.
			Never Smoker	1.00			
			Ex-Smoker	1.49	0.47 - 2.27	> .05	

All-Cause Mortality

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Calendar Period.
			0	1.00			
			1 - 14	1.95	1.51 - 2.51	< .05	
			15 - 24	1.59	1.31 - 1.94	< .05	
			25 - 34	1.38	1.08 - 1.76	< .05	
			> 34	1.41	1.02 - 1.92	< .05	
Toshima, H et al; 1995	1,110	Cohort	No Abstractable Data				Results were presented as proportional hazard model coefficients, which were converted into Hazard Ratios (HR) and are as follows (these represent the hazard associated with each 1 cigarette increase in the number of cigarettes smoked per day): Coronary Heart Disease: HR=1.02 Stroke: HR=1.01 All Cancers: HR=1.01 All Other Causes: HR=0.99 All Causes: HR=1.01 "Cigarette smoking was significant only for Coronary Heart Disease, cancer and for all causes, but not for strokes and 'other causes'."
Tsugane, S et al; 1999	19,231	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Number of Cigarettes per Day.
			Non-Smoker	1.00			
			Current Smoker	1.20	0.83 - 1.73		
Wramner, B et al; 2002	Not Specified	Other	No Abstractable Data				"Concerning mortality all causes a tobacco-related mortality among Polish men has increased more than 50% from the 5-year period 1965-1969 to the period 1990-1994. The analysis for women gives a strongly other picture compared with men showing much lower rates. When comparing the middle age group with the overall population it is interesting to find a faster increase in tobacco-related mortality rates for Polish men and for Swedish women in the age group 45-64 years than in the overall group. " "Swedish men have reduced their smoking habit strongly and far more than Polish men (17 and 42% respectively 1999). " "Concerning the pattern of tobacco use it is obvious that Swedish and Polish women during the last decades have had the same and slowly decreasing smoking prevalence (21 and 23% respectively 1999). "

Asthma

Author	Subjects	Study Type	Data				Comments
Comstock, GW et al; 1973	3,088	Cross Sectional					Prevalence ratios could not be calculated COPD and asthma for the Japanese group because zero nonsmokers had these diseases.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male), ATT Round 1. Adjusted for Age, Geographic Location, Smoking Habits.
			0	1.00			
			1 - 14	0.66			
			15 - 24	1.83			
			> 24	2.00			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male), ATT Round 2. Adjusted for Age, Geographic Location, Smoking Habits.
			0	1.00			
			1 - 14	1.40			
			15 - 24	2.20			
			> 24	3.00			
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.83	1.39 - 2.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.02	3.08 - 5.25		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.07	1.42 - 3.01		
			10 - 19	1.79	1.34 - 2.41		
			> 19	1.74	1.29 - 2.36		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	4.62	2.94 - 5.92		
			10 - 19	4.23	2.9 - 6.18		
			> 19	3.23	1.29 - 8.1		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.98	0.96 - 4.05		
			5 - 9	2.71	1.25 - 5.85		
			> 9	1.02	0.33 - 3.18		

Asthma

Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	8.76	2.99 - 25.68		
Hirayama, T; 1981	91,540	Cohort					The asthma outcome also includes women with emphysema.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			0	1.00			
			1 - 19	1.29			
			> 19	1.49			
Kagamimori, S et al; 1996	Not Specified	Cohort					Asthma endpoint= Wheeze with colds.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-22), Gender (Both), Wheeze with Colds. Adjusted for Age at Entry.
			Non-Smoker	1.00			
			Current Smoker	1.80	1 - 3.2	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (21-29), Gender (Both), Wheeze with Colds. Adjusted for Age at Entry.
			Non-Smoker	1.00			
			Current Smoker	1.40	0.8 - 2.5	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (24-31), Gender (Both), Wheeze with Colds. Adjusted for Age at Entry.
			Non-Smoker	1.00			
			Current Smoker	1.20	0.6 - 2.2	> .05	
Kusaka, Y et al; 1996	703	Cross Sectional	No Abstractable Data				The study found no significant relationship of smoking to asthmatic symptoms.
Nakajima, T et al; 1998	210 Cases 180 Controls	Case-Control; Hospital-Based					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), Atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.96			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Father), Atopic Asthma.
			Not Exposed	1.00			
			Exposed	1.04			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Mother), Atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.32			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Other Household), Atopic Asthma.
			Not Exposed	1.00			
			Exposed	1.29			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), Non-atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.59			

Asthma

Author	Subjects	Study Type	Data				Comments
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Father), Non-atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.42			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Mother), Non-atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.62			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Other Household), Non-atopic Asthma.
			Not Exposed	1.00			
			Exposed	0.98			
Nishima, S et al.; 1983	57,761	Cross Sectional					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), Family History of Major Allergy. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.07			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), No Family History of Major Allergy. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.01			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), Family History of Bronchial Asthma. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.10			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), No Family History of Bronchial Asthma. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.02			
Ono, M et al; 1990	Not Specified	Cross Sectional					805 households were surveyed
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Father).
			Not Exposed	1.00			
			Exposed	1.19			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Mother).
			Not Exposed	1.00			
			Exposed	1.28			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	0.92			
Takemura, Y et al; 2001	2,315 Cases 21,513 Controls	Case-Control					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Parents). Adjusted for Age, Breast Feeding, Gender, Parental History of Asthma.
			Not Exposed	1.00			
			Exposed	0.95	0.866 - 1.032	> .05	
Tominaga, S et al; 1985	7,916	Cross Sectional					Asthma is defined as asthma cases with cough sputum.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS

Asthma

Author	Subjects	Study Type	Data				Comments
							Source (Father).
			1 - 9	1.00			
			20 - 29	3.00			
			> 29	1.60			
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Mother).
			Non-Smoker	1.00			
			Current Smoker	4.75		< .01	
Yokoyama, Y et al; 1985	1,178	Cross Sectional					COPD endpoints=Persistent cough and phlegm. Asthma endpoints=Asthma like attacks.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Within 20 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.46		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), 20-150 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.90		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Within 20 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Current Smoker	1.10		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), 20-150 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Current Smoker	1.92		< .001	

Atherosclerosis

Author	Subjects	Study Type	Data				Comments
Burchfiel, CM et al; 1996	120	Cohort	No Abstractable Data				Smoking was found to be directly associated with myocardial lesions.
Fukuda, H et al; 1996	253	Cross Sectional	No Abstractable Data				Cigarette smoking was found to be a weak but significant positive predictor of the PVH score and was independent of age, hypertension and antihypertensive treatment.
Goldberg, RJ et al; 1995	2,710	Cohort					Cerebrovascular disease outcome: Thromboembolic Stroke.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Blood Pressure, Body Mass Index, Gender, Heart Rate, Hematocrit, Physical Activity, Serum Cholesterol, Serum Glucose, Serum Triglycerides, Serum Uric Acid.
			0	1.00			
			1 - 19	1.65	1.19 - 2.3		
			20	2.14	1.67 - 2.74		
			21 - 80	2.16	1.64 - 2.83		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.35	1.2 - 4.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.43	2.68 - 7.33		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.34	0.45 - 4.01		
			10 - 19	1.95	0.94 - 4.06		
			> 19	3.10	1.56 - 6.15		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.87	0.65 - 5.33		
			10 - 19	6.77	3.78 - 12.12		
			> 19	4.35	0.94 - 20.04		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	3.84	1.05 - 14.03		
			5 - 9	2.74	0.4 - 18.65		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	29.32	11.62 - 73.99		
Hirayama, T; 1981	265,118	Cohort					

Atherosclerosis

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Ex-Smoker	1.34			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 14	1.61			
			15 - 24	1.79			
			25 - 49	2.10			
			> 49	2.82			
Hiyamuta, K et al; 1990	919 Cases 110 Controls	Case-Control	No Abstractable Data				Smoking was concluded to be a risk factor for patients with near normal coronary arteries or a solitary plaque in a branch of the coronary artery.
Inoue, Toji et al; 1995	116	Cross Sectional	No Abstractable Data				Findings indicate significantly higher plasma fibrinogen levels in smokers, compared to non-smokers. Smoking was correlated with Gensini's score (GS), Average sclerotic length (ASL) and Average sclerotic area (ASA).
Kitamura, A et al; 2000	419	Cross Sectional	No Abstractable Data				Results are available for smoking treated as a continuous variable. For each increasing cigarette per day was associated with a 0.039mm increase in IMT thickness ($p<0.01$), after adjustment for age, blood pressure, total cholesterol, HDL cholesterol and diabetes.
Konishi, M et al; 1990	Not Specified	Case-Control	No Abstractable Data				Cigarette smoking was strongly and positively associated to the incidence of myocardial infarction (MI). The age adjusted incidence rate for men who smoked 20 cig or more daily was 7.4 times higher then for non smokers Cigarette smoking was positively associated with the incidence of MI (Cox proportional hazard coefficient for cig/day=0.6939, $p<0.001$)
Mannami, T et al; 1997	1,694	Cohort	No Abstractable Data				Pack-year of smoking was correlated with carotid arterial intimal-medial thickness. Multiple regression coefficients of carotid atherosclerosis and pack-years of smoking: Men: 0.1689 $p<0.001$. Women: 0.1054 $p=0.0038$.
Okumiya, N et al; 1985	1,621	Cohort	No Abstractable Data				In the present study cigarette smoking showed a weakly positive but statistically significant correlation. The standardized regression coefficient of cigarette smoking as a risk factor of coronary atherosclerosis = 0.1302 (t-value= 1.852). Cigarette smoking contributed to 0.0091 of the 0.3348 sum of

Atherosclerosis

Author	Subjects	Study Type	Data				Comments
							R -squares in the multiple stepwise regression analysis of the risk factors contributing to coronary atherosclerosis.
Reed, D et al; 1990	7,591	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	1.08			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.55			
Reed, DM et al; 1987	8,006	Cohort	No Abstractable Data				"Cigarette smoking was also consistently associated with aortic atherosclerosis and inconsistently with coronary atherosclerosis."
Seki, J et al; 1983	296	Cross Sectional					The outcome of interest was peripheral vascular disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	1.05			
Shinozaki, K et al; 1997	40 Cases 24 Controls	Case-Control; Hospital-Based	No Abstractable Data				Cigarettes-years was significantly associated with carotid intima medial wall thickness in stepwise multiple regression models in VAP as well all subjects.
Umeda, T et al; 1998	2,228	Cross Sectional	No Abstractable Data				Serum total cholesterol (TC) decreased with increasing levels of cigarette smoking. Serum high-density-lipoprotein cholesterol (HDL-C) was negatively associated with cigarette smoking. Serum low-density-lipoprotein cholesterol (LDL-C) had an inverse association with cigarette smoking. Current smoking was significantly related to both LDL-C/HDL-C and TC/HDL-C ratios. "The proportions attributable to current smoking were 1.1% (P=0.0001) in LDL-C/HDL-C ratio and 1.6% (p=0.0001 in TC/HDL-C ratio."
Yasaka, M et al; 1993	154 Cases 113 Controls	Case-Control	No Abstractable Data				Smoking was found to be associated with atherosclerosis of the extracranial internal carotid artery and the basilar artery.

Atopy

Author	Subjects	Study Type	Data				Comments
Kuwahara, Y et al; 2001	387	Cross Sectional					Smoking appeared to be positively associated with enhanced eosinophil activity.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Family Smoking Habit, Floor Cover, Frequent Cleaning Habits, History of Allergic Diseases, Intensive Use of Air Conditioner, Living in Heavy Traffic Area, Mold Proliferation, Poor Home Ventilation, Type of Housing, Unvented Combustion Appliances.
			Non-Smoker	1.00			
			Current Smoker	1.31	0.65 - 2.62		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Floor Cover, Frequent Cleaning Habits, History of Allergic Diseases, Intensive Use of Air Conditioner, Living in Heavy Traffic Area, Mold Proliferation, Poor Home Ventilation, Smoking Habits, Type of Housing, Unvented Combustion Appliances.
			Not Exposed	1.00			
			Exposed	1.84	0.91 - 3.68	> .05	

Atrophic Gastritis

Author	Subjects	Study Type	Data				Comments
Kato, I et al; 1990		Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Diffuse). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Exposed	2.67	1.37 - 5.22		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	0.96	0.75 - 1.23		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	0.80	0.56 - 1.13		
			> 19	0.89	0.7 - 1.14		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	0.96	0.62 - 1.49		
			> 19	0.77	0.43 - 1.37		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.14	0.69 - 1.88		

Back Pain

Author	Subjects	Study Type	Data	Comments
Huang, C et al; 1996	645	Cohort	No Abstractable Data	Smoking was not significantly associated with back pain.

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.7 - 2.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	2.60	1.6 - 4.5		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.80	0.4 - 5		
			5 - 14	1.40	0.9 - 2.3		
			15 - 24	2.00	1.3 - 3.3		
			25 - 34	1.70	0.6 - 4.1		
			> 34	2.10	0.5 - 6.1		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.90	0.1 - 4		
			5 - 14	2.20	1.1 - 4.1		
			> 14	1.20	0.1 - 5.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.70	1.1 - 2.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.90	1 - 3.4		
Chyou, PH et al; 1993	7,995	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	1.35	0.7 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	2.86	1.67 - 4.91		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema.

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
							Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.61	1.11 - 2.35		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.29	1.45 - 3.62		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.07	0.57 - 2.02		
			10 - 19	1.60	1.07 - 2.4		
			> 19	1.96	1.32 - 2.91		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.70	0.81 - 3.56		
			10 - 19	2.28	1.13 - 4.59		
			> 19	1.79	0.33 - 9.84		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.29			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.72			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.53			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.69	0.6 - 4.77		
			> 9	1.83	0.58 - 5.75		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			5 - 9	7.95	0.98 - 64.55		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Status				Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.79	1.33 - 2.41		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.27			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	5.00			
			20 - 39	2.30			
			> 39	0.00			
Kato, I et al; 1985	265 Cases 1,412 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	3.52		> .05	
Morrison, Alan S et al; 1984	1,435 Cases 1,852 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United States. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.50			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United Kingdom. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.80			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.00			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United States. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	3.40			

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United Kingdom. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	0.70			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United States. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.40			
			20 - 39	3.20			
			> 39	4.70			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United States. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	4.30			
			> 19	6.20			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United Kingdom. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.90			
			20 - 39	3.20			
			> 39	4.00			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United Kingdom. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	2.10			
			> 19	2.20			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.60			
			20 - 39	2.10			
			> 39	2.80			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Japan. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	4.40			
			> 19	4.20			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United States. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.90	1.3 - 2.8	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United States. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	4.20	2.5 - 7.1	< .05	

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United Kingdom. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	2.20	1.4 - 3.5	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), United Kingdom. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.30	0.8 - 2	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.70	1.1 - 2.9	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Japan. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	4.30	2 - 9.2	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United States. Adjusted for Age, Gender, Residence Location.
			Current Smoker	1.00			
			Ex-Smoker	0.50	0.4 - 0.8	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), United Kingdom. Adjusted for Age, Gender, Residence Location.
			Current Smoker	1.00			
			Ex-Smoker	0.70	0.5 - 0.9	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age, Gender, Residence Location.
			Current Smoker	1.00			
			Ex-Smoker	0.50	0.3 - 0.8	< .05	
Morrison, AS et al; 1982	241 Cases	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.60		> .05	
Murata, Motoi et al; 1996	38 Cases 1,774 Controls	Nested Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 10	2.60			
			11 - 20	2.30			
			> 20	1.30			
Nakata, S et al; 1996	Not Specified	Cross Sectional	No Abstractable Data				Findings indicate that, while cigarette smoking prevalence in males declined in both Japan and the United States, the

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
							incidence of bladder cancer increased. In females, however, both the smoking prevalence and incidence of bladder cancer were stable.
Nakata, S et al; 1995	303 Cases 303 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ever Smoker	2.40	1.42 - 4.04		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 10	1.28	0.68 - 2.42		
			11 - 20	2.87	1.66 - 4.96	< .05	
			> 20	2.78	1.46 - 5.29	< .05	
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 30	1.55	0.8 - 3.01		
			30 - 49	2.33	1.29 - 4.21	< .05	
			> 49	2.56	1.34 - 4.92	< .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 25	1.20	0.63 - 2.27		
			25 - 49	2.89	1.61 - 5.49	< .05	
			> 49	3.09	1.64 - 5.83	< .05	
Nishio, Y et al; 1989	139 Cases 278 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.45	0.972 - 2.155		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.56	0.979 - 2.471		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ever Smoker	3.33	1.942 - 5.701		

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.36	1.734 - 10.963		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.66	0.108 - 4.025		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ever Smoker	3.21	1.405 - 7.318		
Nomura, Abraham et al; 1989	261 Cases 522 Controls	Case-Control; Population-Based					"Bladder cancer" includes urinary bladder (90%), renal pelvis (7%) and ureter (3%) cancers.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	5.10	2.4 - 11.1	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	4.40	2 - 9.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	4.80	2.7 - 8.2	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	2.10	0.8 - 5.6	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.20	0.5 - 2.9	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.60	0.8 - 3	> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 40	3.70			
			> 40	6.20			

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 40	3.40			
			> 40	7.20			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 40	3.90			
			> 40	5.00			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 20	0.90			
			> 20	2.80			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 20	1.40			
			> 20	3.10			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Female). Adjusted for Age, Ethnicity, Gender, Residence Location.
			0	1.00			
			1 - 20	0.60			
			> 20	2.90			
Ohno, Y et al; 1985	293 Cases 589 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-44), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	0.82	0.21 - 3.22		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-64), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.70	0.65 - 4.42		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-89), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	2.37	1.23 - 4.57		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-64), Gender (Female). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	4.50	1.63 - 12.39		

Bladder Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-89), Gender (Female). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	2.72	0.96 - 7.74		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	3.53	1.71 - 7.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.89	1.15 - 3.1		
Wada, S et al; 2001	141 Cases 128 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Ever Smoker	2.07	1.23 - 3.49		
Wilkens, LR et al; 1996	261 Cases 261 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Ethnicity, Fluid Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	4.90	1.6 - 15		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Ethnicity, Fluid Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	2.30	0.7 - 7.3		

Bone Mineral Density

Author	Subjects	Study Type	Data				Comments
Ueda, A et al; 1996	199	Cross Sectional					
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (40-49), Gender (Male), Lumbar Spine. Adjusted for Age.
			Non-Smoker	1.21			
			Current Smoker	1.18			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (50-59), Gender (Male), Lumbar Spine. Adjusted for Age.
			Non-Smoker	1.16			
			Current Smoker	1.15			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (60-69), Gender (Male), Lumbar Spine. Adjusted for Age.
			Non-Smoker	1.04			
			Current Smoker	1.02			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (70-79), Gender (Male), Lumbar Spine. Adjusted for Age.
			Non-Smoker	1.08			
			Current Smoker	1.02			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (40-49), Gender (Male), Femur Neck. Adjusted for Age.
			Non-Smoker	0.96			
			Current Smoker	0.99			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (50-59), Gender (Male), Femur Neck. Adjusted for Age.
			Non-Smoker	0.89			
			Current Smoker	0.93			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (60-69), Gender (Male), Femur Neck. Adjusted for Age.
			Non-Smoker	0.84			
			Current Smoker	0.81			
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (70-79), Gender (Male), Femur Neck. Adjusted for Age.
			Non-Smoker	0.81			
			Current Smoker	0.75			
Yoshimura, N et al; 1996	400	Cross Sectional	No Abstractable Data				Smoking habits were not found to be related to bone mineral density levels.

Brain Tumor

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.23	0.8 - 1.89		
Hirayama, T; 1985	91,450	Cohort					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age.
			0	1.00			
			1 - 19	3.28	1.21 - 8.92		
			> 19	4.92	1.72 - 14.11		
Hirayama, T; 1984	91,540	Cohort					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 14	3.03	1.07 - 8.58		
			15 - 19	6.25	2.01 - 19.43		
			> 19	4.32	1.53 - 12.19		

Breast Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.7 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.10	0.8 - 1.5		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.60	0.1 - 2		
			5 - 14	1.10	0.6 - 1.8		
			> 14	1.00	0.2 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.00	0.6 - 1.6		
Hirayama, T; 1992	265,118	Cohort					Cardiovascular disease endpoint = Ischemic heart disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			Never Smoker	1.00			
			Ex-Smoker	1.07		< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			0	1.00			
			1 - 19	1.55			
			> 19	1.55			
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Ex-Smoker	1.00			
			Current Smoker	1.28	0.93 - 1.76		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	0.94	0.56 - 1.6		
			10 - 19	1.38	0.88 - 2.23		
			> 19	1.03	0.3 - 3.48		

Breast Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.28	0.93 - 1.76		
Hirose, K et al; 1995	1,186 Cases 23,163 Controls	Case-Control; Hospital-Based					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Premenopause. Adjusted for Gender, Menopausal Status.
			Non-Smoker	1.00			
			Current Smoker	1.15	0.91 - 1.46		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Premenopause. Adjusted for Gender, Menopausal Status.
			0	1.00			
			1 - 19	0.81	0.57 - 1.15		
			> 19	1.30	1.02 - 1.65	< .05	
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Postmenopause. Adjusted for Gender, Menopausal Status.
			0	1.00			
			1 - 19	1.55	1.1 - 1.77	< .05	
			> 19	1.28	0.92 - 1.77		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Postmenopause. Adjusted for Gender, Menopausal Status.
			Non-Smoker	1.00			
			Current Smoker	1.39	1.04 - 1.85	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Postmenopause. Adjusted for Gender, Menopausal Status.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.8 - 1.51	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Postmenopause. Adjusted for Gender, Menopausal Status.
			0	1.00			
			1 - 9	0.82	0.38 - 1.77		
			> 9	1.13	0.79 - 1.61		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Premenopause. Adjusted for Gender, Menopausal Status.
			0	1.00			
			1 - 9	1.50	1.04 - 2.17	< .05	
			> 9	1.31	1.02 - 1.69	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Premenopause. Adjusted for Gender, Menopausal Status.
			Non-Smoker	1.00			
			Current Smoker	1.35	1.09 - 1.68	< .01	
Hu, YH et al; 1997	157 Cases 369 Controls	Case-Control					

Breast Cancer

Author	Subjects	Study Type	Data				Comments
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	0.67	0.43 - 1.06		
Kato, I et al; 1989	6,149 Cases 8,920 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Family History of Breast Cancer, Gender, Marital Status, Occupation, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	0.87	0.74 - 1.02		
Kikuchi, S et al; 1990	49 Cases 49 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	0.54		> .05	
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.58	0.34 - 0.99		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.50	0.25 - 0.99		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Age at First Birth, Age at Menarche, Alcohol Consumption, Body Mass Index, Fruit Consumption, Gender, Green Vegetable Consumption, History of Lung Diseases, Number of Live Births, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.58	0.32 - 1.1	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Age at First Birth, Age at Menarche, Alcohol Consumption, Body Mass Index, Fruit Consumption, Gender, Green Vegetable Consumption, History of Lung Diseases, Number of Live Births, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.81	0.44 - 1.5	> .05	
Tajima, K et al; 1990	175 Cases 231 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.12			

Breast Cancer

Author	Subjects	Study Type	Data				Comments
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Never Smoker	1.00			
			Current Smoker	1.60			
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.58			
Yoo, KY et al; 1997		Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at First Birth, Age at Menarche, Age at Menopause, Alcohol Consumption, Breast Feeding, Family History of Cancer, Menstrual History, Occupation, Parity.
			Never Smoker	1.00			
			Ever Smoker	1.25	1.06 - 1.47		

Bulimia

Author	Subjects	Study Type	Data	Comments
Suzuki, K et al; 1995	164 Cases 1,124 Controls	Case-Control	No Abstractable Data	The study found a significant increase in the incidence of smoking among bulimic females, but there was no significant difference between the smoking habits of male groups.

Cancer

Author	Subjects	Study Type	Data				Comments
Benfante, R et al; 1985	8,006	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.78		< .001	
Hara, M et al; 2002	41,484	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	1.69	1.31 - 2.18		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.8 - 1.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.09	0.77 - 1.54		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.61	1.2 - 2.15		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.83	1.14 - 2.95		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	0.89	0.28 - 2.81		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.87	0.28 - 2.72		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.06	1.35 - 3.15		

Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	1.33	0.88 - 2		
			20 - 29	1.41	0.94 - 2.1		
			> 29	1.83	1.34 - 2.51		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	1.03	0.42 - 2.52		
			20 - 29	0.64	0.16 - 2.61		
			> 29	4.51	2.45 - 8.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	1.21	0.89 - 1.64		
			> 29	1.00	0.68 - 1.47		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	1.77	0.6 - 5.17		
			> 29	6.03	1.36 - 26.64		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.52	1.46 - 1.59		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.65	1.56 - 1.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.32	1.24 - 1.41		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.42	1.31 - 1.54		
			10 - 19	1.58	1.49 - 1.67		
			> 19	1.86	1.75 - 1.97		

Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.31	1.2 - 1.44		
			10 - 19	1.33	1.2 - 1.47		
			> 19	1.44	1.18 - 1.78		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.64			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.77			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.49	1.27 - 1.74		
			5 - 9	1.45	1.19 - 1.78		
			> 9	0.95	0.76 - 1.19		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.58	1.02 - 2.43		
			5 - 9	1.21	0.61 - 2.39		
			> 9	1.22	0.62 - 2.41		
Hirayama, T; 1985	91,450	Cohort					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age.
			0	1.00			
			1 - 19	1.11	1.03 - 1.21		
			> 19	1.21	1.1 - 1.32		
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Ex-Smoker	1.39			

Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 14	1.51			
			15 - 24	1.73			
			25 - 49	1.86			
			> 49	2.04			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), < 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	0.97			
			> 4	0.68			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), >= 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	1.03			
			> 4	0.78			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 19	1.53			
			20 - 39	1.81			
			> 39	2.06			
Hiyama, T et al; 1992		Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	2.00		< .01	
			20 - 39	2.20		< .01	
			> 39	2.50		< .01	
Ito, Y et al; 1997		Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Ex-Smoker	0.80	0.37 - 1.71		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.29	0.1 - 0.86		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.31	0.06 - 1.53		

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Never Smoker	0.32	0.13 - 0.77		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption.
			Current Smoker	1.00			
			Ex-Smoker	0.76	0.36 - 1.62		
Kato, I et al; 1985	265 Cases 1,412 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			Never Smoker	1.00			
			Ever Smoker	0.89		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			Never Smoker	1.00			
			Ever Smoker	1.56		> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	1.94		< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	2.17		< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	4.04		> .05	
Kawahara, M et al; 1998	70	Cohort					The outcome was development of a second primary tumor in persons who had survived at least 2 years cancer-free. Upper aerodigestive tract=epithelial regions of the head and neck, lung and oesophagus. Cancer=Smoking-related cancers including cancer of the lung, larynx, oral cavity including pharynx, oesophagus, pancreas, bladder, kidney, stomach and uterine cervix.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	8.00	3.6 - 15.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Ex-Smoker	1.90	0.2 - 6.7		

Cancer

Author	Subjects	Study Type	Data				Comments
Kawaminami, K et al; 2003	10,546	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	1.39	0.99 - 1.93	> .05	
			21 - 40	1.77	1.21 - 2.58	< .05	
			> 40	1.70	0.85 - 3.4	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	0.79	0.32 - 1.94	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.09			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	1.15	0.73 - 1.81	> .05	
			21 - 40	0.75	0.1 - 5.45	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.17	0.8 - 1.7	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.62			
Kinoshita, N et al; 1997	669	Cohort					Outcome = second primary cancer. Upper aerodigestive cancers include oral, laryngeal, pharyngeal, and esophageal cancer cases.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 19	0.64	0.01 - 3.55		
			> 19	3.75	1.87 - 6.7		
Kinoshita, Y et al; 2000	1,631	Cohort					Cancer = Second primary cancer. Aerodigestive cancer= cancer of the esophagus, liver, pancreas, larynx, lung, and bladder.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender, Stage, Type of Adjuvant Therapy.
			Never Smoker	1.00			
			Ex-Smoker	0.95	0.42 - 2.13	> .05	

Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender, Stage, Type of Adjuvant Therapy.
			Never Smoker	1.00			
			Current Smoker	1.82	1.02 - 3.26	< .05	
Morioka, S; 1996	1,308	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1989-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	0.92	0.5 - 1.72	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1990-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	1.02	0.52 - 1.99	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1991-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	0.97	0.46 - 2.06	> .05	
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.92 - 1.4		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.84	0.66 - 1.1		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Miso-soup Consumption, Picked Vegetable Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.91 - 1.4	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Miso-soup Consumption, Picked Vegetable Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.96	0.78 - 1.2	> .05	
Toshima, H et al; 1995	1,110	Cohort	No Abstractable Data				Results were presented as proportional hazard model coefficients, which were converted into Hazard Ratios (HR) and are as follows (these represent the hazard associated with each 1 cigarette increase in the number of cigarettes smoked per day): Coronary Heart Disease: HR=1.02

Cancer

Author	Subjects	Study Type	Data				Comments
							Stroke: HR=1.01 All Cancers: HR=1.01 All Other Causes: HR=0.99 All Causes: HR=1.01 "Cigarette smoking was significant only for Coronary Heart Disease, cancer and for all causes, but not for strokes and 'other causes'."
Tsugane, S et al; 1999	19,231	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Number of Cigarettes per Day.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.59 - 2.04		

Cardiac Complaints

Author	Subjects	Study Type	Data				Comments
Ueda, T et al; 1989	11,574	Cross Sectional					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 20	1.01			
			21 - 40	0.95			
			> 40	1.31			

Cardiovascular Disease

Author	Subjects	Study Type	Data				Comments
Asakawa, H et al; 2000	210	Cross Sectional	No Abstractable Data				Results suggest the progressive mechanism of peripheral vascular disease and CVD might differ from that of CHD, and might also differ across gender groups. Smoking was an independent variable for CVD in females.
Hioki, H et al; 2001	19	Clinical Trial	No Abstractable Data				The study found that platelet-dependent thrombin level is increased in smokers, even when not smoking, and immediately after smoking.
Hirayama, T; 1992	265,118	Cohort					Cardiovascular disease endpoint = Ischemic heart disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			Never Smoker	1.00			
			Ex-Smoker	1.12		< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			0	1.00			
			1 - 19	1.13			
			> 19	1.34		< .01	
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.43		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.26		> .05	
Isaka, Y et al; 1993	40	Cross Sectional	No Abstractable Data				The study concluded that chronic cigarette smoking appears to be associated with a decrease in rCBF in elderly people. The duration of smoking is of the greatest importance in the development of rCBF decrease.
Kambara, H et al; 1992	303	Cross Sectional	No Abstractable Data				Results did not suggest that smoking significantly contributes to the development of coronary artery disease.
Kato, J et al; 2001	485	Cohort					Cardiovascular disease endpoint = coronary artery lesion.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Smoking Habits.
			Non-Smoker	1.00			
			Current Smoker	4.48	1.13 - 17.82		
Kodama, K et al; 1999	58 Cases 5,912 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	2.13	0.77 - 5.92	> .05	

Cardiovascular Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	2.91	1.27 - 6.7	< .05	
Menotti, A et al; 1990	8,287	Cohort	No Abstractable Data				Cigarette consumption had a positive but weak relation with CHD (simple linear regression slope= 1.75, p>0.05) Cox proportional hazard coefficient for cigarette smoking on stroke was (0.0063, t-value: 1.26) - Table 6, page 313.
Minami, J et al; 2002	35	Clinical Trial	No Abstractable Data				The results demonstrated that 1-week smoking cessation produced a significant increase in HDL cholesterol levels and significant decrease in serum lipoprotein and plasma PAI-1 levels in Japanese male smokers.
Nobuyoshi, M et al; 1992	604	Cohort	No Abstractable Data				Study concluded that smoking is the most significant risk factor in discriminating between patients with and without coronary artery spasm.
Sugiishi, M et al; 1993	175 Cases 176 Controls	Case-Control					Cardiovascular disease endpoint = coronary artery disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	2.41	1.53 - 3.82		
Takahashi, K et al; 1999	279	Cohort	No Abstractable Data				The findings indicate that smoking is not correlated with middle cerebral artery lesions in Japanese.
Takaoka, K et al; 2000	315 Cases 224 Controls	Case-Control	No Abstractable Data				Cigarette smoking was found to be a significant and crucial risk factor for coronary spasm.
Yamagishi, K et al; 2003	3,626	Cohort					Coronary heart disease endpoint= modified from WHO criteria Cerebrovascular disease endpoint=Stroke (rapid onset neurological disorder persisting for >24 hours, or until death) Cardiovascular disease endpoint= combined CHD and/or stroke
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.7 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			0	1.00			
			1 - 20	1.50	1 - 2.2		
			> 20	2.10	1.5 - 3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			0	1.00			
			1 - 20	1.40	0.9 - 2		
			> 20	1.90	1.3 - 2.7		

Cardiovascular Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.6 - 1.6		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
Abbott, Robert D et al; 1986	7,872	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hemorrhagic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	6.10	2.4 - 15.7	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Ischemic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	3.00	1.8 - 5.1	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	3.50	2.3 - 5.5	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hemorrhagic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.80	0.4 - 9	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Ischemic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.7 - 3.8	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.50	1 - 2.3	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Ischemic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			0	1.00			
			1 - 9	1.79			
			10 - 19	1.60			
			20 - 29	2.34			
			30 - 39	1.68			
			> 39	1.68			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hemorrhagic Stroke. Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			0	1.00			
			1 - 9	1.70			
			10 - 19	1.63			
			20 - 29	1.95			
			30 - 39	4.08			
			> 39	3.00			

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Diastolic Blood Pressure, Ethnicity, Gender, Hematocrit, History of Heart Disease, Serum Cholesterol.
			0	1.00			
			1 - 9	1.80			
			10 - 19	1.57			
			20 - 29	2.15			
			30 - 39	2.32			
			> 39	1.93			
Asakawa, H et al; 2000	210	Cross Sectional	No Abstractable Data				Results suggest the progressive mechanism of peripheral vascular disease and CVD might differ from that of CHD, and might also differ across gender groups. Smoking was an independent variable for CVD in females.
Benfante, R et al; 1985	8,006	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	2.84		< .001	
Fujishima, Masatoshi et al; 1992	3,651	Cohort					Stroke endpoint = thrombotic stroke.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Male). Adjusted for Age, Ethnicity, Gender.
			0	1.00			
			1 - 19	1.44			
			> 19	0.73			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Female). Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	0.75		> .05	
Goldberg, RJ et al; 1995	2,710	Cohort					Cerebrovascular disease outcome: Thromboembolic Stroke.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Blood Pressure, Body Mass Index, Gender, Heart Rate, Hematocrit, Physical Activity, Serum Cholesterol, Serum Glucose, Serum Triglycerides, Serum Uric Acid.
			0	1.00			
			1 - 19	2.08	1.18 - 3.65		
			20	2.38	1.5 - 3.77		
			21 - 80	2.13	1.31 - 3.46		
Hashimoto, T et al; 1970	758	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 19	1.00			
			> 19	0.40			
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male), Subarachnoid

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Status				Hemorrhage. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.56			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.20	0.37 - 3.89		
			5 - 9	1.06	0.22 - 5.22		
			> 9	1.20	0.31 - 4.65		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			0	1.00			
			1 - 4	6.69	2.85 - 15.71		
			> 9	1.43	0.08 - 25.93		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.08	1.03 - 1.13		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.18	1.11 - 1.26		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.23	1.14 - 1.32		
			10 - 19	1.07	1.01 - 1.12		
			> 19	0.96	0.91 - 1.02		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.17	1.07 - 1.28		
			10 - 19	1.09	0.99 - 1.21		
			> 19	1.34	1.1 - 1.64		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.22	1.06 - 1.42		
			5 - 9	0.82	0.66 - 1.03		
			> 9	0.80	0.65 - 0.99		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.50	0.99 - 2.28		
			5 - 9	1.49	0.84 - 2.64		
			> 9	1.61	0.93 - 2.79		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.82	1.27 - 2.59		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.71	1.32 - 2.22		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.21	0.68 - 2.16		
			10 - 19	1.66	1.13 - 2.43		
			> 19	3.88	2.77 - 5.44		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.77	1.23 - 2.54		
			10 - 19	1.39	0.88 - 2.17		
			> 19	2.07	0.94 - 4.55		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.65			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.44			
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	0.83			
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.66		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Subarachnoid Hemorrhage. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.20		< .05	

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cerebral Hemorrhage. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.02		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Cerebral Hemorrhage. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.33		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cerebral Thrombosis. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.10		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Cerebral Thrombosis. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.96		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Stroke. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.26		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Stroke. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.20		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Heart Failure. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.34		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Heart Failure. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.48		< .05	
Jacobs, David R et al; 1999	12,763	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.86 - 1.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			0	1.00			
			1 - 9	1.10	0.83 - 1.45		
			> 9	1.50	1.24 - 1.82		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
Kagan, A et al; 1985	7,895	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Race.
			0	1.00			
			1 - 9	1.85			
			10 - 19	1.93			
			20 - 39	2.45			
			> 39	1.86			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Thromboembolic Stroke. Adjusted for Age, Gender, Race.
			0	1.00			
			1 - 9	2.06			
			10 - 19	2.22			
			20 - 39	2.68			
			> 39	1.71			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Intracranial Hemorrhage. Adjusted for Age, Gender, Race.
			0	1.00			
			1 - 9	1.02			
			10 - 19	1.47			
			20 - 39	2.53			
			> 39	2.94			
Kiyohara, Y et al; 1990	1,603	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for 2-Hour Glucose, Age, Alcohol Consumption, Blood Pressure, Body Mass Index, ECG Abnormalities, Gender, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	1.48	0.85 - 2.57	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	0.76	0.41 - 1.42	> .05	
Kono, S et al; 1985	5,477	Cohort					Upper aerodigestive cancer: Cancer with ICD 8th codes 140-150 (Malignant neoplasm of buccal cavity, pharynx and oesophagus), 160 (Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses) and 161 (Malignant neoplasm of larynx).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.31	0.81 - 2.13		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.42	0.91 - 2.21		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	2.15	1.25 - 3.7		
			10 - 19	1.28	0.76 - 2.15		
			> 19	0.96	0.53 - 1.76		
Kubota, M et al; 2001	127 Cases 127 Controls	Case-Control					Cerebrovascular cases were consecutive patients with aneurysmal subarachnoid hemorrhage.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Admission Period, Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	4.40	1.94 - 9.98	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Admission Period, Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.97	0.87 - 4.48	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Admission Period, Age, Alcohol Consumption, Family History/Index Disease, Gender, Hypertension.
			Non-Smoker	1.00			
			Current Smoker	2.78	1.83 - 3.99	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Admission Period, Age, Gender.
			0	1.00			
			1 - 20	2.24	1.24 - 4.06	< .01	
			> 20	2.72	1.34 - 5.53	< .01	
Morioka, S; 1996	1,308	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1989-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	7.90	0.8 - 78.3	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1990-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	7.90	0.8 - 78.3	> .05	
Naito, Y et al; 1997	5,326	Cohort	No Abstractable Data				Results are available for smoking treated as a continuous variable. The regression coefficient for increasing cigarettes per day was 0.057 ($p<0.001$), after adjustment for age, total energy consumption, body mass index, diastolic blood pressure, total serum cholesterol, and drinking.
Nakayama, T et al; 2000	2,302	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-64), Gender (Male). Adjusted for Age, Atrial Fibrillation, Hypertension.
			Non-Smoker	1.00			
			Current Smoker	1.77	0.96 - 3.27		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-64), Gender (Both). Adjusted for Age, Atrial Fibrillation, Gender, Hypertension.
			Non-Smoker	1.00			
			Current Smoker	1.84	1 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Atrial Fibrillation, Hypertension.
			Non-Smoker	1.00			
			Current Smoker	1.11	0.58 - 2.14		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Atrial Fibrillation, Gender, Hypertension.
			Non-Smoker	1.00			
			Current Smoker	1.00	0.53 - 1.88		
Nakayama, T et al; 1997	2,302	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cerebral Infarction. Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Blood Pressure, Body Mass Index, ECG Abnormalities, Gender, Glycosuria, Hematocrit, History of CHD, Ophthalmologist, Physical Activity, Proteinuria, Serum Cholesterol.
			< 20	1.00			
			> 20	2.81	1.28 - 6.16		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), All Strokes. Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Blood Pressure, Body Mass Index, ECG Abnormalities, Gender, Glycosuria, Hematocrit, History of CHD, Ophthalmologist, Physical Activity, Proteinuria, Serum Cholesterol.
			< 20	1.00			
			> 20	2.11	1.18 - 3.76		
Okada, Hiroshi et al; 1976	4,737	Cohort					Stroke endpoint = cerebral thrombosis and cerebral hemorrhage.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both), Thrombotic Stroke. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.70			
			10 - 19	1.90			
			> 19	2.40			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both), Hemorrhagic Stroke. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.90			
			10 - 19	1.50			
			> 19	1.20			
Rodriguez, BL et al; 2002	8,305	Cohort	No Abstractable Data				Cigarette smoking was found to be associated with consistent elevation of each stroke type.
Sankai, T et al; 2000	12,372	Cohort					Cerebrovascular cases of subarachnoid hemorrhage.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Blood Pressure, Body Mass Index, Diabetes, Total Cholesterol.
			Non-Smoker	1.00			
			Current Smoker	1.30	0.4 - 4		

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
Sasaki, A et al; 1995	1,939	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 20	1.29			
			> 20	1.13			
Shintani, Shuzo et al; 1998	270	Cross Sectional	No Abstractable Data				The smoking habit was not statistically significant between the normal group and the other groups (see Table 3).
Stemmermann, GN et al; 1984	8,006	Cohort	No Abstractable Data				The study found that men with hemorrhagic lesions had a higher cigarette use.
Tanizaki, Y et al; 2000	1,621	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Atrial Fibrillation, Blood Pressure, ECG Abnormalities, Glucose Tolerance, Left Ventricular Hypertrophy.
			Never Smoker	1.00			
			Current Smoker	2.20	1.3 - 3.9	< .05	
Toshima, H et al; 1995	1,110	Cohort	No Abstractable Data				Results were presented as proportional hazard model coefficients, which were converted into Hazard Ratios (HR) and are as follows (these represent the hazard associated with each 1 cigarette increase in the number of cigarettes smoked per day): Coronary Heart Disease: HR=1.02 Stroke: HR=1.01 All Cancers: HR=1.01 All Other Causes: HR=0.99 All Causes: HR=1.01 "Cigarette smoking was significant only for Coronary Heart Disease, cancer and for all causes, but not for strokes and 'other causes'."
Uchiyama, S et al; 1992	923	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Cigarette Smoking, ECG Abnormalities, Emaciation, Long Portal to Portal Hours, Managerial Position, Obesity, Sleeping Hours.
			Never Smoker	1.00			
			Current Smoker	2.40	1 - 5.5		
Ueshima, H; 2001	10,000	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Blood Pressure.
			Never Smoker	1.00			
			Ex-Smoker	1.50			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Blood Pressure.
			0	1.00			
			1 - 39	1.50			
			> 39	2.20			
Ueshima, H; 1995	9,768	Cohort					

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 20	1.12	0.53 - 2.35	> .05	
			> 20	1.16	0.48 - 2.8	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 20	1.02	0.51 - 2.02	> .05	
			> 20	0.84	0.34 - 2.09	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 20	1.43	0.83 - 2.48	> .05	
			21 - 40	1.42	0.77 - 2.62	> .05	
			> 40	0.54	0.11 - 2.55	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 20	1.14	0.66 - 1.97	> .05	
			> 20	1.04	0.46 - 2.35	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.43	0.47 - 4.32	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.06	0.34 - 3.25	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.89	1.13 - 3.15	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.64	0.93 - 2.88	> .05	
Wang, H et al; 2001	67 Cases 67 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Blood Pressure, Gender.
			0	1.00			
			1 - 10	0.65	0.1 - 4.29		
			> 10	0.77	0.13 - 4.42		
Yamagishi, K et al; 2003	3,626	Cohort					Coronary heart disease endpoint= modified from WHO criteria Cerebrovascular disease endpoint=Stroke (rapid onset

Cerebrovascular Disease

Author	Subjects	Study Type	Data				Comments
							neurological disorder persisting for >24 hours, or until death) Cardiovascular disease endpoint= combined CHD and/or stroke
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.5 - 1.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			0	1.00			
			1 - 20	1.20	0.8 - 1.8		
			> 20	1.90	1.3 - 2.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			0	1.00			
			1 - 20	1.10	0.7 - 1.7		
			> 20	1.60	1.1 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.5 - 1.3		
Yamashita, Kazuya et al; 1996	365	Cross Sectional	No Abstractable Data				"Silent brain infarction was identified in 32 (26.9%) of 119 smokers and in 54 (22.8%) of 246 nonsmokers…There was no significant difference in the distribution of periventricular hyperintensity grades (Fig. 1) or in the regional cerebral blood flow (69.0 +- 9.9 ml/100 g/min vs.. 68.6 +- 11.6 ml/100 g/min) between smokers and nonsmokers."

Cervical Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.57	1.3 - 1.89		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.73	1.34 - 2.23		
			10 - 19	1.33	0.96 - 1.83		
			> 19	2.36	1.42 - 3.92		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	2.32	0.75 - 7.16		
Hirayama, T; 1981	91,540	Cohort					The asthma outcome also includes women with emphysema.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			0	1.00			
			1 - 19	1.15			
			> 19	1.14			
Hirose, K et al; 1998	416 Cases 20,985 Controls	Case-Control					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-69), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	1.42	1.13 - 1.79	< .01	
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-69), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 19	1.09	0.79 - 1.51		
			> 19	1.66	1.29 - 2.15	< .001	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-44), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	1.39	0.95 - 2.04		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-44), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 19	0.88	0.49 - 1.57		
			> 19	1.69	1.13 - 2.53		

Cervical Cancer

Author	Subjects	Study Type	Data				Comments
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	2.27	1.39 - 3.7	< .01	
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 19	1.55	0.77 - 3.11		
			> 19	2.62	1.56 - 4.38	< .01	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (55-69), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	1.04	0.71 - 1.51		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (55-69), Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 19	1.01	0.62 - 1.62		
			> 19	1.09	0.68 - 1.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-69), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	2.31	1.84 - 2.92	< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-69), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 9	1.52	0.91 - 2.53		
			> 9	2.59	2.02 - 3.31	< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-44), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 9	0.87	0.38 - 1.99		
			> 9	2.66	1.88 - 3.77	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-44), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	2.15	1.54 - 2.99	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	2.26	1.38 - 3.7	< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 9	2.28	0.82 - 6.33		
			> 9	2.28	1.34 - 3.9	< .01	

Cervical Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (55-69), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			0	1.00			
			1 - 9	2.28	0.97 - 5.39		
			> 9	2.44	1.53 - 3.91	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (55-69), Gender (Female). Adjusted for Age, Age at First Pregnancy, Marital Status, Number of Pregnancies.
			Non-Smoker	1.00			
			Current Smoker	2.38	1.55 - 3.64	< .01	
Hirose, K et al; 1996	556 Cases 26,751 Controls	Case-Control; Hospital-Based					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.30	1.07 - 1.59	< .01	
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 19	1.00	0.76 - 1.33		
			> 19	1.55	1.24 - 1.94	< .01	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			0	1.00			
			1 - 9	1.32	0.83 - 2.11		
			> 9	2.50	2.01 - 3.11	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	2.19	1.78 - 2.69		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.26 - 4.5		
Sasagawa, T et al; 1997	123 Cases 778 Controls	Case-Control					Cervical Cancer Outcome= Squamous Intraepithelial Lesion (SIL) of the cervix.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, HPV Status.
			Non-Smoker	1.00			
			Current Smoker	1.60	0.63 - 4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, HPV Status.
			Non-Smoker	1.00			
			Current Smoker	2.50	1.1 - 5.7		
Tajima, K et al; 1990	56 Cases	Case-Control;					

Cervical Cancer

Author	Subjects	Study Type	Data				Comments
	231 Controls	Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	2.58		< .01	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Never Smoker	1.00			
			Current Smoker	2.29		< .01	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age at Menarche, Body Mass, Family Size, Height, Parity, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.89			

Cessation

Author	Subjects	Study Type	Data	Comments
Arai, Y et al; 1997	20,538	Cross Sectional	No Abstractable Data	Results are available for the mean scores of the personality dimensions from the EPQ-R (E= extroversion/introversion, N= Neuroticism, P= Psychoticism and L= Lie) by smoking status (current, ex and non-smokers) for both gender. P and E were higher for current and ex- smokers in both gender. Table 2. Smoking start before the legal age of 20 divided the sample in "early starters" and "late starters". Early starters had a significantly higher P score than the late starters in both genders and later starters had a significantly lower L score than early starters among males. Table 4. Table 5 and Figures 1-3 show the analysis of personality characteristics in current smokers by daily consumption of cigarettes. Heavy smokers are higher in psychoticism and neuroticism but lower in lie.
Kadowaki, T et al; 2000		Other	No Abstractable Data	Overall cessation rate was 8.4% Prevalence of smoking decreased from 62.9% to 56.7%. Study concluded that a willingness to quit smoking is effective in impacting the overall smoking rate.
Kawakami, M; 2000		Longitudinal	No Abstractable Data	Non-smokers were found to think more actively about smoking intervention than current smokers. Study concluded that Japanese medical students, as future doctors, do not demonstrate a satisfactory level of awareness on the harmful effects of smoking nor did they see the need to perform smoking intervention in future.
Kitajima, T et al; 2002	1,572	Cohort	No Abstractable Data	Main results in Table 1 with 8% new smokers and 6% quitters " nicotine dependency measured by the Fagerstrom scale increased from 3.9 in the first survey to 4.3% in the second." " as smoking initiator factors, no concern about harmful effects of passive smoking and the fact that the mother, friends, and superiors at work were smokers, were proved to be statistically significant" "as quitting factors the idea that health professionals should not smoke and living with the family were proved to be statistically significant" Risk factors for smoking and smoking cessation factors proved not to be significant between the followed up and the lost to follow up. (table 5)
Muto, T et al; 1998		Other	No Abstractable Data	Study found abstinence rates for experimental group and control group to be 22.9% and 5.7% respectively. Using a net abstinence rate of 13% as the cutoff point, the one-

Cessation

Author	Subjects	Study Type	Data	Comments
				year rate of 17.2% obtained in the study calls for larger experiments to give more statistically significant results.
Nishi, N et al; 1998		Meta-analysis	No Abstractable Data	Results demonstrate a positive effect of exercise on smoking cessation, however, these results are inconclusive due to the small number of studies and the small sample size in each study.

Circulatory System

Author	Subjects	Study Type	Data				Comments
Hara, M et al; 2002	41,484	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.11	0.73 - 1.69		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	1.67	1.2 - 2.34		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.41	0.97 - 2.03		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	0.99	0.67 - 1.43		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.48	0.91 - 6.78		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.99	1.75 - 5.11		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	2.72	1.45 - 5.07		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	2.51	0.9 - 6.99		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	1.02	0.6 - 1.73		
			20 - 29	1.44	0.9 - 2.31		
			> 29	1.41	0.95 - 2.12		

Circulatory System

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			0	1.00			
			< 19	3.37	1.52 - 7.47		
			20 - 29	2.12	0.65 - 6.95		
			> 29	1.51	0.35 - 6.57		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	0.93	0.61 - 1.41		
			> 29	1.20	0.76 - 1.88		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet, Education, Gender, History of Hypertension, Medication, Physical Activity.
			< 19	1.00			
			20 - 29	0.15	0.01 - 1.56		
			> 29	1.25	0.11 - 13.76		

Colon Adenoma

Author	Subjects	Study Type	Data				Comments
Honjo, S et al; 1995	504 Cases 3,101 Controls	Case-Control; Hospital-Based					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Sigmoid), Smoking in Past 10 Years. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 7.5	2.10	1.5 - 2.8		
			7.55 - 12.5	2.20	1.7 - 2.9		
			> 12.5	2.50	1.8 - 3.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Sigmoid), Smoking until 10 Years ago. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 17	1.90	1.4 - 2.6		
			18 - 23	2.20	1.6 - 3		
			> 23	2.10	1.5 - 2.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Sigmoid). Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 22	1.70	1.2 - 2.3		
			23 - 33	2.30	1.7 - 3.2		
			> 33	2.30	1.6 - 3.2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Sigmoid), Smoking in Past 10 Years. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Smoking until 10 Years Ago, Study Center.
			0	1.00			
			1 - 7	1.90	1.3 - 2.8		
			8 - 12	2.10	1.4 - 3		
			> 12	3.00	1.9 - 4.7		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Sigmoid), Smoking until 10 Years ago. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Smoking in the past 10 Years, Study Center.
			0	1.00			
			1 - 17	1.20	0.8 - 1.8		
			18 - 23	1.20	0.8 - 1.8		
			> 23	0.90	0.5 - 1.4		
Honjo, Satoshi et al; 1992	116 Cases 930 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Sigmoid). Adjusted for Alcohol Consumption, Body Mass Index, SDF Rank.
			Never Smoker	1.00			
			Ex-Smoker	2.20	1.1 - 4.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Sigmoid). Adjusted for Alcohol Consumption, Body Mass Index, SDF Rank.
			0	1.00			
			1 - 24	3.30	1.8 - 6.3		
			> 24	2.80	1.3 - 5.9		

Colon Adenoma

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Sigmoid). Adjusted for Alcohol Consumption, Body Mass Index, SDF Rank.
			0	1.00			
			1 - 19	2.30	1.1 - 4.6		
			20 - 39	2.90	1.5 - 5.4		
			> 39	3.20	1.6 - 6.5		
Inoue, H et al; 2001	205 Cases 220 Controls	Case-Control; Hospital-Based					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), GSTM1Positive;GSTT1 Positive. Adjusted for Alcohol Consumption, Body Mass Index, Hospital, Rank.
			0	1.00			
			< 20	0.90	0.3 - 3.2		
			> 20	5.10	1.8 - 14.8		
Inoue, H et al; 2000	205 Cases 220 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.6 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Hospital, Rank.
			0	1.00			
			1 - 24	3.50	2 - 6.1		
			> 24	3.80	2 - 7.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Hospital, Rank.
			0	1.00			
			1 - 19	1.40	0.8 - 2.6		
			20 - 39	2.20	1.3 - 3.6		
			> 39	4.10	2.1 - 8.2		
Stemmermann, GN et al; 1988	8,006	Cohort	No Abstractable Data				"No significant differences were observed between subjects with and without adenomas in intake of dietary fat, proteins, or carbohydrates, and in body mass index, level of physical activity, serum cholesterol, or cigarette smoking history." (Table 4) Age-adjusted mean number of cigarettes per day among current smokers at baseline for subjects: with adenomatous polyps=13.2 without adenomatous polyps=12.3, p=0.704. (Table 4) Age-adjusted mean pack-years among past or current smokers is 32.1 and 30.7, respectively (p=0.736). (Table 4)
Todoroki, I et al; 1995	228 Cases 1,484 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Physical Activity, Rank.
			0	1.00			
			1 - 19	2.10	1.2 - 3.4		

Colon Adenoma

Author	Subjects	Study Type	Data				Comments
			20 - 40	2.80	1.8 - 4.3		
			> 40	3.50	2.1 - 5.8		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Adenomas). Adjusted for Alcohol Consumption, Body Mass Index, Physical Activity, Rank.
			0	1.00			
			1 - 19	2.00	1 - 4.1		
			20 - 40	3.20	1.7 - 6		
			> 40	3.00	1.4 - 6.1		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Adenomas). Adjusted for Alcohol Consumption, Body Mass Index, Physical Activity, Rank.
			0	1.00			
			1 - 19	2.30	1.1 - 5		
			20 - 40	2.70	1.4 - 5.4		
			> 40	4.60	2.2 - 9.7		

Colon Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ever Smoker	0.90	0.6 - 1.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.20	0.9 - 1.6		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.90	0.2 - 2.6		
			5 - 14	1.00	0.7 - 1.6		
			15 - 24	1.10	0.7 - 1.6		
			25 - 34	1.20	0.5 - 2.4		
			> 34	1.80	0.6 - 4.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.10	0.4 - 2.4		
			5 - 14	0.90	0.5 - 1.4		
			> 14	0.50	0.1 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.10	0.8 - 1.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	0.90	0.6 - 1.3		
Chyou, Po-Huang et al; 1996	7,945	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.42	1.09 - 1.85		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.27	0.95 - 1.7		

Colon Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 15	1.33	0.94 - 1.88		
			16 - 30	1.10	0.79 - 1.54		
			> 30	1.48	1.13 - 1.94		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.06	0.85 - 1.31		
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.00			
			20 - 39	1.80			
			> 39	4.10			
Hoshiyama, Y et al; 1993	79 Cases 653 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.30	0.1 - 0.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 29	0.30	0.1 - 0.7		
			> 29	0.30	0.1 - 1		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 40	0.30	0.1 - 0.7		
			> 40	0.20	0 - 0.7		
Inoue, M et al; 1995	432 Cases 31,782 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Proximal Colon Adenoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	0.70	0.4 - 1.4		

Colon Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Distal Colon Adenoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.00	0.6 - 1.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Proximal Colon Adenoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	0.90	0.4 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Distal Colon Adenoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.10	0.6 - 2.3		
Kato, I et al; 1990	3,327 Cases 16,600 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Proximal Colon. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	0.57	0.46 - 0.69	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Distal Colon. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	0.66	0.56 - 0.77	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by All Colon. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	0.62	0.56 - 0.7	< .01	
Le Marchand, Loic et al; 1997	825 Cases 825 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Right Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.5 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Right Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	0.70	0.3 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Left Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.9 - 2.4		

Colon Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Left Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	0.90	0.4 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Right Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	2.40	1 - 5.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Right Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.10	0.4 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Left Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Ex-Smoker	1.10	0.6 - 2		
			Never Smoker	1.00			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Left Colon. Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Current Smoker	0.70	0.3 - 1.5		
			Never Smoker	1.00			
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.30	0.65 - 2.4		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.75	0.37 - 1.5		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.54 - 2.4	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.58 - 2.2	> .05	
Tajima, K et al; 1985	27 Cases 111 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Education, Gender, Time of Interview.
			Never Smoker	1.00			

Colon Cancer

Author	Subjects	Study Type	Data				Comments
			Current Smoker	0.59		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			Never Smoker	1.00			
			Current Smoker	0.61		> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			0	1.00			
			< 30	0.33		> .05	
			> 29	0.82		> .05	

Colorectal Adenoma

Author	Subjects	Study Type	Data				Comments
Nagata, Chisato et al; 1999	259 Cases 18,361 Controls	Nested Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.44	0.93 - 2.33		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.21	0.75 - 2.01		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 29	1.10	0.69 - 1.84		
			> 29	1.60	1.02 - 2.62		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.36	0.88 - 2.2		
			> 19	1.29	0.79 - 2.17		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.14	0.71 - 1.9		
			> 19	1.52	0.97 - 2.46		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.42	0.84 - 2.47		
			> 9	1.04	0.57 - 1.88		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.18	1.05 - 5.31		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.14	1 - 5.31		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 29	1.75	0.8 - 4.4		
			> 29	2.62	1.23 - 6.4		

Colorectal Adenoma

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 19	2.19	1.06 - 5.3		
			> 19	2.11	0.94 - 5.34		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.76	0.8 - 4.42		
			> 19	2.53	1.21 - 6.15		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Proximal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.81	1.24 - 7.19		
			> 9	1.59	0.62 - 4.36		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.50	0.91 - 2.64		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.95	0.53 - 1.75		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 29	0.74	0.41 - 1.38		
			> 29	1.81	1.08 - 3.22		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.26	0.76 - 2.22		
			> 19	1.26	0.71 - 2.33		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.96	0.54 - 1.76		
			> 19	1.52	0.91 - 2.68		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male), Distal Colon. Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.18	0.61 - 2.28		
			> 9	0.81	0.38 - 1.67		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ever Smoker	2.17	1.22 - 3.69	< .001	

Colorectal Adenoma

Author	Subjects	Study Type	Data				Comments
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 29	1.49	0.68 - 2.93		
			> 29	4.54	2.04 - 9.08		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	2.39	1.17 - 4.47		
			> 4	2.13	0.87 - 4.45		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	2.05	1 - 3.84		
			> 14	2.87	1.18 - 5.99		
Takeshita, T et al; 2000	69 Cases 131 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Physical Activity, Rank.
			< 20	1.00			
			> 19	3.00	1.6 - 5.7		

Colorectal Cancer

Author	Subjects	Study Type	Data				Comments
Kato, I et al; 1985	265 Cases 1,412 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	0.85		> .05	
Kobayashi, Y et al; 1990	5 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls ($p<0.05$). Heavy smokers were also more prevalent among MPC cases than among controls ($p<0.1$)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases ($p<0.1$)"
Kono, Suminori et al; 1987		Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	0.89	0.42 - 1.87		
			> 19	0.93	0.39 - 2.21		
Yamada, K et al; 1997	66 Cases 390 Controls	Case-Control; Hospital-Based					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 20	0.80	0.3 - 2.2		
			21 - 40	1.20	0.5 - 3		
			> 40	2.60	0.9 - 7.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			Never Smoker	1.00			
			Ex-Smoker	1.80	0.7 - 4.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	1.20	0.4 - 3.8		
			16 - 30	0.80	0.3 - 2.1		
			> 30	2.40	0.7 - 8.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Carcinoma in situ). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	2.20	1 - 4.6		
			16 - 30	2.60	1.3 - 5.1		
			> 30	3.10	1.3 - 7.5		

Colorectal Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Carcinoma in situ). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.5 - 1.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Carcinoma in situ). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 20	1.40	0.7 - 2.7		
			21 - 40	2.80	1.4 - 5.4		
			> 40	2.50	1.3 - 5.1		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Carcinoma in situ), Smoking in Past 20 years. Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	1.30	0.7 - 2.4		
			16 - 30	2.20	1.2 - 4.1		
			> 30	3.70	1.6 - 8.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Carcinoma in situ), Smoking until 20 years ago. Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	1.20	0.7 - 2		
			16 - 30	2.10	1 - 4		
			> 30	0.70	0.3 - 2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Smoking until 20 years ago. Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	1.00	0.4 - 2.4		
			16 - 30	3.40	1.2 - 9.2		
			> 30	5.00	1.3 - 18.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Smoking in Past 20 years. Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Study Center.
			0	1.00			
			1 - 15	1.10	0.5 - 2.7		
			16 - 30	1.20	0.5 - 2.9		
			> 30	2.90	0.9 - 9.4		

Comorbidity

Author	Subjects	Study Type	Data				Comments
Wang, L et al; 2002	241 Cases 165 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Family History of Diabetes, Fiber Intake, Gender, Psychological Stress.
			Non-Smoker	1.00			
			Current Smoker	3.30	1.37 - 7.99		

COPD

Author	Subjects	Study Type	Data				Comments
Comstock, GW et al; 1973	3,088	Cross Sectional					Prevalence ratios could not be calculated COPD and asthma for the Japanese group because zero nonsmokers had these diseases.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male), ATT Round 1. Adjusted for Age, Geographic Location, Smoking Habits.
			0	1.00			
			1 - 14	1.44			
			15 - 24	2.88			
			> 24	4.88			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (White), Gender (Male), ATT Round 2. Adjusted for Age, Geographic Location, Smoking Habits.
			0	1.00			
			1 - 14	1.85			
			15 - 24	3.28			
			> 24	5.28			
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.09			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.67			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.10			
Jacobs, David R et al; 1999	12,763	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.5 - 2.07		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			0	1.00			
			1 - 9	2.90	1.75 - 4.85		
			> 9	3.50	2.3 - 5.31		
Toyama, T et al; 1978	22,590	Cross Sectional	No Abstractable Data				Prevalence of smoking in rural area was 76% and 10% in males and females respectively; whereas it was 74% in males and 19% on females in the urban area

COPD

Author	Subjects	Study Type	Data				Comments
							Prevalence of pulmonary symptoms higher in males aged 40-59 in are with population >1000 Km square vs. <1000 km square irrespective of smoking status
Tsunetoshi, Y et al; 1971	36,374	Cross Sectional	No Abstractable Data				Prevalence of chronic bronchitis is 3-4 times higher in each group in male smokers of 21 cigarettes or more compared to non-smokers in each group. Prevalence of chronic bronchitis is 5-6 times higher in each group in female smokers of 11 cigarettes or more compared to non-smokers in each group. Approximately 30% of the male non-smokers used to have a smoking habit in the past
Wang, Q et al; 2001	7,847	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Ever Smoker	5.20		< .01	
Yamaguchi, S et al; 1989	3,432	Cross Sectional					COPD endpoint=Chronic bronchitis symptoms prevalence.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.10		< .01	
			> 9	2.22		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.47		< .05	
Yokoyama, Y et al; 1985	1,178	Cross Sectional					COPD endpoints=Persistent cough and phlegm. Asthma endpoints=Asthma like attacks.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Within 20 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.76		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), 20-150 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.10		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Within 20 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Current Smoker	4.40		< .001	

COPD

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), 20-150 Meters of Roadside. Adjusted for Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.64		< .001	

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
Benfante, R et al; 1990	1,480	Cohort	No Abstractable Data				Study found that daily cigarette smoking was an independent predictor of coronary heart disease in elderly men over 65 years.
Benfante, R et al; 1985	8,006	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	2.35		< .001	
Benfante, Richard et al; 1991	1,394	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-74), Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Diabetes, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Current Smoker	1.62	1.01 - 2.61	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (51-59), Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Diabetes, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Current Smoker	1.80	1.25 - 2.61	< .05	
Friedman, Gary D et al; 1979	4,289	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, CHD Risk, Education, Emotional Disturbance, Gender, Marital Status, Occupational Hazard, Serious Disease.
			Never Smoker	1.00			
			Current Smoker	3.60		< .001	
Glantz, SA et al; 1991		Meta-analysis					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	
			Not Exposed	1.00			
			Exposed	1.30	1.2 - 1.4		
Goldberg, RJ et al; 1995	2,710	Cohort					Cerebrovascular disease outcome: Thromboembolic Stroke.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Blood Pressure, Body Mass Index, Gender, Heart Rate, Hematocrit, Physical Activity, Serum Cholesterol, Serum Glucose, Serum Triglycerides, Serum Uric Acid.
			0	1.00			
			1 - 19	1.66	1.08 - 2.55		
			20	2.14	1.55 - 2.96		
			21 - 80	2.33	1.63 - 3.27		
Hirayama, T; 1990	Not Specified	Cohort					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender, Time Period.
			0	1.00			
			1 - 19	1.08	0.9 - 1.3		
			> 19	1.30	1.06 - 1.6		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.73	1.55 - 1.93		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.90	1.7 - 2.13		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.68	1.44 - 1.97		
			10 - 19	1.63	1.44 - 1.83		
			> 19	1.95	1.73 - 2.19		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.69	1.43 - 2.01		
			10 - 19	2.25	1.91 - 2.65		
			> 19	3.77	2.91 - 4.88		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.94			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.71			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.69			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.50	1.09 - 2.07		
			5 - 9	1.73	1.19 - 2.54		
			> 9	0.94	0.59 - 1.5		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.41	0.07 - 2.4		
			5 - 9	1.19	0.27 - 5.21		
			> 9	0.91	0.17 - 4.9		
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
							Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	1.08			
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.71		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.78		< .05	
Hirayama, T; 1981	91,540	Cohort					The asthma outcome also includes women with emphysema.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			0	1.00			
			1 - 19	0.97			
			> 19	1.03			
Hirayama, T; 1981	265,118	Cohort					
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), < 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	0.71			
			> 4	0.55			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), >= 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	1.18			
			> 4	1.03			
Irie, F et al; 2001	96,664	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Blood Glucose, Blood Pressure, Body Mass Index, Gender, HDL Cholesterol, Proteinuria, Serum Creatinine, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.9 - 2.8	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Blood Glucose, Blood Pressure, Body Mass Index, Gender, HDL Cholesterol, Proteinuria, Serum Creatinine, Total Cholesterol.
			0	1.00			
			1 - 20	2.50	1.4 - 4.5	< .05	
			> 20	2.40	1.4 - 4.1	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Blood Glucose, Blood Pressure, Body Mass Index, Gender, HDL Cholesterol, Proteinuria, Serum Creatinine, Total Cholesterol.
			0	1.00			
			1 - 20	2.40	1 - 5.5		
			> 20	7.10	3 - 16.9	< .05	

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
Jacobs, David R et al; 1999	12,763	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.88 - 1.36		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			0	1.00			
			1 - 9	1.20	0.99 - 1.44		
			> 9	1.80	1.61 - 2.11		
Kashihara, H et al; 2000	Not Specified	Case-Control					Coronary Heart Disease: cases of myocardial infarction or Angina Pectoris.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Fasting Plasma Glucose Level, History of CHD, Hypertension, Serum Cholesterol, Serum Triglycerides, Systolic Blood Pressure.
			0	1.00			
			< 20	1.30	1.1 - 1.54	< .01	
			20 - 40	2.20	1.34 - 3.63	< .01	
			40 - 60	3.73	1.62 - 8.57	< .01	
			> 60	6.31	1.97 - 20.24	< .01	
Kimura, N; 1977	Not Specified	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 19	3.17		< .05	
			> 19	3.50		< .05	
Kiyohara, Y et al; 1990	1,603	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	2.38	1.3 - 3.22	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Serum Cholesterol.
			Never Smoker	1.00			
			Current Smoker	2.22	1.04 - 4.75	< .05	
Kodama, K et al; 1990	19,961	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	2.40			
			10 - 19	1.90			
			20 - 29	2.70			
			> 29	2.60			

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			0	1.00			
			1 - 9	1.60			
			10 - 19	1.90			
			20 - 29	1.50			
			> 29	0.00			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, ECG Abnormalities, Gender, Glycosuria, Serum Cholesterol, Systolic Blood Pressure.
			Non-Smoker	1.00			
			Current Smoker	1.39			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, ECG Abnormalities, Glycosuria, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Current Smoker	1.50			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, ECG Abnormalities, Glycosuria, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			
			Current Smoker	1.18			
Konishi, M et al; 1987	10,785	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 19	1.32			
			> 19	4.62			
Kono, S et al; 1985	5,477	Cohort					Upper aerodigestive cancer: Cancer with ICD 8th codes 140-150 (Malignant neoplasm of buccal cavity, pharynx and oesophagus), 160 (Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses) and 161 (Malignant neoplasm of larynx).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.79	0.98 - 3.28		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	2.14	1.23 - 3.73		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	1.51	0.68 - 3.36		
			10 - 19	2.12	1.13 - 3.97		
			> 19	3.01	1.61 - 5.65		
Kurosaka, K et al; 2000	104 Cases	Case-Control					

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
	111 Controls						
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Diabetes, Hypertension, Marital Status, Serum Apolipoprotein AI, Serum Apolipoprotein B, Serum Apolipoprotein E, Serum Cholesterol, Serum Lipoprotein, Serum Triglycerides, Uric Acid.
			Non-Smoker	1.00			
			Current Smoker	3.07	1.448 - 6.503	< .01	
Marmot, MG et al; 1975	11,900	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	1.85			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Japan. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	2.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), California. Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	1.35			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), California. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.54			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hawaii. Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	2.06			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hawaii. Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.17			
Miwa, K et al; 2000	176 Cases 135 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Diabetes, Serum HDL Cholesterol, Serum Lipoprotein.
			Non-Smoker	1.00			
			Current Smoker	0.69	0.48 - 0.99	< .05	
Miyake, Y; 2000	384 Cases 656 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-64), Gender (Both). Adjusted for Age, Alcohol Consumption, Angina Pectoris, Body Mass Index, Diabetes, Gender, Hypercholesterolemia, Hypertension, Physical Activity, Residence Location.
			Never Smoker	1.00			

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
			Ex-Smoker	1.10	0.5 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-79), Gender (Both). Adjusted for Age, Alcohol Consumption, Angina Pectoris, Body Mass Index, Diabetes, Gender, Hypercholesterolemia, Hypertension, Physical Activity, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.6 - 2.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-79), Gender (Both). Adjusted for Age, Alcohol Consumption, Angina Pectoris, Body Mass Index, Diabetes, Gender, Hypercholesterolemia, Hypertension, Physical Activity, Residence Location.
			0	1.00			
			1 - 19	1.00	0.5 - 2		
			> 19	2.80	1.4 - 6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Both). Adjusted for Age, Alcohol Consumption, Angina Pectoris, Body Mass Index, Diabetes, Gender, Hypercholesterolemia, Hypertension, Physical Activity, Residence Location.
			0	1.00			
			1 - 19	0.70	0.3 - 2		
			> 19	4.30	2.2 - 8.2		
Morioka, S; 1996	1,308	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1989-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	2.43	0.96 - 6.17	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1990-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	2.98	1.09 - 8.2	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1991-1994. Adjusted for Age, Past History, Walking.
			Non-Smoker	1.00			
			Current Smoker	5.43	1.37 - 21.6	< .01	
Ogawa, K et al; 1996	133 Cases 133 Controls	Case-Control					Coronary Heart Disease outcome= ischemic heart disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	10.28		< .05	
Owada, M et al; 1999	29 Cases 958 Controls	Case-Control					The coronary heart disease outcome represents persons whose sudden death as due to coronary artery disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Autonomic Disturbance, Gender, Long-term Stress, Occupation, Short-term Stress.
			Non-Smoker	1.00			
			Current Smoker	4.64	1.44 - 14.96	< .05	
Robertson, Thomas L et al; 1977	1,963	Cohort					Endpoint = myocardial infarction.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Male), Japan. Adjusted for Age, Ethnicity, Gender.
			0	1.00			
			1 - 10	0.95			

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
			11 - 20	0.68			
			> 20	1.59			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Male), Hawaii. Adjusted for Age, Ethnicity, Gender.
			0	1.00			
			11 - 20	2.73			
			> 20	4.80			
Sasaki, A et al; 1995	1,939	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 20	0.89			
			> 20	0.86			
Sato, I et al; 1992		Cohort					Coronary heart disease outcome=Myocardial infarction.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Ex-Smoker	1.00			
			Current Smoker	3.40	1.1 - 9.8	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Hypertension, Total Cholesterol.
			Ex-Smoker	1.00			
			Current Smoker	3.10	1 - 9.8	< .05	
Shimozato, M et al; 1996	2,329	Cohort					Coronary Heart Disease outcome: Myocardial infarction.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	8.00			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Blood Pressure, Body Mass Index, ECG Abnormalities, Gender, Glycosuria, Ophthalmologist, Proteinuria, Serum Cholesterol.
			< 20	1.00			
			> 20	4.07	1.26 - 13.11	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			< 20	1.50			
			> 20	6.20			
Stehle, G et al; 1992	15,652	Cross Sectional	No Abstractable Data				Smoking is found to be the most important risk factor in Japan. Smoking and Hypertension are the most important risk factors in China In Germany, the most important risk factors are obesity and hyperlipidemia.
Szatrowski, TP et al; 1984	16,711	Cohort	No Abstractable Data				"When Coronary heart disease (CHD) incidence in individuals on whom smoking information was obtained in cycle 4 was examined in cycle 5 forward over a risk period of 8 and 1/2

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
							years, smoking showed a significant (estimated RR=1.62) relationship with CHD incidence in univariate analysis but not in the presence of other factors. The size of the relative risk estimates for smokers does not change greatly when other risk factors are accounted for, but loses statistical significance, this may reflect only an insufficient number of cases or limited information on smoking habits available in the study. Otherwise the effects of smoking in this population may well be mediated by, or at least explained by changes in, other risk factors."
Takeya, Y et al; 1984	9,261	Cohort	No Abstractable Data				Cigarette smoking was found to be only a significant risk factor for thrombo-embolic stroke in Japan. The study concluded that it seems unlikely that smoking accounts for the difference in stroke frequency between migrant and indigenous Japanese.
Tomono, S et al; 1990	51 Cases 871 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.13			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			> 59	2.84			
Toshima, H et al; 1995	1,110	Cohort	No Abstractable Data				Results were presented as proportional hazard model coefficients, which were converted into Hazard Ratios (HR) and are as follows (these represent the hazard associated with each 1 cigarette increase in the number of cigarettes smoked per day): Coronary Heart Disease: HR=1.02 Stroke: HR=1.01 All Cancers: HR=1.01 All Other Causes: HR=0.99 All Causes: HR=1.01 "Cigarette smoking was significant only for Coronary Heart Disease, cancer and for all causes, but not for strokes and 'other causes'."
Yamagishi, K et al; 2003	3,626	Cohort					Coronary heart disease endpoint= modified from WHO criteria Cerebrovascular disease endpoint=Stroke (rapid onset neurological disorder persisting for >24 hours, or until death) Cardiovascular disease endpoint= combined CHD and/or stroke
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			Never Smoker	1.00			
			Ex-Smoker	4.20	1.4 - 12.6		

Coronary Heart Disease

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Community, Gender.
			0	1.00			
			1 - 20	4.20	1.5 - 12.1		
			> 20	4.50	1.6 - 12.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			0	1.00			
			1 - 20	4.10	1.4 - 11.8		
			> 20	4.60	1.6 - 12.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Atrial Fibrillation, Body Mass, Community, Diabetes, Fundus Changes, Gender, Proteinuria, ST-T Elevation, Systemic Medication, Systolic Blood Pressure, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	3.70	1.2 - 11.2		
Yano, K et al; 1988	9,223	Cohort	No Abstractable Data				Cigarette smoking was a significant predictor of coronary heart disease mortality. The interquartile relative risk of fatal coronary heart disease for lifetime smoking (cigarettes smoked/day x years of smoking) was 1.97 (p=0.001) adjusted for age, systolic blood pressure, BMI, serum cholesterol, serum triglyceride, serum uric acid, serum glucose, hematocrit and alcohol intake.
Yano, Katsuhiko et al; 1984	7,705	Cohort	No Abstractable Data				"Cigarette smoking was closest to systolic blood pressure as a potent and consistent risk factor for total CHD, fatal CHD, and acute coronary insufficiency, and showed an even stronger association with nonfatal myocardial infarction."

Deafness

Author	Subjects	Study Type	Data				Comments
Itoh, A et al; 2001	496 Cases 2,807 Controls	Case-Control					Deafness = Hearing loss in elderly.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Aspartate Aminotransferase, Body Mass Index, Fasting Plasma Glucose Level, gamma-glutamyl Transpeptidase, Gender, Hemoglobin, Lung Function, Serum Triglycerides, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.22	0.89 - 1.67		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Aspartate Aminotransferase, Body Mass Index, Fasting Plasma Glucose Level, gamma-glutamyl Transpeptidase, Gender, Hemoglobin, Lung Function, Serum Triglycerides, Total Cholesterol.
			Never Smoker	1.00			
			Current Smoker	2.10	1.53 - 2.89		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Aspartate Aminotransferase, Body Mass Index, Fasting Plasma Glucose Level, gamma-glutamyl Transpeptidase, Gender, Hemoglobin, Lung Function, Serum Triglycerides, Total Cholesterol.
			0	1.00			
			1 - 20	2.23	1.49 - 3.35		
			> 20	2.01	1.46 - 2.87		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Aspartate Aminotransferase, Body Mass Index, Fasting Plasma Glucose Level, gamma-glutamyl Transpeptidase, Gender, Hemoglobin, Lung Function, Serum Triglycerides, Total Cholesterol.
			0	1.00			
			< 19.95	1.27	1.12 - 2.21		
			20 - 39.95	1.37	0.97 - 1.93		
			> 39.95	1.76	1.26 - 2.44		
Mizoue, T et al; 2003	4,624	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), 1000Hz Not Exposed.
			0	1.00			
			1 - 14	1.20	0.6 - 2.7		
			15 - 24	1.30	0.9 - 1.9		
			> 24	1.10	0.7 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 1000Hz Not Exposed.
			Non-Smoker	1.00			
			Current Smoker	1.14	0.82 - 1.58		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 4000Hz Not Exposed.
			0	1.00			
			1 - 14	1.80	1.1 - 2.9		
			15 - 24	1.90	1.4 - 2.4		
			> 24	2.10	1.6 - 2.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 4000Hz Not Exposed.
			Non-Smoker	1.00			
			Current Smoker	1.57	1.31 - 1.89		

Deafness

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 1000Hz Exposed.
			0	1.00			
			1 - 14	0.90	0.3 - 2.8		
			15 - 24	1.00	0.6 - 1.8		
			> 24	1.00	0.5 - 1.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 4000Hz Exposed.
			0	1.00			
			1 - 14	1.20	0.6 - 2.6		
			15 - 24	1.60	1.2 - 2.2		
			> 24	2.60	1.8 - 3.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 1000Hz Exposed.
			Non-Smoker	1.55	0.98 - 2.45		
			Current Smoker	1.50	1.05 - 2.15		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by 4000Hz Exposed.
			Non-Smoker	1.77	1.36 - 2.3		
			Current Smoker	2.56	2.12 - 3.07		
Nakamura, M et al; 2001	164 Cases 20,313 Controls	Case-Control					Deafness = Idiopathic sudden deafness.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by High Frequency. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	0.84	0.1 - 7.46		
			> 19	2.35	0.6 - 9.25		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Low Frequency. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	0.66	0.17 - 2.5		
			> 19	0.45	0.14 - 1.41		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Flat type. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	0.73	0.21 - 2.5		
			> 19	1.96	0.91 - 4.23		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Profound type. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	2.18	0.37 - 12.9		
			> 19	3.76	0.6 - 23.43		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Control I. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	0.81	0.41 - 1.63		
			> 19	1.28	0.77 - 2.13		

Deafness

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Control II. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	1.14	0.53 - 2.49		
			> 19	1.35	0.75 - 2.44		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Others. Adjusted for Age, Alcohol Consumption, Diet, Gender, Residence Location, Sleeping Hours.
			0	1.00			
			1 - 19	1.00	0.28 - 3.57		
			> 19	0.99	0.36 - 2.73		
Nakanishi, N et al; 2000	1,554	Cross Sectional					Deafness is indicated by development of hearing impairment.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Low Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			Never Smoker	1.00			
			Ex-Smoker	1.12	0.57 - 2.17		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by High Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			Never Smoker	1.00			
			Ex-Smoker	1.70	0.85 - 3.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Low Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			0	1.00			
			1 - 20	1.21	0.65 - 2.25		
			21 - 30	1.35	0.7 - 2.61		
			> 30	1.82	0.98 - 3.38		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by High Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			0	1.00			
			1 - 20	1.82	0.92 - 3.59		
			21 - 30	2.00	0.98 - 4.08		
			> 30	2.20	1.09 - 4.42		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Low Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			0	1.00			
			0.1 - 19.9	1.15	0.51 - 2.61		
			20 - 29.9	1.07	0.47 - 2.42		
			30 - 39.9	1.09	0.51 - 2.33		
			> 40	1.58	0.87 - 2.87		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by High Frequency. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Hematocrit.
			0	1.00			
			0.1 - 19.9	1.74	0.67 - 4.53		
			20 - 29.9	2.27	1.01 - 5.11		
			30 - 39.9	1.69	0.73 - 3.9		
			> 40	2.45	1.28 - 4.7		

Dementia

Author	Subjects	Study Type	Data				Comments
Nojiri, M et al; 1991	1,662	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.79			
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.38			
			> 19	0.41			
Yamada, M et al; 2003	1,774	Cohort	No Abstractable Data				"Smoking, alcohol intake, [physical activity index], [body mass index], other dietary habits, and radiation dose did not show any significant effects on prevalence of [vascular dementia] or [Alzheimer's disease]."

Dental Caries

Author	Subjects	Study Type	Data				Comments
Tada, A et al; 2002	575	Cross Sectional					Dental Disease outcome: Missing teeth.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Dental Checkup, Dental Floss, Employment, Family Situation, Gender, Toothbrushing.
			Never Smoker	1.00			
			Ex-Smoker	1.11	0.29 - 4.26	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Dental Checkup, Dental Floss, Employment, Family Situation, Gender, Toothbrushing.
			Never Smoker	1.00			
			Current Smoker	5.29	2.62 - 10.66	< .05	

Dental Disease

Author	Subjects	Study Type	Data				Comments
Imaki, M et al; 1997	1,611	Cross Sectional	No Abstractable Data				Smoking was adversely affected with higher Community Periodontal Index of Treatment Needs in individuals with high plaque which was measured by the Simplified Debris Index.
Ogawa, Y et al; 1998	2,000	Cross Sectional					
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-29), Gender (Male), Missing Teeth. Adjusted for Age.
			Never Smoker	0.24	0.05		
			Current Smoker	0.50	0.07		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (30-39), Gender (Male), Missing Teeth. Adjusted for Age.
			Never Smoker	0.75	0.13		
			Current Smoker	1.33	0.16		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (40-49), Gender (Male), Missing Teeth. Adjusted for Age.
			Never Smoker	1.16	0.14		
			Current Smoker	1.88	0.15		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (50-59), Gender (Male), Missing Teeth. Adjusted for Age.
			Never Smoker	1.83	0.28		
			Current Smoker	2.98	0.29		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-59), Gender (Male), Missing Teeth. Adjusted for Age.
			Never Smoker	0.92	0.08		
			Current Smoker	1.51	0.18		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-29), Gender (Male), Decayed Teeth. Adjusted for Age.
			Never Smoker	0.72	0.14		
			Current Smoker	1.15	0.13		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (30-39), Gender (Male), Decayed Teeth. Adjusted for Age.
			Never Smoker	0.84	0.21		
			Current Smoker	1.11	0.13		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (40-49), Gender (Male), Decayed Teeth. Adjusted for Age.
			Never Smoker	0.48	0.10		
			Current Smoker	0.86	0.11		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (50-59), Gender (Male), Decayed Teeth. Adjusted for Age.
			Never Smoker	0.59	0.12		
			Current Smoker	0.90	0.23		

Dental Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-59), Gender (Male), Decayed Teeth. Adjusted for Age.
			Never Smoker	0.70	0.08		
			Current Smoker	0.96	0.06		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-29), Gender (Male), Filled Teeth. Adjusted for Age.
			Never Smoker	8.50	0.30		
			Current Smoker	8.58	0.38		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (30-39), Gender (Male), Filled Teeth. Adjusted for Age.
			Never Smoker	10.12	0.36		
			Current Smoker	10.54	0.56		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (40-49), Gender (Male), Filled Teeth. Adjusted for Age.
			Never Smoker	9.25	0.32		
			Current Smoker	10.30	0.43		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (50-59), Gender (Male), Filled Teeth. Adjusted for Age.
			Never Smoker	7.46	0.52		
			Current Smoker	8.38	0.45		
			Active Smoking Status	**Mean**	**Std. Dev./ Error**	**P-Value**	Stratified by Age (20-59), Gender (Male), Filled Teeth. Adjusted for Age.
			Never Smoker	9.09	0.18		
			Current Smoker	9.26	0.23		
Shizukuishi, S et al; 1998	310	Cross Sectional					Dental disease outcome= Community Periodontal Index (CPI) in the upper 25th percentile.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Brushing Teeth at Cervical Area, Frequency of Toothbrushing, Gender, Use of Interdental Cleaners.
			Ever Smoker	1.00			
			Current Smoker	2.11	1.17 - 3.81		
Tada, A et al; 2002	575	Cross Sectional					Dental Disease outcome: Missing teeth.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Dental Checkup, Dental Floss, Employment, Family Situation, Gender, Toothbrushing.
			Never Smoker	1.00			
			Ex-Smoker	0.32	0.06 - 1.45	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Dental Checkup, Dental Floss, Employment, Family Situation, Gender, Toothbrushing.
			Never Smoker	1.00			
			Current Smoker	2.54	1.35 - 4.77	< .01	

Diabetes Mellitus

Author	Subjects	Study Type	Data				Comments
Kawakami, N et al; 1997	2,312	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			Current Smoker	1.00			
			Ex-Smoker	0.84	0.32 - 2.19		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			Never Smoker	1.00			
			Ex-Smoker	2.25	0.67 - 7.49		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			0	1.00			
			1 - 15	1.13	0.3 - 4.26		
			16 - 25	3.27	1.18 - 9.09		
			> 25	3.21	1.05 - 9.83		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			1 - 15	1.00			
			16 - 25	2.30	0.91 - 5.83		
			> 25	1.98	0.68 - 5.74		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			1 - 15	1.00			
			16 - 25	2.90	0.97 - 8.7		
			> 25	2.68	0.79 - 9.11		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			1 - 10	1.00			
			11 - 20	2.00	0.52 - 7.62		
			> 20	1.90	0.4 - 8.9		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Education, Family History of Diabetes, Occupation, Physical Activity, Workshift.
			1 - 10	1.00			
			11 - 20	2.51	0.66 - 9.49		
			> 20	3.07	0.49 - 18.9		
Kawakami, N et al; 1995	63	Cross Sectional	No Abstractable Data				Study found that number of cigarettes smoked per day significantly and positively associated with glycosylated hemoglobin ($p<0.01$), after adjusting for age, occupation, profile of mood states and each catecholamine.
Sugimori, H et al; 1998	2,573	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Cholesterol, Diet, Family History/Index Disease, Gender, Glucose Tolerance, High Blood Pressure, Hypercholesterolemia.
			Non-Smoker	1.00			
			Current Smoker	1.37	1.03 - 1.82		

Diabetes Mellitus

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Cholesterol, Diet, Family History/Index Disease, Glucose Tolerance, High Blood Pressure, Hypercholesterolemia.
			Non-Smoker	1.00			
			Current Smoker	1.42	1.1 - 1.83		
Uchimoto, S et al; 1999	8,410	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Family History of Diabetes, Fasting Plasma Glucose Level, Gender, Haematocrit, HDL, Physical Activity, Serum Triglycerides, Total Cholesterol.
			Never Smoker	1.00			
			Current Smoker	1.47	1.14 - 1.92		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Family History of Diabetes, Fasting Plasma Glucose Level, Gender, Haematocrit, HDL, Physical Activity, Serum Triglycerides, Total Cholesterol.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.79 - 1.53		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Family History of Diabetes, Fasting Plasma Glucose Level, Gender, Haematocrit, HDL, Physical Activity, Serum Triglycerides, Total Cholesterol.
			0	1.00			
			1 - 20	1.40	1.05 - 1.86		
			21 - 30	1.40	1.03 - 1.93		
			> 30	1.73	1.2 - 2.48		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass, Family History of Diabetes, Fasting Plasma Glucose Level, Gender, Haematocrit, HDL, Physical Activity, Serum Triglycerides, Total Cholesterol.
			0	1.00			
			1 - 20	1.22	0.89 - 1.67		
			20.1 - 30	1.57	1.16 - 1.67		
			30.1 - 40	1.55	1.06 - 2.26		
			> 40	1.73	1.15 - 2.6		
Wang, L et al; 2002	241 Cases 165 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Family History of Diabetes, Fiber Intake, Gender, Psychological Stress.
			Non-Smoker	1.00			
			Ever Smoker	2.50	1.11 - 5.68		

Diabetic Nephropathy

Author	Subjects	Study Type	Data				Comments
Horikawa, Y et al; 1999	67	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Blood Pressure, Body Mass Index, Duration of Diabetes, HbA1c, Serum Lipids.
			Never Smoker	1.00			
			Current Smoker	0.15	0.02 - 1.23	> .05	
Ikeda, Y et al; 1997	148	Cross Sectional					Diabetic Nephropathy outcome= Albuminuria.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.00	0.6 - 6.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Current Smoker	4.50	1.9 - 11.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.60	2 - 11.9		
Yokoyama, H et al; 1998	426	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	1.15	0.6 - 2.22	> .05	

Difficulty Initiating Sleep

Author	Subjects	Study Type	Data				Comments
Kim, K et al; 1999	4,000	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.00		> .05	

Difficulty Maintaining Sleep

Author	Subjects	Study Type	Data				Comments
Kim, K et al; 1999	4,000	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.07		> .05	

Diminished Health Status

Author	Subjects	Study Type	Data				Comments
Arima, K et al; 1992	40 Cases 221 Controls	Case-Control	No Abstractable Data				The study concluded that cigarette smoking suppressed the outbreak of summer-type hypersensitivity pneumonitis, but smoking had no effect once the disease was established.
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	1.69			
Kuwahara, Y et al; 2001	426	Cross Sectional					Smoking appeared to be positively associated with enhanced eosinophil activity.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Family Smoking Habit, Floor Cover, Frequent Cleaning Habits, History of Allergic Diseases, Intensive Use of Air Conditioner, Living in Heavy Traffic Area, Mold Proliferation, Poor Home Ventilation, Type of Housing, Unvented Combustion Appliances.
			Non-Smoker	1.00			
			Current Smoker	1.64	0.92 - 2.91	> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Floor Cover, Frequent Cleaning Habits, History of Allergic Diseases, Intensive Use of Air Conditioner, Living in Heavy Traffic Area, Mold Proliferation, Poor Home Ventilation, Smoking Habits, Type of Housing, Unvented Combustion Appliances.
			Not Exposed	1.00			
			Exposed	0.99	0.59 - 1.66		
Nakanishi, N et al; 2002	5,275	Cross Sectional	No Abstractable Data				The results indicate that cigarette smoking has no effect on the strong association between WBC count and MS.
Ueshima, H; 1997	9,768	Cohort	No Abstractable Data				In this paper, the outcome was defined as "mortality and deteriorated activities of daily life (ADL)." The regression coefficient associated with each unit increase in smoking (0=never smoker, 1=former smoker, 2=current smoker) was -0.312 (p=0.001) for males and -0.238 (p=0.020) for females, after adjustment for history of stroke, history of myocardial infarction, alcohol intake, age, BMI, blood pressure, and total serum cholesterol.

Dyslipidemia

Author	Subjects	Study Type	Data				Comments
Wang, L et al; 2002	241 Cases 165 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Family History of Diabetes, Fiber Intake, Gender, Psychological Stress.
			Non-Smoker	1.00			
			Current Smoker	2.54	1.43 - 4.52		

Early Morning Awakening

Author	Subjects	Study Type	Data				Comments
Kim, K et al; 1999	4,000	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.78		> .05	

Endometrial Cancer

Author	Subjects	Study Type	Data				Comments
Hirose, K et al; 1996	416 Cases 26,751 Controls	Case-Control; Hospital-Based					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.09	0.76 - 1.57		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 19	1.02	0.63 - 1.65		
			> 19	1.14	0.73 - 1.76		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			0	1.00			
			1 - 9	0.52	0.13 - 2.12		
			> 9	0.75	0.38 - 1.49		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	0.69	0.37 - 1.27		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.30	0.4 - 3.9		

Erectile Dysfunction

Author	Subjects	Study Type	Data				Comments
Nicolosi, A et al; 2003	600	Cross Sectional					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Country, Depression, Diabetes, Education, Employment, Gender, Heart Disease, Hypertension, Marital Status, Physical Activity, Prostate Disease, Ulcer.
			0	1.00			
			1 - 30	1.00	0.8 - 1.26		
			> 30	1.74	1.11 - 2.74		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Country, Depression, Diabetes, Education, Employment, Gender, Heart Disease, Hypertension, Marital Status, Physical Activity, Prostate Disease, Ulcer.
			Never Smoker	1.00			
			Current Smoker	1.03	0.79 - 1.34		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Country, Depression, Diabetes, Education, Employment, Gender, Heart Disease, Hypertension, Marital Status, Physical Activity, Prostate Disease, Ulcer.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.68 - 1.2		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ever Smoker	2.80	1.3 - 6.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	3.30			
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.90	0.2 - 2.5		
			5 - 14	2.00	1.4 - 2.8		
			15 - 24	2.40	1.7 - 3.3		
			25 - 34	2.10	1.1 - 3.8		
			> 34	2.50	1 - 5.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.80	0.5 - 4.3		
			> 4	1.70	1 - 2.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	2.20	1.6 - 3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.70	1.1 - 2.7		
Hanaoka, T et al; 1994	141 Cases 141 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption.
			0	1.00			
			1 - 5	1.89	0.76 - 4.7		
			5 - 14	2.92	0.99 - 8.62		
			15 - 24	4.35	1.81 - 10.49		
			> 24	1.42	0.59 - 3.44		
Haruma, K et al; 1991	21 Cases 358 Controls	Case-Control; Hospital-Based					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0 - 19	1.00			
			> 19	4.11	1.4 - 12.5		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.11	1.7 - 2.62		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.24	1.72 - 2.91		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.75	1.21 - 2.51		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.62	1.09 - 2.41		
			10 - 19	2.04	1.54 - 2.71		
			> 19	2.69	2.05 - 3.53		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.74	1.04 - 2.91		
			10 - 19	2.45	1.53 - 3.93		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.53	0.7 - 3.38		
			5 - 9	1.13	0.35 - 3.64		
			> 9	1.96	0.88 - 4.38		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.17			
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
			Current Smoker	3.08			
Hirayama, T; 1981	98 Cases 480 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.01			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Diet, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.44			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	3.90			
			20 - 39	7.30		< .01	
			> 39	6.60		< .01	
Hori, Hikaru et al; 1997	94 Cases 70 Controls	Case-Control; Population-Based	No Abstractable Data				There were no significant differences between healthy controls and patients with esophageal cancer in the polymorphisms of the CYP1A1, GSTM1 and CYP11E1 genes'. There were significant differences in the ADH2 and ALDH2 polymorphism between healthy controls and esophageal cancer cases. The ADH21/ALDH21 and ALDH21/ALDH22 genotypes were significantly and independently higher in esophageal carcinoma cases than healthy controls Polymorphism of alcohol metabolizing enzymes and not tobacco metabolizing enzymes have been shown to be significantly associated with esophageal cancer.
Kinjo, Yoshihide et al; 1998	220,272	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Occupation, State of Residence, Tea Consumption, Vegetable Intake.
			Never Smoker	1.00			
			Ex-Smoker	1.50	0.8 - 2.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Occupation, State of Residence, Tea Consumption, Vegetable Intake.
			0	1.00			
			1 - 14	1.80	1.3 - 2.5		
			> 14	1.90	1.4 - 2.7		
Kobayashi, Y et al; 1990	11 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
							(p<0.05). Heavy smokers were also more prevalent among MPC cases than among controls (p<0.1)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases (p<0.1)"
Kolonel, L; 1979	8,636	Cross Sectional	No Abstractable Data				Caucasian men had a greatest lifetime cigarette use while Chinese and Filipino men had the lowest. Smoking cigarettes was highest among Caucasian women and lowest among Chinese. Data did not explain unusually high incidence of lung and esophageal cancer in Hawaiian males.
Kono, Suminori et al; 1987		Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	0.51	0.08 - 3.23		
			> 19	2.11	0.49 - 9.16		
Kumimoto, H et al; 2001	91 Cases 241 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by LL Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.38	0.37 - 5.11	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by LS Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Non-Smoker	1.00			
			Current Smoker	7.49	2.65 - 21.16	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by SS Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.26	0.65 - 16.44	> .05	
Matsuo, K et al; 2001	102 Cases 241 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.19	1.34 - 7.58		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	9.78	4.49 - 21.3		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			0	1.00			
			1 - 50	7.27	3.17 - 16.7		
			> 50	17.20	6.61 - 44.7		
Matsuo, K et al; 2001	91 Cases 241 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (43-60). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.32	0.33 - 5.22		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (61-76). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	9.42	2.04 - 43.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (43-60). Adjusted for Age, Gender.
			0	1.00			
			1 - 50	1.94	0.54 - 6.9		
			> 50	17.70	4.08 - 76.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (61-76). Adjusted for Age, Gender.
			0	1.00			
			1 - 50	13.80	2.93 - 66.7		
Nakachi, K et al; 1988	343 Cases 343 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	2.38	0.995 - 5.69		
Sasaki, R et al; 1990	201 Cases 403 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Nagoya Hospital Cases-Controls. Adjusted for Age, Gender, Hospital Type, Time of Interview.
			Never Smoker	1.00			
			Ever Smoker	5.00	2.1 - 11.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Wakayama Hospital Cases-Control. Adjusted for Age, Gender, Hospital Type, Time of Interview.
			Never Smoker	1.00			
			Ever Smoker	4.30	1.7 - 11.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Nagoya Hospital Cases-Controls. Adjusted for Age, Gender, Hospital Type, Time of Interview.
			Never Smoker	1.00			
			Ever Smoker	0.90	0.3 - 2.6		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Wakayama Hospital Cases-Control. Adjusted for Age, Gender, Hospital Type, Time of Interview.
			Never Smoker	1.00			
			Ever Smoker	2.30	0.8 - 6.8		
Takezaki, T et al; 2000	284 Cases 11,936 Controls	Case-Control; Hospital-Based					Upper aerodigestive cancer are results for cancer of the hypopharynx or esophagus combined.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Upper Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.3 - 3.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.60	1.1 - 6.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Lower Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.5 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.9 - 2.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Upper Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	3.00	0.9 - 9.7		
			> 19	2.00	0.7 - 5.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	4.50	1.8 - 11.3		
			> 19	6.50	2.8 - 15.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Lower Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	1.90	0.7 - 4.9		
			> 19	1.90	0.8 - 4.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	3.10	1.8 - 5.5		
			> 19	3.50	2.1 - 5.9		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	3.10	1.6 - 5.9		
			20 - 29	3.50	1.9 - 6.5		
			30 - 39	4.60	2.3 - 9.1		
			> 39	5.20	2.6 - 10.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Upper Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Current Smoker	2.40	0.8 - 6.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Current Smoker	5.80	2.5 - 13.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Lower Esophageal Cancer. Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Current Smoker	2.10	0.9 - 4.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Current Smoker	3.50	2.1 - 5.8		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 29	2.20	1.1 - 4.4		
			> 29	3.60	2.1 - 6		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 9	2.30	1.3 - 4.2		
			> 9	1.30	0.7 - 2.3		
Yokoyama, A et al; 2002	234 Cases 634 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Smoking Habits.
			0	1.00			
			1 - 29	1.42	0.68 - 2.97		
			> 29	2.90	1.54 - 5.47		
Yokoyama, A et al; 1996		Cross Sectional					Oropharyngeal cancer outcome includes laryngeal cancer cases. Upper aerodigestive cancer outcome includes esophageal cancer, gastric cancer, and oropharyngolaryngeal cancer.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Type of Alcohol.
			< 50	1.00			
			> 49	2.80	1.4 - 5.7		

Esophageal Cancer

Author	Subjects	Study Type	Data				Comments
Yokoyama, A et al; 1995	629	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Distinct Iodine Unstained. Adjusted for Age, Alcohol Consumption, Smoking Habits.
			0	1.00			
			1 - 19	1.38			
			20 - 29	2.25			
			> 29	2.13			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Superficial. Adjusted for Age, Alcohol Consumption, Smoking Habits.
			0	1.00			
			1 - 19	1.33			
			20 - 29	1.00			
			> 29	2.13			

Excessive Daytime Sleepiness

Author	Subjects	Study Type	Data				Comments
Doi, Y et al; 2002	3,909	Cross Sectional					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Asthma, Caffeine Consumption, Depression, Difficulty Sleeping, Education, Marital Status, Muscle-joint Pain, Peptic Ulcer, Sleeping Hours, Sleeping Medication, Sleep-wake Schedule, Snoring, Type of Work.
			0	1.00			
			1 - 19	0.65	0.42 - 1.02		
			20 - 39	0.70	0.46 - 1.08		
			> 39	2.15	0.85 - 5.43		

Gall Bladder Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.23	0.91 - 1.65		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.32	0.99 - 1.75		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.29	0.82 - 2.03		
			10 - 19	1.11	0.8 - 1.55		
			> 19	1.21	0.87 - 1.69		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.47	1 - 2.16		
			10 - 19	1.27	0.81 - 2		
			> 19	1.89	0.85 - 4.2		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.73	0.79 - 3.8		
			> 9	0.41	0.07 - 2.37		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			> 9	3.59	0.68 - 18.94		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.27	1.03 - 1.56		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.66	0.24 - 1.9		

Gallstones

Author	Subjects	Study Type	Data				Comments
Kono, S et al; 2002	278 Cases 7,637 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.34	0.85 - 2.1		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			0	1.00			
			1 - 25	1.48	0.96 - 2.28		
			> 25	1.42	0.86 - 2.34		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Newly Diagnosed. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.22	0.71 - 2.09		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Newly Diagnosed. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			0	1.00			
			1 - 25	1.67	1.01 - 2.76		
			> 25	1.31	0.71 - 2.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	0.99	0.59 - 1.65		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			0	1.00			
			1 - 25	0.77	0.46 - 1.31		
			> 25	0.62	0.31 - 1.23		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by New Dx Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.16	0.75 - 1.78		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by New Dx Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Hospital, Rank.
			0	1.00			
			1 - 25	0.85	0.54 - 1.32		
			> 25	0.89	0.52 - 1.51		
Kono, S et al; 1995	2,228	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Body Mass Index, Exercise, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.5 - 2.7		

Gallstones

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Body Mass Index, Exercise, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Current Smoker	1.00	0.6 - 1.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gallstone + Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Exercise, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.3 - 2.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gallstone + Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Exercise, Glucose Tolerance, Hospital, Rank.
			Never Smoker	1.00			
			Current Smoker	0.80	0.6 - 1.4		
Kono, S et al; 1992	2,756	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent Disease. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.6 - 2.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Prevalent Disease. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			0	1.00			
			1 - 25	1.60	0.7 - 3.3		
			> 25	1.80	0.8 - 4.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.50	0.6 - 3.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Postcholecystectomy State. Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			0	1.00			
			1 - 25	0.60	0.2 - 1.8		
			> 25	1.50	0.6 - 4.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.7 - 2.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Body Mass Index, Glucose Tolerance, Rank.
			0	1.00			
			1 - 25	1.20	0.6 - 2.1		
			> 25	1.70	0.9 - 3.3		

Gastritis

Author	Subjects	Study Type	Data	Comments
Yamagiwa, H; 1970	434	Case Series	No Abstractable Data	1) "No significant relationship was found between the intestinal metaplasia and drinking or smoking." "The gastric ulcer was frequently found in smokers, and female was predominant in non-smokers." "If smoking has any unfavorable influence on duodenal ulcers, it may be due to any indirect factor described in the duodenal gastric ulcer." "Effects of drinking and smoking on the gastric carcinoma were not clear."

Graves' Disease

Author	Subjects	Study Type	Data				Comments
Bednarczuk, T et al; 2003	573 Cases 357 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Both). Adjusted for Age at Diagnosis, CTLA-4 Genotype, Race.
			Non-Smoker	1.00			
			Current Smoker	1.70	0.9 - 2.9	< .05	
Yoshiuchi, K et al; 1998	228 Cases	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Coping Skills, Daily Hassles, Gender, Life Events.
			0	1.00			
			1 - 10	3.70	1.3 - 11	< .05	
			11 - 20	3.50	1.2 - 10	< .05	
			21 - 40	5.10	1 - 27	< .001	

Health-related Behavior

Author	Subjects	Study Type	Data	Comments
Inaba, S et al; 1998		Other	No Abstractable Data	"When we compared the lifestyles of smokers and nonsmokers after separating them by their spouses' smoking status, the following variables were statistically significantly lower in smokers than in nonsmokers, irrespective of sex ($p < 0.05$): (1) intakes of fiber, calcium, carotene, vitamin B1, vitamin B2, vitamin C and vitamin E among male smokers with nonsmoking wives, (2) intakes of fiber, calcium, carotene, vitamin B2 and vitamin C among male smokers with wives who also smoked, (3) intakes of energy and vitamin B1 among female smokers with nonsmoking husbands, (4) intakes of fiber, calcium, carotene, vitamin B1, vitamin C and vitamin E among female smokers with husbands who also smoked and (5) participation rates in both stomach and lung cancer screening programs among male smokers with nonsmoking wives and among female smokers with husbands who also smoked."

Helicobacter Pylori

Author	Subjects	Study Type	Data				Comments
Komoto, K et al; 1998		Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Cardia. Adjusted for Age, Alcohol Consumption, Blood Type, Coffee, Family History of Cancer, Gender, Helicobacter pylori.
			Non-Smoker	1.00			
			Current Smoker	4.32	0.9 - 20.86		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Non-Cardia. Adjusted for Age, Alcohol Consumption, Blood Type, Coffee, Family History of Cancer, Gender, Helicobacter pylori.
			Non-Smoker	1.00			
			Current Smoker	2.00	1.04 - 3.85		
Namekata, T et al; 2000	776	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	1.77	1 - 3.14		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	2.39	1.14 - 5.03		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 1st Generation. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	0.86	0.3 - 2.51		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 1st Generation. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	0.35	0.09 - 1.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 2nd-4th Generations. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	1.57	0.83 - 2.97		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 2nd-4th Generations. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	1.29	0.83 - 2.01		
Ogihara, A et al; 2000	8,837	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.82	0.74 - 0.91		

Helicobacter Pylori

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.91	0.79 - 1.04		
			20 - 49	0.82	0.73 - 0.91		
			> 49	0.65	0.47 - 0.88		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.97	0.83 - 1.13		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (39-44), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.99	0.72 - 1.36		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (39-44), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.67	0.56 - 0.81		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.85	0.74 - 0.99		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.94	0.74 - 1.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>55), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.99	0.76 - 1.29		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>55), Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.96	0.79 - 1.17		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>55), Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.01	0.78 - 1.29		
			20 - 49	0.90	0.73 - 1.11		
			> 50	1.18	0.59 - 2.35		

Helicobacter Pylori

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-54), Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.91	0.74 - 1.12		
			20 - 49	0.85	0.73 - 1		
			> 50	0.70	0.44 - 1.13		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (39-44), Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.81	0.62 - 1.06		
			20 - 49	0.69	0.57 - 0.84		
			> 50	0.38	0.22 - 0.67		
Toyonaga, A et al; 2000	365	Cross Sectional	No Abstractable Data				Multivariate analysis showed no association between smoking and H Pylori prevalence

Hemoglobin Level

Author	Subjects	Study Type	Data	Comments
Yamada, M et al; 2003	4,858	Cohort	No Abstractable Data	"Compared with non-smokers the average Hb level of male ever-smokers was increased by 0.21 g/dL [95% confidence interval (CI): 0.08-0.34] whereas the increase was 0.36 g/dL (95% CI: 0.27-0.45) for female ever-smokers."

Hepatoblastoma

Author	Subjects	Study Type	Data				Comments
Kobaashi, N et al; 1990	81 Cases 2,641 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	
			Non-Smoker	1.00			
			Current Smoker	2.10			

Holoprosencephalus

Author	Subjects	Study Type	Data				Comments
Matsunaga, E et al; 1977	103 Cases 206 Controls	Case-Control					Maternal smoking habits were found not to be associated with holoprosencephaly.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Parity.
			Never Smoker	1.00			
			Ever Smoker	0.69		> .05	

Hyperuricemia

Author	Subjects	Study Type	Data	Comments
Kono, S et al; 1994	2,487	Cohort	No Abstractable Data	Past smoking was found to be positively associated with serum uric acid level.
Nakanishi, N et al; 1999	1,445	Cohort		

Active Smoking Status	Risk Estimate	95% CI	P-Value
Never Smoker	1.00		
Ex-Smoker	0.95	0.64 - 1.48	> .05

Stratified by Gender (Male).
Adjusted for Age, Alcohol Consumption, Blood Pressure, Blood Urea Nitrogen, Body Mass Index, HDL, Hematocrit, Hemoglobin, Log Triglyceride, Total Cholesterol, Total Protein.

Active Smoking Status	Risk Estimate	95% CI	P-Value
Never Smoker	1.00		
Current Smoker	0.73	0.52 - 1.02	> .05

Stratified by Gender (Male).
Adjusted for Age, Alcohol Consumption, Blood Pressure, Blood Urea Nitrogen, Body Mass Index, HDL, Hematocrit, Hemoglobin, Log Triglyceride, Total Cholesterol, Total Protein.

Idiopathic Spontaneous Pneumothorax

Author	Subjects	Study Type	Data	Comments
Nakamura, H et al; 1983	2,433 Cases 1,906 Controls	Case-Control	No Abstractable Data	The study indicates a statistically significance difference in the level of tobacco consumption between individuals with IPT and healthy subjects.

Intraocular Pressure

Author	Subjects	Study Type	Data	Comments
Yoshida, M et al; 2003	569	Cross Sectional	No Abstractable Data	Results found that: "the adjusted mean intraocular pressure increased in men with the increasing level of the three cigarette consumption categories (p trend <0.001)." The adjusted mean intraocular pressure in women was not significant for cigarette consumption.

Intrauterine Growth Retardation

Author	Subjects	Study Type	Data				Comments
Matsubara, F et al; 2000	7,411	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Ex-Smoker	0.79	0.48 - 1.29		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Current Smoker	1.79	1.05 - 3.04		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 5	1.00	0.36 - 2.83		
			6 - 10	2.89	1.49 - 5.62		
			> 10	1.43	0.43 - 4.8		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Never Smoker	1.00			
			Ex-Smoker	0.93	0.29 - 3.01		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Never Smoker	1.00			
			Current Smoker	0.95	0.72 - 1.26		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 10	1.09	0.72 - 1.65		
			11 - 20	0.93	0.67 - 1.29		
			> 20	0.82	0.5 - 1.35		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Not Exposed	1.00			
			Exposed	0.95	0.71 - 1.26		
			Hours / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			< 2	1.14	0.82 - 1.57		
			> 1	0.72	0.49 - 1.07		

Joint Pain

Author	Subjects	Study Type	Data				Comments
Huang, C et al; 1997	690	Cross Sectional					Osteoporosis endpoints=predictors of joint pain in postmenopausal women.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Body Mass, Bone Mineral Density, Extremity Fracture, Gender, Non-Spine Fractures, Physical Activity, Vertebral Fractures.
			Non-Smoker	1.00			
			Current Smoker	0.38	0.12 - 1.07	> .05	

Kidney Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.3 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.10	0.5 - 2.5		
Hinds, MW et al; 1980		Other	No Abstractable Data				"A significant positive association between cigarette smoking and renal cancer was noted in the TNCS (Third National Cancer Survey) study and in the Hawaiian Study of Five Ethnic Groups." "The Third National Cancer Survey and the Hawaiian Study of Five Ethnic Groups have also reported a positive association [between smoking and laryngeal cancer]." "In the Third National Cancer Survey and in the Hawaiian Study of Five Ethnic Groups, there was a significant positive relationship between smoking and pancreatic cancer."
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.06	0.6 - 1.85		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.24	0.05 - 1.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.20	0.5 - 2.88		
			10 - 19	0.94	0.5 - 1.76		
			> 19	1.21	0.65 - 2.24		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	0.55	0.1 - 3.01		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).

Kidney Cancer

Author	Subjects	Study Type	Data			Comments
			Status			Adjusted for Age, Gender.
			Never Smoker	1.00		
			Current Smoker	0.38	0.49 - 1.4	

Laryngeal Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	13.70	0.5 - 346		
			5 - 14	17.00	3.6 - 304		
			15 - 24	25.70	5.5 - 458		
			25 - 34	76.90	14 - 1427		
			> 34	73.40	5.3 - 420		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	23.80	5.3 - 420		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.80	0.4 - 6		
Hinds, MW et al; 1980		Other	No Abstractable Data				"A significant positive association between cigarette smoking and renal cancer was noted in the TNCS (Third National Cancer Survey) study and in the Hawaiian Study of Five Ethnic Groups." "The Third National Cancer Survey and the Hawaiian Study of Five Ethnic Groups have also reported a positive association [between smoking and laryngeal cancer]." "In the Third National Cancer Survey and in the Hawaiian Study of Five Ethnic Groups, there was a significant positive relationship between smoking and pancreatic cancer."
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	11.22	4.99 - 25.23		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	32.50	8.69 - 121.93		

Laryngeal Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.29	1.45 - 7.43		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	16.33	3.15 - 84.7		
			10 - 19	30.64	7.97 - 117.8		
			> 19	45.02	13.28 - 152.56		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.21	0.19 - 7.62		
			10 - 19	3.45	1.06 - 11.26		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			5 - 9	27.48	4.34 - 174.18		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.07			
Iwamoto, H; 1975	6,360	Case Series	No Abstractable Data				Ninety-seven percent of male patients and 85% of female patients surveyed were smokers; the percentage of smoking in the general population of Japan is less than 40% and as result according to the author it must be considered as a significant causal factor in laryngeal carcinoma.
Kihara, M et al; 1997	158 Cases 474 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	24.40	4.9 - 121.4	< .001	
Kobayashi, Y et al; 1990	40 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls ($p<0.05$). Heavy smokers were also more prevalent among MPC cases than among controls ($p<0.1$)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases ($p<0.1$)"

Leukemia

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.4 - 2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	0.70	0.4 - 1.4		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.15	0.84 - 1.58		
Wakabayashi, I et al; 1994	142 Cases 284 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Acute Non-Lymphocytic). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.76	0.96 - 3.23		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Acute). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.68	0.99 - 2.84		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Chronic). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.86	0.39 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Acute Non-Lymphocytic). Adjusted for Age, Gender.
			0	1.00			
			1 - 10	0.90	0.24 - 3.4		
			11 - 20	2.16	0.98 - 4.75	< .05	
			21 - 30	1.11	0.28 - 4.4		
			> 30	2.99	0.66 - 13.47		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Histology (Acute). Adjusted for Age, Gender.
			0	1.00			
			1 - 10	0.87	0.27 - 2.83		
			11 - 20	1.58	0.79 - 3.13		
			21 - 30	1.71	0.53 - 5.54		
			> 30	4.06	1.09 - 15.16	< .05	

Leukemia

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	Risk Estimate	95% CI	P-Value	Stratified by Histology (Chronic). Adjusted for Age, Gender.
			0	1.00			
			1 - 10	1.05	0.2 - 5.44		
			11 - 20	0.50	0.16 - 1.56		
			21 - 30	1.89	0.33 - 10.76		
			> 30	1.42	0.23 - 8.82		

Liver Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.60	1.1 - 2.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.80	1.4 - 2.5		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.10	0.5 - 2		
			5 - 14	1.60	1.3 - 2		
			15 - 24	1.40	1.2 - 1.8		
			25 - 34	1.60	1.1 - 2.4		
			> 34	1.90	1.1 - 3.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.40	0.7 - 2.5		
			5 - 14	1.40	1 - 2		
			> 14	2.50	1.3 - 4.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.50	1.2 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.60	1.2 - 2		
Chiba, T et al; 1996	412	Cohort					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Alpha-fetoprotein Level, Blood Transfusion, Family History of Liver Cancer, Gender, Hepatitis B Viral Markers, Hepatitis C Viral Markers, Stage, Surgical Procedure.
			0	1.00			
			1 - 19	1.67	0.75 - 3.73		
			> 19	2.46	1.11 - 5.49		
Goodman, MT et al; 1995	36,133	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	4.56	1.95 - 10.7		

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			Never Smoker	1.00			
			Current Smoker	4.26	1.87 - 9.72		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.66	0.76 - 3.63		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			Never Smoker	1.00			
			Current Smoker	1.58	0.86 - 2.88		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			0	1.00			
			1 - 13	5.60	2.15 - 14.6		
			14 - 23	4.11	1.58 - 10.7		
			> 23	4.04	1.54 - 10.6		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			0	1.00			
			1 - 9	10.40	2.51 - 43.5		
			10 - 24	1.03	0.25 - 4.24		
			> 24	2.31	0.72 - 7.43		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			0	1.00			
			1 - 22	6.47	2.74 - 15.3		
			23 - 40	4.43	1.87 - 10.5		
			> 40	3.09	1.31 - 7.29		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at Time of Hiroshima Bombing, Gender, Radiation Dose to Liver, Residence Location.
			0	1.00			
			1 - 15	1.81	0.86 - 3.78		
			> 15	1.51	0.72 - 3.16		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.55	1.36 - 1.78		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Status				Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.50	1.27 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.66	1.35 - 2.05		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.48	1.14 - 1.93		
			10 - 19	1.49	1.23 - 1.8		
			> 19	1.59	1.32 - 1.93		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.80	1.13 - 2.87		
			5 - 9	2.56	1.57 - 4.19		
			> 9	1.07	0.54 - 2.14		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.68	0.36 - 7.77		
			5 - 9	3.04	0.67 - 13.71		
Hirayama, T; 1989	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	3.14	1.82 - 5.42		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.28			
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	1.18			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).

Liver Cancer

Author	Subjects	Study Type	Data				Comments
							Adjusted for Age, Gender.
			1 - 19	0.90			
			20 - 39	1.10			
			> 39	0.90			
Kato, I et al; 1987	241	Cohort	No Abstractable Data				The O/E ratio for all causes of death was almost equal for the 2 groups (smokers and non smokers), but the O/E ratio for malignant neoplasms, especially liver cancer were slightly higher in smokers than in non smokers (53.28 vs. 35.43, NS). The O/E ratio for liver cirrhosis was statistically significant only in non-smokers. (Table VI- page 1190)
Kono, Suminori et al; 1987		Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	1.14	0.59 - 2.2		
			> 19	1.04	0.49 - 2.23		
Mizoue, Tetsuya et al; 2000	4,050	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.90	1 - 8.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	3.30	1.2 - 9.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			0	1.00			
			1 - 24	3.50	1.2 - 10.2		
			> 24	2.80	0.8 - 9.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), History of Liver Disease. Adjusted for Age at Entry, Alcohol Consumption, Area, Gender, History of Liver Disease.
			Never Smoker	1.00			
			Current Smoker	3.50	1 - 11.7		
Mori, Mitsuru et al; 2000	3,059	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Race (Asian), Gender (Both). Adjusted for Age, Gender, Member of National Insurance, Residence Location.
			Non-Smoker	1.00			
			Ever Smoker	2.10	0.61 - 7.23	< .001	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>30), Race (Asian), Gender (Both). Adjusted for Age, Gender, Member of National Insurance, Residence Location.
			0	1.00			
			1 - 9	3.26	0.38 - 28.2		
			> 9	1.97	0.57 - 6.87		

Liver Cancer

Author	Subjects	Study Type	Data				Comments
Mukaiya, M et al; 1998	104 Cases 104 Controls	Case-Control; Hospital-Based					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0 - 19	1.00			
			> 19	3.33	1.339 - 8.3	< .05	
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0 - 4	1.00			
			> 4	3.33	1.339 - 8.3	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Current Smoker	1.00			
			Non-Smoker	0.29	0.115 - 0.708	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Non-Drinker. Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	9.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Non-Drinker. Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	15.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Drinker. Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	17.90			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Drinker. Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	17.30			
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.20	0.45 - 3.2		
Oshima, Akira et al; 1984	Not Specified	Nested Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Hepatitis B Virus Infection.
			< 10	1.00			
			10 - 30	1.70	0.4 - 6.4		
			> 30	5.80	1 - 34.2		
Shibata, A et al; 1990	1,316	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cohort II. Adjusted for Age, Alcohol Consumption.
			0	1.00			

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			1 - 19	2.10	0.44 - 9.95		
			> 19	1.86	0.37 - 9.4		
Shibata, Akira et al; 1986	1,316	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Area, Gender, Sake Drinking, Shochu Drinking.
			0	1.00			
			1 - 19	2.00	0.44 - 9.78		
			> 19	1.80	0.36 - 8.86		
Tanaka, K et al; 1998	100	Cohort	No Abstractable Data				"Current smoking status (3 categories of never, past, and current smokers; P=0.54 for males and 0.40 for females) or pack-years (P=0.69 for males and 0.88 for females by the Cox model) was also not significantly related to risk increase."
Tanaka, K et al; 1995	762 Cases 1,027 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Study Center.
			Never Smoker	1.00			
			Ex-Smoker	2.80	1.1 - 6.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Study Center.
			Never Smoker	1.00			
			Current Smoker	1.80	0.9 - 3.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Study Center.
			0	1.00			
			0.1 - 12.9	2.40	1.1 - 4.9		
			> 12.9	1.80	0.8 - 3.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Family History of Cancer, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Study Center.
			Never Smoker	1.00			
			Ever Smoker	2.20	1.2 - 4.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Family History of Cancer, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.90	1.2 - 2.8		
Tanaka, K et al; 1995	334 Cases 351 Controls	Case-Control; Hospital-Based					Results from Fukuoka 2 Case-Control Study.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location, Time Period.
			Never Smoker	1.00			
			Ex-Smoker	3.90		> .05	

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location, Time Period.
			Never Smoker	1.00			
			Current Smoker	2.70		> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location, Time Period.
			0	1.00			
			0.1 - 12.9	6.40		> .05	
			> 12.9	1.50		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Family History of Cancer, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Residence Location, Time Period.
			Never Smoker	1.00			
			Ever Smoker	1.70	0.8 - 3.7		
Tanaka, K et al; 1995	224 Cases 266 Controls	Case-Control; Hospital-Based					Results from the Osaka Case-Control Study.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.90		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Ex-Smoker	1.00			
			Current Smoker	2.20		> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			0.1 - 12.9	3.80		> .05	
			> 12.9	2.10		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Family History of Cancer, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion.
			Never Smoker	1.00			
			Ever Smoker	2.20	1 - 5		
Tanaka, K et al; 1995	204 Cases 410 Controls	Case-Control; Hospital-Based					Results from Fukuoka 1 Case-Control Study.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.70		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00		> .05	

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			0.1 - 12.9	1.00		> .05	
			> 12.9	1.50		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Family History of Cancer, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion.
			Never Smoker	1.00			
			Ever Smoker	1.80	0.9 - 3.4		
Tanaka, K et al; 1988	124 Cases 250 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), All Subject, Whole Life. Adjusted for Age, Alcohol Consumption, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Residence Location.
			0	1.00			
			1 - 24	1.30	0.6 - 2.9		
			25 - 49	1.80	0.8 - 4.2		
			> 49	2.40	0.8 - 7.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), All Subject, Until Age 40. Adjusted for Age, Alcohol Consumption, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Residence Location.
			0	1.00			
			1 - 24	1.30	0.5 - 3.1		
			25 - 49	1.10	0.5 - 2.4		
			> 49	1.40	0.6 - 3.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), HB (-) & No Hist of Blood Trans, Lifetim. Adjusted for Age, Alcohol Consumption, Gender, Residence Location.
			0	1.00			
			1 - 24	1.30	0.5 - 3.2		
			25 - 49	2.20	0.9 - 5.5		
			> 49	3.80	1.1 - 12.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), HB & Blood Trans His (-), up to 40 Yrs. Adjusted for Age, Alcohol Consumption, Gender, Residence Location.
			0	1.00			
			1 - 24	1.00	0.3 - 2.9		
			25 - 49	1.00	0.4 - 2.5		
			> 49	1.80	0.7 - 4.7		
Tanaka, Keitaro et al; 1992	204 Cases 410 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Both). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.60	0.9 - 2.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Both). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.50	0.9 - 2.5		

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Both). Adjusted for Age, Gender, Residence Location.
			1 - 10.9	1.00			
			11 - 26.2	1.40	0.8 - 2.3		
			26.3 - 35.9	1.20	0.7 - 2.1		
			> 35.9	1.40	0.8 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.80	0.9 - 3.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.70	0.9 - 3.2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Male). Adjusted for Age, Gender, Residence Location.
			1 - 10.9	1.00			
			11 - 26.2	1.40	0.8 - 2.5		
			26.3 - 35.9	1.20	0.7 - 2.1		
			> 35.9	1.40	0.8 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Female). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.70	0.4 - 7.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Female). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.00	0.3 - 3.2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Female). Adjusted for Age, Gender, Residence Location.
			1 - 10.9	1.00			
			> 11	1.40	0.4 - 4.7		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-69), Gender (Both). Adjusted for Age, Alcohol Consumption, Family History/Index Disease, Gender, Hepatitis B Surface Antigen (HBsAg), History of Blood Transfusion, Residence Location.
			1 - 10.9	1.00			
			11 - 26.2	1.40	0.8 - 2.4		
			26.3 - 35.9	1.30	0.7 - 2.5		
			> 36	1.30	0.7 - 2.5		
Tsukuma, H et al; 1993	917	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Alpha-fetoprotein Level, Gender, Hepatitis B Viral Markers, Hepatitis C Viral Markers, Stage.
			Never Smoker	1.00			
			Ex-Smoker	1.68	0.63 - 4.47		

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Alpha-fetoprotein Level, Gender, Hepatitis B Viral Markers, Hepatitis C Viral Markers, Stage.
			Never Smoker	1.00			
			Current Smoker	2.30	0.9 - 5.86		
Tsukuma, H et al; 1990	229 Cases 266 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.3 - 2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.30	1.1 - 4.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.70	0.3 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.50	1.4 - 4.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	3.40			
			20 - 39	2.50			
			> 39	1.00			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0 - 19	1.00			
			20 - 39	1.60	0.9 - 2.8		
			40 - 59	1.90	1.1 - 3.4		
			> 59	0.90	0.5 - 1.7		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0 - 19	1.00			
			20 - 39	1.70	1 - 2.8		
			40 - 59	1.80	1 - 3.1		
			> 59	1.00	0.5 - 1.8		
Yamaguchi, G; 1993	466 Cases 466 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Admission.
			Non-Smoker	1.00			

Liver Cancer

Author	Subjects	Study Type	Data				Comments
			Current Smoker	1.16			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Admission.
			Non-Smoker	1.00			
			Current Smoker	1.00			

Liver Cirrhosis

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1989		Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.17	1 - 1.36		

Low Birth Weight

Author	Subjects	Study Type	Data				Comments
Kitamura, K; 1984	1,219 Cases 1,388 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Calendar Period, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.28			
Maruoka, K et al; 1998	23,132	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Gender, History of LBW Infant, Live Birth Order.
			Non-Smoker	1.00			
			Current Smoker	1.30	0.94 - 1.8	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Live Birth Order: First. Adjusted for Gender, History of LBW Infant, Live Birth Order.
			0	1.00			
			1 - 9	1.35	1.23 - 1.49		
			10 - 19	1.14	0.98 - 1.33		
			> 19	1.61	1.12 - 2.32		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Live Birth Order: Second. Adjusted for Gender, History of LBW Infant, Live Birth Order.
			0	1.00			
			1 - 9	3.25	2.9 - 3.6		
			10 - 19	2.71	2.42 - 3.05		
			> 19	1.78	0.88 - 3.61		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Live birth Order: Third. Adjusted for Gender, History of LBW Infant, Live Birth Order.
			0	1.00			
			1 - 9	0.96	0.57 - 1.61		
			10 - 19	1.35	0.94 - 1.93		
			> 19	3.27	1.55 - 6.88		
Matsubara, F et al; 2000	7,411	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Ex-Smoker	0.68	0.44 - 1.05		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Current Smoker	1.89	1.09 - 3.26		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 5	0.82	0.28 - 2.48		
			6 - 10	2.70	1.27 - 5.75		
			> 10	3.00	1.09 - 8.23		

Low Birth Weight

Author	Subjects	Study Type	Data				Comments
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Never Smoker	1.00			
			Ex-Smoker	1.05	0.43 - 2.61		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Never Smoker	1.00			
			Current Smoker	0.92	0.71 - 1.2		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 10	1.24	0.84 - 1.83		
			11 - 20	0.76	0.55 - 1.05		
			> 20	1.02	0.66 - 1.57		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Not Exposed	1.00			
			Exposed	0.99	0.75 - 1.3		
			Hours / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Gestational Age, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			< 2	1.12	0.82 - 1.54		
			> 1	0.83	0.59 - 1.19		
Nelson, EA et al; 2001	4,656	Cohort	No Abstractable Data				"Mothers who smoked had infants of lower mean birth weight (3213g, SD 615) than mothers who did not smoke (2257g, SD 552) (F=45, p<0.0001).
Ohmi, H et al; 2001	Not Specified	Cross Sectional	No Abstractable Data				Study concluded that the increase in smoking prevalence and the decrease in body mass index in young women, appear to be responsible for the increase in LBW babies.

Lung Cancer

Author	Subjects	Study Type	Data				Comments
Achiwa, H et al; 1999	130	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.62	0.45 - 5.816	> .05	
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	2.50	1.5 - 4.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	5.10			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.7 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	3.90	2.9 - 5.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			0	1.00			
			1 - 14	3.50	2.2 - 6		
			15 - 24	6.10			
			> 24	9.10	5.4 - 15.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Female). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			0	1.00			
			1 - 14	3.60	2.6 - 5		
			15 - 24	5.80	3.3 - 9.5		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	2.50	1.4 - 4.3		
			5 - 14	3.30	2.6 - 4.3		
			15 - 24	5.40	4.3 - 6.9		
			25 - 34	7.10	5.1 - 9.7		
			> 34	8.40	5.7 - 12.3		

Lung Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.90	1 - 3.2		
			5 - 14	2.50	1.9 - 3.3		
			> 14	3.10	1.8 - 5.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	4.50	3.6 - 5.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	2.50	2 - 3.2		
Akiba, S et al; 1986	92 Cases 252 Controls	Nested Case-Control					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender, In Another Study, Residence Location.
			0	1.00			
			1 - 19	1.30	0.7 - 2.3		
			20 - 29	1.50	0.8 - 2.8		
			> 29	2.10	0.7 - 2.5		
			Source: Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender, In Another Study, Residence Location.
			0	1.00			
			1 - 19	2.10	1 - 4.3		
			20 - 39	1.50	0.8 - 2.7		
			> 39	1.30	0.7 - 2.5		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Non-smoker. Adjusted for Age, Gender, In Another Study, Residence Location.
			Not Exposed	1.00			
			Exposed	1.50		> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse), Smoker. Adjusted for Age, Gender, In Another Study, Residence Location.
			Not Exposed	1.00			
			Exposed	3.60		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Husband Non-smoker. Adjusted for Age, Gender, In Another Study, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	2.20		> .05	
Ando, M et al; 2003	100,734	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			

Lung Cancer

Author	Subjects	Study Type	Data				Comments
			Current Smoker	4.46	3.1 - 6.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.38	1.61 - 3.51		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.56	1.12 - 5.83		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.58	2.24 - 5.73		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 30	1.20	0.6 - 2.5		
			30 - 39	3.30	2.1 - 8.2		
			> 39	5.40	3.7 - 7.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 10	2.30	1.1 - 4.6		
			10 - 19	3.20	2.1 - 8.2		
			20 - 29	5.20	3.5 - 7.6		
			> 29	7.90	5.2 - 12		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 20	2.10	1.1 - 3.8		
			20 - 39	3.10	2.1 - 4.7		
			40 - 59	5.90	4 - 8.7		
			> 59	7.70	5 - 11.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 20	0.70	0.3 - 1.7		
			20 - 39	1.70	1 - 2.9		
			40 - 59	3.00	1.8 - 5.1		
			> 59	5.00	3 - 8.5		

Lung Cancer

Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 5	4.30	2.7 - 6.9		
			5 - 9	2.20	1.2 - 4		
			10 - 14	1.90	1 - 3.6		
			> 14	0.80	0.4 - 1.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 10	0.50	0.1 - 3.9		
			10 - 19	1.30	0.7 - 2.4		
			20 - 29	2.30	1.4 - 3.7		
			> 29	3.50	2.1 - 5.7		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 30	0.70	0.3 - 1.4		
			30 - 39	2.10	1.2 - 3.7		
			> 39	4.30	2.7 - 6.9		
Chyou, PH et al; 1993	7,961	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	3.10	1.6 - 5.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	11.40	6.5 - 20.1		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 24.99	2.20	1.1 - 4.8		
			25 - 49.99	3.10	1.4 - 7.1		
			> 49.99	6.30	2.6 - 15.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 24.99	4.30	2.1 - 9		
			25 - 49.99	9.80	5.5 - 17.6		
			> 49.99	23.30	12.9 - 41.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	16.00			

Lung Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	6.80			
Chyou, PH et al; 1992	7,760	Cohort					Oral cancer refers to "Oral-bladder cancer".
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.20	1.6 - 6.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Current Smoker	12.00	6.7 - 21.6		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Gender.
			0	1.00			
			1 - 30	6.30	3.3 - 12.3		
			31 - 45	9.00	4.8 - 17.1		
			> 45	23.30	12.8 - 42.6		
Cullen, JW et al; 1986		Review	No Abstractable Data				Findings show that systematic smoking control strategies for lung cancer control are being emphasized over traditional approaches like reducing cigarette tar and nicotine levels.
Esaki, H et al; 1977	245 Cases 245 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			< 15	1.10			
			15 - 29	2.23			
			> 29	5.95			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.46			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.90			
Gao, CM et al; 1993	282 Cases 282 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	3.56	1.83 - 6.91		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	6.61	3.47 - 12.58		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 19	3.46	1.57 - 7.19		
			20 - 29	7.53	3.71 - 15.3		
			> 29	10.63	5.08 - 22.22		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 4	5.14	2.31 - 11.4		
			5 - 9	3.48	1.15 - 8.01		
			10 - 14	3.83	1.55 - 9.46		
			15 - 19	3.35	1.05 - 10.66		
			> 19	1.38	0.51 - 3.74		
Hinds, MW et al; 1981	375 Cases 1,812 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Gender, Socioeconomic Status (SES).
			Never Smoker	1.00			
			Ever Smoker	4.90	3.2 - 7.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Socioeconomic Status (SES).
			Never Smoker	1.00			
			Ever Smoker	4.00	2.3 - 6.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Epidermoid Carcinoma). Adjusted for Age, Gender, Socioeconomic Status (SES).
			Never Smoker	1.00			
			Ever Smoker	12.70	5 - 32.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Large Cell Carcinoma). Adjusted for Age, Gender, Socioeconomic Status (SES).
			Never Smoker	1.00			
			Ever Smoker	4.60	1.6 - 12.8		
Hirayama, T; 1992	265,118	Cohort					Cardiovascular disease endpoint = Ischemic heart disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			Never Smoker	1.00			
			Ex-Smoker	1.49		< .01	

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Occupation.
			0	1.00			
			1 - 19	1.50			
			> 19	1.93			
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.45	3.72 - 5.31		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.34	1.94 - 2.82		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.06	1.57 - 2.71		
			10 - 19	4.00	3.32 - 4.82		
			> 19	6.24	5.24 - 7.42		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.25	1.73 - 2.93		
			10 - 19	2.56	1.95 - 3.36		
			> 19	4.47	2.95 - 6.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.31			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	4.22			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	5.10			

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Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	2.03	1.21 - 3.39		
			5 - 9	1.59	0.76 - 3.31		
			> 9	1.38	0.68 - 2.81		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	3.72	1.36 - 10.22		
			5 - 9	3.29	0.74 - 14.67		
			> 9	0.97	0.05 - 17.74		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.06			
			10 - 14	3.57			
			15 - 19	4.78			
			20 - 29	6.14			
			30 - 39	5.90			
			40 - 49	7.37			
			> 49	15.09			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	2.11			
			5 - 9	2.31			
			10 - 19	2.56			
			20 - 29	4.44			
			> 29	4.67			
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age of Spouse, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.36	0.85 - 2.18		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Age of Spouse, Gender.
			0	1.00			
			1 - 14	1.42	1.01 - 2.01		
			15 - 19	1.58	0.98 - 2.38		
			> 19	1.91	1.34 - 2.71		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.66	3.19 - 4.2		
Hirayama, T; 1986	265,118	Cohort					

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.12			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 4	0.87			
			> 4	0.51			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Daily Green-Yellow Vegetable Intake.
			0	1.00			
			1 - 4	0.30			
			> 4	0.30			
Hirayama, T; 1985	91,450	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			Never Smoker	1.00			
			Ex-Smoker	1.36			
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			0	1.00			
			1 - 14	1.42			
			15 - 19	1.53			
			> 19	1.91			
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	6.64			
Hirayama, T; 1984	Not Specified	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.36			
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 14	1.42			
			15 - 19	1.53			
			> 19	1.91			

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Author	Subjects	Study Type	Data				Comments
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 19	2.14	0.98 - 4.65		
			> 19	2.31	0.9 - 5.94		
Hirayama, T; 1981	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			Never Smoker	1.00			
			Ex-Smoker	2.01			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 9	2.03			
			10 - 14	3.71			
			15 - 24	5.04			
			25 - 49	6.83			
			> 49	8.57			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Ex-Smoker	2.00			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 14	3.09			
			15 - 24	5.09			
			25 - 49	6.33			
			> 49	6.80			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), < 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	0.34			
			> 4	0.28			
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), >= 200,000 Lifetime Cigarettes.
			0	1.00			
			1 - 4	0.95			
			> 4	0.36			
Hirayama, T; 1981	91,540	Cohort					The asthma outcome also includes women with emphysema.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			0	1.00			
			1 - 19	1.61			
			> 19	2.08			

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Author	Subjects	Study Type	Data				Comments
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			Not Exposed	1.00			
			Exposed	1.78			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.50			
			20 - 39	3.10			
			> 39	1.10			
Ito, H et al; 2002	138 Cases 241 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Ser Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.07	0.4 - 1.06		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Ser Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.89	0.47 - 7.68		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Cys Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.84	0.31 - 2.26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Cys Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.92	0.38 - 2.25		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Cys/Cys Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.54	0.42 - 5.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Cys/Cys Genotype. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.47	0.5 - 12.24		
Jacobs, David R et al; 1999	12,763	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			Never Smoker	1.00			

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Author	Subjects	Study Type	Data				Comments
			Ex-Smoker	0.50	0.2 - 1.26		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, Cardiovascular Disease, Country, Gender, Serum Cholesterol, Systolic Blood Pressure.
			0	1.00			
			1 - 9	2.40	1.4 - 4.08		
			> 9	6.50	4.22 - 9.96		
Katada, H et al; 1988	25 Cases 50 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.21		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	10.00		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.06		< .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types), ETS Time (Lifetime). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	7.29		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), ETS Time (Lifetime). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	2.67		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), ETS Time (Lifetime). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	4.73		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types), ETS Time (Adulthood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	6.67		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), ETS Time (Adulthood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	2.67		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), ETS Time (Adulthood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	5.33		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types), ETS Time (Childhood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	7.43		> .05	

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Author	Subjects	Study Type	Data				Comments
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), ETS Time (Childhood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	3.00		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), ETS Time (Childhood). Adjusted for Age, Gender.
			Not Exposed	1.00			
			Exposed	12.00		> .05	
Kato, I et al; 1985	265 Cases 1,412 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	5.04		< .05	
Kawahara, M et al; 1998	70	Cohort					The outcome was development of a second primary tumor in persons who had survived at least 2 years cancer-free. Upper aerodigestive tract=epithelial regions of the head and neck, lung and oesophagus. Cancer=Smoking-related cancers including cancer of the lung, larynx, oral cavity including pharynx, oesophagus, pancreas, bladder, kidney, stomach and uterine cervix.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Etoposide, Gender, Intercurrent Smoking, Performance Status, Radiation Exposure.
			0 - 44	1.00			
			> 44	0.90	0.2 - 3.3	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Etoposide, Gender, Intercurrent Smoking, Performance Status, Radiation Exposure.
			Non-Smoker	1.00			
			Current Smoker	4.30	1.1 - 15.9	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	5.40	2.7 - 9.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Ex-Smoker	1.60	0.3 - 4.6		
Kawajiri, K et al; 1996	187	Cohort	No Abstractable Data				Findings suggest that polymorphisms associated with genetic predisposition for lung cancer, is related to smoking-associated p53 mutations. p53 mutations were observed more in heavy smokers than never smokers.
Kawajiri, K et al; 1990	2,500	Cohort	No Abstractable Data				The study found that the genetically susceptible patients with genotype C contracted lung cancer with less cigarette dose than other types.
Kawaminami, K et al; 2003	10,546	Cohort					

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	2.35	0.62 - 8.91	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	6.76			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	5.99	1.84 - 19.51	< .05	
			21 - 40	11.16	3.31 - 37.66	< .05	
			> 40	13.10	2.88 - 59.7	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.67			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Body Mass Index, Gender, Residence Location.
			0	1.00			
			1 - 20	3.40	1.29 - 8.93		
			21 - 40	10.25	1.19 - 88.26		
Kihara, M et al; 1995	447 Cases 469 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Squamous Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ever Smoker	6.82			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Squamous Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	9.50			
			40 - 59	26.20			
			> 59	30.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Squamous Cell Carcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	0.40			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Squamous Cell Carcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	2.90			
			40 - 59	3.60			
			> 59	3.60			

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	8.50			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	14.80			
			40 - 59	35.30			
			> 59	36.20			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	5.70			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	8.80			
			40 - 59	18.70			
			> 59	15.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	7.30			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	11.00			
			40 - 59	28.80			
			> 59	32.10			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Large Cell Carcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	5.90			
			> 59	6.30			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Adenocarcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	1.50			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Adenocarcinoma), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	1.60			
			40 - 59	1.40			
			> 59	1.70			

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Adenocarcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	0.80			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Adenocarcinoma), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	2.10			
			40 - 59	2.40			
			> 59	2.10			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Other), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	0.40			
			40 - 59	0.70			
			> 59	0.90			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Other), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	10.40			
			40 - 59	12.60			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Other), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	1.70			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (All types), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	1.80			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (All types), GSTM1-Positive. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	2.50			
			40 - 59	3.60			
			> 59	3.40			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (All types), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			Never Smoker	1.00			
			Ex-Smoker	1.70			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (All types), GSTM1-Negative. Adjusted for GSTM1 Genotype.
			0	1.00			
			< 40	3.60			
			40 - 59	6.50			
			> 59	6.40			

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Author	Subjects	Study Type	Data				Comments
Kihara, M et al; 1994	178 Cases 201 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.22	0.36 - 4.14		
			20 - 30	1.49	0.53 - 4.22		
			> 30	3.18	0.98 - 10.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.87	0.23 - 3.26		
			20 - 30	2.44	0.72 - 8.73		
			> 30	3.66	0.64 - 27.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.32	0.54 - 3.24		
			20 - 30	1.49	0.53 - 4.22		
			> 30	1.22	0.33 - 4.55		
Kobayashi, Y et al; 1990	22 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls ($p<0.05$). Heavy smokers were also more prevalent among MPC cases than among controls ($p<0.1$)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases ($p<0.1$)"
Kolonel, L; 1979		Cross Sectional	No Abstractable Data				Caucasian men had a greatest lifetime cigarette use while Chinese and Filipino men had the lowest. Smoking cigarettes was highest among Caucasian women and lowest among Chinese. Data did not explain unusually high incidence of lung and esophageal cancer in Hawaiian males.
Kondo, K et al; 1996	53	Cross Sectional	No Abstractable Data				Findings suggest the frequency of p53 mutation correlated with the amount of the tobacco smoked.
Kono, S et al; 1985	5,477	Cohort					Upper aerodigestive cancer: Cancer with ICD 8th codes 140-150 (Malignant neoplasm of buccal cavity, pharynx and oesophagus), 160 (Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses) and 161 (Malignant neoplasm of larynx).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	0.69	0.16 - 3.1		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	4.31	1.5 - 12.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	1.87	0.41 - 8.38		
			10 - 19	3.78	1.2 - 11.9		
			> 19	7.47	2.44 - 22.9		
Kono, Suminori et al; 1987		Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	3.18	1.57 - 6.45		
			> 19	8.15	4.12 - 16.1		
Kumimoto, H et al; 2002	191 Cases 241 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by LL Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ever Smoker	0.92	0.32 - 2.68	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by LS Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ever Smoker	2.30	1.05 - 5.04	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by SS Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ever Smoker	3.19	0.92 - 11.06	> .05	
Le Marchand, L et al; 1995	1,353	Ecological Study	No Abstractable Data				A stepwise regression model of lung cancer incidence on smoking produced a regression coefficient for pack-years (continuous) of -0.6 (P = 0.92, adjusted for gender, gender x pack-years, lutein, vitamin E, height, cholesterol, and yellow-orange vegetable intake).
Minowa, M et al; 1991	96 Cases 86 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Hospital Type.
			Non-Smoker	1.00			
			Ex-Smoker	7.69		< .05	

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Hospital Type.
			Non-Smoker	1.00			
			Ever Smoker	6.52		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Kreyberg I & II. Adjusted for Age, Asbestos Exposure, Gender, Hospital Type.
			Non-Smoker	1.00			
			Ever Smoker	6.01		< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Hospital Type.
			0	1.00			
			1 - 19	6.78		< .01	
			> 19	6.42		< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Kreyberg I. Adjusted for Age, Asbestos Exposure, Gender, Hospital Type.
			Non-Smoker	1.00			
			Ever Smoker	13.51		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Kreyberg II. Adjusted for Age, Asbestos Exposure, Gender, Hospital Type.
			Non-Smoker	1.00			
			Ever Smoker	1.64		> .05	
Mizoue, Tetsuya et al; 2000	4,050	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.5 - 3.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.10	0.8 - 5.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			0	1.00			
			1 - 24	1.40	0.5 - 4		
			> 24	5.00	1.7 - 14.9		
Mizuno, S et al; 1989	Not Specified	Other	No Abstractable Data				"For nonsmokers, the estimated lung cancer mortality rate was comparable to the rates reported in the US or Britain, assigning 20 to 25% proportions of nonsmokers." "For smokers, the estimated duration of smoking was shorter than would be expected from the age when smoking was started according to various epidemiological surveys." "The estimated average numbers of cigarettes smoked per day by smokers were similar to those obtained by epidemiological

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Author	Subjects	Study Type	Data				Comments
							studies".
Mizuno, S et al; 1989	49,013	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			5 - 14	1.00			
			15 - 24	1.70			
			25 - 34	2.50			
			> 34	2.70			
Mulder, I et al; 2000	12,763	Cohort	No Abstractable Data				This article presented an analysis of lung cancer among never- and current smokers in different areas of the Seven Countries Study. The RRs (adjusted for age and cigarettes per day) were as follows: Japan: 1.00 (Reference) Serbia: 1.67 (0.83-3.35) Mediterranean southern Europe: 1.61 (0.93-2.79) Inland southern Europe: 2.08 (1.22-3.54) United States: 2.67 (1.57-4.54) Northern Europe: 5.40 (3.25-8.97)
Nakachi, K et al; 1995	80 Cases 160 Controls	Case-Control; Hospital-Based	No Abstractable Data				"The risk ratio of genotype C or Val/Val to A or Ile/Ile for adenocarcinoma was unaltered at different cigarette dose levels, although the risk ratio for squamous cell carcinoma has been decreased at a higher dose level."
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.90	0.81 - 4.4		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.39	0.11 - 1.4		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, History of Lung Diseases, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.80	0.67 - 4.6	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, History of Lung Diseases, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.53	0.18 - 1.5	> .05	
Pierce, JP et al; 1992	Not Specified	Other	No Abstractable Data				Tobacco-consumption model was used to estimate future lung cancer mortality rates. Analysis shows that lung cancer mortality rates will increase in most European countries by the year 2000, but afterwards the

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Author	Subjects	Study Type	Data				Comments
							epidemic will mostly occur in Asia.
Sakai, R; 1989	64 Cases 128 Controls	Case-Control; Hospital-Based					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			< 20	4.30	1.3 - 13.5		
			20	3.30	0.9 - 4.6		
			> 20	4.50	1.5 - 13.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age.
			0	1.00			
			< 20	3.00	0.7 - 12.6		
			20	6.00	1.3 - 28.9		
			> 20	9.00	1.4 - 58.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	2.50	1.2 - 5.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	6.30	1.9 - 21		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			
			Current Smoker	2.90	1.09 - 5.4		
Sakurai, R et al; 1989	1,083	Longitudinal	No Abstractable Data				The observed/expected ratio was 20 for smoking patients vs. 4.5 in non smokers and was significantly different (p<0.001).
Satoh, H et al; 1999	877	Cross Sectional	No Abstractable Data				"The percentage of non-smokers in female patients was significantly higher (77.5% 172/222 cases) compared to that in male patients (10.4% 68/655 cases) (p=0.0001). In female patients, the percentage of non-smoking patients in histological subtypes other than SCLC [small cell lung cancer] was higher than 50%. However, in male patients, the percentage of non-smoking patients in each subtypes was lower than 20%. Among the female patients, percentage of non-smoker in SCLC (42.1%) and SqLC [squamous cell lung cancer] (35%) was lower than that of lung adenocarcinoma (83.1%) (p=0.0001, p=0.0001, respectively)."
Sekine, I et al; 1999	3,312	Cross Sectional	No Abstractable Data				"Among female patients, 39% in both age groups were smokers (former or current), but heavy smokers (40 cigarettes per day or more) were found only in the older group. Among male patients, in contrast, there were fewer smokers (former or current) in the young group (84%) than in the older group (95%) (P<0.0001). In addition, heavy smokers were more numerous in the older male group (18%) than in the young

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Author	Subjects	Study Type	Data				Comments
							group (7%) (p=0.056)."
Sekine, I et al; 1998	109	Cohort					Outcome of interest = p53 mutation in lung cancer patients.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Histology.
			< 30	1.00			
			30 - 59	1.92	0.55 - 7.94	> .05	
			> 59	4.21	1.09 - 19	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Histology.
			Non-Smoker	1.00			
			Current Smoker	3.23	0.48 - 25.4	> .05	
Shimizu, H et al; 1994	605 Cases 183 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	10.30	2.8 - 37.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age.
			0	1.00			
			1 - 20	5.00	1.1 - 21.7		
			> 20	18.60	4.9 - 70.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age.
			0	1.00			
			1 - 20	8.20	2.1 - 30.4		
			> 20	15.50	4.4 - 55.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			0	1.00			
			1 - 20	1.10	0.6 - 2.3		
			> 20	2.10	1 - 4.5		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age.
			0	1.00			
			1 - 40	5.10	1.2 - 21.2		
			> 40	16.50	3.8 - 70.5		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age.
			0	1.00			
			1 - 40	6.00	1.4 - 25.3		
			> 40	20.70	5.2 - 82		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			0	1.00			
			1 - 40	1.10	0.5 - 2.2		
			> 40	2.20	0.9 - 5.6		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	12.80	5.1 - 32.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.50	0.8 - 2.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.60	0.8 - 3.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Tubular Type. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.70	0.7 - 4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Tubular Type. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.90	0.7 - 5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.00	0.5 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.10	0.6 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	7.40	2.2 - 25.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	10.70	3.2 - 35.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Peripheral. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.80	0.9 - 3.6		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Central. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	0.50	0.1 - 3.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Central. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.30	0.2 - 7.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Peripheral. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.00	0.6 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	6.50	1.6 - 26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	4.40	0.8 - 25.7		
Shimizu, H et al; 1988	90 Cases 163 Controls	Case-Control; Hospital-Based					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	1.10		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Mother). Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	2.10		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Father). Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	1.10		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Other Household), Husband's Father. Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	3.20		< .05	

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Author	Subjects	Study Type	Data				Comments
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Other Household), Husband's Mother. Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	0.80		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Other Household), Children. Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	0.80		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Residence), ETS Source (Siblings). Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	0.80		> .05	
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Not Specified), ETS Location (Workplace), ETS Source (Not Specified). Adjusted for Age, Date of Admission, Gender, Hospital Type, Occupational Exposure to Iron, Smoking by Father, Smoking by Mother.
			Not Exposed	1.00			
			Exposed	1.20		> .05	
Shimizu, H et al; 1986	751 Cases 1,473 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	3.70	2.7 - 5.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	3.40	2.1 - 5.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	1.90	1.3 - 3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	2.90	1.7 - 5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	4.30	2.8 - 6.7		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	6.40	2.3 - 17.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	3.90	2 - 7.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	4.50	1.8 - 10.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	3.40	1.8 - 6.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Large Cell Carcinoma). Adjusted for Age, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	4.00	1.6 - 10.3		
Sobue, T et al; 2002	91,738	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.20	1.4 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	4.50	3 - 6.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.70	1.4 - 10.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	4.20	2.4 - 7.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	5.10	1.8 - 14.6		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	12.70	4.7 - 34.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	10.80	1.2 - 94.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	17.50	4.9 - 62.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.7 - 2.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.80	1.6 - 4.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	4.30	1.3 - 13.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.00	0.8 - 5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 19	3.50	0.9 - 13.9		
			20 - 39	13.40	4.8 - 37.1		
			40 - 59	15.90	5.6 - 45.1		
			> 59	15.20	5 - 46.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 19	2.70	1.5 - 4.9		
			20 - 39	4.50	2.9 - 6.9		
			40 - 59	4.80	3 - 7.6		
			> 59	6.40	3.8 - 10.7		

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Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 19	2.60	1.2 - 5.7		
			20 - 39	2.80	1.5 - 5.2		
			40 - 59	2.90	1.5 - 5.6		
			> 59	3.00	1.3 - 7		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 10	3.00	1.9 - 5		
			10 - 19	1.80	1 - 3.3		
			> 19	1.00	0.4 - 2.4		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 10	8.00	2.7 - 23.7		
			10 - 19	4.00	1.1 - 14.2		
			> 19	1.00	0.1 - 9.3		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			0	1.00			
			1 - 10	2.00	1 - 4.1		
			10 - 19	0.60	0.2 - 1.9		
			> 19	1.10	0.4 - 3.5		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			< 24	1.00			
			25 - 34	1.90	0.8 - 4.6		
			35 - 44	2.80	1.1 - 7.4		
			> 44	4.00	1.3 - 12		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			< 24	1.00			
			25 - 34	7.90	0.8 - 75.1		
			35 - 44	9.10	0.9 - 92.3		
			> 44	13.90	1.2 - 160.7		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			< 24	1.00			
			25 - 34	1.60	0.4 - 6.3		
			35 - 44	3.50	0.7 - 15.9		
			> 44	4.90	0.8 - 29.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Area, Gender.
			< 19	1.00			
			20 - 29	1.20	0.9 - 1.7		
			30 - 39	1.40	0.9 - 2.2		
			> 39	1.60	1 - 2.6		

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma and Squamous Cell Carcinoma). Adjusted for Age, Area, Gender.
			< 19	1.00			
			20 - 29	1.50	1 - 2.5		
			30 - 39	1.30	0.7 - 2.7		
			> 39	2.00	1 - 4.1		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Area, Gender.
			< 19	1.00			
			20 - 29	1.10	0.7 - 1.9		
			30 - 39	1.30	0.6 - 2.6		
			> 39	0.80	0.3 - 2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Area, Gender.
			0	1.00			
			< 29	3.30	1.7 - 6.5		
			> 29	10.10	4 - 25.1		
Sobue, T et al; 1994	1,376 Cases 2,230 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	13.10	5.2 - 33.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	18.10	7.9 - 41.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.50	0.9 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.90	1.3 - 3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	9.20	1.5 - 56.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	21.40	5.3 - 87.1		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	2.60	0.7 - 10		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	3.80	1.2 - 12.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	5.60	2.3 - 13.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	9.70	5.5 - 16.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.70	1 - 3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.30	0.9 - 2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	4.70	1.3 - 17.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	12.10	6.3 - 23.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Large Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	4.10	1.4 - 32.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Large Cell Carcinoma). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	3.70	1.1 - 11.7		

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Author	Subjects	Study Type	Data				Comments
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			1 - 29	1.00			
			30 - 39	2.10	1.2 - 3.8		
			40 - 49	4.30	2.4 - 7.7		
			> 49	8.00	4.3 - 14.9		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			1 - 29	1.00			
			30 - 39	1.10	0.7 - 1.8		
			40 - 49	2.00	1.3 - 2.2		
			> 49	2.10	1.2 - 3.7		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age.
			1 - 29	1.00			
			30 - 39	2.40	0.9 - 6.2		
			40 - 49	4.30	1.7 - 10.9		
			> 49	7.60	2.8 - 20		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age.
			1 - 29	1.00			
			30 - 39	1.30	0.5 - 3.2		
			40 - 49	2.10	0.8 - 5.3		
			> 49	1.60	0.5 - 4.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age.
			1 - 19	1.00			
			20 - 29	1.50	1 - 2.3		
			> 29	1.90	1.2 - 2.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age.
			1 - 19	1.00			
			20 - 29	1.20	0.8 - 1.8		
			> 29	1.20	0.8 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age.
			1 - 19	1.00			
			20 - 29	0.80	0.4 - 1.5		
			> 29	2.30	1.3 - 4.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age.
			1 - 19	1.00			
			20 - 29	2.10	0.8 - 5.3		
			> 29	2.60	1 - 6.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	2.80	1.9 - 4.2		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	4.10	2.8 - 5.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	2.80	2 - 3.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	2.10	1.4 - 3.2		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types).
			1 - 29	1.00			
			30 - 39	1.50	1 - 2.2		
			40 - 49	2.80	2 - 4.1		
			> 49	4.10	2.7 - 6.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types).
			1 - 19	1.00			
			20 - 29	1.30	1 - 1.8		
			> 29	1.70	1.2 - 2.3		
Sobue, T et al; 1993	776 Cases 772 Controls	Case-Control; Hospital-Based					
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (55-64), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.85	0.49 - 1.47		
			5 - 9	0.47	0.25 - 0.92		
			> 9	0.34	0.18 - 0.64		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.87	0.5 - 1.49		
			5 - 9	0.61	0.34 - 1.1		
			> 9	0.35	0.2 - 0.59		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (65-74), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.96	0.51 - 1.8		
			5 - 9	0.69	0.36 - 1.32		
			> 9	0.41	0.23 - 0.72		

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Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (70-79), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.85	0.43 - 1.7		
			5 - 9	0.49	0.23 - 1.06		
			> 9	0.50	0.27 - 0.94		
Sobue, T; 1990	144 Cases 713 Controls	Case-Control; Hospital-Based					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Childhood), ETS Source (Father). Adjusted for Age, Education, Gender.
			Not Exposed	1.00			
			Exposed	0.79	0.52 - 1.21		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Childhood), ETS Source (Other Household). Adjusted for Age, Education, Gender.
			Non-Smoker	1.00			
			Exposed	1.18	0.76 - 1.84		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Education, Gender.
			Not Exposed	1.00			
			Exposed	1.13	0.78 - 1.63		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Age at Hospitalization, Education, Gender, Mother Smoked in Childhood, Use of Wood or Straw Cooking Fuels.
			Not Exposed	1.00			
			Exposed	1.50	1.01 - 2.22		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Mother). Adjusted for Age, Age at Hospitalization, Education, Gender, Other Household Member Smoked, Use of Wood or Straw Cooking Fuels.
			Not Exposed	1.00			
			Exposed	1.28	0.71 - 2.31		
Sobue, T et al; 1988	2,083 Cases	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	6.90	4.9 - 9.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), Central. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	8.30	4.6 - 15.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	7.20	4.8 - 10.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	6.10	3.4 - 11.1		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	5.20	4.2 - 6.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Large Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	4.10	2.4 - 7.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Small Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	6.90	4.6 - 10.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.10	2.4 - 3.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.80	1.4 - 2.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Large Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.80	1.5 - 9.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Small Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	14.40	9.3 - 22.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), Peripheral. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	4.70	3.4 - 6.5		
Soda, H et al; 2000	7,977	Cohort	No Abstractable Data				The study suggests that cigarettes increase the risk of lung adenocarcinoma as well as squamous cell carcinoma. Smoking prevention has an effect in reducing the incidence of lung adenocarcinoma among smokers.
Stellman, SD et al; 2001	371 Cases 373 Controls	Case-Control; Hospital-Based					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Interview, Education, Hospital.
			0	1.00			
			< 20	10.90	4.4 - 28		
			20 - 29	53.40	23.1 - 135.2		

Author	Subjects	Study Type	Data				Comments
			> 29	73.30	32.5 - 181.6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Date of Interview, Education, Hospital.
			0	1.00			
			< 20	7.00	2.2 - 22.4		
			20 - 29	37.30	12.7 - 109.7		
			> 29	54.60	18.8 - 158.4		
Stellman, SD et al; 2001	410 Cases 411 Controls	Case-Control; Hospital-Based					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Interview, Education, Hospital.
			0	1.00			
			< 20	1.60	0.7 - 3.9		
			20 - 29	3.50	1.5 - 8.4		
			> 29	6.20	2.6 - 15		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Date of Interview, Education, Hospital.
			0	1.00			
			< 20	0.60	0.2 - 1.8		
			20 - 29	2.20	0.8 - 5.9		
			> 29	3.30	1.2 - 8.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Date of Interview, Education, Hospital.
			0	1.00			
			< 20	7.40	1.3 - 42.2		
			20 - 29	13.70	2.5 - 76.2		
			> 29	31.80	5.4 - 185.8		
Sugimura, H et al; 1995	322 Cases 328 Controls	Case-Control; Hospital-Based	No Abstractable Data				"When the cases were categorized by lifetime smoking dose, and analysis was performed in squamous cell carcinoma, the OR of Val-containing genotype for lung cancer cases increases as the smoking dose decreased (OR = 1.97 for patients with smoking history of more than 60 pack-years vs. OR = 2.92 for smokers with less than 40 pack-years.)
Sugimura, H et al; 1987	72 Cases 143 Controls	Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			< 2.5	1.00			
			2.5 - 20	6.30			
			> 20	3.40			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female).
			< 2.5	1.00			
			2.5 - 20	0.00			
			> 20	2.30			

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Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			< 2.5	1.00			
			2.5 - 20	2.20			
			> 20	2.30			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Unicentric Lung Cancer.
			< 20	1.00			
			20 - 40	1.59			
			40 - 80	1.75			
			> 80	2.16			
Sugita, M et al; 1998		Meta-analysis					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), All Countries.
			Not Exposed	1.00			
			Exposed	1.28	1.13 - 1.46		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), Greece.
			Not Exposed	1.00			
			Exposed	2.01	1.33 - 3.04		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), Hong Kong.
			Not Exposed	1.00			
			Exposed	1.46	0.94 - 2.29		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), Japan.
			Not Exposed	1.00			
			Exposed	1.41	1.14 - 1.75		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), United States.
			Not Exposed	1.00			
			Exposed	1.11	0.97 - 1.28		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), Europe.
			Not Exposed	1.00			
			Exposed	1.17	0.79 - 1.73		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by ETS Time (Not Specified), ETS Source (Not Specified), China.
			Not Exposed	1.00			
			Exposed	1.08	0.71 - 1.66		
Suzuki, H et al; 1992	30	Cross Sectional	No Abstractable Data				Findings show the presence of p53 mutation among lung cancer patients is closely associated with lifetime cigarette consumption.
Suzuki, T et al; 1990	238 Cases 476 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	3.20	1.52 - 6.63		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	5.00	2.71 - 9.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.48 - 5.51		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	2.40	1.19 - 4.86		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Well Differentiated. Adjusted for Age, Gender, Hospital Type.
			0	1.00			
			1 - 29	1.20	0.32 - 4.26		
			30 - 59	1.90	0.61 - 5.89		
			> 59	15.60	1.7 - 143		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Moderately Differentiated. Adjusted for Age, Gender, Hospital Type.
			0	1.00			
			1 - 29	3.90	0.95 - 15.7		
			30 - 59	6.50	2.09 - 20.4		
			> 59	22.10	2.58 - 87.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Poorly Differentiated. Adjusted for Age, Gender, Hospital Type.
			0	1.00			
			1 - 29	6.60	1.5 - 29		
			30 - 59	7.80	2.14 - 28		
			> 59	17.50	3.48 - 88.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Well Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.23 - 4.44		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Well Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	2.10	0.8 - 5.67		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Moderately Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	4.10	1.26 - 13.1		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Moderately Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	7.70	2.58 - 23.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Poorly Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	8.50	1.87 - 38.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Poorly Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	7.90	2.3 - 26.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Well Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	1.70	0.32 - 9.06		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Well Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	1.30	0.41 - 4.37		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Moderately Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	2.30	0.77 - 6.66		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Poorly Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	10.60	1.25 - 89		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Moderately Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	4.10	1.25 - 13.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Poorly Differentiated. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	9.90	2.1 - 47.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Tubular Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	4.70	1.4 - 15.6		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Tubular Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	3.70	1.37 - 10.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	6.10	2.78 - 13.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	2.50	0.97 - 6.42		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Tubular Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	2.00	0.13 - 32		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.37 - 5.52		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma), Papillary Type. Adjusted for Age, Gender, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	1.40	0.6 - 3.06		
Tsugane, S et al; 1987	185 Cases 185 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			Never Smoker	1.00			
			Current Smoker	0.80			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			Never Smoker	1.00			
			Current Smoker	4.85		> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			< 10	1.00			
			10 - 29	0.35	0.16 - 0.76		
			> 29	0.30	0.34 - 1.89		

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			0				
			1 - 15	0.94	0.38 - 2.36		
			> 15	0.87	0.38 - 1.96		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			Never Smoker	1.00			
			Ever Smoker	0.89	0.42 - 1.92	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			Never Smoker	1.00			
			Ever Smoker	0.55	0.18 - 1.68	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			Never Smoker	1.00			
			Current Smoker	0.55			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location, Year of Interview.
			< 10	1.00			
			10 - 29	3.00	0.28 - 31.7		
			> 29	21.00	2.6 - 170		
Wakai, K et al; 2001	33,654	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	5.16	3.56 - 7.49		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			< 4	4.84	3 - 7.79		
			5 - 9	3.19	1.84 - 5.53		
			10 - 14	2.03	1.02 - 4.03		
			15 - 19	1.29	0.46 - 3.63		
			> 19	0.99	0.047 - 2.08		
Wakai, K et al; 1997	333 Cases 666 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	2.43	1.16 - 5.06	< .05	

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	4.40	2.19 - 8.85	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Gender, Residence Location.
			Ever Smoker	1.00			
			Ex-Smoker	5.33	1.21 - 23.5	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (All types). Adjusted for Age, Gender, Residence Location.
			Ex-Smoker	1.00			
			Current Smoker	4.37	2.21 - 8.62	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	6.16	1.42 - 26.7	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	9.82	2.36 - 41	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	9.76	0.85 - 112	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	28.20	7.55 - 105	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.59 - 3.31	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	2.18	1 - 4.76	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	2.69	0.68 - 10.6	> .05	

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	1.14	0.49 - 2.61	> .05	
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			5 - 9	2.48	1.04 - 5.92	< .05	
			10 - 19	3.63	1.56 - 8.44	< .01	
			> 19	1.00	0.35 - 2.83	> .05	
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			5 - 9	7.47	1.58 - 35.3	< .05	
			10 - 19	8.95	1.91 - 42	< .01	
			> 19	2.05	0.33 - 12.8	> .05	
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			5 - 9	1.23	0.42 - 3.64	> .05	
			10 - 19	2.49	0.95 - 6.53	> .05	
			> 19	0.54	0.14 - 2.16	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.80	0.81 - 4.02	> .05	
			20 - 29	4.01	1.91 - 8.41	< .001	
			> 29	9.19	4.2 - 20.1	< .001	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	3.95	0.86 - 18.1	> .05	
			20 - 29	10.40	2.43 - 44.3	< .01	
			> 29	24.00	5.46 - 105	< .001	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.30	0.52 - 3.21	> .05	
			20 - 29	1.93	0.84 - 4.44	> .05	
			> 29	4.53	1.89 - 10.9	< .001	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (All types). Adjusted for Age, Age Started Smoking, Fraction Smoked per Cigarette, Gender, Residence Location, Smoke Inhalation, Type of Cigarette.
			1 - 19	1.00			
			20 - 29	2.07	1.24 - 3.46	< .01	
			> 29	4.80	2.68 - 8.59	< .001	

Lung Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma).
			1 - 19	1.00			
			20 - 29	2.63	1.31 - 5.29	< .01	Adjusted for Age, Age Started Smoking, Fraction Smoked per Cigarette, Gender, Residence Location, Smoke Inhalation, Type of Cigarette.
			> 29	5.64	2.64 - 12.1	< .001	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Adenocarcinoma).
			1 - 19	1.00			Adjusted for Age, Age Started Smoking, Fraction Smoked per Cigarette, Gender, Residence Location, Smoke Inhalation, Type of Cigarette.
			20 - 29	1.38	0.69 - 2.77	> .05	
			> 29	3.22	1.5 - 6.93	< .01	
Yamaguchi, N et al; 2000	Not Specified	Cohort	No Abstractable Data				The increase in the age-specific lung cancer mortality rates over time was found to correlate with a proportional increase in cumulative cigarette consumption.
Yamaguchi, N et al; 1992	144 Cases 676 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Never Smoker	1.00			Adjusted for Age, Gender, Hospital Type.
			Ex-Smoker	2.90	1.43 - 5.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			Adjusted for Age, Gender, Hospital Type.
			1 - 20	3.75	1.89 - 7.47		
			> 20	12.14	5.1 - 28.9		

Lung Function

Author	Subjects	Study Type	Data	Comments
Baba, Y et al; 1985	176	Cohort	No Abstractable Data	The results indicate that there were no significant differences in pulmonary function indices between smokers and non-smokers, although value for smokers were lower.
Burchfiel, Cecil M et al; 1996	4,451	Cohort	No Abstractable Data	"...For continuous or never smokers, the age-adjusted mean rate of FEV1 decline decreases progressively with increasing quintiles of subscapular skinfold and body mass index (for each category, test fro trend p<0.05)…" "...Continuous smokers are 1.65 times more likely to experience a rapid FEV1 decline than others. An increase of 10 cigarettes pack-year is associated with a rapid FEV1 decline in all subjects or in continuous smokers (OR: 1.04 and 1.07, respectively)."
Comstock, GW et al; 1973	3,088	Cross Sectional		Prevalence ratios could not be calculated COPD and asthma for the Japanese group because zero nonsmokers had these diseases.
			Cigarettes / Day / **Risk Estimate** / **95% CI** / **P-Value** 0 / 1.00 1 - 14 / 0.98 15 - 24 / 0.92 > 24 / 0.89	Stratified by Race (White), Gender (Male), ATT Round 1. Adjusted for Age, Geographic Location, Smoking Habits.
			Cigarettes / Day / **Risk Estimate** / **95% CI** / **P-Value** 0 / 1.00 1 - 14 / 0.98 15 - 24 / 0.89 > 24 / 0.90	Stratified by Race (White), Gender (Male), ATT Round 2. Adjusted for Age, Geographic Location, Smoking Habits.
			Cigarettes / Day / **Risk Estimate** / **95% CI** / **P-Value** 0 / 1.00 1 - 14 / 1.01 15 - 24 / 0.99 > 24 / 1.00	Stratified by Race (Japanese), Gender (Male). Adjusted for Age, Geographic Location, Smoking Habits.
Katoh, T et al; 2001	1,739	Cohort	No Abstractable Data	This cohort study followed residents of an agricultural town for 12 years, measuring lung function, height and weight. The adjusted FCV change/year (IQR) was as follows: Never smokers: -20.0 (-43.3, -0.1) Former smokers: -22.5 (-43.0, -5.50) Continuing smokers: -29.6 (-50.7, -290) *p<0.05 Quitter: -30.7 (-52.6, -13.2) *p<0.05 (It is unclear exactly what "Quitter" represents) The adjusted FEV1change/year (IQR) was as follows: Never smokers: -0.9 (-21.0, 10.7) Former smokers: -3.9 (-14.1, 11.9) Continuing smokers: -10.7 (-32.2, 1.2) *p<0.05 Quitter: -8.1 (-23.3, 2.8) *p<0.05

Lung Function

Author	Subjects	Study Type	Data				Comments
Yamaguchi, S et al; 1989		Cross Sectional					COPD endpoint=Chronic bronchitis symptoms prevalence.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.79		< .01	
			> 9	1.82		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.79		< .01	

Lymphomas

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.04	0.79 - 1.36		
Matsuo, K et al; 2001	333 Cases 55,904 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.90	1.16 - 3.07		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ever Smoker	1.16	0.88 - 1.53		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.11	0.79 - 1.57		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	1.75	1 - 3.06		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	3.08	1.12 - 8.42		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.50	0.97 - 2.33		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.04	0.73 - 1.47		
			> 19	1.12	0.81 - 1.53		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 19	1.08	0.7 - 1.69		
			> 19	1.06	0.74 - 1.52		

Lymphomas

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			0	1.00			
			1 - 19	1.19	0.65 - 2.17		
			> 19	1.68	0.85 - 3.34		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.10	0.83 - 1.46		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.37	0.85 - 2.19		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.06	0.75 - 1.5		

Macular Degeneration

Author	Subjects	Study Type	Data				Comments
Tamakoshi, Akiko et al; 1997	56 Cases 82 Controls	Case-Control; Hospital-Based					Macular degeneration outcome = neovascular form of age-related macular degeneration.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	2.09	0.71 - 6.13		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	2.97	1 - 8.84	< .05	
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age.
			0	1.00			
			< 30	1.86	0.59 - 5.84		
			30 - 39	2.38	0.77 - 7.35		
			> 39	3.79	1.13 - 12.7	< .05	

Maxillary Sinus Cancer

Author	Subjects	Study Type	Data				Comments
Fukuda, K et al; 1990	169 Cases 338 Controls	Case-Control; Hospital-Based					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			< 10	2.67			
			10 - 19	2.50			
			20 - 39	2.91			
			> 39	4.60			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	10.58		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	12.73		< .05	
Fukuda, K et al; 1988	116 Cases 232 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-79), Gender (Male). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	3.30	1.29 - 8.06	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-79), Gender (Female). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.80	0.57 - 5.87	> .05	
Fukuda, K et al; 1987	106 Cases 212 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Heating System, History of Compulsory Education, History of Sinusitis, Nasal Polyps, Nasal Trauma, Occupation.
			Never Smoker	1.00			
			Ever Smoker	3.00		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma). Adjusted for Heating System, History of Compulsory Education, History of Sinusitis, Nasal Polyps, Nasal Trauma, Occupation.
			Never Smoker	1.00			
			Ever Smoker	1.60		> .05	
Hirayama, T; 1985		Cohort					
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			0	1.00			
			1 - 14	2.27			
			15 - 19	2.56			
			> 20	3.34			

Maxillary Sinus Cancer

Author	Subjects	Study Type	Data				Comments
Kihara, M et al; 1997	158 Cases 474 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.70	0.72 - 19.3	> .05	
Shimizu, H et al; 1989	66 Cases 132 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.00	0.6 - 6.2		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.50	0.2 - 1.3		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Squamous Cell Carcinoma), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.50	0.7 - 3.2		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.40	0.4 - 13.4		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Squamous Cell Carcinoma), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.80	0.2 - 3.3		

Mental Health

Author	Subjects	Study Type	Data	Comments
Ezoe, S et al; 1994	2,800	Cross Sectional	No Abstractable Data	Cigarette smoking was significantly associated with the grade of psychological distress or its 3 components in females.
Mino, Y et al; 2001	782	Cross Sectional	No Abstractable Data	The study did not observe any difference in the mental health of male smokers and non-smokers. Female smokers showed poorer mental health than non-smokers, even after 2 years.
Takemura, Y et al; 1999	2,669	Cross Sectional		

Active Smoking Status	Risk Estimate	95% CI	P-Value	Comments
Never Smoker	1.00			Adjusted for Age.
Ex-Smoker	0.82	0.61 - 1.12	> .05	

Cigarettes / Day	Risk Estimate	95% CI	P-Value	Comments
0	1.00			Adjusted for Age.
1 - 20	1.10	0.88 - 1.37	> .05	
> 20	0.89	0.76 - 1.05	> .05	

Mucocutaneous Lymph Node Syndrome

Author	Subjects	Study Type	Data	Comments
Matsuoka, S et al; 1997	1,165 Cases 5,825 Controls	Case-Control	No Abstractable Data	The study found significantly fewer households of children with Kawasaki disease reported cigarette smoking (49% vs. 59%; P<0.01) versus control children.

Myelodysplastic Syndrome

Author	Subjects	Study Type	Data	Comments
Ido, M et al; 1996	116 Cases 116 Controls	Case-Control		

Active Smoking Status	Risk Estimate	95% CI	P-Value	Comments
Non-Smoker	1.00			Stratified by Gender (Male). Adjusted for Age, Gender, Hospital Type.
Ever Smoker	1.43	0.54 - 3.75		

Active Smoking Status	Risk Estimate	95% CI	P-Value	Comments
Non-Smoker	1.00			Stratified by Gender (Female). Adjusted for Age, Gender, Hospital Type.
Ever Smoker	2.67	0.71 - 10.1		

Active Smoking Status	Risk Estimate	95% CI	P-Value	Comments
Non-Smoker	1.00			Stratified by Gender (Both). Adjusted for Age, Gender, Hospital Type.
Ever Smoker	1.80	0.83 - 3.89		

Active Smoking Status	Risk Estimate	95% CI	P-Value	Comments
Non-Smoker	1.00			Stratified by Gender (Both), Refractory Anemia. Adjusted for Age, Gender, Hospital Type.
Ever Smoker	1.83	0.67 - 4.93		

Neuroblastoma

Author	Subjects	Study Type	Data	Comments
Kobaashi, N et al; 1990	339 Cases 2,383 Controls	Case-Control		

Active Smoking Status	Risk Estimate	95% CI	P-Value
Non-Smoker	1.00		
Current Smoker	1.67		

Nicotine Dependence

Author	Subjects	Study Type	Data	Comments
Hashimoto, E et al; 2001	1,357	Cross Sectional	No Abstractable Data	Results were available in the form of prevalence of tobacco dependence in current smokers in alcohol-dependent and non-alcohol-dependent individuals. Using ICD-10 criteria "prevalence of tobacco dependence was 58.1% in alcohol-dependent subjects, 42.5% in heavy drinkers and 12.8% in non drinkers or social drinkers Using the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (4th ed.) criteria for nicotine withdrawal, the prevalence of nicotine physical dependence was 2.4% in alcohol-dependent individuals, 2.2% in heavy drinkers and 0.3% in non drinkers or social drinkers.
Kawakami, N et al; 2000	136	Cross Sectional	No Abstractable Data	Results were available for the different personality characteristics. "Neuroticism scores were significantly higher in those who were diagnosed as tobacco/nicotine dependent than in non nicotine dependent ever-smokers. Lie scale scores were significantly lower in those who were diagnosed as tobacco/nicotine dependent than in non nicotine dependent ever-smokers. Extroversion was significantly higher in those currently smoking than in those who were past smokers. Multiple logistic regression analysis showed that Neuroticism was associated with higher risk of nicotine dependence where Lie was inversely associated.
Kawakami, N et al; 1999	370	Cross Sectional	No Abstractable Data	Results were available for the three different samples, providing alpha cronbach values in the range of .74 to .81, Table 2. Analysis of the performance of the tests; TDS and FTQ were made by means of Receiver Operator Characteristics (ROC) Curves, Figure 1, showing the better performance of the TDS, these results parallel to the specificity and sensibility values in Table 3. Table 4 offers data on spearman's correlation coefficients of TDS and FTQ with variables from the different sample participants.
Kawakami, N et al; 1998	170	Cross Sectional	No Abstractable Data	Results were available for 170 males smokers and ex smokers showing the prevalence according to the different diagnostic criteria ranging from 16% to 48%, Table 1. Multivariate analysis in Table 2 showed higher life-time risks of nicotine dependence for increasing length of smoking and number of cigarettes per day Figure 1 showed the relationship of age and cumulative rate of dependence according to the different criteria by birth cohort. Younger cohort showed higher rates but not significant.

Obesity

Author	Subjects	Study Type	Data				Comments
Ishizaki, M et al; 1999	3,833	Cross Sectional	No Abstractable Data				Study found that smoking status was unrelated to increase in waist to hip ratio.
Mizoue, T et al; 1998	7,324	Cross Sectional	**Active Smoking Status**	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >25. Adjusted for Age, Alcohol Consumption, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	0.86	0.72 - 1.03		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >28. Adjusted for Age, Alcohol Consumption, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	0.71	0.51 - 0.98		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >25. Adjusted for Age, Alcohol Consumption, Physical Activity.
			0	1.00			
			2 - 4	1.41	0.92 - 2.16		
			5 - 7	1.10	0.74 - 1.65		
			8 - 10	1.12	0.77 - 1.64		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >28. Adjusted for Age, Alcohol Consumption, Physical Activity.
			0	1.00			
			2 - 4	1.18	0.57 - 2.25		
			5 - 7	0.70	0.31 - 1.56		
			8 - 10	1.03	0.53 - 2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >25. Adjusted for Age, Alcohol Consumption, Physical Activity.
			0	1.00			
			1 - 24	0.79	0.64 - 0.96		
			> 24	0.97	0.78 - 1.19		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by BMI >28. Adjusted for Age, Alcohol Consumption, Physical Activity.
			0	1.00			
			1 - 24	0.66	0.46 - 0.96		
			> 24	0.80	0.55 - 1.16		

Oral Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 14	2.20	1 - 5.2		
			15 - 24	2.70	1.3 - 6.3		
			25 - 34	4.20	1.3 - 12.8		
			> 34	4.00	0.6 - 16.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.70	0.1 - 7.9		
			5 - 14	1.10	0.3 - 3.1		
			> 14	2.30	0.1 - 10.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	2.50	1.3 - 5.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.30	0.5 - 3.2		
Chyou, PH et al; 1992	8,006	Cohort					Oral cancer refers to "Oral-bladder cancer".
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.60	1.1 - 2.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Gender.
			Never Smoker	1.00			
			Current Smoker	2.70	1.8 - 3.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Gender.
			0	1.00			
			1 - 30	2.30	1.4 - 3.6		
			31 - 45	9.00	4.8 - 17.1		
			> 45	23.30	12.8 - 42.6		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.17	1.2 - 3.91		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).

Oral Cancer

Author	Subjects	Study Type	Data				Comments
			Status				
			Current Smoker	1.00			
			Never Smoker	0.11			
Hirayama, T; 1982	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Alcohol Consumption, Gender, Socioeconomic Status (SES), Tea Consumption.
			Non-Smoker	1.00			
			Current Smoker	2.18	1.2 - 3.98		
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.00			
			20 - 39	25.80		< .01	
			> 39	48.70		< .01	
Katoh, T et al; 1999	92 Cases 146 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.64	1.73 - 4.66		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.40	0.46 - 4.29		
			20 - 39	1.88	0.67 - 5.25		
			> 39	3.36	1.04 - 10.88		
Kihara, M et al; 1997	158 Cases 474 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.70	1 - 7.51	< .05	
Kurumatani, N et al; 1999	Not Specified	Cohort	No Abstractable Data				The time trend in mortality due to oro/hypopharyngeal cancer was correlated to cigarette consumption. There was an increasing trend in mortality due to oro/hypopharyngeal cancer in males.
Takezaki, T et al; 1996	266 Cases 36,527 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			Never Smoker	1.00			

Oral Cancer

Author	Subjects	Study Type	Data				Comments
			Ever Smoker	3.40	1.8 - 6.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.70	0.9 - 3.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.40	1.5 - 3.6		
			20 - 39	2.80	1.8 - 4.5		
			> 39	3.50	1.8 - 7		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.30	1.4 - 3.8		
			20 - 29	2.50	1.6 - 3.9		
			> 39	2.90	1.6 - 5.2		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			0	2.50	1.7 - 3.7		
			1 - 4	4.10	2.1 - 7.9		
			5 - 14	1.60	0.8 - 3.2		
			> 14	1.70	0.8 - 3.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender, Smoking Habits, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	2.30	1.6 - 3.4		

Oropharyngeal Cancer

Author	Subjects	Study Type	Data				Comments
Kobayashi, Y et al; 1990	11 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls ($p<0.05$). Heavy smokers were also more prevalent among MPC cases than among controls ($p<0.1$)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases ($p<0.1$)"
Yokoyama, A et al; 1996		Cross Sectional					Oropharyngeal cancer outcome includes laryngeal cancer cases. Upper aerodigestive cancer outcome includes esophageal cancer, gastric cancer, and oropharyngolaryngeal cancer.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Type of Alcohol.
			< 50	1.00			
			> 49	5.10	1.3 - 19.5		

Osteoporosis

Author	Subjects	Study Type	Data				Comments
Egami, I et al; 2003	163	Cross Sectional	No Abstractable Data				There was no association between number of cigarettes/day and bone mineral density examined by Spearman's correlation coefficient.
Fujiwara, Saeko et al; 1997	4,573	Cohort	No Abstractable Data				Smoking as assessed by this study was not associated with hip fracture.
Hirota, Y et al; 1993	118 Cases 236 Controls	Case-Control					Osteoporosis = Idiopathic osteonecrosis of the femoral head.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Body Mass Index, Energy Intake, Ethnicity, Gender, Liver Dysfunction, Occupation, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	3.30	0.9 - 11.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Body Mass Index, Energy Intake, Ethnicity, Gender, Liver Dysfunction, Occupation, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	4.70	1.5 - 14.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Body Mass Index, Energy Intake, Ethnicity, Gender, Liver Dysfunction, Occupation, Smoking Habits.
			0	1.00			
			1 - 20	1.70	0.6 - 4.5		
			> 20	2.60	1.1 - 6		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Body Mass Index, Energy Intake, Ethnicity, Gender, Liver Dysfunction, Occupation, Smoking Habits.
			0	1.00			
			1 - 9	1.60	0.4 - 6.3		
			10 - 19	6.60	1.7 - 25.7		
			> 19	6.50	1.9 - 21.9		
Shibata, A et al; 1996	64 Cases 128 Controls	Case-Control; Hospital-Based					Osteoporosis = Idiopathic avascular necrosis of the femoral head (IANF).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Flushing Pattern, History of Liver Disease, Occupation.
			Never Smoker	1.00			
			Ex-Smoker	2.24	0.53 - 9.49		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Flushing Pattern, History of Liver Disease, Occupation.
			Never Smoker	1.00			
			Current Smoker	1.06	0.28 - 4.06		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Flushing Pattern, History of Liver Disease, Occupation.
			0	1.00			
			1 - 9	0.83	0.01 - 66.34		
			10 - 19	0.41	0.09 - 1.9		
			> 19	0.62	0.2 - 1.93		

Osteoporosis

Author	Subjects	Study Type	Data				Comments
			Pack Years	Risk Estimate	95% CI	P-Value	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index, Flushing Pattern, History of Liver Disease, Occupation.
			0	1.00			
			1 - 9	1.27	0.06 - 29.6		
			10 - 19	3.11	0.46 - 21.02		
			20 - 29	2.80	0.37 - 21.22		
			> 29	1.68	0.23 - 12.39		
Vogel, JM et al; 1997	1,303	Cohort	No Abstractable Data				Current and past smokers had significantly lower bone density. The findings indicate that the adverse effect of smoking appeared to be greater in cancellous than cortical bones.

Ovarian Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.19	0.72 - 1.97		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.55	0.83 - 2.91		
			10 - 19	0.78	0.3 - 2.05		
			> 19	1.18	0.21 - 6.61		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.19	0.72 - 1.96		
Kato, I et al; 1989		Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Gender, Marital Status, Occupation, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	0.78	0.56 - 1.08		
Mori, M et al; 1996	78 Cases 346 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.60	0.78 - 3.27		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Source (Father). Adjusted for Age.
			Not Exposed	1.00			
			Exposed	0.79	0.48 - 1.3		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Source (Mother). Adjusted for Age.
			Not Exposed	1.00			
			Exposed	0.35	0.1 - 1.19		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Source (Spouse). Adjusted for Age.
			Not Exposed	1.00			
			Exposed	1.22	0.69 - 2.14		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			Non-Smoker	1.00			

Ovarian Cancer

Author	Subjects	Study Type	Data			Comments
			Current Smoker	1.70	0.58 - 5.2	Adjusted for Age, Gender.

Pancreatic Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.4 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.20	0.8 - 1.9		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.10	0.3 - 2.7		
			5 - 14	1.50	1.1 - 2.1		
			15 - 24	1.60	1.2 - 2.2		
			25 - 34	1.20	0.6 - 2.2		
			> 34	1.30	0.4 - 2.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.60	0.1 - 1.9		
			5 - 14	1.90	1.2 - 2.8		
			> 14	1.40	0.4 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.50	1.1 - 2.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.60	1.1 - 2.3		
Goto, R et al; 1990	28 Cases 56 Controls	Case-Control; Population-Based					
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			> 20	6.50	1.32 - 32.11	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			> 10	4.67	1.21 - 18.05	< .05	
Hinds, MW et al; 1980		Other	No Abstractable Data				"A significant positive association between cigarette smoking and renal cancer was noted in the TNCS (Third National Cancer Survey) study and in the Hawaiian Study of Five Ethnic Groups."

Pancreatic Cancer

Author	Subjects	Study Type	Data				Comments
							"The Third National Cancer Survey and the Hawaiian Study of Five Ethnic Groups have also reported a positive association [between smoking and laryngeal cancer]." "In the Third National Cancer Survey and in the Hawaiian Study of Five Ethnic Groups, there was a significant positive relationship between smoking and pancreatic cancer."
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.52	1.26 - 1.83		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.56	1.22 - 1.99		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.44	1.09 - 1.92		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.51	1.05 - 2.18		
			10 - 19	1.46	1.12 - 1.9		
			> 19	1.66	1.28 - 2.16		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.91	0.55 - 1.5		
			10 - 19	2.10	1.46 - 3.02		
			> 19	0.98	0.31 - 3.14		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	0.74	0.27 - 1.99		
			5 - 9	0.33	0.05 - 1.99		
			> 9	1.15	0.45 - 2.91		

Pancreatic Cancer

Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.76	0.27 - 11.67		
Hirayama, T; 1989	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.56	1.22 - 1.99		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.45	1 - 1.92		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 14	1.47			
			15 - 29	1.58			
			30 - 39	1.70			
			40 - 49	1.84			
			> 49	2.63			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	0.00			
			20 - 39	0.00			
			> 39	2.80			
Ishii, K et al; 1973	353 Cases 122,621 Controls	Case-Control	No Abstractable Data				The cigarette smoking frequencies was significantly higher in both groups of calcifying pancreatitis and carcinoma of pancreas than in the control group ($p<0.05$)
Lin, Y et al; 2002	99,527	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.61 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			Never Smoker	1.00			
			Ex-Smoker	1.80	0.67 - 5		

Pancreatic Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			0	1.00			
			1 - 19	1.60	0.91 - 2.9		
			20 - 39	1.30	0.74 - 2.4		
			> 39	3.30	1.38 - 8.1		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			0	1.00			
			1 - 19	2.00	0.89 - 4.4		
			20 - 39	1.70	0.95 - 3.1		
			40 - 59	1.40	0.73 - 2.6		
			> 59	1.70	0.7 - 4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			Never Smoker	1.00			
			Current Smoker	1.60	0.95 - 2.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			Never Smoker	1.00			
			Current Smoker	1.70	0.85 - 3.4		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			0	1.00			
			1 - 24	1.30	0.27 - 6.2		
			25 - 34	2.00	0.8 - 4.9		
			35 - 44	1.70	0.91 - 3.2		
			> 44	1.50	0.81 - 2.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			Never Smoker	1.00			
			Current Smoker	1.60	0.95 - 2.7		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Body Mass Index, History of Diabetes mellitus, History of Gallbladder Diseases.
			0	1.00			
			1 - 9	1.40	0.7 - 2.6		
			10 - 19	0.85	0.36 - 2		
			> 19	0.85	0.36 - 2		
Mizuno, Soichi et al; 1992	124 Cases 124 Controls	Case-Control; Hospital-Based					
							Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Site (e.g. Hospital).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Site (e.g. Hospital).
			Never Smoker	1.00			
			Ever Smoker	2.40	1.13 - 5.31	< .05	

Pancreatic Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Site (e.g. Hospital).
			Never Smoker	1.00			
			Current Smoker	2.80	1.19 - 6.37	< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Site (e.g. Hospital).
			0	1.00			
			1 - 12	6.24	1.71 - 22.79		
			13 - 22	1.87	0.71 - 4.9		
			> 22	2.47	0.81 - 7.55		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both), Smoking in Past 10 Years. Adjusted for Age, Gender, Site (e.g. Hospital).
			0	1.00			
			1 - 12	4.50	1.53 - 13.18		
			13 - 22	2.57	1.01 - 6.51		
			> 22	2.56	0.93 - 7.04		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.20	0.45 - 3.1		
Ohba, S et al; 1996	141 Cases 282 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.25	0.73 - 2.13		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender, Residence Location.
			Non-Smoker	1.00			
			Current Smoker	0.81			

Pancreatitis

Author	Subjects	Study Type	Data				Comments
Ishii, K et al; 1973	353 Cases 122,261 Controls	Case-Control	No Abstractable Data				The cigarette smoking frequencies was significantly higher in both groups of calcifying pancreatitis and carcinoma of pancreas than in the control group ($p<0.05$)
Lin, Y et al; 2001	91 Cases 175 Controls	Case-Control; Hospital-Based					Pancreatitis= Chronic pancreatitis.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender, Hospital, Time of First Hospital Visit.
			Non-Smoker	1.00			
			Current Smoker	1.11			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender, Hospital, Time of First Hospital Visit.
			0	1.00			
			1 - 19	5.23			
			20 - 39	2.84			
			> 39	6.38			

Parkinson's Disease

Author	Subjects	Study Type	Data				Comments
Watanabe, K; 1994	95 Cases 190 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	1.45	0.79 - 2.66	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	2.12	0.94 - 4.79	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Current Smoker	0.79	0.25 - 2.52	> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			< 25	1.84	0.92 - 3.71	> .05	

Peptic Ulcer Disease

Author	Subjects	Study Type	Data				Comments
Araki, S; 1985	74 Cases 74 Controls	Case-Control	No Abstractable Data				"Significantly more tobacco was smoked by workers with active gastric ulcers" [26 +/- 11(SD) cigarettes per day] than by the matched controls [10 +/-9 cigarettes per day]. (Table 3) "Smoking was associated with gastric, but not duodenal ulcer."
Araki, S et al; 1985	74 Cases 74 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Occupation, Rank.
			Never Smoker	1.00			
			Current Smoker	2.70		< .05	
Hamajima, N et al; 2001	151 Cases 90 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by GG Genotype. Adjusted for Age, Alcohol Consumption, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.56			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by GA/AA Genotypes. Adjusted for Age, Alcohol Consumption, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.57			
Hamajima, N et al; 1987	54 Cases 54 Controls	Case-Control					Peptic Ulcer Disease outcome= gastric ulcer.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Meal Time, Occupation, Psychological Factors, Sleeping Hours.
			0	1.00			
			1 - 9	11.90	1.6 - 89.4		
			> 9	9.90	2.6 - 37.7		
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	1.54			
Kaneko, E et al; 1989	276	Cohort	No Abstractable Data				"Only cigarette smoking influenced the ulcer status adversely" (Table VII: $p<0.01$). "Smoking appears to be the main adverse factor." " The present study confirmed that smoking affects ulcer healing adversely."
Kato, Ikuko et al; 1992	7,624	Cohort					Peptic Ulcer endpoint = incident gastric or duodenal ulcer (reported separately).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			

Peptic Ulcer Disease

Author	Subjects	Study Type	Data				Comments
			Current Smoker	3.40	2.4 - 4.7	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.70	1.2 - 2.5	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	3.00	1.9 - 4.7	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.50	0.9 - 2.6	> .05	
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			0	1.00			
			1 - 23.9	1.50			
			24 - 40	3.10			
			> 40	3.80			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			0	1.00			
			1 - 23.9	1.80			
			24 - 40	2.40			
			> 40	3.30			
Kurata, J et al; 1994	Not Specified	Review	No Abstractable Data				High gastric ulcer mortality rate is a reflection of high smoking exposure in Japan. A study of endoscopy in Japan who smoke regularly showed a risk ratio of 3.32 for gastric ulcer and 2.99 for duodenal ulcer.
Stemmermann, G et al; 1977	32 Cases 101 Controls	Case-Control					Peptic ulcer disease outcome = gastric ulcer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hawaiian Japanese. Adjusted for Age, Nativity.
			Never Smoker	1.00			
			Ever Smoker	1.22			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Nisei. Adjusted for Age, Nativity.
			Never Smoker	1.00			
			Ever Smoker	1.70			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Hawaiian Japanese. Adjusted for Age, Nativity.
			Never Smoker	1.00			
			Ever Smoker	3.60			

Peptic Ulcer Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Nisei. Adjusted for Age, Nativity.
			Never Smoker	1.00			
			Ever Smoker	3.30			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hawaiian Japanese. Adjusted for Age, Nativity.
			1 - 19	1.00			
			> 19	0.54			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Nisei. Adjusted for Age, Nativity.
			1 - 19	1.00			
			> 19	0.43			
Stemmermann, GN et al; 1989	5,933	Cohort					Peptic Ulcer endpoint = incident gastric or duodenal ulcer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	2.09		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.19		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Gastric Ulcer. Adjusted for Age, Ethnicity, Gender.
			Current Smoker	1.00			
			Ex-Smoker	0.57		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	3.00		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.56		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male), Duodenal Ulcer. Adjusted for Age, Ethnicity, Gender.
			Current Smoker	1.00			
			Ex-Smoker	0.52		< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male). Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	2.44		< .001	

Peptic Ulcer Disease

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male). Adjusted for Age, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.41		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Other), Gender (Male). Adjusted for Age, Ethnicity, Gender.
			Current Smoker	1.00			
			Ex-Smoker	0.58		< .001	
Watanabe, Y et al; 1992	717 Cases 588 Controls	Case-Control					Peptic ulcer disease outcome= Gastric ulcer and/or duodenal ulcer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Gastric Ulcer.
			Non-Smoker	1.00			
			Current Smoker	3.32	2.34 - 4.71	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Duodenal Ulcer.
			Non-Smoker	1.00			
			Current Smoker	2.99	2.02 - 4.42	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Gastric Ulcer. Adjusted for Age, Alcohol Consumption, Gender, Salty Food Consumption.
			Non-Smoker	1.00			
			Current Smoker	3.10	2.08 - 4.62	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Duodenal Ulcer. Adjusted for Age, Alcohol Consumption, Gender, Salty Food Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.90	1.24 - 2.92	< .001	

Pharyngeal Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	0.40	0.1 - 1.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.10			
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.09	0.79 - 5.55		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	3.00	1.56 - 5.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.05	0.47 - 2.37		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.05	0.79 - 5.29		
			10 - 19	2.97	1.5 - 5.88		
			> 19	3.35	1.7 - 6.57		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	0.80	0.21 - 3		
			10 - 19	1.23	0.37 - 4.04		
			> 19	3.92	1.01 - 15.27		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			5 - 9	3.03	0.49 - 18.67		
			> 9	1.80	0.21 - 15.62		
Kihara, M et al; 1997	158 Cases	Case-Control					

Pharyngeal Cancer

Author	Subjects	Study Type	Data				Comments
	474 Controls						
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.10	1.37 - 7.14	< .01	
Kurumatani, N et al; 1999	Not Specified	Cohort	No Abstractable Data				The time trend in mortality due to oro/hypopharyngeal cancer was correlated to cigarette consumption. There was an increasing trend in mortality due to oro/hypopharyngeal cancer in males.
Takezaki, T et al; 2000	62 Cases 11,936 Controls	Case-Control; Hospital-Based					Upper aerodigestive cancer are results for cancer of the hypopharynx or esophagus combined.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.70	0.2 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			Never Smoker	1.00			
			Current Smoker	2.20	0.9 - 5.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			< 19	2.10	0.7 - 5.8		
			> 19	2.40	0.9 - 5.9		

Postoperative Complications

Author	Subjects	Study Type	Data				Comments
Nakagawa, M et al; 2001	288	Retrospective Cohort					The outcome was postoperative pulmonary complications.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			< 10	1.00			
			> 10	1.10	0.9 - 1.33	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Duration of Surgery, Gender, Pulmonary Function Test.
			Non-Smoker	1.00			
			Ex-Smoker	1.03	0.47 - 2.26	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Duration of Surgery, Gender, Pulmonary Function Test.
			Non-Smoker	1.00			
			Current Smoker	2.09	0.83 - 5.25	> .05	

Preeclampsia

Author	Subjects	Study Type	Data				Comments
Ioka, A et al; 2003	493	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Gender, Household Smoking Exposure.
			Non-Smoker	1.00			
			Current Smoker	1.20	0.63 - 1.51	> .05	

Preterm Birth

Author	Subjects	Study Type	Data				Comments
Matsubara, F et al; 2000	7,411	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Ex-Smoker	1.43	0.96 - 2.14		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			Non-Smoker	1.00			
			Current Smoker	0.66	0.28 - 1.52		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 5	0.62	0.15 - 2.56		
			6 - 10	0.79	0.25 - 2.54		
			> 10	0.50	0.07 - 3.66		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
				1.00			
				0.62	0.15 - 2.56		
			Never Smoker	1.00			
			Ex-Smoker	1.99	0.84 - 4.72		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
				1.00			
				0.62	0.15 - 2.56		
			Never Smoker	1.00			
			Current Smoker	1.04	0.78 - 1.4		
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Residence), ETS Source (Spouse). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			1 - 10	0.80	0.49 - 1.3		
			11 - 20	1.11	0.79 - 1.55		
			> 20	1.24	0.78 - 1.96		
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
				1.00			
				0.80	0.49 - 1.3		
			Not Exposed	1.00			
			Exposed	0.92	0.68 - 1.23		
			Hours / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Pregnancy), ETS Location (Total), ETS Source (Not Specified). Adjusted for Alcohol Consumption, Body Mass Index, Education, Environmental Tobacco Smoke, Height, Infant Gender, Maternal Age, Parity, Working During Pregnancy.
			0	1.00			
			< 2	0.94	0.67 - 1.34		
			> 1	0.85	0.58 - 1.25		

Prostate Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	3.10	1.4 - 6.4		
			5 - 14	1.00	0.7 - 1.6		
			15 - 24	0.90	0.6 - 1.4		
			25 - 34	0.80	0.2 - 2.1		
			> 34	3.00	1 - 7.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.10	0.7 - 1.5		
Furuya, Y et al; 1998	329 Cases 188 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			Non-Smoker	1.00			
			Current Smoker	0.99	0.69 - 1.41		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00	0.73 - 1.37		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00	0.73 - 1.38		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.32	0.83 - 2.11		
			10 - 19	0.93	0.65 - 1.32		
			> 19	0.92	0.64 - 1.32		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.14	0.42 - 3.11		
			5 - 9	1.02	0.26 - 3.94		
			> 9	1.00	0.29 - 3.43		

Prostate Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	0.04			
Nomura, AM et al; 2000	249 Cases 249 Controls	Nested Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, In Original Cohort.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.8 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, In Original Cohort.
			Never Smoker	1.00			
			Current Smoker	1.30	0.8 - 2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, In Original Cohort.
			0	1.00			
			1 - 30	1.40	0.7 - 2.9		
			> 30	1.20	0.8 - 2		
Oishi, K et al; 1989	117 Cases 296 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), BPH Controls. Adjusted for Age, Date of Admission, Hospital Type.
			Never Smoker	1.00			
			Ever Smoker	1.36	0.76 - 2.45		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), BPH Controls. Adjusted for Age, Date of Admission, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	0.77	0.44 - 1.35		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hospital Controls. Adjusted for Age, Date of Admission, Hospital Type.
			Never Smoker	1.00			
			Current Smoker	0.59	0.34 - 1.03		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hospital Controls. Adjusted for Age, Date of Admission, Hospital Type.
			Never Smoker	1.00			
			Ex-Smoker	1.41	0.81 - 2.48		

Proteinuria

Author	Subjects	Study Type	Data				Comments
Hashimoto, Y et al; 1999	5,174	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Normal Glycosylated Hemoglobin. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Family History of Diabetes, Family History of Hypertension, Glycosylated Hemoglobin.
			Never Smoker	1.00			
			Ever Smoker	1.02	0.65 - 1.6	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by High Glycosylated Hemoglobin. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Family History of Diabetes, Family History of Hypertension, Glycosylated Hemoglobin.
			Never Smoker	1.00			
			Ever Smoker	11.53	1.44 - 92.19	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, Family History of Diabetes, Family History of Hypertension, Glycosylated Hemoglobin.
			Never Smoker	1.00			
			Ever Smoker	1.18	0.77 - 1.8	> .05	
Tozawa, M et al; 2002	5,403	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Anemia, Diabetes, Gender, Hematocrit, Hypercholesterolemia, Hypertension, Hypertriglyceridemia, Hyperuricemia, Obesity, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.32	1 - 1.74	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Anemia, Diabetes, Gender, Hematocrit, Hypercholesterolemia, Hypertension, Hypertriglyceridemia, Hyperuricemia, Obesity, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.28	0.96 - 1.72	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Anemia, Diabetes, Gender, Hematocrit, Hypercholesterolemia, Hypertension, Hypertriglyceridemia, Hyperuricemia, Obesity, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.30	0.44 - 3.8	> .05	

Pustulosis Palmaris et Plantaris

Author	Subjects	Study Type	Data	Comments
Akiyama, T et al; 1995	409	Cohort	No Abstractable Data	The findings suggest that heavy smoking may be associated with onset and exacerbation of pustulosis palmaris et plantaris.

Rectal Adenoma

Author	Subjects	Study Type	Data				Comments
Honjo, S et al; 1995	504 Cases 3,101 Controls	Case-Control; Hospital-Based					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Smoking in Past 10 Years. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 7.5	0.80	0.3 - 1.8		
			7.55 - 12.5	2.20	1.3 - 3.8		
			> 12.5	1.10	0.5 - 2.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Smoking until 10 Years ago. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 17	0.80	0.4 - 1.6		
			18 - 23	1.50	0.8 - 2.7		
			> 23	1.00	0.5 - 1.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Study Center.
			0	1.00			
			1 - 22	0.60	0.3 - 1.2		
			23 - 33	1.70	0.9 - 3.2		
			> 33	1.00	0.5 - 2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Smoking in Past 10 Years. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Smoking until 10 Years Ago, Study Center.
			0	1.00			
			1 - 7	1.20	0.4 - 3.2		
			8 - 12	3.50	1.4 - 8.5		
			> 12	2.00	0.6 - 6.7		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Smoking until 10 Years ago. Adjusted for Admission Period, Alcohol Consumption, Body Mass Index, Rank, Smoking in the past 10 Years, Study Center.
			0	1.00			
			1 - 17	0.50	0.2 - 1.3		
			18 - 23	0.50	0.2 - 1.5		
			> 23	0.40	0.1 - 1.3		
Nagata, Chisato et al; 1999	259 Cases 18,361 Controls	Nested Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.49	0.65 - 4.01		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.46	0.61 - 4.06		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 29	1.26	0.52 - 3.51		
			> 29	1.68	0.72 - 4.6		

Rectal Adenoma

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.62	0.72 - 4.32		
			> 19	1.10	0.41 - 3.24		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	1.37	0.57 - 3.8		
			> 19	1.55	0.67 - 4.2		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>35), Race (Asian), Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	2.06	0.81 - 5.89		
			> 9	0.77	0.22 - 2.58		

Rectal Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.8 - 2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.00	0.7 - 1.4		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.40	0.5 - 3.2		
			5 - 14	1.30	0.9 - 1.9		
			15 - 24	1.40	1 - 2		
			25 - 34	1.50	0.7 - 2.9		
			> 34	1.10	0.3 - 2.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	0.50	0.1 - 1.7		
			5 - 14	0.90	0.9 - 1.5		
			> 14	2.10	0.8 - 4.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.40	1 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	0.90	0.6 - 1.5		
Chyou, Po-Huang et al; 1996	7,945	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.95	1.25 - 3.04		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.31	0.78 - 2.2		

Rectal Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 15	1.05	0.54 - 2.05		
			16 - 30	1.59	0.93 - 2.72		
			> 30	1.92	1.23 - 2.99		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.14	0.93 - 1.4		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.22	0.96 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.99	0.7 - 1.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.42	0.97 - 2.09		
			10 - 19	1.19	0.89 - 1.58		
			> 19	1.25	0.94 - 1.67		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	0.76	0.43 - 1.34		
			10 - 19	1.38	0.86 - 2.21		
			> 19	0.66	0.15 - 2.83		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.06	0.44 - 2.54		
			5 - 9	2.19	1.01 - 4.75		
			> 9	0.79	0.25 - 2.51		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			> 9	10.10	4.01 - 25.45		
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary

Rectal Cancer

Author	Subjects	Study Type	Data				Comments
							cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	2.10			
			20 - 39	0.00			
			> 39	2.30			
Hoshiyama, Y et al; 1993	102 Cases 653 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.40	0.6 - 3.1		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 29	1.70	0.9 - 3.4		
			> 29	1.00	0.3 - 2.6		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			1 - 40	1.60	0.8 - 3		
			> 40	1.50	0.6 - 3.6		
Inoue, M et al; 1995	432 Cases 31,782 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.90	1.1 - 3.2		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age.
			Never Smoker	1.00			
			Ever Smoker	1.70	1 - 3.1		
Kato, I et al; 1990		Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	0.74	0.66 - 0.84	< .01	
Le Marchand, Loic et al; 1997	350 Cases 350 Controls	Case-Control; Population-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			

Rectal Cancer

Author	Subjects	Study Type	Data				Comments
			Ex-Smoker	1.40	0.8 - 2.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	0.80	0.4 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.7 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Alcohol Consumption, Body Mass Index 5 Years Ago, Calcium Intake, Calorie Intake, Egg Intake, Family History/Index Disease, Fiber Intake, Gender, Physical Activity.
			Never Smoker	1.00			
			Current Smoker	1.30	0.5 - 3.7		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.80	0.85 - 3.9		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.10	0.42 - 2.9		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.90	0.87 - 4.2	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Meat Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	1.60	0.75 - 3.4	> .05	
Tajima, K et al; 1985	25 Cases 111 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Education, Gender, Time of Interview.
			Never Smoker	1.00			
			Current Smoker	1.13		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			Never Smoker	1.00			
			Current Smoker	1.02		> .05	

Rectal Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			0	1.00			
			< 30	1.06		> .05	
			> 29	0.93		> .05	

Renal Failure

Author	Subjects	Study Type	Data				Comments
Takei, I et al; 1995	37 Cases 37 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	1.64			

Respiratory Symptoms

Author	Subjects	Study Type	Data				Comments
Kagamimori, S et al; 1996	Not Specified	Cohort					Asthma endpoint= Wheeze with colds.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (21-29), Gender (Both), Persistent Cough. Adjusted for Age at Entry.
			Never Smoker	1.00			
			Current Smoker	3.70	2.1 - 11	< .001	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-22), Gender (Both), Persistent Cough. Adjusted for Age at Entry.
			Never Smoker	1.00			
			Current Smoker	2.30	0.6 - 6.6	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (24-31), Gender (Both), Persistent Cough. Adjusted for Age at Entry.
			Never Smoker	1.00			
			Current Smoker	3.30	1.3 - 8.1	< .01	
Kumagai, S et al; 1993	667	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Conduit Repair Workers. Adjusted for Age, Employment Duration, Job Title.
			Non-Smoker	1.00			
			Current Smoker	1.52			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Clerical/Engineering Workers. Adjusted for Age, Employment Duration, Job Title.
			Non-Smoker	1.00			
			Current Smoker	2.02			
Nishima, S et al.; 1983	57,761	Cross Sectional					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), Family History of Major Allergy. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.20			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), No Family History of Major Allergy. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.02			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), Family History of Bronchial Asthma. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.39			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Location (Residence), No Family History of Bronchial Asthma. Adjusted for Family History .
			Not Exposed	1.00			
			Exposed	1.05			
Okuma, M; 1994	10,137	Cross Sectional					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood).
			Not Exposed	1.00			
			Exposed	1.09			
Ono, M et al; 1990	Not Specified	Cross Sectional					805 households were surveyed
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time

Respiratory Symptoms

Author	Subjects	Study Type	Data				Comments
							(Childhood), ETS Source (Father), Cough.
			Exposed	1.20			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Mother), Cough.
			Not Exposed	1.00			
			Exposed	1.00			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Father), Sputum.
			Not Exposed	1.00			
			Exposed	1.44			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Mother), Sputum.
			Not Exposed	1.00			
			Exposed	0.83			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Father), Wheeze.
			Not Exposed	1.00			
			Exposed	1.08			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Mother), Wheeze.
			Not Exposed	1.00			
			Exposed	0.97			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Father), Cold.
			Not Exposed	1.00			
			Exposed	0.89			
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (4-11), Gender (Both), ETS Time (Childhood), ETS Source (Mother), Cold.
			Not Exposed	1.00			
			Exposed	1.15			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Male), Cough. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	5.38			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female), Cough. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	2.18			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Male), Sputum. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.96			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female), Sputum. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.86			

Respiratory Symptoms

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Male), Cough with Sputum. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	3.63			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female), Cough with Sputum. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	4.80			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Male), Wheeze. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	2.31			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female), Wheeze. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.16			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Male), Breathlessness. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	2.26			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-49), Gender (Female), Breathlessness. Adjusted for Gender.
			Non-Smoker	1.00			
			Current Smoker	1.12			

Sick Building Syndrome

Author	Subjects	Study Type	Data	Comments
Mizoue, T et al; 2001	1,281	Cross Sectional	No Abstractable Data	Workplace ETS exposure among nonsmokers (hours/day) and the associated OR for sick building syndrome: <1: 1 (reference) 1-<4: 2.4 (1.0-5.7) 4+: 2.7 (1.6-4.8) Adjusted for age, gender, type of building, job position, history of asthma, video terminal use, overtime, interest in work, work overload, control over work, support from colleagues, distress over human relations at work, sports activity, and hours of sleep per night. "…a clear trend association was observed between hours of ETS exposure and SBS symptoms among nonsmokers; the odds ratio was significantly elevated for workers with the greatest amount of ETS exposure…. Odds ratios were relatively high for symptoms pertaining to the nose, throat, and eyes. A similar finding was obtained when analysis was limited to subjects who worker in the main building (data not shown). Subjects in workplaces with strict restrictions on smoking, such as a total ban or a workroom ban, had reduced odds ratios for symptoms of the nose (OR = 0.5, 95 percent CI: 0.3, 0.9), throat (OR = 0.6, 95 percent CI: 0.4, 1.0), and skin (OR = 0.6, 95 percent CI: 0.3, 1.0) compared with subjects in workplaces with milder restrictions."

Smoking Behavior

Author	Subjects	Study Type	Data	Comments
Kawabata, T et al; 1999	2,090	Cohort	No Abstractable Data	Results were available for self-esteem in the cognitive and physical domains, stratified by gender and elementary and junior high school students. Never smokers had significantly higher cognitive self esteem, Figure 2. Ever smokers presented higher and statistically significant physical self esteem. Figure 3.
Kawahara, K et al; 2000	Not Specified	Cross Sectional	No Abstractable Data	Results were available for prevalence of current smoking by gender Table 1, male doctors 27.8% vs. female doctors 5.2%. Prevalence of past smoking by age cohort was shown in Figure 1. With highest prevalence of the age cohorts 55-59 and 70+. Non-smoking doctors were significantly more prompt to explain patients the risks of smoking, and to ask new patients about smoking habits.
Ohida, T et al; 2001	446	Cohort	No Abstractable Data	Results were available for prevalence of smoking " as for smoking status after 1 year , Table 1, for the subjects from vocational schools of nursing, 13% started smoking and 3% quit, resulting in a 10% increase in smoking prevalence. For nursing school/universities 5% started and 2% quit resulting in a 3% increase in smoking prevalence. "results from the multivariate logistic regression analyses showed that the factors "my friends smoke" now and "I live alone" are significantly affecting initiation of smoking. Table 2.
Ohida, T et al; 2000	Not Specified	Cross Sectional	No Abstractable Data	Results were available for prevalence "14.6% of female nurses were smoking nearly on the same level as the general women's and 75% of male nurses were smoking much more than the general men did" Table 1. "The highest smoking prevalence was noted with the psychiatric department while the pediatric was the lowest" Table 3 provides data on consciousness about smoking and anti-smoking behavior of smokers. "more than 96% of the nurses had an opinion that a hospital or clinic as a working place for them should be kept as non-smoking area"
Ohida, T et al; 2000	13,998	Cross Sectional	No Abstractable Data	Results were available for "the proportion of smokers (daily smokers plus occasional smokers) was 44.7% for males and 3.1% for females, rates lower than those in the general population. Table 1 "almost all male and female teachers agreed with total ban on smoking in schools (Table 2)" "It was found that twenty-one percent of male smokers and five percent of female smokers smoked in the teachers' room even though smoking was banned (Table 3) . "Almost all teachers males and females agreed that there is a need for anti-smoking education (Table 4)
Smith, M et al; 2000	356	Cross Sectional	No Abstractable Data	Results were available for" general health knowledge is high among both ever-smokers and non-smokers. The majority

Smoking Behavior

Author	Subjects	Study Type	Data	Comments
				knows that smoking causes cancer. However, significantly more non smokers agree that smoking causes cancer (Table 4)". "Regarding perceptions and attitudes towards smoking significant differences were found. 39.4% of ever-smokers and 17.0% of non smokers agree that cigarettes make one look more fashionable. 37.95 of ever-smokers and 13.1% of non smokers agreed that smoking facilitates communication. (Table 5)" "from and economic stand point, 80,3% of ever-smokers and 70.6% of non smokers believe that tobacco industry is good for the economy (Table 6).
Takakura, M et al; 2001	1,466	Cross Sectional	No Abstractable Data	Results were available for "overall prevalence of smoking; 17.4%. Prevalence of smoking was significantly higher among male students, vocational high school students, and those whose parental education level was less than high school, Table 1" "Table 2 shows that all health risk behaviors were significantly higher for current smokers than among non-smokers except for physical inactivity in total sample and females, and nonuse of seat belts in females" Table 3 show the OR for health-risk behaviors among the smokers compared to the never smokers by gender and total. Current drinking, sexual intercourse and non use of seatbelts were significantly associated to smoking among both gender. Weight loss activities were significantly associated in females.

Smoking Habits

Author	Subjects	Study Type	Data	Comments
Hiraoka, Y et al; 1988	1,451	Cross Sectional	No Abstractable Data	Results were available on factors related to smoking habits in youth. " permissive consciousness and attitudes towards smoking, not to keep school rules and prohibition when in high school, lack of recognition of the hazardousness o smoking were items determining the smoking probability of smoking in male students" "indecision regarding the right to hate smoking, inability to choose a sports activity according to one's feeling were items determining the smoking probability in female students"
Nakamura, Y et al; 1996	3,826	Cross Sectional	No Abstractable Data	Results were available for prevalence; Table 1 shows the prevalence of current smokers by age with a total of 53.5% and higher rates at younger age declining with age. Tables 2 and 3 showed the relationship between smoking status and habitual exercise and physical activity both showing no significance. Table 4 shows the relationship between alcohol drinking and smoking habits. "Former drinkers were more likely to be former and current smokers. Habitual drinkers were also likely to be former and current smokers" Figure 1 shows the dose-response alcohol-smoking habits.
Ohida, T et al; 2001	3,771	Cross Sectional	No Abstractable Data	"Smoking prevalence among physicians was 27.1% for men and 6.8% for women, about half of the general population in Japan (male, 54%; female, 14.5%)." "Smoking prevalence among Japanese physicians has decreased year by year." Nonsmoking physicians carry out smoking-cessation guidance more actively and have stricter views on smoking than do physicians who smoke."
Ohida, T et al; 1999	2,207	Cross Sectional	No Abstractable Data	"The prevalence of smoking among female nurses was 18.6% which was higher than the rates of the two studies in the general female population." "The prevalence of smoking among all working nurses is somewhat higher than among nurses in national hospitals, if the % of LPNs is taken into consideration." "Prevalence of smoking indicates that smoking was less common in hospitals where the number of patients was greater." Smoking was more common in those working in the departments of psychiatry than in other departments."
Osaki, Y et al; 1999	69,402	Cross Sectional	No Abstractable Data	"Experimenter's rates for Jiangxi boys were higher in each grade than those of Japanese boys."

Smoking Habits

Author	Subjects	Study Type	Data	Comments
				"Current smokers' rates were similar in both areas, whereas the regular smokers' rates were higher for Japanese boys." "Experimenter's rate, current smoker's rate and regular smokers' rate were all lower for Jiangxi girls than those of Japanese girls." "Friend's smoking status was strongly related to smoking experience among both sexes in both areas."
Osaki, Y et al; 1996	57,189	Cross Sectional	No Abstractable Data	"The proportion of boys smoking 1-9 cigarettes per day decrease ($p<0.01$), and the proportion of those smoking 10 or more cigarettes per day increased in each grade ($p<0.01$)." "The percentage of girls smoking 1-9 cigarettes per day did not decrease while the percentage of girls smoking 10-19 cigarettes per day increased in each grade until the 12th grade." "The major source of cigarettes reported by current smokers was vending machines (Table 3)." "The proportions of boys who buy cigarettes from vending machines or tobacconist shops significantly increased in each grade (Table 3)."
Shibata, A et al; 1990	4,689	Cross Sectional	No Abstractable Data	The prevalence of smoking among male senior high school students in ordinary school for non-smokers, ex-smokers, and smokers was 54%, 34.1%, 11.8%, respectively. (Table 1) The prevalence of smoking among female senior high school students in ordinary school for non-smokers, ex-smokers, and smokers was 81.8%, 14.8%, 3.4%, respectively. (Table 1) The prevalence of smoking among male senior high school students in vocational school for non-smokers, ex-smokers, and smokers was 21.9%, 35.5%, 42.6%, respectively. (Table 1) Results also available for reasons for smoking the first cigarette, source of the first cigarette, places where cigarette smoking begins, reasons for giving up smoking, and other factors related to smoking (spending money, parental smoking, friend smoking).
Sobue, T et al; 2001	110,896	Cohort	No Abstractable Data	"The age-adjusted proportion of current and former smokers was 54.8% and 21.8% in males, and 8.3% and 2.1% in females, respectively, for the 11 public health centers combined." "The average number of cigarettes smoked per day tended to decrease in the older age group in males, while there was little difference in females." Results also available for age at initiation of smoking.
Wada, K; 2001	6,115	Cross Sectional	No Abstractable Data	"The % of Lifetime smokers, who had at least one incidence of cigarette smoking was 30.7% for male subjects, 14.9% of

Smoking Habits

Author	Subjects	Study Type	Data	Comments
				females subjects, and 22.9% of all subjects. These percentages were broken down into 17.1% of 1st grade students, 26.5% of 2nd grade students, and 24.9% of 3rd grade students."
Wada, K et al; 1994	5,240	Cross Sectional	No Abstractable Data	"Of all students, 30.5% of male subjects, 13.3% of female subjects and 22.2% of the total were lifetime smokers." Results also available for opinions on tobacco smoking, and the relationship between smoking tobacco and drinking alcohol.

Snoring

Author	Subjects	Study Type	Data				Comments
Kimura, H et al; 1993	5,706	Cross Sectional					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Mild Snoring.
			< 10	1.00			
			11 - 20	1.18			
			> 20	1.13			
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Severe Snoring.
			< 10	1.00			
			11 - 20	1.08			
			> 20	1.95			

Social Factors

Author	Subjects	Study Type	Data	Comments
Ohida, T et al; 2001	31,627	Cross Sectional	No Abstractable Data	"The present study showed that the smoking prevalence in men was higher than women (Table 2)." "The overall influence of social factors on smoking is assumed to be greater in women than in men." "Smoking prevalence among both men and women becomes lower as they become older." "As to occupation, male wage earners were more likely to smoke than those not earning, but that was not found significantly in the case of women." "As shown in Table 5, no correlation between the smoking prevalence and a household size of two and three-generation was observed for men." "The present study showed that women who lived alone were more likely to be smokers than those living in three-generational households."
Ohida, T et al; 2000	10,069	Cross Sectional	No Abstractable Data	Table 2 shows that place of residence and age were associated with the habit of smoking both in men and women." "Household size was also associated with the habit of smoking in women, that association was not observed for men." "Women between the age of 20-34 and 40-59 who lived alone were more likely to be smokers than women living in larger households." "The influence of smoking in women from social factors such as place of residence, occupation, and household size, is assumed to be greater than in males, as shown in Table 2."

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
Akiba, S; 1994	61,505	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Ex-Smoker	1.30	1.1 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Race (Asian), Gender (Both). Adjusted for Age, Gender, Residence Location, Smoking Habits.
			Never Smoker	1.00			
			Current Smoker	1.40	1.2 - 1.7		
Akiba, S et al; 1990	256,000	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.40	1 - 1.8		
			5 - 14	1.40	1.3 - 1.6		
			15 - 24	1.50	1.4 - 1.7		
			25 - 34	1.40	1.1 - 1.7		
			> 34	1.70	1.3 - 2.2		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			0	1.00			
			1 - 4	1.20	0.8 - 1.7		
			5 - 14	1.30	1.1 - 1.5		
			> 14	0.80	0.5 - 1.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.50	1.3 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Date of Examination, Occupation, Residence Location, Study Center.
			Never Smoker	1.00			
			Ever Smoker	1.20	1 - 1.4		
Hamada, GS et al; 2002	96 Cases 192 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hospitalized Controls. Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.3 - 1.9		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			0	1.00			
			< 30	0.60	0.3 - 1.3		
			30 - 50	1.10	0.4 - 2.7		
			> 50	0.50	0.2 - 1.5		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.60	0.3 - 1.2		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Hospitalized Controls. Adjusted for Age, Gender.
			0	1.00			
			< 30	0.70	0.3 - 1.6		
			30 - 50	1.20	0.5 - 3.3		
			> 50	0.80	0.2 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Hospitalized Controls. Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.3 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.70	0.3 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00	0.4 - 2.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Current Smoker	0.90	0.3 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Current Smoker	0.70	0.3 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Country of Birth, Gender.
			Never Smoker	1.00			
			Current Smoker	0.80	0.4 - 2		
Hanaoka, T et al; 2001	432 Cases 428 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Ser Genotype. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Ever Smoker	1.99	1.18 - 2.41		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Ser/Cys + Cys/Cys Genotype. Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Ever Smoker	1.18	0.58 - 2.41		
Hirayama, T; 1990	265,118	Cohort					Coronary Heart Disease = ischemic heart disease. Atherosclerosis = aneurysm. Chronic Obstructive Pulmonary Disease = emphysema. Pharyngeal Cancer = buccal/pharynx cancer. Gall Bladder Cancer = bile duct/gall bladder cancer.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.45	1.33 - 1.57		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.18	1.05 - 1.33		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.45	1.28 - 1.64		
			10 - 19	1.41	1.29 - 1.54		
			> 19	1.49	1.36 - 1.63		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 9	1.26	1.06 - 1.48		
			10 - 19	1.11	0.91 - 1.34		
			> 19	0.76	0.46 - 1.26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-59), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.27			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (60-69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.49			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>69), Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.50			

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.54	1.21 - 1.95		
			5 - 9	1.59	1.18 - 2.13		
			> 9	0.87	0.61 - 1.24		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			0	1.00			
			1 - 4	1.42	0.63 - 3.22		
			5 - 9	1.82	0.68 - 4.87		
			> 9	1.40	0.45 - 4.34		
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.37	1.28 - 1.46		
Hirayama, T; 1986	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Current Smoker	1.00			
			Never Smoker	0.50			
Hirayama, T; 1985	91,450	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			Never Smoker	1.00			
			Ex-Smoker	1.15			
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse).
			0	1.00			
			1 - 14	1.00			
			15 - 19	1.00			
			> 19	1.01			
Hirayama, T; 1985	122,261	Cohort					Diminished Health Status = Pneumonia, bronchitis Coronary Health Disease = Ischemic Heart Disease
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Alcohol Consumption, Meat Consumption, Vegetable Intake.
			Non-Smoker	1.00			
			Current Smoker	0.71			
Hirayama, T; 1984	91,540	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.15			

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Gender.
			0	1.00			
			1 - 14	1.00			
			15 - 19	1.00			
			> 19	1.01			
Hirayama, T; 1984	265,118	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			> 25	1.50			
Hirayama, T; 1981	91,540	Cohort					The asthma outcome also includes women with emphysema.
			Source: Cigs / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Occupation.
			0	1.00			
			1 - 19	1.02			
			> 19	0.99			
Hiyama, T et al; 1992	472	Cohort					Outcome of interest = development of secondary primary cancer following laryngeal cancer. Cancer= cancer from all sites for which results are available, except larynx.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			0	1.00			
			1 - 19	2.30			
			20 - 39	0.80			
			> 39	1.50			
Hoshino, H et al; 1985	460 Cases 460 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Both), No Family History of Gastric Cancer. Adjusted for Age, Family History of Cancer, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.08			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Both), No Family History of Gastric Cancer. Adjusted for Age, Family History of Cancer, Gender.
			Non-Smoker	1.00			
			Current Smoker	2.83			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Both), Family History of Gastric Cancer. Adjusted for Age, Family History of Cancer, Gender.
			Non-Smoker	1.00			
			Current Smoker	3.49			
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Both), Family History of Gastric Cancer. Adjusted for Age, Family History of Cancer, Gender.
			Non-Smoker	1.00			
			Current Smoker	5.31			
Hoshiyama, Y et al; 1992	251 Cases	Case-Control					

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
	483 Controls						
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Single. Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.10	0.6 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Single. Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.50	0.9 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Multiple. Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	0.90	0.3 - 3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Multiple. Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.40	0.5 - 4.3		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Single. Adjusted for Age.
			0	1.00			
			1 - 800	1.40	0.8 - 2.3		
			> 800	1.30	0.8 - 2.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Multiple. Adjusted for Age.
			0	1.00			
			1 - 800	1.10	0.3 - 3.3		
			> 800	1.30	0.4 - 4.2		
Hoshiyama, Yoshiharu et al; 1992	294 Cases 496 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Population Based Controls. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.6 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Population Based Controls. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 29	1.80	1.1 - 3		
			> 29	1.80	0.9 - 3.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Population Based Controls. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 40	1.50	0.9 - 2.4		
			> 40	1.60	0.9 - 2.8		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Hospitalized Controls. Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	0.60	0.3 - 1.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Hospitalized Controls. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 29	1.00	0.5 - 1.7		
			> 29	0.70	0.3 - 1.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Hospitalized Controls. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 40	0.90	0.5 - 1.6		
			> 40	0.70	0.3 - 1.4		
Huang, X et al; 1999	887 Cases 28,619 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	2.22	1.68 - 2.93	< .001	
Inoue, M et al; 1994	668 Cases 668 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	2.56	1.74 - 3.77		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.18	0.71 - 1.97		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			1 - 19	2.70	1.61 - 4.54		
			> 19	2.70	1.77 - 4.14		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			> 9	2.27	1.39 - 3.69		
			1 - 9	2.51	1.52 - 4.14		
			< 1	2.64	1.17 - 5.19		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	4.44	1.75 - 11.3		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.79	1.04 - 3.05		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	2.89	1.65 - 5.07		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			1 - 20	4.28	1.59 - 11.5		
			> 20	5.94	2.04 - 17.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			1 - 20	2.17	1.21 - 3.9		
			> 20	1.35	0.62 - 2.97		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			1 - 20	3.01	1.64 - 5.53		
			> 20	2.97	1.45 - 6.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	4.71	1.81 - 12.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.93	1.1 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	3.01	1.68 - 5.42		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	4.12	1.55 - 11		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.61	0.89 - 2.91		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Exposed	2.74	1.5 - 5.01		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			< 1	6.85	1.88 - 25		
			1 - 9	4.68	1.6 - 13.7		
			> 9	2.81	0.92 - 13.7		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			< 1	3.63	0.77 - 5.76		
			1 - 9	1.41	0.67 - 2.95		
			> 9	1.70	0.86 - 3.36		
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			0	1.00			
			< 1	2.14	0.73 - 6.05		
			1 - 9	3.03	1.52 - 6.05		
			> 9	2.72	1.52 - 5.36		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Cardia. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.28	0.52 - 3.11		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Middle. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.00	0.48 - 2.09		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Antrum. Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.31	0.66 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.95	1.43 - 2.66	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Gastric Cardia). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	2.68	1.45 - 4.96	< .05	

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Middle). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	1.48	0.96 - 2.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Antrum). Adjusted for Age, Gender, Time of First Hospital Visit.
			Never Smoker	1.00			
			Ever Smoker	2.20	1.44 - 3.35	< .05	
Inoue, Manami et al; 1999	995 Cases 43,846 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.70	1.28 - 2.26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	2.50	1.9 - 3.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.18	1.4 - 3.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	3.25	2.17 - 4.86		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.35	0.93 - 1.95		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.88	1.3 - 2.71		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.37	0.8 - 2.34		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.74	1.28 - 2.36		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.14	1.11 - 4.14		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.66	1.1 - 2.48		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.32 - 1.99		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.99	1.24 - 3.21		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.93	1.3 - 2.86		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	2.73	1.86 - 3.99		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.37	1.15 - 4.88		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	3.96	2.04 - 7.68		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.65	1.03 - 2.65		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	2.03	1.27 - 3.25		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.23	0.49 - 3.09		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.60	0.91 - 2.81		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.49	0.74 - 8.32		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-59), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.45	0.62 - 3.39		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	0.72	0.17 - 3.03		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.86	0.88 - 3.91		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.50	0.99 - 2.26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	2.32	1.59 - 3.38		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.21	1.25 - 3.91		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	3.01	1.8 - 5.05		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	0.92	0.51 - 1.66		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.60	0.91 - 2.81		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	1.42	0.74 - 2.72		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.76	1.21 - 2.54		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	2.01	0.92 - 4.41		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (18-60), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	1.68	1.05 - 2.67		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Ex-Smoker	0.85	0.26 - 2.76		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>60), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			Never Smoker	1.00			
			Current Smoker	2.08	1.13 - 3.8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.50	1.9 - 3.49		
			> 19	2.50	1.84 - 3.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.72	1.83 - 4.03		
			> 19	2.76	1.78 - 4.28		

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.33	1.58 - 3.45		
			> 19	2.29	1.5 - 3.5		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	3.32	2.18 - 5.07		
			> 19	3.18	2.06 - 4.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	4.10	2.06 - 8.17		
			> 19	3.81	1.88 - 7.72		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	3.05	1.77 - 5.25		
			> 19	2.98	1.71 - 5.19		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Male), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.65	0.93 - 2.94		
			> 19	1.35	0.61 - 2.95		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Male), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.99	1.22 - 3.22		
			> 19	2.17	1.2 - 3.96		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Male). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.87	1.28 - 2.73		
			> 19	1.87	1.16 - 3.03		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.99	1.21 - 3.26		
			> 19	2.19	0.5 - 9.58		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.78	0.82 - 3.89		
			> 19	3.09	0.39 - 24.28		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	2.12	1.14 - 3.95		
			> 19	1.73	0.23 - 13.25		

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.66	1.02 - 2.71		
			> 19	1.95	0.6 - 6.26		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.41	0.57 - 3.48		
			> 19	1.82	0.24 - 13.73		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<60), Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.64	1.07 - 2.51		
			> 19	1.88	0.68 - 5.17		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.73	1.25 - 2.38		
			> 19	1.94	0.85 - 4.47		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Differentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.55	0.86 - 2.81		
			> 19	2.22	0.53 - 9.36		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Undifferentiated). Adjusted for Age, Age at First Hospital Visit, Alcohol Consumption, Family History/Index Disease, Fruit Intake, Preference for Salty Food, Year and Season of Hospital Visit.
			0	1.00			
			1 - 19	1.76	1.19 - 2.58		
			> 19	1.87	0.68 - 5.14		
Kato, I et al; 1992	3,914	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.17	0.47 - 2.94		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.08	0.36 - 3.26		
			> 19	2.24	0.92 - 5.44		
Kato, I et al; 1990	1,841 Cases 3,014 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Diffuse). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	2.67	1.37 - 5.22		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.81	1.17 - 2.79		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	1.93	1.13 - 3.3		
			> 19	2.81	1.83 - 4.29		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	0.63	0.22 - 1.79		
			> 19	1.53	0.63 - 3.74		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Non-Smoker	1.00			
			Ex-Smoker	1.28	0.52 - 3.14		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Diffuse). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	1.76	0.73 - 4.22		
			> 19	3.32	1.71 - 6.44		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Intestinal). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.58	0.91 - 2.75		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Intestinal). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	2.25	1.16 - 4.34		
			> 19	2.95	1.7 - 5.09		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Diffuse). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.01	0.3 - 3.39		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Diffuse). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	0.49	0.12 - 2.07		
			> 19	1.09	0.33 - 3.62		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Intestinal). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.18	0.26 - 5.34		

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Histology (Intestinal). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	0.78	0.17 - 3.58		
			> 19	2.73	0.75 - 9.91		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			Never Smoker	1.00			
			Ex-Smoker	1.90	1.19 - 3.03		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Gender, History of Gastric Ulcer, Residence Location.
			0	1.00			
			1 - 19	1.83	1.02 - 3.28		
			> 19	2.84	1.79 - 4.51		
Kato, I et al; 1985	265 Cases 1,412 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Site of Cancer, Year of Diagnosis.
			0 - 29	1.00			
			> 29	1.74		> .05	
Kato, Ikuko et al; 1992	9,753	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.56	0.81 - 8.12		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.58	1.09 - 6.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	4.87	0.64 - 36.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.69	0.39 - 7.31		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Cooking Method, Family History/Index Disease, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.62	0.97 - 7.05		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Cooking Method, Family History/Index Disease, Gender.
			Never Smoker	1.00			
			Current Smoker	2.18	1.07 - 4.43		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.61	0.97 - 7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.29	1.15 - 4.56		
Kobayashi, Y et al; 1990	17 Cases	Nested Case-Control	No Abstractable Data				"For second lung cancer, smokers (current and ex-smokers) were prevalent among all MPC cases and in 81% controls ($p<0.05$). Heavy smokers were also more prevalent among MPC cases than among controls ($p<0.1$)" "For second oropharyngeal cancer, heavy smokers were prevalent in 42% of controls but in none of MPC cases ($p<0.1$)"
Komoto, K et al; 1998	141 Cases 105 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Intestinal). Adjusted for Age, Alcohol Consumption, Blood Type, Coffee, Family History of Cancer, Gender, Helicobacter pylori.
			Non-Smoker	1.00			
			Current Smoker	3.05	1.58 - 5.93		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Diffuse). Adjusted for Age, Alcohol Consumption, Blood Type, Coffee, Family History of Cancer, Gender, Helicobacter pylori.
			Non-Smoker	1.00			
			Current Smoker	2.18	0.77 - 6.16		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Histology (Adenoma). Adjusted for Age, Alcohol Consumption, Blood Type, Coffee, Family History of Cancer, Gender, Helicobacter pylori.
			Non-Smoker	1.00			
			Current Smoker	3.05	0.7 - 5.3		
Kono, S et al; 1988	139 Cases 2,852 Controls	Case-Control					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Controls: Hospital Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.20		> .05	
			> 19	1.90			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Controls: Hospital Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	2.50		< .05	
			> 19	1.40		> .05	

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Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Controls: Hospital Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.70		< .05	
			> 19	2.50		< .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Controls: General Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.10		> .05	
			> 19	1.80		> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Controls: General Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.10		> .05	
			> 19	1.00		> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Controls: General Population. Adjusted for Age, Gender, Residence Location.
			0	1.00			
			1 - 19	1.10		> .05	
			> 19	1.80		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Controls: General Population. Adjusted for Age, Fruit Consumption, Gender, Green Tea Consumption, Mandarin Orange Consumption, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.30	0.8 - 2.2	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Controls: Hospital Population. Adjusted for Age, Fruit Consumption, Gender, Green Tea Consumption, Mandarin Orange Consumption, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	1.80	1.1 - 2.9	< .01	
Kono, S et al; 1985	5,477	Cohort					Upper aerodigestive cancer: Cancer with ICD 8th codes 140-150 (Malignant neoplasm of buccal cavity, pharynx and oesophagus), 160 (Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses) and 161 (Malignant neoplasm of larynx).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	0.78	0.37 - 1.64		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	1.40	0.77 - 2.55		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	0.91	0.35 - 2.35		
			10 - 19	1.82	0.94 - 3.52		
			> 19	1.19	0.55 - 2.56		

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Author	Subjects	Study Type	Data				Comments
Kono, Suminori et al; 1987		Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	1.66	1.07 - 2.59		
			> 19	1.79	1.09 - 2.96		
Kuwahara, Y et al; 2000	566	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Atrophic gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.6 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Atrophic gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.7 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Atrophic gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			0	1.00			
			1 - 25	0.90	0.6 - 1.5		
			> 25	1.00	0.6 - 1.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Atrophic gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			0	1.00			
			1 - 25	0.90	0.6 - 1.5		
			> 25	1.00	0.6 - 1.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Moderate Atrophic Gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.6 - 1.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Moderate Atrophic Gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			0	1.00			
			1 - 25	0.60	0.3 - 1.1		
			> 25	0.60	0.3 - 1.4		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Severe Atrophic Gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			0	1.00			
			1 - 25	1.40	0.8 - 2.7		
			> 25	1.70	0.8 - 3.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Severe Atrophic Gastritis). Adjusted for Alcohol Consumption, H pylori, Rank.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.6 - 2.3		
Mizoue, Tetsuya et al; 2000	4,050	Cohort					

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.20	0.8 - 6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			Never Smoker	1.00			
			Current Smoker	2.20	0.8 - 5.7		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age at Entry, Alcohol Consumption, Area, Gender.
			0	1.00			
			1 - 24	2.20	0.8 - 6		
			> 24	1.90	0.6 - 6.4		
Namekata, T et al; 2000	776	Cross Sectional					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	0.76	0.32 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	0.76	0.24 - 2.42		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	1.06	0.43 - 3.26		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, Gender, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	1.18	0.19 - 6.04		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 1st Generation. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	1.31	0.3 - 5.81		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 1st Generation. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	0.49	0.04 - 6.06		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 2nd-4th Generations. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Current Smoker	1.04	0.36 - 3.02		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), 2nd-4th Generations. Adjusted for 1-Hour Postload Glucose, Age, Alcohol Consumption, H pylori Positive Peptic Ulcer, History of Peptic Ulcers, Parental History of Gastric Cancer, Years of Living in Japan.
			Never Smoker	1.00			
			Ex-Smoker	0.81	0.39 - 1.7		
Nishimoto, IN et al; 2002	236 Cases 236 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Education, Gender, Race.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.6 - 2.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Diet, Education, Gender, Race.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.6 - 2.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Education, Gender, Race.
			Never Smoker	1.00			
			Ex-Smoker	1.30	0.6 - 2.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Education, Gender, Race.
			Never Smoker	1.00			
			Ex-Smoker	1.20	0.6 - 2.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Education, Gender, Race.
				1.00			
				0.90	0.5 - 1.6		
				2.50	1.3 - 4.5		
			> 50	2.00	1.1 - 3.8		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Diet, Education, Gender, Race.
				1.00			
				0.90	0.5 - 1.6		
				2.10	1.1 - 3.9		
			> 50	2.10	1.1 - 4.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Education, Gender, Race.
			Never Smoker	1.00			
			Current Smoker	1.70	1.1 - 2.7		

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Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Diet, Education, Gender, Race.
			Never Smoker	1.00			
			Current Smoker	1.60	1 - 2.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Education, Gender, Race.
			Never Smoker	1.00			
			Current Smoker	1.70	1.1 - 2.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Diet, Education, Gender, Race.
			Never Smoker	1.00			
			Current Smoker	1.60	0.9 - 2.6		
Nishino, Y et al; 2001	9,675	Cohort					
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Spouse). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.95	0.58 - 1.6		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Source (Other Household). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	0.90	0.52 - 1.5		
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Spouse). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Miso-soup Consumption, Picked Vegetable Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.98	0.59 - 1.6	> .05	
			Source: Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), ETS Time (Adulthood), ETS Location (Residence), ETS Source (Other Household). Adjusted for Age, Alcohol Consumption, Fruit Consumption, Gender, Green Vegetable Consumption, Miso-soup Consumption, Picked Vegetable Consumption, Study Area, Yellow Vegetable Consumption.
			Non-Smoker	1.00			
			Current Smoker	0.87	0.54 - 1.4	> .05	
Nomura, Abraham et al; 1990	7,990	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-65), Race (Asian), Gender (Male). Adjusted for Age at Examination, Gender, Race.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.6 - 1.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-65), Race (Asian), Gender (Male). Adjusted for Age at Examination, Gender, Race.
			Never Smoker	1.00			
			Current Smoker	2.70	1.8 - 4.1		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-65), Race (Asian), Gender (Male). Adjusted for Age at Examination, Gender, Race.
			0	1.00			
			1 - 10	2.70	1.5 - 5.1		
			11 - 30	2.90	1.9 - 4.6		
			> 30	2.40	1.4 - 4.1		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (45-65), Race (Asian), Gender (Male). Adjusted for Age at Examination, Gender, Race.
			0	1.00			
			1 - 25	3.50	1.9 - 6.6		
			26 - 35	1.50	0.9 - 2.7		
			> 35	3.50	2.2 - 5.6		
Nomura, AM et al; 1995	8,006	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Never Smoker	1.00			
			Ex-Smoker	1.10	0.7 - 1.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption.
			Never Smoker	1.00			
			Current Smoker	2.30	1.7 - 3.2		
Sasazuki, S et al; 2002	19,657	Cohort					Cardia Cancer= tumor located in esophagogastric junction or upper 1/3 of stomach.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Gastric Cardia). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Ex-Smoker	1.60	0.5 - 5.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Ex-Smoker	2.00	1.1 - 3.7		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Ex-Smoker	0.90	0.5 - 1.8		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Ex-Smoker	1.60	1.1 - 2.4		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			1 - 19	1.50	0.9 - 2.3		
			20	2.00	1.4 - 3		
			> 21	1.50	1 - 2.4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			0.05 - 20.9	1.40	0.9 - 2.1		
			21 - 33	1.90	1.3 - 2.8		
			> 33.15	1.70	1.2 - 2.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Gastric Cardia). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			0.05 - 20.9	1.70	0.5 - 5.9		
			21 - 33	2.80	0.9 - 8.9		
			> 33.15	1.60	0.5 - 5.5		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			0.05 - 20.9	1.30	0.7 - 2.6		
			21 - 33	2.70	1.5 - 4.9		
			> 33.15	2.20	1.2 - 4		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			0.05 - 20.9	1.00	0.5 - 2		
			21 - 33	0.50	0.2 - 1.1		
			> 33.15	0.60	0.3 - 1.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Gastric Cardia). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			1 - 19	2.00	0.6 - 7.2		
			20	3.00	0.9 - 9.6		
			> 21	2.20	0.6 - 8		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			1 - 19	1.90	1 - 3.7		
			20	2.20	1.2 - 4.1		
			> 21	2.60	1.3 - 4.9		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			0	1.00			
			1 - 19	0.90	0.4 - 1.8		
			20	0.60	0.3 - 1.3		
			> 21	0.30	0.1 - 0.8		

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Gastric Cardia). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Current Smoker	2.40	0.8 - 7.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Differentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Current Smoker	2.10	1.2 - 3.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Histology (Undifferentiated). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Current Smoker	0.60	0.3 - 1.1		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Area, Body Mass Index, Diet.
			Never Smoker	1.00			
			Current Smoker	1.70	1.2 - 2.4		
Stemmermann, GN et al; 1990	350	Cohort					Stomach cancer = Intestinal metaplasia of the stomach.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Ex-Smoker	0.97	0.7 - 1.36		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Never Smoker	1.00			
			Current Smoker	1.07	0.79 - 1.46		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 20	0.92	0.64 - 1.31		
			21 - 40	0.80	0.56 - 1.14		
			> 40	1.37	0.95 - 1.96		
Tajima, K et al; 1985	59 Cases 111 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Education, Gender, Time of Interview.
			Never Smoker	1.00			
			Current Smoker	2.06		> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			Never Smoker	1.00			
			Current Smoker	1.99		> .05	

Stomach Cancer

Author	Subjects	Study Type	Data				Comments
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender, Time of Interview.
			0	1.00			
			< 30	1.18		> .05	
			> 29	2.76		> .05	
Unakami, M et al; 1989	1,347 Cases 221 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Gastric Cardia.
			Non-Smoker	1.00			
			Current Smoker	2.82		< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Gastric Cardia.
			Non-Smoker	1.00			
			Current Smoker	1.35		> .05	
Yokoyama, A et al; 1996		Cross Sectional					Oropharyngeal cancer outcome includes laryngeal cancer cases. Upper aerodigestive cancer outcome includes esophageal cancer, gastric cancer, and oropharyngolaryngeal cancer.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Type of Alcohol.
			< 50	1.00			
			> 49	2.00	0.7 - 5.4		

Stomach Pain

Author	Subjects	Study Type	Data				Comments
Ueda, T et al; 1989	11,574	Cross Sectional					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male).
			0	1.00			
			1 - 20	1.43			
			21 - 40	1.52			
			> 40	1.71			

Stroke

Author	Subjects	Study Type	Data				Comments
Detels, R et al; 1982	1,673	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Cerebral Hemorrhage. Adjusted for Alcohol Consumption, Blood Pressure, Cholesterol, Glucose Tolerance.
			0 - 20	1.00			
			> 20	2.09			
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), Cerebral Infarction. Adjusted for Alcohol Consumption, Blood Pressure, Cholesterol, Glucose Tolerance.
			0 - 20	1.00			
			> 20	1.06			
Kagan, A et al; 1980	8,006	Cohort	No Abstractable Data				The study found that, after age adjustment, the number of cigarettes smoked daily was related to the incidence of thrombo-embolic stroke.
Ohkuma, H et al; 2003	390 Cases 390 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender, Proxy Respondent Use.
			Non-Smoker	1.00			
			Current Smoker	3.12	2.05 - 4.77		
Sankai, T et al; 1999	12,372	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), No Heavy Drinking. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	1.30	0.4 - 4	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Heavy Drinking. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	6.00	1.8 - 20.1	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), No Hypertension. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	1.80	0.4 - 8.5	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), Hypertension. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	6.10	1.3 - 28.7	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), No Hypertension. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	3.90	1.5 - 10.1	< .01	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female), Hypertension. Adjusted for Age, Blood Pressure, Body Mass Index, Cholesterol, History of Diabetes mellitus.
			Never Smoker	1.00			
			Current Smoker	6.30	1.4 - 28	< .01	
Takeya, Y et al; 1984		Cohort	No Abstractable Data				Cigarette smoking was found to be only a significant risk factor

Stroke

Author	Subjects	Study Type	Data				Comments
							for thrombo-embolic stroke in Japan. The study concluded that it seems unlikely that smoking accounts for the difference in stroke frequency between migrant and indigenous Japanese.
Tanaka, H et al; 1985	2,299	Cohort					
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Blood Pressure, Cholesterol, Gender, Glucose Tolerance, Hematocrit.
			0 - 20	1.00			
			> 20	1.33			

Sudden Death

Author	Subjects	Study Type	Data				Comments
Kondo, H et al; 2001	242 Cases 505 Controls	Nested Case-Control					
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Job Title, Work Place.
			0	1.00			
			1 - 19.9	0.96	0.52 - 1.78		
			20 - 39.9	1.57	0.91 - 2.7		
			> 40	2.86	1.4 - 5.84		
Owada, M et al; 1999	91 Cases 958 Controls	Case-Control					The coronary heart disease outcome represents persons whose sudden death as due to coronary artery disease.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Autonomic Disturbance, Chest Symptoms, Diabetes, Gender, Heart Disease, Hypercholesterolemia, Hypertension, Long-term Stress, Occupation, Short-term Stress.
			Non-Smoker	1.00			
			Current Smoker	1.91	1.02 - 3.59	< .05	

Sudden Infant Death Syndrome (SIDS)

Author	Subjects	Study Type	Data				Comments
Tanaka, T et al; 1999	386 Cases 386 Controls	Case-Control					
			Exposure	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both), ETS Time (Childhood), ETS Source (Parents). Adjusted for Age, Birth Weight, Breast Feeding, Controlling the Head, Developmental or Growth Problems, Gender, Residence Location, Room Temperature, Sleeping Position, Thickness of Clothes and Linens, Turn during Sleep, Weeks of Delivery.
			Not Exposed	1.00			
			Exposed	3.02	1.8 - 5.06	< .05	

Systemic Lupus Erythematosus

Author	Subjects	Study Type	Data				Comments
Nagata, C et al; 1995	282 Cases 292 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	2.31	1.34 - 3.97		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.07	0.37 - 3.1		

Teratoma

Author	Subjects	Study Type	Data				Comments
Kobaashi, N et al; 1990	106 Cases 2,616 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	
			Non-Smoker	1.00			
			Current Smoker	1.59			

Tuberculosis

Author	Subjects	Study Type	Data				Comments
Une, H et al; 1993	292 Cases 292 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Education, Gender, Irregular Meal Times, Marital Status, Occupation, Residence Location, Source of Income, Unbalanced Diet.
			Non-Smoker	1.00			
			Current Smoker	1.43	0.9 - 2.27		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Education, Gender, Irregular Meal Times, Marital Status, Residence Location, Source of Income, Unbalanced Diet.
			Non-Smoker	1.00			
			Current Smoker	0.94	0.36 - 2.44		

Ulcerative Colitis

Author	Subjects	Study Type	Data				Comments
Higashi, A et al; 1991	50 Cases 50 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.00	0.03 - 36.49	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00	0.21 - 4.73	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.80	0.18 - 3.41	> .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Gender.
			Never Smoker	1.00			
			Current Smoker	0.50	0.02 - 6.98	> .05	
Nakamura, Y et al; 1994	384 Cases 384 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.44	0.73 - 2.85		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.30	0.16 - 0.56		
Nakamura, Y et al; 1994	384 Cases 384 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.25	0.6 - 2.59		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.23	0.12 - 0.46		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.27	0.91 - 5.66		

Ulcerative Colitis

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.41	0.17 - 0.98		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 14	0.56	0.28 - 1.13		
			15 - 24	0.21	0.1 - 0.43		
			> 24	0.22	0.09 - 0.57		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 4	1.44	0.54 - 3.86		
			5 - 14	0.30	0.14 - 0.65		
			> 14	0.16	0.07 - 0.36		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 4	0.86	0.42 - 1.79		
			5 - 24	0.16	0.07 - 0.34		
			> 24	0.14	0.06 - 0.46		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 14	1.15	0.55 - 2.38		
			15 - 24	1.83	0.86 - 3.88		
			> 24	2.87	0.86 - 9.58		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 4	0.78	0.3 - 1.97		
			5 - 14	1.25	0.53 - 2.84		
			> 14	3.71	1.29 - 10.6		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender.
			0	1.00			
			1 - 4	1.43	0.64 - 3.16		
			5 - 24	1.14	0.53 - 2.44		
			> 24	5.37	1.01 - 28.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<19). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.77	0.03 - 23		

Ulcerative Colitis

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (<19). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	1.00	0.15 - 6.66		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.41	0.77 - 7.58		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (20-29). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.56	0.21 - 1.48		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	0.87	0.29 - 2.63		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (30-39). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.14	0.04 - 0.49		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	3.46	0.9 - 13.3		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (40-49). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.18	0.05 - 0.61		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.44	0.19 - 10.9		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (50-59). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.30	0.04 - 2.62		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.23	0.31 - 15.9		

Ulcerative Colitis

Author	Subjects	Study Type	Data				Comments
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Age (>59). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.29	0.05 - 1.57		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.67	0.97 - 2.88		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both). Adjusted for Age, Alcohol Consumption, Gender.
			Never Smoker	1.00			
			Current Smoker	0.30	0.18 - 0.5		
No authors listed; 1995	101 Cases 143 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender, Inpatient Status, Region.
			Never Smoker	1.00			
			Ex-Smoker	2.40	1 - 6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender, Inpatient Status, Region.
			0	1.00			
			1 - 20	0.60	0.2 - 1.7		
			> 20	0.70	0.2 - 2		
No authors listed; 1994	101 Cases 143 Controls	Case-Control; Hospital-Based					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender, Inpatient Status, Region.
			Never Smoker	1.00			
			Ex-Smoker	2.40	1 - 6		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Adjusted for Age, Alcohol Consumption, Gender, Inpatient Status, Region.
			0	1.00			
			1 - 20	0.60	0.2 - 1.7		
			> 20	0.70	0.2 - 2		

Upper Aerodigestive Cancer

Author	Subjects	Study Type	Data				Comments
Chyou, Po-Huang et al; 1995	7,995	Cohort					Upper aerodigestive cancer includes esophagus, buccal cavity, pharynx, or larynx.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	3.15	1.69 - 5.88	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	1.69	0.82 - 3.48	> .05	
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			0	1.00			
			1 - 19	2.17	0.99 - 4.75		
			20 - 29	2.41	1.22 - 4.74		
			> 29	2.98	1.54 - 5.76		
			Years Smoked	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			0	1.00			
			1 - 24	2.05	0.97 - 4.3		
			25 - 34	2.70	1.37 - 5.31		
			> 34	2.95	1.46 - 5.93		
Kato, Ikuko et al; 1992	6,701	Cohort					Upper-aerodigestive-tract cancer includes oral-pharynx, esophagus, and larynx.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Current Smoker	3.60	1.7 - 7.6	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Ex-Smoker	2.70	1.2 - 6.1	< .05	
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), < 30 ml of Alcohol per day. Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Ever Smoker	3.30	1.3 - 8.4		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male), => 30 ml of Alcohol per day. Adjusted for Age, Alcohol Consumption, Ethnicity, Gender.
			Never Smoker	1.00			
			Ever Smoker	17.30	6.7 - 44.2		
Kawahara, M et al; 1998	70	Cohort					The outcome was development of a second primary tumor in persons who had survived at least 2 years cancer-free. Upper aerodigestive tract=epithelial regions of the head and neck, lung and oesophagus. Cancer=Smoking-related cancers including cancer of the lung,

Upper Aerodigestive Cancer

Author	Subjects	Study Type	Data				Comments
							larynx, oral cavity including pharynx, oesophagus, pancreas, bladder, kidney, stomach and uterine cervix.
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Current Smoker	14.80	5.9 - 30.6		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			Non-Smoker	1.00			
			Ex-Smoker	2.20	0 - 12.1		
Kinoshita, N et al; 1997	669	Cohort					Outcome = second primary cancer. Upper aerodigestive cancers include oral, laryngeal, pharyngeal, and esophageal cancer cases.
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Both).
			0	1.00			
			1 - 19	12.50	0.16 - 69.55		
			> 19	10.00	1.12 - 36.1		
Kono, S et al; 1985	5,477	Cohort					Upper aerodigestive cancer: Cancer with ICD 8th codes 140-150 (Malignant neoplasm of buccal cavity, pharynx and oesophagus), 160 (Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses) and 161 (Malignant neoplasm of larynx).
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Ex-Smoker	1.86	0.17 - 20.5		
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			Non-Smoker	1.00			
			Current Smoker	5.87	0.75 - 46		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age.
			0	1.00			
			1 - 9	2.32	0.14 - 37.5		
			10 - 19	4.89	0.55 - 43.7		
			> 19	8.89	1.03 - 76.5		
Kono, Suminori et al; 1987	5,130	Cohort					For upper aerodigestive cancer results: Cancer with ICD 8th codes 140-150 (malignant neoplasm of buccal cavity, pharynx and oesophagus) and 161 (Malignant neoplasm of larynx).
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Sake Drinking.
			0	1.00			
			1 - 19	1.16	0.3 - 4.53		
			> 19	2.98	0.86 - 10.38		
Morita, M et al; 1994	30 Cases	Case-Control					

Upper Aerodigestive Cancer

Author	Subjects	Study Type	Data				Comments
	113 Controls						
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Family History of Cancer.
			Never Smoker	1.00			
			Current Smoker	5.30	0.8 - 34.3		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Family History of Cancer.
			0	1.00			
			1 - 14	5.00	0.6 - 43.9		
			15 - 29	5.70	0.9 - 38		
			> 29	17.50	3.2 - 94.7		
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Family History of Cancer.
			0	1.00			
			1 - 24	1.20	0 - 84		
			25 - 49	2.80	0.3 - 26.4		
			> 49	12.70	2.1 - 19.5		
Takezaki, T et al; 2000	346 Cases 11,936 Controls	Case-Control; Hospital-Based					Upper aerodigestive cancer are results for cancer of the hypopharynx or esophagus combined.
			Years Quit	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			< 14	1.00	0.5 - 1.8		
			8 - 14	1.60	0.9 - 2.9		
			1 - 7	1.80	1 - 3.1		
			Cigarettes / Day	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Age, Alcohol Consumption, Date of Admission, Diet, Gender.
			0	1.00			
			1 - 19	2.80	1.7 - 4.6		
			20 - 29	3.00	1.9 - 4.8		
			30 - 39	3.50	2.1 - 6		
			> 39	3.40	2 - 6		
Yokoyama, A et al; 1996	1,000	Cross Sectional					Oropharyngeal cancer outcome includes laryngeal cancer cases. Upper aerodigestive cancer outcome includes esophageal cancer, gastric cancer, and oropharyngolaryngeal cancer.
			Pack Years	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Male). Adjusted for Alcohol Consumption, Type of Alcohol.
			< 50	1.00			
			> 49	2.00	1.1 - 3.7		

Uterine Cancer

Author	Subjects	Study Type	Data				Comments
Hirayama, T; 1990	265,118	Cohort					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Gender.
			Non-Smoker	1.00			
			Current Smoker	1.57	1.3 - 1.89		
Kato, I et al; 1989	2,396 Cases 8,920 Controls	Case-Control					
			Active Smoking Status	**Risk Estimate**	**95% CI**	**P-Value**	Stratified by Gender (Female). Adjusted for Age, Alcohol Consumption, Gender, Marital Status, Occupation, Residence Location.
			Never Smoker	1.00			
			Ever Smoker	0.45	0.27 - 0.76		

White Blood Cell Count

Author	Subjects	Study Type	Data	Comments
Nakanishi, N et al; 2002	2,953	Cross Sectional	No Abstractable Data	The study found that white blood cell count could predict the development of impaired fasting glucose or type II diabetes mellitus, primarily in non-smokers.