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On the Brink of Elimination:
Preventing the Resurgence of Drug-Resistant Malaria

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Introduction

Around the world, malaria persists in tropical regions as a life-threatening disease that burdens communities and healthcare systems (Fikadu and Ashenafi 2023). This global disease is caused by infection of a protozoan endoparasite from the genus *Plasmodium*, which is transmitted between individuals through *Anopheles* mosquitoes (Service 2012). Patients infected with malaria experience debilitating symptoms, including high fevers and body chills, which can interfere with daily life and reduce economic productivity (Lukwa et al. 2019). In a developing country, such as Cambodia, inadequate healthcare infrastructure and socioeconomic disparities limit access to life-saving drug treatments, especially in rural communities (Sorn 2025). Such barriers have significant effects on family households, where children with more severe infections may have long-term cognitive effects (Vorasan et al. 2015).

Despite intense ongoing efforts to limit the spread of the disease, progress in decreasing the global malaria burden has stalled (Weiss et al. 2025). Additionally, not only does malaria heavily strain healthcare systems in developing regions, but its treatment is also steadily becoming less effective as the parasite evolves resistance to current medications (WHO 2025). Due to the growing antimalarial drug resistance, eradication of malaria must be a top priority to improve the quality of life for millions of people around the world.

Geographic Localization and Epidemiology

History of Malaria

Throughout human history, numerous malaria epidemics have occurred, ranging from the fall of the Roman Empire to modern-day Sri Lanka (Sallares 2002; Wijesundere and Ramasamy 2017). Malaria infection significantly impairs the capacity for affected individuals to carry out daily tasks and perform work, thereby hindering economic productivity (Lukwa et al. 2019). Eradication of malaria would therefore benefit not only the quality of life for citizens but also the financial prosperity of the country.

From 1975 to 1979, the Communist Khmer Rouge regime seized power and dismantled the healthcare system in its mission to eliminate Western influences, thereby contributing to malaria outbreaks that were poorly documented (Hiebert 2017). One of the most common diseases among Cambodian refugees was malaria, where 55% of the cases were caused by *Plasmodium falciparum* infection (Dahlberg 1980). Since then, Cambodia has been gradually rebuilt with modern healthcare infrastructure, enabling the approach toward malaria elimination by the end of 2025 (Doum et al. 2025).

Current Malaria Distribution and Future Eradication

Malaria thrives in tropical regions around the world due to the favorable warm, humid conditions that support mosquito breeding (Hamza and Rayah 2016). The disease is primarily found in sub-Saharan Africa, where four countries were responsible for slightly more than half of global malaria deaths in 2024 (WHO 2025). Although Africa currently experiences the highest malaria burden, it is also important to sustain efforts in historically endemic regions to achieve eradication. Located near the equator, Cambodia possesses wetlands and mangrove marshes that serve as hotspot breeding sites for mosquitoes (Boyer et al. 2025). The Pailin province was historically known as a malaria hotspot, but now, there are few to no infections, thanks to active case detection (Hustedt et al. 2016).

However, malaria still exists in *Anopheles* mosquito vectors, so the current efforts must be maintained to achieve eradication and prevent the resurgence of resistant malaria infections (Boyer et al. 2025). Vector monitoring and control must be focused on jungle regions such as the Mondulkiri forest, which not only contains *Plasmodium*-infected mosquitoes but also hosts natural mosquito breeding grounds that cannot be eliminated (Boyer et al. 2025). By targeting forested areas and continuing malaria testing in rural communities, eradication of malaria in Cambodia may become realized.

Climate Change Threatens Eradication Efforts

Climate change expands the fundamental niche of mosquitoes further from the equator and toward higher altitudes by increasing ambient temperatures (Lyberger et al. 2025). Previously hostile geographical barriers, such as mountains, are becoming less effective at restricting mosquito migration, especially in Africa (Carlson et al. 2023). Besides natural range expansion, mosquitoes can spread into new regions by human mobility and wind dispersal (Acosta et al. 2025). Future plans to control malaria must take the potential range expansion of mosquitoes into account by also monitoring regions that are slightly outside of the current known range of mosquitoes to detect early malaria cases.

Vector Biology

Lifecycle of Anopheles Mosquitoes

Anopheles mosquitoes thrive in tropical climates with consistently warm, humid conditions (Hamza and Rayah 2016). These mosquitoes prefer to lay their eggs on unpolluted bodies of water, ranging from puddles and marshes to rivers and ricefields (Boyer et al. 2025; Munga et al. 2005). On sheltered water surfaces, blood-fed female adults lay 50–200 boat-shaped eggs, one at a time (Munga et al. 2005; Service 2012). These brown to black eggs contain air-filled floats and are sensitive to desiccation (Berenbaum 1995; Service 2012). After 2–3 days of incubation at tropical temperatures, or optimally around 27°C, the eggs hatch into larvae (Christiansen-Jucht et al. 2015; Service 2012).

As larvae progress through four instars, or developmental phases, they avoid predation by rapidly swimming to the bottom of the water in response to shadows or vibrations, followed by resurfacing in seconds to minutes (Service 2012). After about 7 days under tropical conditions, larvae metamorphosize into comma-shaped pupae for 2–3 days (Service 2012). Pupae have conical respiratory trumpets and continue to respond to disturbances, though their swimming movements are more vigorous and janky (Service 2012).

Most species are either crepuscular or nocturnal (Service 2012). Common major vectors in Southeast Asia include *Anopheles dirus* and *Anopheles minimus*, both of which prefer shaded areas (Obsomer et al. 2013; Service 2012). The former typically feeds outdoors while the latter feeds indoors, for females require blood meals for proper egg development (Berenbaum 1995; Service 2012). Therefore, traps for adult mosquitoes should be placed in shaded areas, both outside and inside buildings.

Measuring Vector Presence and Abundance

To detect the presence and abundance of mosquitoes, measures should prioritize rural villages, where mosquitoes are expected to be most abundant due to human hosts (Guo et al. 2025). However, uninhabited areas should also contain a few traps to effectively monitor migrations where mosquitoes may not only breed and lay eggs but also feed on alternative hosts (Guo et al. 2025). Mosquito traps containing high concentrations of carbon dioxide mimic the attractant of exhaled breath from humans and should be set to monitor adult populations (Wu et al. 2025). The surfaces of water must also be sampled through dip cups to monitor larval and pupal abundances (Mamai et al. 2019). Although sampling should occur year-round, a higher frequency of sampling should take place during the wet season since the increased humidity further supports mosquito breeding and maturation (Hamza and Rayah 2016).

Strategies to Reduce Vector Population

To effectively reduce the mosquito population, multiple stages of its life cycle must be targeted simultaneously (Guo et al. 2025). To target the larval stage of *Anopheles* mosquitoes, larvicides should be used at an effective dose deemed safe for non-target arthropods, fish, and humans (Cameron and Lorenz 2013). Reducing mating success can be achieved by introducing males that are sterile or carry deleterious genes that harm fitness (Cameron and Lorenz 2013). Additionally, insecticide-treated nets that surround beddings and windows should be provided to

rural villages to inhibit blood feeding (Matthews 2011). The effectiveness of these control measures should be evaluated by continuously monitoring mosquito populations at multiple stages, including sampling hotspot breeding sites for larval abundance and adult trapping (Guo et al. 2025). These measures would be deemed successful by a marked decrease in mosquito abundance for all life stages around rural communities and uninhabited jungle regions.

Pathogen Biology

Plasmodium Causes Malaria

Malaria is caused by infection of a protozoan endoparasite from the genus *Plasmodium*, which is transmitted through *Anopheles* mosquitoes (Service 2012). Five *Plasmodium* species naturally infect humans: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale* and *P. knowlesi* (Sato 2021). In Cambodia, *P. falciparum*, *P. vivax*, and *P. knowlesi* are the top three species responsible for malaria cases (Jeyaprakasam et al. 2020; Siv et al. 2016). Control efforts have been targeting *P. falciparum* due to its growing resistance to artemisinin, leading to a significant drop in its incidence (Siv et al. 2016). Although effective progress has been made to reduce the total prevalence of malaria, not only does the narrow focus on *P. falciparum* contribute to *P. vivax* being overlooked, but *P. vivax* also has a relatively low parasitemia that increases the chances of false negative diagnoses and relapses (Siv et al. 2016). Unlike *P. falciparum* and *P. vivax*, *P. knowlesi* has natural reservoirs in macaque monkeys, making eradication particularly challenging (Jeyaprakasam et al. 2020; Sato 2021; van de Straat et al. 2022).

Lifecycle of Plasmodium

All *Plasmodium* species enter the blood of a human as sporozoites through the bite of an infected female *Anopheles* mosquito (Frischknecht and Matuschewski 2017). These sporozoites rapidly migrate to the liver and multiply inside the liver cells, where they differentiate into merozoites (Amino et al. 2006; Prudêncio et al. 2006; Roques et al. 2023). The merozoites then

exit through lysis and infect erythrocytes to reproduce asexually, followed by lysis and infection of new erythrocytes in a repeated cycle of merozoite propagation (Gerald et al. 2011; Sturm et al. 2006). Some merozoite differentiate into gametocytes that are then transmitted into a female mosquito during a blood meal (Bancells et al. 2019; Josling and Llinás 2015).

Within the midgut of the mosquito, the gametocytes develop into male or female gametes, which fuse to form a zygote (Bennink et al. 2016). After differentiating into a mobile ookinete, it penetrates the midgut wall and gives rise to an oocyst that ruptures upon maturation, releasing sporozoites into the haemolymph (Bennink et al. 2016; Smith and Jacobs-Lorena 2010; Siciliano et al. 2020). These sporozoites migrate to the salivary glands of the mosquito, where they wait for the opportunity of a blood meal to infect the next human host (Smith and Jacobs-Lorena 2010).

Detection and Diagnostic Methods

To detect the *Plasmodium* pathogen in reservoir animal populations, regular blood samples should be collected from captive macaque monkeys stationed as strategic points between villages, followed by ELISA analysis for the presence of antibodies against *Plasmodium*-associated antigens (Beshir et al. 2022). Occasional blood samples should also be collected from domestic animals in rural villages, such as dogs and pigs, since they may serve as additional reservoirs for the parasite (Munirah et al. 2021). Positive detection of *Plasmodium* in the animals will provide early warnings to the local villages at risk of malaria.

Broad monitoring of *Plasmodium* in human populations should be facilitated by rapid diagnostic tests (RDTs), which can quickly test for the presence of *Plasmodium*-associated antigens in a patient's blood at a low cost (Orish et al. 2018). Although these RDTs are portable and thus readily deployable in rural villages, they may provide false positives (Lee et al. 2014). To confirm an active infection and identify the specific *Plasmodium* species, the sample should be sent to a medical institution for further analysis with microscopy and a polymerase chain

reaction (PCR), which are more expensive but far more accurate (Ghosh et al. 2017; Srisutham et al. 2020). In case the RDTs provide false negative results for asymptomatic or low-parasitemia cases, a few random blood samples collected from villagers should undergo evaluation by microscopy and PCR, which examines a blood smear for the presence of the parasite and tests for the presence of parasite DNA material, respectively (Watson et al. 2019). The broad deployment of the RDTs, combined with the accuracy of microscopy and PCR, should cover enough of the Cambodian population with sufficient sensitivity to provide early warnings of an epidemic.

Disease Pathology and Treatment

Pathology of Malaria in Humans

Symptoms of malaria vary in length and severity among individuals (Bartoloni and Zammarchi 2012). Typically, nonspecific flu-like symptoms begin about 7–30 days after a mosquito bite, when the parasite lyses red blood cells as a consequence of its intracellular multiplication (Fikadu and Ashenafi 2023). Such lysis triggers fever and chills, which raise the core body temperature to increase the efficiency of the immune response (Walter et al. 2016). A hallmark of malaria is intense, periodic fevers that last 6–8 hours, whose cycle length varies by species due to the timing of erythrocyte lysis during asexual propagation, though this periodic characteristic may be absent in some cases (Bartoloni and Zammarchi 2012). Other nonspecific symptoms include soreness and tiredness from both the growth of the parasite and the high energy requirements of the immune response (Idokoko et al. 2017).

Serious infection results in severe complications, including anemia and jaundice from the lysis of red blood cells and liver cells, respectively (Giribaldi et al. 2015). As the parasite digests hemoglobin in red blood cells, it aggregates toxic heme into insoluble inert crystals that further triggers inflammation (Giribaldi et al. 2015). Left untreated, the disease may progress to kidney failure, resulting from the rapid accumulation of erythrocyte debris (Batte et al. 2025).

Hyperventilation may occur in an attempt to restore blood pH during acidosis, caused by lactate produced from fermentation by the parasite and human tissues under hypoxic conditions (Graça et al. 2020). Neurological dysfunctions, including mental confusion, seizures, and coma, may also be present if infected red blood cells become sequestered in the vasculature of the central nervous system and compromise the blood-brain barrier, which is more common in *P. falciparum* infections (Grau and Craig 2012).

Current Treatment and Care Strategies

For centuries, quinine was used to treat malaria, long before its causative agent was identified (Achan et al. 2011). Recently developed drug treatments include chloroquine in 1934 and mefloquine in the 1970s (Payne 1987; Trenholme et al. 1975). Interestingly, chloroquine-resistant strains emerged by 1960 in Cambodia, within 30 years of the drug's introduction (Payne 1987). Thus, antimalarial drug resistance can develop rapidly, underscoring the need for sustained efforts to prevent drug-resistant malaria.

After identifying the strain of the parasite, the appropriate antimalarial drug treatment of artemisinin derivatives or quinine derivatives, such as lumefantrine or amodiaquine, should be immediately administered either orally or intravenously, depending on severity (Alghamdi et al. 2024; Nyaaba et al. 2022). These drugs target vital proteins that inhibit growth and disrupt the life cycle of the parasite (Cui and Su 2009; Sullivan 2017). The entire course of the drug treatment must be completed, even under asymptomatic conditions, to prevent the development of drug resistance and subsequent recurrent infections (Shibeshi et al. 2020). To alleviate symptoms such as fevers, over-the-counter medications, such as acetaminophen, may also be used (Birbeck et al. 2024).

Proposed Logistical Plan under Resource-Poor Conditions

To prevent the re-introduction of malaria into urban environments, communication between rural villagers and medical officials must be prioritized. Due to relatively low literacy rates in populations over the age of 25, visual graphics should be used heavily in low-cost print materials, such as pamphlets (NIS 2025). In-person talks should also be given in villages by medical officials or local residents trained by medical officials, which not only provides education on the disease but also facilitates a relationship of trust between villagers and scientists (Sovannaroeth et al. 2022). Using the provided information, villagers can independently implement preventive measures that are personalized to their village, ultimately lowering total operational costs (Canavati et al. 2016).

Local officials must be immediately alerted to the presence of malaria, which can be accomplished by phone calls, emails, and in-person visits (Sovannaroeth et al. 2022). Central governmental entities and medical institutions must be notified about early warning signs of an epidemic, including confirmed cases, and implement targeted, proactive measures to limit the spread of malaria, including diverting diagnostic and treatment resources to the affected region (Kheang et al. 2020). Temporary clinics for malaria treatment should be established in villages experiencing an active outbreak, equipped with essential drug treatments and a light microscope to diagnose suspected infections to provide immediate care in a timely, low-cost manner (Kesteman et al. 2017). To further minimize operational costs, patients with mild symptoms can remain at home to rest so that limited resources are effectively directed to the most severe cases (Kua et al. 2024). Most importantly, the required efficiency of communication and responsive action relies on the existing trust and coordination established with villagers (Iuliano et al. 2023).

Public Health and Education

Strategies to Educate Policymakers and the Public

To educate policymakers about malaria, strategies must center around community engagement where conversations about disease control and prevention can take place. These conversations help demonstrate to the policymakers that public interest exists in malaria elimination. From there, policymakers can dedicate the resources from a specialized governmental agency, such as the National Malaria Center of Cambodia, toward disease elimination (CNM 2011).

In rural Cambodian communities, education of malaria has been facilitated by medical officials or local residents trained by medical officials through in-person talks, which provides informative, actionable options to combat the disease and a streamlined means of communication between villagers and experts (Sovannaroeth et al. 2022). When local residents provide these talks, they can adapt the information to the local dialect and culture best suited for the village (Sovannaroeth et al. 2022). Workers have also disseminated paper pamphlets that primarily rely on visual graphics, accounting for the relatively lower literacy rates in populations over the age of 25 (NIS 2025). These strategies enable villagers to independently implement preventive measures that are tailored to their specific living conditions, preserving agency over their livelihoods and ultimately lowering total operational costs (Canavati et al. 2016). Because of their effectiveness, these strategies should continue to be used in order to educate the public, thereby preventing disease transmission and future epidemics.

Proposed Communication Means of Information

To empower policymakers and the public towards reducing infection rates and treating existing infections, medical experts and health workers not only must inform them of the devastating effects of the disease, ranging from the individual's quality of life to nationwide economic productivity, but also recommend evidence-based modern tools to not only treat but

also prevent the disease (Lukwa et al. 2019). Policymakers would be more interested in suggestions that can be applied at scale, such as agency-run policies and projects. To persuade them of the viability to implement a policy that combats malaria at the governmental level, they must be presented with financial budgeting proposals that outline logistical equipment costs, including larvicides, insecticide-treated nets, adult mosquito traps, rapid diagnostic tests, antimalarial drug treatments, and governmental vehicles (Alghamdi et al. 2024; Cameron and Lorenz 2013; Guo et al. 2025; Matthews 2011; Nyaaba et al. 2022; Orish et al. 2018).

Meanwhile, the public would be more interested in actions that they could take immediately (Onyinyechi et al. 2023). Using community-directed approaches in educating the public gives residents independent agency, as previously discussed, and improves the effectiveness of implementing preventative practices, like using insecticide-treated nets in day-to-day life (Onyinyechi et al. 2023). To distribute the information as wide as possible, it must be disseminated on both the Internet, especially social media platforms, and hard-copy materials, such as graphical pamphlets. By making the information freely available, more people in the population become aware that malaria continues to pose a threat in the modern day, thereby motivating them to adopt achievable, preventable actions in everyday life that battle against potential malaria resurgence.

Conclusion

As a life-threatening tropical disease, malaria lies on the verge of elimination in Cambodia, yet the danger of drug resistance and climate change risks expanding the range of resistant malaria strains that lack a cure. Malaria is caused by *Plasmodium* protozoans, which are transmitted by *Anopheles* mosquitoes—both parasite and vector must be monitored and targeted to achieve elimination. Affected patients experience varied symptoms that differ in severity in duration, but they can progress toward death if left untreated. To prevent disease transmission, communication and coordination between rural villagers and medical officials must

be prioritized to efficiently distribute resources and educate the public. Local residents can be professionally trained to provide in-person talks personalized to their village, while policymakers must be presented with a defined plan that outlines financial requirements to be applied at scale. Prioritizing the elimination of malaria as rapidly as possible will prevent the resurgence of drug-resistant malaria, thereby preserving healthcare infrastructure, boosting economic productivity, and improving the quality of life for millions of Cambodians.

References

- Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, Rosenthal PJ, D'Alessandro U. 2011. Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. *Malar J.* 10:144. <https://doi.org/10.1186/1475-2875-10-144>.
- Acosta AL, Castro MC, Laporta GZ, Conn JE, Sallum MAM. 2025. Future global distribution and climatic suitability of *Anopheles stephensi*. *Sci Rep.* 15(1):22268. <https://doi.org/10.1038/s41598-025-07653-8>.
- Alghamdi JM, Al-Qahtani Arwa A., Alhamlan FS, Al-Qahtani Ahmed A. 2024. Recent Advances in the Treatment of Malaria. *Pharmaceutics.* 16(11):1416. <https://doi.org/10.3390/pharmaceutics16111416>.
- Alvarez-Costa A, Leonardi MS, Giraud S, Schilman PE, Lazzari CR. 2024. Challenging Popular Belief, Mosquito Larvae Breathe Underwater. *Insects.* 15(2):99. <https://doi.org/10.3390/insects15020099>.
- Amino R, Thiberge S, Martin B, Celli S, Shorte S, Frischknecht F, Ménard R. 2006. Quantitative imaging of *Plasmodium* transmission from mosquito to mammal. *Nat Med.* 12(2):220–224. <https://doi.org/10.1038/nm1350>.
- Bancells C, Llorà-Batlle O, Poran A, Nötzel C, Rovira-Graells N, Elemento O, Kafack BFC, Cortés A. 2019. Revisiting the initial steps of sexual development in the malaria parasite *Plasmodium falciparum*. *Nat Microbiol.* 4(1):144–154. <https://doi.org/10.1038/s41564-018-0291-7>.
- Bartoloni A, Zammarchi L. 2012. Clinical aspects of uncomplicated and severe malaria. *Mediterr J Hematol Infect Dis.* 4(1):e2012026. <https://doi.org/10.4084/MJHID.2012.026>.
- Batte A, Nakulima V, Namazzi R, Aujo JC, Starr MC, Schwaderer AL, Lintner-Rivera M, Ahumwire A, Ogwal D, Tenywa E, et al. 2025. Malaria associated pathogenesis of chronic kidney disease (MAP-CKD): a prospective study of children hospitalized with severe malaria. *BMC Nephrol.* 26(1):390. <https://doi.org/10.1186/s12882-025-04333-7>.

- Bennink S, Kiesow MJ, Pradel G. 2016. The development of malaria parasites in the mosquito midgut. *Cell Microbiol.* 18(7):905–918. <https://doi.org/10.1111/cmi.12604>.
- Berenbaum M. 1995. *Bugs in the system: insects and their impact on human affairs*. Reading, Mass: Addison-Wesley. p. 230–237.
- Beshir KB, Parr JB, Cunningham J, Cheng Q, Rogier E. 2022. Screening strategies and laboratory assays to support *Plasmodium falciparum* histidine-rich protein deletion surveillance: where we are and what is needed. *Malar J.* 21(1):201. <https://doi.org/10.1186/s12936-022-04226-2/>
- Birbeck GL, Seydel KB, Mwanza S, Tembo D, Chilombe M, Watts A, Ume-Ezeoke I, Mathews M, Patel AA, Mwenechanya M, et al. 2024. Acetaminophen and Ibuprofen in Pediatric Central Nervous System Malaria: A Randomized Clinical Trial. *JAMA Neurol.* 81(8):857–865. <https://doi.org/10.1001/jamaneurol.2024.1677>.
- Boyer S, Doeurk B, Rakotonirina A, Chy S, Vong C, Piv E, Tat B, Ea M, Chhin C, Phen S, et al. 2025. Anopheles mosquitoes in Mondulkiri forest, Cambodia: abundance, distribution, seasonal patterns and *Plasmodium* prevalence. *Malar J.* 24(1):6. <https://doi.org/10.1186/s12936-024-05166-9>
- Cameron MM, Lorenz LM, editors. 2013. *Biological and environmental control of disease vectors*. Oxfordshire, UK: CABI.
- Canavati SE, Lawpoolsri S, Quintero CE, Nguon C, Ly P, Pukrittayakamee S, Sintasath D, Singhasivanon P, Peeters Grietens K, Whittaker MA. 2016. Village malaria worker performance key to the elimination of artemisinin-resistant malaria: a Western Cambodia health system assessment. *Malar J.* 15(1):282. <https://doi.org/10.1186/s12936-016-1322-6>.
- Carlson CJ, Bannon E, Mendenhall E, Newfield T, Bansal S. 2023. Rapid range shifts in African *Anopheles* mosquitoes over the last century. *Biol Lett.* 19(2):20220365. <https://doi.org/10.1098/rsbl.2022.0365>.

- Christiansen-Jucht CD, Parham PE, Saddler A, Koella JC, Basáñez M-G. 2015. Larval and adult environmental temperatures influence the adult reproductive traits of *Anopheles gambiae* s.s. *Parasit Vectors*. 8:456. <https://doi.org/10.1186/s13071-015-1053-5>.
- Cui L, Su X. 2009. Discovery, mechanisms of action and combination therapy of artemisinin. *Expert Rev Anti Infect Ther*. 7(8):999–1013. <https://doi.org/10.1586/eri.09.68>.
- Dahlberg K. 1980. Medical Care of Cambodian Refugees. *JAMA*. 243(10):1062. <https://doi.org/10.1001/jama.1980.03300360034021>.
- Doum D, Mclver DJ, Chen I, Keo V, Sovannaroeth S, Lek D, Cunningham JM, Lovin DD, Daniel NW, Quan M, et al. 2025. Asymptomatic malaria reservoirs are the last challenge in the elimination in Cambodia. *Malar J*. 24(1):110. <https://doi.org/10.1186/s12936-025-05343-4>.
- Fikadu M, Ashenafi E. Malaria: An Overview. *Infect Drug Resist*. 2023;16:3339-3347. doi:10.2147/IDR.S405668.
- Frischknecht F, Matuschewski K. 2017. Plasmodium Sporozoite Biology. *Cold Spring Harb Perspect Med*. 7(5):a025478. <https://doi.org/10.1101/cshperspect.a025478>.
- Gerald N, Mahajan B, Kumar S. 2011. Mitosis in the human malaria parasite *Plasmodium falciparum*. *Eukaryot Cell*. 10(4):474–482. <https://doi.org/10.1128/EC.00314-10>.
- Ghosh P, Bhattacharjee D, Nasipuri M. 2017. Automatic System for Plasmodium Species Identification from Microscopic Images of Blood-Smear Samples. *J Healthc Inform Res*. 1(2):231–259. <https://doi.org/10.1007/s41666-017-0009-2>.
- Giribaldi G, D'Alessandro S, Prato M, Basilico N. 2015. Etiopathogenesis and Pathophysiology of Malaria. *Human and Mosquito Lysozymes*. Cham: Springer International Publishing, 2014. p. 1–18. https://doi.org/10.1007/978-3-319-09432-8_1.
- Graça Luísa, Abreu IG, Santos AS, Graça Luís, Dias PF, Santos ML. 2020. Descriptive Acute Respiratory Distress Syndrome (ARDS) in adults with imported severe *Plasmodium*

- falciparum malaria: A 10 year-study in a Portuguese tertiary care hospital. *PLoS One*. 15(7):e0235437. <https://doi.org/10.1371/journal.pone.0235437>.
- Grau GER, Craig AG. 2012. Cerebral malaria pathogenesis: revisiting parasite and host contributions. *Future Microbiol*. 7(2):291–302. <https://doi.org/10.2217/fmb.11.155>.
- Guo S, Huang J, Liu Y, Zhang R, Ren J, Shi X, Sun J. 2025. Integrated mosquito control in Matatang village, Northern Zhejiang, China: an effectiveness assessment. *Front Public Health*. 13:1628116. <https://doi.org/10.3389/fpubh.2025.1628116>.
- Hamza AM, Rayah EAE. 2016. A Qualitative Evidence of the Breeding Sites of *Anopheles arabiensis* Patton (Diptera: Culicidae) in and Around Kassala Town, Eastern Sudan. *Int J Insect Sci*. 8:65–70. <https://doi.org/10.4137/IJIS.S40071>.
- Hiebert, MS. 2017. Genocide, Revolution, and Starvation under the Khmer Rouge. *Genocide Studies International*. 11(1), 68–86. <https://www.jstor.org/stable/26986060>.
- Hustedt J, Canavati SE, Rang C, Ashton RA, Khim N, Berne L, Kim S, Sovannarothe S, Ly P, Ménard D, et al. 2016. Reactive case-detection of malaria in Pailin Province, Western Cambodia: lessons from a year-long evaluation in a pre-elimination setting. *Malar J*. 15:132. <https://doi.org/10.1186/s12936-016-1191-z>.
- Idokoko A, Ajayi I, Falade C, Soyawo O, 2017. Pain in malaria: An assessment of its prevalence, characteristics and determinants in Ibadan, Nigeria. *Afr J Biomed Res*. 20: 111–119.
- Iuliano A, Shittu F, Colbourn T, Salako J, Bakare D, Bakare AAA, King C, Graham H, McCollum ED, Falade AG, et al. 2023. Community perceptions matter: a mixed-methods study using local knowledge to define features of success for a community intervention to improve quality of care for children under-5 in Jigawa, Nigeria. *BMJ Open*. 13(11):e069213. <https://doi.org/10.1136/bmjopen-2022-069213>.

- Jeyaprakasam NK, Liew JWK, Low VL, Wan-Sulaiman W-Y, Vythilingam I. 2020. Plasmodium knowlesi infecting humans in Southeast Asia: What's next? *PLoS Negl Trop Dis*. 14(12):e0008900. <https://doi.org/10.1371/journal.pntd.0008900>.
- Josling GA, Llinás M. 2015. Sexual development in Plasmodium parasites: knowing when it's time to commit. *Nat Rev Microbiol*. 13(9):573–587. <https://doi.org/10.1038/nrmicro3519>.
- Kesteman T, Randrianarivelosia M, Rogier C. 2017. The protective effectiveness of control interventions for malaria prevention: a systematic review of the literature. *F1000Res*. 6:1932. <https://doi.org/10.12688/f1000research.12952.1>.
- Kheang ST, Sovannaroeth S, Barat LM, Dysoley L, Kapella BK, Po L, Nguon S, Gimnig J, Slot R, Samphornarann T, et al. 2020. Malaria elimination using the 1-3-7 approach: lessons from Sampov Loun, Cambodia. *BMC Public Health*. 20(1):544. <https://doi.org/10.1186/s12889-020-08634-4>.
- Kua KP, Lee SWH, Chongmelaxme B. 2024. The impact of home-based management of malaria on clinical outcomes in sub-Saharan African populations: a systematic review and meta-analysis. *Trop Med Health*. 52(1):7. <https://doi.org/10.1186/s41182-023-00572-2>.
- Lee J-H, Jang JW, Cho CH, Kim JY, Han ET, Yun SG, Lim CS. 2014. False-positive results for rapid diagnostic tests for malaria in patients with rheumatoid factor. *J Clin Microbiol*. 52(10):3784–3787. <https://doi.org/10.1128/JCM.01797-14>.
- Lukwa AT, Mawoyo R, Zablun KN, Siya A, Alaba O. Effect of malaria on productivity in a workplace: the case of a banana plantation in Zimbabwe. *Malar J*. 2019 Dec 3;18(1):390. doi: 10.1186/s12936-019-3021-6.
- Lyberger K, Robinson AR, Couper L, Delwel I, Glidden C, Qian C, Burslem A, Fernandez F, Gao B, Garcia G, et al. 2025. A systematic review of climate-change driven range shifts in mosquito vectors. *bioRxiv*. 2025.03.25.645279. <https://doi.org/10.1101/2025.03.25.645279>.

- Mamai W, Maiga H, Gárdos M, Bán P, Bimbilé Somda NS, Konczal A, Wallner T, Parker A, Balestrino F, Yamada H, et al. 2019. The efficiency of a new automated mosquito larval counter and its impact on larval survival. *Sci Rep*. 9(1):7413.
<https://doi.org/10.1038/s41598-019-43333-0>.
- Matthews GA. 2011. *Integrated vector management: controlling vectors of malaria and other insect vector borne diseases*. Chichester, West Sussex, UK; Ames, Iowa: Wiley-Blackwell.
- Munga S, Minakawa N, Zhou G, Barrack O-OJ, Githeko AK, Yan G. 2005. Oviposition site preference and egg hatchability of *Anopheles gambiae*: effects of land cover types. *J Med Entomol*. 42(6):993–997. <https://doi.org/10.1093/jmedent/42.6.993>.
- Munirah M, Wahyuni S, Wahid I, Hamid F. 2021. Preliminary Evidence of Human Plasmodium in Domestic Animals from a Malaria-Endemic Region in Indonesia. *F1000Res*. 10:645.
<https://doi.org/10.12688/f1000research.53946.4>.
- National Institute of Statistics (NIS). 2025. Adult Literacy Rate by Age and Sex Cambodia 2019 and 2024. *Cambodian General Department of Digital Economy*.
https://data.mef.gov.kh/datasets/pd_68550f631b4d5f000166ac46.
- National Center for Parasitology, Entomology and Malaria Control (CNM). 2011. *PCSP Group Co., Ltd*. <https://www.cnm.gov.kh/>.
- Nyaaba N, Andoh NE, Amoh G, Amuzu DSY, Ansong M, Ordóñez-Mena JM, Hirst J. 2022. Comparative efficacy and safety of the artemisinin derivatives compared to quinine for treating severe malaria in children and adults: A systematic update of literature and network meta-analysis. *PLoS One*. 17(7):e0269391.
<https://doi.org/10.1371/journal.pone.0269391>.
- Obsomer V, Dufrene M, Defourny P, Coosemans M. 2013. *Anopheles* species associations in Southeast Asia: indicator species and environmental influences. *Parasit Vectors*. 6:136.
<https://doi.org/10.1186/1756-3305-6-136>.

- Onyinyechi OM, Mohd Nazan AIN, Ismail S. 2023. Effectiveness of health education interventions to improve malaria knowledge and insecticide-treated nets usage among populations of sub-Saharan Africa: systematic review and meta-analysis. *Front Public Health*. 11:1217052. <https://doi.org/10.3389/fpubh.2023.1217052>.
- Orish VN, De-Gaulle VF, Sanyaolu AO. 2018. Interpreting rapid diagnostic test (RDT) for *Plasmodium falciparum*. *BMC Res Notes*. 11(1):850. <https://doi.org/10.1186/s13104-018-3967-4>.
- Payne D. 1987. Spread of chloroquine resistance in *Plasmodium falciparum*. *Parasitol Today*. 3(8):241–246. [https://doi.org/10.1016/0169-4758\(87\)90147-5](https://doi.org/10.1016/0169-4758(87)90147-5).
- Prudêncio M, Rodriguez A, Mota MM. 2006. The silent path to thousands of merozoites: the *Plasmodium* liver stage. *Nat Rev Microbiol*. 4(11):849–856. <https://doi.org/10.1038/nrmicro1529>.
- Roques M, Bindschedler A, Beyeler R, Heussler VT. 2023. Same, same but different: Exploring *Plasmodium* cell division during liver stage development. *PLoS Pathog*. 19(3):e1011210. <https://doi.org/10.1371/journal.ppat.1011210>.
- Sallares R. 2002. *Malaria and Rome: a history of malaria in ancient Italy*. Oxford University Press.
- Sato S. 2021. *Plasmodium*-a brief introduction to the parasites causing human malaria and their basic biology. *J Physiol Anthropol*. 40(1):1. <https://doi.org/10.1186/s40101-020-00251-9>.
- Service MW. *Medical Entomology for Students*. 5th ed. Cambridge University Press, 2012. p. 13–45.
- Shibeshi MA, Kifle ZD, Atnafie SA. 2020. Antimalarial Drug Resistance and Novel Targets for Antimalarial Drug Discovery. *Infect Drug Resist*. 13:4047–4060. <https://doi.org/10.2147/IDR.S279433>.

- Siciliano G, Costa G, Suárez-Cortés P, Valleriani A, Alano P, Levashina EA. 2020. Critical Steps of *Plasmodium falciparum* Ookinete Maturation. *Front Microbiol.* 11:269. <https://doi.org/10.3389/fmicb.2020.00269>.
- Siv S, Roca-Feltre A, Vinjamuri SB, Bouth DM, Lek D, Rashid MA, By NP, Popovici J, Huy R, Menard D. 2016. *Plasmodium vivax* Malaria in Cambodia. *Am J Trop Med Hyg.* 95(6 Suppl):97–107. <https://doi.org/10.4269/ajtmh.16-0208>.
- Smith RC, Jacobs-Lorena M. 2010. *Plasmodium*-Mosquito Interactions: A Tale of Roadblocks and Detours. *Adv In Insect Phys.* 39:119–149. <https://doi.org/10.1016/B978-0-12-381387-9.00004-X>.
- Sorn V. Achieving Universal Health Coverage in Cambodia: Barriers, Strategies, and Policy Recommendations. *Health Sci Rep.* 2025 Sep 16;8(9):e71259. doi: 10.1002/hsr2.71259.
- Sovannaroeth S, Ngor P, Khy V, Dunn JC, Burbach MK, Peng S, Mak S, Siv K, Manzoni G, Guintran JO, et al. 2022. Accelerating malaria elimination in Cambodia: an intensified approach for targeting at-risk populations. *Malar J.* 21(1):209. <https://doi.org/10.1186/s12936-022-04234-2>.
- Srisutham S, Suwannasin K, Mathema VB, Sriprawat K, Smithuis FM, Nosten F, White NJ, Dondorp AM, Imwong M. 2020. Utility of *Plasmodium falciparum* DNA from rapid diagnostic test kits for molecular analysis and whole genome amplification. *Malar J.* 19(1):193. <https://doi.org/10.1186/s12936-020-03259-9>.
- Sturm A, Amino R, van de Sand C, Regen T, Retzlaff S, Rennenberg A, Krueger A, Pollok J-M, Menard R, Heussler VT. 2006. Manipulation of host hepatocytes by the malaria parasite for delivery into liver sinusoids. *Science.* 313(5791):1287–1290. <https://doi.org/10.1126/science.1129720>.
- Sullivan DJ. 2017. Quinolines block every step of malaria heme crystal growth. *Proc Natl Acad Sci U S A.* 114(29):7483–7485. <https://doi.org/10.1073/pnas.1708153114>.

- Trenholme CM, Williams RL, Desjardins RE, Frischer H, Carson PE, Rieckmann KH, Canfield CJ. 1975. Mefloquine (WR 142,490) in the treatment of human malaria. *Science*. 190(4216):792–794. <https://doi.org/10.1126/science.1105787>.
- van de Straat B, Sebayang B, Grigg MJ, Staunton K, Garjito TA, Vythilingam I, Russell TL, Burkot TR. 2022. Zoonotic malaria transmission and land use change in Southeast Asia: what is known about the vectors. *Malar J*. 21(1):109. <https://doi.org/10.1186/s12936-022-04129-2>.
- Vorasan N, Pan-Ngum W, Jittamala P, Maneeboonyang W, Rukmanee P, Lawpoolsri S. Long-term impact of childhood malaria infection on school performance among school children in a malaria endemic area along the Thai-Myanmar border. *Malar J*. 2015 Oct 9;14:401. doi: 10.1186/s12936-015-0917-7.
- Walter EJ, Hanna-Jumma S, Carraretto M, Forni L. 2016. The pathophysiological basis and consequences of fever. *Crit Care*. 20(1):200. <https://doi.org/10.1186/s13054-016-1375-5>.
- Watson OJ, Sumner KM, Janko M, Goel V, Winskill P, Slater HC, Ghani A, Meshnick SR, Parr JB. 2019. False-negative malaria rapid diagnostic test results and their impact on community-based malaria surveys in sub-Saharan Africa. *BMJ Glob Health*. 4(4):e001582. <https://doi.org/10.1136/bmjgh-2019-001582>.
- Weiss DJ, Dzianach PA, Saddler A, et al. Mapping the global prevalence, incidence, and mortality of Plasmodium falciparum and Plasmodium vivax malaria, 2000–22: a spatial and temporal modelling study. *Lancet*. 2025;405(10483):979–990. doi:10.1016/S0140-6736(25)00038-8.
- Wijesundere DA, Ramasamy R. 2017. Analysis of Historical Trends and Recent Elimination of Malaria from Sri Lanka and Its Applicability for Malaria Control in Other Countries. *Front Public Health*. 5:212. <https://doi.org/10.3389/fpubh.2017.00212>.
- World Health Organization (WHO). *World malaria report 2025: Addressing the threat of antimalarial drug resistance*. Geneva: World Health Organization, 2025.

Wu Y, Zhang C, Peng Y, Sun J, Gong Z, Ling F. 2025. Efficacy of CO₂-baited mosquito catchers in controlling vector mosquitoes in residential areas of China. *Front Vet Sci.* 12:1671416. <https://doi.org/10.3389/fvets.2025.1671416>.