Risk and Control of Mosquito-Borne Diseases in Southeast Asian Rubber Plantations

Julie-Anne A. Tangena,[1,2,*] Phoutmany Thammavong,[1] Anne L. Wilson,[2] Paul Brey,[1,‡] and Steve W. Lindsay[2,‡]

[1]Entomology Department, Institut Pasteur du Laos, Vientiane, Laos

[2]School of Biological and Biomedical Sciences, Durham University, Durham, UK

*Correspondence: jtangena@pasteur.la (Tangena, J-A.A.).

Keywords: rubber plantation; mosquito-borne diseases; Southeast Asia; malaria; dengue; vector control.

[‡]Joint senior author.

Unprecedented economic growth in Southeast Asia (SEA) has encouraged the expansion of rubber plantations. This land-use transformation is changing the risk of mosquito-borne diseases. Mature plantations provide ideal habitats for the mosquito vectors of malaria, dengue, and chikungunya. Migrant workers may introduce pathogens into plantation areas, most worryingly artemisinin-resistant malaria parasites. The close proximity of rubber plantations to natural forest also increases the threat from zoonoses, where new vector-borne pathogens spill over from wild animals into humans. There is therefore an urgent need to scale up vector control and access to health care for rubber workers. This requires an intersectoral approach with strong collaboration between the health sector, rubber industry, and local communities.

Mosquito-borne Diseases in SEA

In **SEA** (see Glossary) the most important **vector**-borne diseases are **malaria** and **dengue**. The World Health Organization (WHO) estimates that from 2000–2014 there was a reduction in global malaria cases from 2.9 million to 1.6 million, with malaria mortality rates falling by 60% [1]. The malaria mortality rate declined by 85% in the SEA region and by 65% in the Western Pacific region (Figure 1A). This remarkable decline has been achieved by the massive deployment of long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS), improved access to diagnosis, and effective treatment with **artemisinin combination therapies (ACTs)** [1]. Consequently, many countries in SEA are now planning for malaria elimination. By contrast, in many parts of SEA, dengue cases have increased and the disease is endemic in many places (Figure 1B), with recent epidemics recorded in China, Lao PDR, Malaysia, Singapore, and the Philippines [2].

The risk of both malaria and dengue depends intimately on the environment, with major land-use changes often increasing the risk of transmission [3]. Over the past 30 years there has been an unprecedented increase in **rubber plantations** in SEA as a consequence of the economic development in the region. Here we examine the potential threat posed by the growth of rubber plantations and suggest ways of protecting plantation workers from **mosquito-borne diseases**, focusing on **vector control**.

Expansion of Rubber Plantations

Monocultures of the rubber tree *Hevea brasiliensis* are hugely important commercial crops with plantations in SEA supplying more than 90% of the global demand for **natural rubber** (http://www.rubberstudy.com). The growth of the Chinese economy resulted in a high demand

for rubber, with record high rubber prices, which lead to an expansion of rubber plantations. In 2010, SEA had 9.2 million ha of rubber plantations, with the largest plantations in Indonesia (2.9 million ha), Thailand (2.6 million ha), and Malaysia (1.1 million ha) (Figure 1C) (http://www.fao.org). Although rubber prices have dropped (http://www.anrpc.org) since the onset of the 2008 global financial crisis when world industrial production contracted [4], it is anticipated that large acreages of rubber will continue to be cultivated across SEA in the future. Rubber plantations are essentially manmade forests with generally higher humidity and lower temperatures under the canopy than non-tree crops, making them ideal environments for long-lived forest vectors, including the important malaria vectors *Anopheles dirus sensu lato* and the dengue and **chikungunya** vector *Aedes albopictus* [5,6]. There is a shift in vector species as natural primary and secondary forest is removed, bare land is cultivated for rubber plantations, and the rubber plantations mature (Table 1). Plantations provide a wide range of larval habitats, including **latex**-collecting cups, water-storage containers, slow-running streams, water pools, and puddles, able to support diverse vector fauna [6,7].

The expansion of rubber plantations has created a high demand for labour. We estimate that in the next decade 4.5–6 million people will work on rubber plantations in SEA (assuming 13.5–17.7 million ha of rubber plantations by 2024, with one person tapping 3 ha [8]). In many plantations workers are largely poor itinerant workers. This mobile, migrant, and sometimes illegal population may be non-immune and working in disease-endemic countries or they may be carrying pathogens into disease-free areas, both leading to increased cases in the migrant workforce or in local communities, respectively [9,10]. The risk from vector-borne diseases is increased further because plantation workers often do not interact with official health-care providers due to difficult accessibility of health services, economic factors, lack of local

language skills, lack of knowledge on mosquito-borne diseases, fear of deportation, or a combination of these [11,12].

Malaria in Rubber Plantations

The first account of malaria in rubber plantations dates from 1907 in Malaysia, when a malaria epidemic swept through rubber plantations with non-immune immigrant workers [13]. Since then malaria outbreaks have been reported in rubber plantations regularly throughout SEA, most frequently in Thailand [1,14–17].

The relative importance of malaria vector species in rubber plantations varies according to the site and time of year. For example, in Malaysia *Anopheles umbrosus sensu lato* was the primary malaria vector in lowland rubber plantations while *Anopheles maculatus sensu lato* was dominant in highland plantations [18]. In Thailand *An. dirus s.l.* was the primary vector in rubber plantations during the dry season, together with the secondary vector *Anopheles minimus sensu lato* [19], while in the rainy season *An. dirus s.l.*, *An. minimus s.l.*, *An. maculatus s.l.*, and *Anopheles aconitus* were the main vectors [20]. Mature rubber plantations also support other malaria vectors including *Anopheles barbirostris sensu lato* and *Anopheles latens* [21,22]. Although many species of malaria vectors have been collected from rubber plantations, it is unclear which of these actually breed in the plantations. *Anopheles baimaii* larvae (from the *An. dirus s.l.* complex) have been collected from rubber plantations in Thailand [23], while *An. aconitus* and *Anopheles annularis* larvae were found in Indonesian plantations [24]. In Borneo and Thailand, *An. maculatus s.l.*, *An. barbirostris s.l.*, *An. dirus s.l.*, and *An. umbrosus s.l.* were recorded breeding on the edges of plantations but not within [25,26]. Although evidence for anopheline larvae in rubber plantations is limited, potential breeding sites for malaria vectors

abound, particularly partially shaded slow-running streams, pools, and puddles next to the unpaved roads used for transporting latex, and domestic water containers.

In general, *An. dirus s.l.* and *An. minimus s.l.* are considered the principal vectors in rubber plantations because both prefer breeding in shaded forest [20,23,27–29]. *An. dirus s.l.* is a highly **anthropophilic** forest mosquito that is present mostly in the rainy season and *An. minimus s.l.* is a more **zoophilic** mosquito that is common in the drier season (Table 2). *An. dirus s.l.* breeds in shaded, temporary bodies of fresh, stagnant water in hilly or mountainous zones, including ground pools, puddles, and wells found in natural forests and rubber plantations [21,29]. *An. minimus s.l.* breeds in partially shaded margins of slow-running streams in low hill forests [31]. In areas where *An. dirus s.l.* is the main vector, the replacement of deforested bare areas with rubber leads to increased malaria [27]. Although not yet investigated, a similar trend is expected for *An. minimus s.l.*.

The risk of malaria transmission in rubber plantations depends on the daily activities of the rubber workers and the seasonality of their work. Rubber-plantation workers in SEA, unlike those in Africa, tap latex at night when latex yields are highest (Box 1), exposing them to malaria vectors. For example, Thai tappers work from 21.00 to 05.00 h, which coincides with peak malaria vector biting times [21]. Whole families may live and work in the rubber plantations, also exposing them to evening-biting mosquitoes when resting in their poorly constructed houses [32,33]. Moreover, as rubber tapping is seasonal work, disease incidence can increase markedly due to the influx of workers during the tapping season [11]. In southern Lao, an influx of malaria-infected workers from neighbouring countries, some of whom worked in rubber plantations, increased the number of malaria cases from 17 529 in 2011 to 46 140 in 2012 (http://www.who.int).

The most common malaria parasites in SEA are *Plasmodium falciparum* and *Plasmodium vivax*, with fewer cases of *Plasmodium malariae*, *Plasmodium knowlesi*, and *Plasmodium ovale* [1]. Currently there is great interest in the artemisinin-tolerant *P. falciparum* strains that originally developed in Cambodia and are now present in most of mainland SEA [34]. Recent studies on the Thailand–Myanmar and Thailand–Cambodia borders have shown the important role of migrant rubber workers in spreading malaria, especially *P. falciparum* and *P. vivax* multidrug resistance [15,18]. *Plasmodium knowlesi* has been reported in all SEA countries except Lao PDR and occurs in rubber plantations [35,36]. Unlike other malaria species, *P. knowlesi* is naturally infective to macaques, including *Macaca fascicularis*, the long-tailed macaque, which is found in rubber plantations [37]. *P. knowlesi* cases have been reported in rubber workers on the Thai–Myanmar border [38]. The combination of primate reservoir hosts, *Anopheles* mosquitoes, and plantation workers makes it likely that rubber tapping is a high-risk practice for *knowlesi* malaria.

Dengue in Rubber Plantations

The key reason for the rapid spread of the dengue virus is its adaptation to the highly anthropophagic day-biting mosquitoes *Aedes aegypti* and *Aedes albopictus* (Table 2). Dengue is principally an urban disease, where it is transmitted by *Ae. aegypti*, but in rural areas *Ae. albopictus* thrives and is often responsible for outbreaks [39]. Although there are few data on dengue epidemics in rubber plantations, since these plantations make ideal habitats for *Ae. albopictus* [40] the threat from dengue must be taken seriously. Recent epidemics include 16 367 cases in 2010 in a Malaysian rubber plantation [41] and 3760 cases in 2012 in an Indian plantation [42].

Ae. albopictus thrives in rubber plantations since they provide a variety of potential breeding sites including latex-collection cups, tree holes, and water-storage containers around the homes of rubber workers [43,44]. As rubber workers and their families live within or close to the rubber plantations, they are exposed to these day-biting mosquitoes. According to one study in Thailand, rubber-plantation houses have 18.3-times higher odds of having at least one container with *Aedes* larvae (not identified to species) than town houses [45]. Importantly, *Ae. albopictus* frequently lay their eggs in latex-collection cups that fill with rain water and can produce adult mosquitoes during the long tapping break outside the main rainy season or due to interruptions in tapping during the rainy season. *Aedes* mosquitoes thrive in these collecting cups as they contain latex residues and decaying leaves for nutrients. In one Malaysian study, 96% of the adult and larval mosquitoes collected in rubber plantations were *Ae. albopictus* [5]. Similarly, *Ae. albopictus* was dominant in an Indian plantation, where mosquito larvae were found in 80% of collection cups outside the tapping season, with 98% of these cups containing *Ae. albopictus* larvae [46]. Other *Aedes* mosquitoes collected in rubber plantations include *Ae. aegypti*, *Aedes chrysolineatus*, *Aedes niveus*, *Aedes vexans*, and *Aedes vittatus* [6].

The risk of dengue is further increased by the close proximity of rubber plantations to the natural forest where the sylvatic cycle of dengue is present [47]. In Viet Nam 79% of the rubber plantations in the central highlands were planted in partly deforested forests (http://www.tropenbos.org). In such situations the risk of dengue transmission is enhanced as dengue-infected non-human primates like *Presbytis* and *Macaca* species enter the rubber plantations to feed, exposing the dengue vectors in the rubber plantations to the forest arbovirus. Additionally, rubber workers who visit the natural forest in search of food can be exposed to dengue vectors from the forest [37]. Although data on dengue cases in rubber plantations is

limited, the presence of the vector, the proximity of the sylvatic cycle, and the high exposure risk of rubber workers suggest a substantial risk of dengue in rubber plantations.

Chikungunya: An Emerging Disease in Rubber Plantations

Since many new and **emerging infectious diseases** are vector borne [48], it is possible that rubber plantations, with their close proximity to the natural forests, a large work force, and the presence of anthropophilic vectors [6], could be a nidus for pathogens to spill over from forest animals into local human communities. Although information on new and emerging diseases in rubber plantations is limited, the rich diversity of mosquito species found in these environments highlights the potential risk of exposure to new pathogens [6,7].

Chikungunya is one example of a virus with a sylvatic cycle that has spilled over to rubber-plantation workers. The chikungunya virus has spread across many parts of SEA, where it has resulted in severe outbreaks. Chikungunya in SEA has been mostly an urban disease, typically found in dengue-endemic areas. However, like dengue, chikungunya cases are becoming more common in rural areas [49,50]. In Kerala, India, a province with large rubber plantations, a chikungunya epidemic occurred with 24 052 cases in 2006–2007. A post-epidemic survey found a 78% seroprevalence among males, with 74% of them involved in rubber plantation-related activities [51]. More recently, in 2012 there were 14 277 cases in India, with many of those infected working in rubber plantations where *Aedes* mosquitoes were breeding in coconut shells used for latex collection [42]. Although knowledge on the diseases and vectors circulating in the rubber plantations remains limited, there is a clear indication that these habitats can become significant areas for vector-borne disease transmission. Surveillance of rubber tappers and their

families for febrile illnesses of unknown aetiology should be encouraged to assess the risk of pathogens emerging in this vulnerable population.

Vector Control in Rubber Plantations

There is an urgent need to identify appropriate vector control methods to reduce the risk of vector-borne diseases in rubber plantations. Investing in the health of rubber-plantation workers is likely to be financially beneficial to the rubber industry and economies of SEA because vector-borne disease outbreaks result in high vector control costs, medical costs, absenteeism, and lower productivity [52,53]. A historical analysis suggested that a malaria outbreak could increase costs by 20%, due to sick workers forcing the employment of expensive skilled labour to keep production stable [14]. In India the economic burden of malaria is estimated at US$1940 million, of which 75% was due to loss of earnings for patients and supporting family [54]. In Viet Nam a country-wide dengue outbreak cost the economy US$12 million for vector control, surveillance, information, education, communication, and direct and indirect costs [55].

Vector control in rubber plantations should involve a combination of interventions targeting both indoor- and outdoor-biting mosquitoes, providing protection against daytime and night-time biting, and using both insecticide-based and non-insecticide-based vector control methods. Vector control should draw on vector control measures both from within and outside the health sector. In the present example, this would entail collaboration between the health sector, rubber industry, and local communities of plantation workers. Vector control should be supported by strong entomological and epidemiological surveillance to determine the most appropriate tools and implementation strategies and monitor and evaluate their effects. This is essentially **integrated vector management (IVM)**, a WHO-recommended adaptive management approach

to vector control [56]. Complementary strategies that should be implemented alongside vector control in rubber plantations include the training of migrant community volunteers, improved health communication, improved interaction with health workers, and improved access to basic health services for prompt and effective diagnosis and treatment of vector-borne diseases [57]. Currently many different **community protection** and **personal protection** strategies are suggested for preventing mosquito-borne diseases, with the choice of vector control interventions urgently needing further research in a variety of settings [58,59]. Here we provide some guidance on possible interventions in rubber plantations.

Protection Against Indoor Biting

Many vector control methods against indoor biting exist. LLINs and IRS, the key indoor interventions used for indoor malaria control [1], can be effective even against vectors that are generally considered **exophilic**, such as *An. dirus s.l.*, *An. minimus s.l.*, and *Ae. albopictus*. However, both interventions are threatened by the rise of insecticide-resistant vectors [60]. A general recommendation is that LLINs should be targeted at plantation workers and their families, since even in the presence of pyrethroid-resistant vectors nets provide a physical barrier against malaria transmission.

Good housing is protective against indoor-biting mosquitoes [61], with traditional houses made from bamboo having more gaps in walls and floors for mosquitoes to enter compared with modern houses. House screening or the use of insecticide-treated curtains should be considered for protecting against malaria and dengue in rubber plantations [62,63]. Houses raised on platforms with few entry points for mosquitoes are also protective, as is keeping cattle away

from houses [32,33]. Although rebuilding houses for rubber workers might be too costly, simple measures for screening houses should be recommended.

Spatial repellents such as mosquito coils or metofluthrin-impregnated plastic strips for use in the home may be effective at reducing densities of mosquitoes indoors [64,65]. Although epidemiological data on the impact of spatial repellents on disease transmission is limited [66], several studies have shown protection by spatial repellents against malaria. In China transfluthrin coils provided 77% protection against malaria, which increased to 94% protection when combined with LLINs [64], while in Indonesia metofluthrin-treated coils showed 52% protection against malaria [67]. These studies are encouraging but further research is needed before they can be recommended as public-health tools for rubber plantations.

Protection from Outdoor Biting

Protecting people against outdoor-biting mosquitoes is one of the biggest challenges facing vector control today, with our current tools representing, at best, partial protection [58]. The topical application of mosquito repellent is perhaps the most common method used for protection outdoors (Figure 2A). Examples of topical repellents include citronella, para-menthane-3,8-diol, lemon eucalyptus (*Eucalyptus maculata citriodon*), picaridin, and the best known, *N,N*-diethyl-m-toluamide (DEET) [68]. While they protect individuals from mosquitoes for several hours [69], a recent systematic review and meta-analysis concluded that topical repellents are not protective against *falciparum* or *vivax* malaria [70]. This lack of efficacy against clinical disease may be because topical repellents do not protect for long enough and require high user compliance to be protective [71]. Therefore, while topical repellents are useful for personal protection, they cannot be recommended as public-health interventions. New approaches are

therefore needed that function in an automated fashion and for longer periods and require lower user compliance.

Although to our knowledge no scientific study has assessed the protective efficacy of long-sleeved clothing, organisations like the WHO recommend wearing long-sleeved clothing to protect from mosquito bites (http://www.who.int). Greater protection would be achieved by using insecticide-treated clothing, especially on large industrial plantations where it can be incorporated in workers' clothing for greater acceptability (Figure 2B) [72]. Insecticide-treated clothing is protective against bites from *Anopheles* and *Aedes* mosquitoes [73,74] and personal protection is enhanced when an insecticide and repellent are combined [75,76]. However, there is only weak evidence that treated clothing is protective against clinical malaria [73]. Before insecticide-treated clothing can be used routinely by rubber-plantation workers, further research is needed to make insecticide-treated clothing more resistant to washing, UV light exposure, and wear and tear [74].

Another method of outdoor protection is the use of spatial repellents fitted to the individual, such as a metofluthrin-emitting machine worn on a belt (Figure 2C). Metofluthrin emanators can reduce exposure to *Ae. albopictus* by 70% for about 3 h while the individual is mobile [77]. Similarly, mosquito coils, although most commonly burned indoors, can be inserted into a metal case and worn by a moving person (Figure 2D). More studies are needed to understand the true value of personal spatial repellents for both indoor and outdoor protection. If these interventions are effective for longer periods, they could be a convenient solution for protecting rubber workers.

Larval Source Management (LSM)

LSM is an important complementary method for vector control that could be used in rubber plantations. Environmental management has been practised successfully for malaria control throughout SEA from the early 1900s [78] but is used less today. In situations where *Anopheles* breeds in streams, small dams could be constructed and water released periodically to flush the streams. In India, flushing resulted in an 85% reduction in positive dips of *Anopheles* larvae and pupae [79]. For dengue and chikungunya control a simple intervention would be inverting the latex-collection cups and storing them in rain-proof shelters when not tapping for long periods. Rain guards that stop water from running into the latex cups could also be used for larva control. These guards are already used on some plantations to stop rainwater and debris falling into the latex. Rain guards decreased water in latex cups fivefold compared with cups without a guard and showed higher latex yields [80]. Around the home and peridomestic environment of rubber workers, mosquito-breeding sites should be prevented by removing garbage and covering water containers [2,81].

Larvicides could be applied in rubber plantations to reduce vectors, but we know of no studies where this has been done. The disadvantage of larvicides is that in many cases sites need retreatment every 7–14 days. Larvicides can therefore be cost-effective only where breeding sites are few, fixed, and findable [82]. Biological control agents are used infrequently for vector control. One of the best examples is *Mesocyclops*, a copepod that feeds on mosquito larva. Community-based programmes introduced these copepods into large water-storage jars in Viet Nam so successfully that they eliminated dengue from large parts of the country [83]. However, the success of these programmes was dependent on large water-storage jars being the dominant breeding sites for *Ae. aegypti*, which may not be the case in rubber plantations. Larvivorous fishes such as *Gambusia* spp. and *Poecilia reticulate* could potentially be released in the large

water-storage jars close to tappers' houses. Although a recent systematic review found that there was a lack of evidence that fish were effective control agents [84], additional well-conducted studies are needed before a recommendation can be made. Other examples of natural predators include the entomophilic mermithid nematode *Romanomermis iyengari* and the naturally occurring predatory mosquito *Toxorhynchites splendens*, which have been effective at reducing *Ae. albopictus* larvae in rubber plantations [44,85]. One drawback of this approach is that every latex-collection cup needs to be reseeded monthly with the predator.

Genetic Control

In the future, **genetic control** of mosquitoes may be an effective method of vector control that could be used in rubber plantations. Currently, apart from the release of sterile males and insects with a dominant lethal gene (RIDL), most control methods remain at an early stage of development [86–88]. Genetic control has been studied for several vector species, including the chikungunya and dengue vectors *Ae. aegypti* and *Ae. albopictus* [86,87]. As genetic control is species specific, in rubber plantations there are opportunities for dengue vector control, with only the vector *Ae. albopictus* being important in this habitat.

Concluding Remarks

For the foreseeable future, large acreages of rubber plantations will continue to be cultivated for latex across SEA. There is a threat that these plantations may become malaria hot spots, making it difficult to eliminate this disease. The presence of high numbers of *Ae. albopictus* in rubber plantations suggests that dengue and chikungunya could be introduced easily in these

environments. Moreover, there is concern that as yet unknown pathogens may spill over to the rubber-worker population from animals living in or close to the rubber plantations.

Future mosquito-borne disease control in rubber plantations should focus on developing IVM strategies alongside prompt and effective treatment of vector-borne diseases and education about vector-borne disease transmission and prevention. For malaria vector control, large-scale deployment of LLINs, and in some sites stream flushing and larvicides, would be protective. For dengue and chikungunya control, inverting the latex-collection cups after latex collection and storing them in rain-proof shelters is essential. Although we lack methods of personal outdoor protection, wash-proof insecticide-treated clothing or spatial repellent emanators may provide long-term protection for plantation workers. Understanding the migration patterns of plantation workers in SEA within countries and cross-border is a crucial challenge for effective disease control and is even more urgent with the rapid spread of ACT-tolerant malaria parasites across the region (see Outstanding Questions). National and international cooperation is imperative for successful control and management of vector-borne diseases, not only strengthening the capacity for mosquito control but also identifying vulnerable population groups and residual transmission areas. Importantly, this is an issue that threatens the growth and productivity of the rubber industry in the region, so control implementation should be a partnership between the health sector, local communities, and industry.

Acknowledgments

References

1 World Health Organization (2015) *World Malaria Report 2015*, WHO

2 World Health Organization (2009) *Dengue Guidelines for Diagnosis, Treatment, Prevention and Control*, WHO

3 Foley, J.A. *et al.* (2005) Global consequences of land use. *Science* 309, 570–574

4 Nissanke, M. (2010) *The Global Financial Crisis and the Developing World: Transmission Channels and Fall-Outs for Industrial Development*, United Nations Industrial Development Organization

5 Sulaiman, S. and Jeffery, J. (1986) The ecology of *Aedes albopictus* (Skuse) (Diptera: Culicidae) in a rubber estate in Malaysia. *Bull. Entomol. Res.* 76, 553–557

6 Jomon, K.V. and Valamparampil, T.T. (2014) Medically important mosquitoes in the rubber plantation belt of central Kerala, India. *Southeast Asian J. Trop. Med. Public Health* 45, 796

7 Sumodan, P.K. (2012) Species diversity of mosquito breeding in rubber plantations of Kerala, India. *J. Am. Mosq. Control. Assoc.* 28, 114–115

8 National Agriculture and Forestry Research Institute (2011) *Review of Rubber Plantations*, Ministry of Agriculture and Forestry

9 Martens, P. and Hall, L. (2000) Malaria on the move: human population movement and malaria transmission. *Emerg. Infect. Dis.* 6, 103–109

11 Satitvipawee, P. *et al.* (2012) Predictors of malaria-association with rubber plantations in Thailand. *BMC Public Health* 12, 1115

12 Wangroongsarb, P. *et al.* (2011) Respondent-driven sampling on the Thailand–Cambodia border. II. Knowledge, perception, practice and treatment-seeking behaviour of migrants in malaria endemic zones. *Malar. J.* 10, 117

13 Guyant, P. *et al.* (2015) Malaria and the mobile and migrant population in Cambodia: a population movement framework to inform strategies for malaria control and elimination. *Malar. J.* 14, 252

14 Watson, M. (1921) *The Prevention of Malaria in the Federated Malay States, a Record of 20 Years Progress*, E.P. Dutton

15 Bhumiratana, A. *et al.* (2013) Border malaria associated with multidrug resistance on Thailand–Myanmar and Thailand–Cambodia borders: transmission dynamic, vulnerability, and surveillance. *Biomed Res. Int.* 2013, 363417

16 Singhasivanon, P. *et al.* (1999) Malaria in tree crop plantations in south-eastern and western provinces of Thailand. *Southeast Asian J. Trop. Med. Public Health* 30, 399–404

17 Garros, C. *et al.* (2008) Distribution of *Anopheles* in Vietnam, with particular attention to malaria vectors of the *Anopheles minimus* complex. *Malar. J.* 7, 11

18 Wangroongsarb, P. *et al.* (2012) Characteristics and malaria prevalence of migrant populations in malaria-endemic areas along the Thai–Cambodian border *Southeast Asian J. Trop. Med. Public Health* 43, 261–269

19 Singh, J. and Tham, A.S. (1988) *Case History on Malaria Vector Control Through the Application of Environmental Management in Malaysia*, WHO

20 Rosenberg, R. *et al.* (1990) Highly efficient dry season transmission of malaria in Thailand. *Trans. R. Soc. Trop. Med. Hyg.* 84, 22–28

21 Bhumiratana, A. *et al.* (2013) Malaria-associated rubber plantations in Thailand. *Travel Med. Infect. Dis.* 11, 37–50

22 Sinka, M.E. *et al.* (2011) The dominant *Anopheles* vectors of human malaria in the Asia–Pacific region: occurrence data, distribution maps and bionomic *précis*. *Parasit. Vectors* 4, 89

23 Sallum, M.A.M. *et al.* (2005) Six new species of the *Anopheles leucosphyrus* group, reinterpretation of *An. elegans* and vector implications. *Med. Vet. Entomol.* 19, 158–199

24 Stoops, C.A. *et al.* (2008) Remotely-sensed land use patterns and the presence of *Anopheles* larvae (Diptera: Culicidae) in Sukabumi, West Java, Indonesia. *J. Vector Ecol.* 33, 30–39

25 Ropes, R. (1914) An account of some anopheline mosquitos found in British North Borneo, with description of a new species. *Bull. Entomol. Res.* 5, 137–147

26 Kaewwaen, W. and Bhumiratana, A. (2015) Landscape ecology and epidemiology of malaria associated with rubber plantations in Thailand: integrated approaches to malaria ecotoping. *Interdiscip. Perspect. Infect. Dis.* 2015, 17

27 Yasuoka, J. and Levins, R. (2007) Impact of deforestation and agricultural development on anopheline ecology and malaria epidemiology. *Am. J. Trop. Med. Hyg.* 76, 450–460

28 Sinka, M. *et al.* (2011) The dominant *Anopheles* vectors of human malaria in the Asia–Pacific region: occurrence data, distribution maps and bionomic *précis*. *Parasit. Vectors* 4, 89

29 Obsomer, V. *et al.* (2007) The *Anopheles dirus* complex: spatial distribution and environmental drivers. *Malar. J.* 6, 26

30 Tainchum, K. *et al.* (2015) *Anopheles* species diversity and distribution of the malaria vectors of Thailand. *Trends Parasitol.* 31, 109–119

31 Suwonkerd, W. *et al.* (2013) Vector biology and malaria transmission in Southeast Asia. In *Anopheles Mosquitoes – New Insights into Malaria Vectors* (Manguin, S., ed.), InTech

32 Lwetoijera, D. *et al.* (2013) A need for better housing to further reduce indoor malaria transmission in areas with high bed net coverage. *Parasit. Vectors* 6, 57

33 Hiscox, A. *et al.* (2013) Risk factors for mosquito house entry in the Lao PDR. *PLoS One* 8, e62769

34 Ashley, E.A. *et al.* (2014) Spread of artemisinin resistance in *Plasmodium falciparum* malaria. *N. Engl. J. Med.* 371, 411–423

35 Moyes, C.L. *et al.* (2014) Defining the geographical range of the *Plasmodium knowlesi* reservoir. *PLoS Negl. Trop. Dis.* 8, e2780

36 Vythilingam, I. and Hii, J. (2013) Simian malaria parasites: special emphasis on *Plasmodium knowlesi* and their *Anopheles* vectors in Southeast Asia. In *Anopheles Mosquitoes – New Insights into Malaria Vectors* (Manguin, S., ed.), InTech

37 Kwa, B.H. (2008) Environmental change, development and vectorborne disease: Malaysia's experience with filariasis, scrub typhus and dengue. *Environ. Dev. Sustain.* 10, 209–217

38 Sermwittayawong, N. *et al.* (2012) Human *Plasmodium knowlesi* infection in Ranong province, southwestern border of Thailand. *Malar. J.* 11, 36

39 Tsuda, Y. *et al.* (2006) Different spatial distribution of *Aedes aegypti* and *Aedes albopictus* along an urban–rural gradient and the relating environmental factors examined in three villages in northern Thailand. *J. Am. Mosq. Control Assoc.* 22, 222–228

40 Sumodan, P.K. *et al.* (2015) Rubber plantations as a mosquito box amplification in South and Southeast Asia. In *Socio-Ecological Dimensions of Infectious Diseases in Southeast Asia* (Morand, S., ed.), pp. 160–165, Springer

41 Albar Bin Nusyirwan, S. (2010) *Overview of Dengue Mortality in Selangor State: 2010*, Selangor State Health Department

42 Palaniyandi, M. (2014) The environmental aspects of dengue and chikungunya outbreaks in India: GIS for epidemic control. *Int. J. Mosq. Res.* 1, 35–40

43 Thammapalo, S. *et al.* (2009) Biting time of *Aedes albopictus* in the rubber plantations and the orchards, the southern-most of Thailand. *J. Vector Borne Dis.* 6, 1–6

44 Paily, K.P. *et al.* (2013) Efficacy of a mermithid nematode *Romanomermis iyengari* (Welch) (Nematoda: Mermithidae) in controlling tree hole-breeding mosquito *Aedes albopictus* (Skuse) (Diptera: Culicidae) in a rubber plantation area of Kerala, India. *Parasitol. Res.* 112, 1299–1304

45 Thammapalo, S. *et al.* (2005) Socio-demographic and environmental factors associated with *Aedes* breeding places in Phuket, Thailand. *Southeast Asian J. Trop. Med. Public Health* 36, 426–433

46 Sumodan, P.K. (2003) Potential of rubber plantations as breeding source for *Aedes albopictus* in Kerala, India. *Dengue Bull.* 27, 197–198

47 Vasilakis, N. *et al.* (2011) Fever from the forest: prospects for the continued emergence of sylvatic dengue virus and its impact on public health. *Nat. Rev. Microbiol.* 9, 532–541

48 Woolhouse, M.E.J. (2002) Population biology of emerging and re-emerging pathogens. *Trends Microbiol.* 10, S3–S7

49 Staples, J.E. *et al.* (2009) Chikungunya fever: an epidemiological review of a re-emerging infectious disease. *Clin. Infect. Dis.* 49, 942–948

50 Soulaphy, C. *et al.* (2013) Emergence of chikungunya in Moonlapamok and Khong Districts, Champassak Province, the Lao People's Democratic Republic, May to September 2012. *Western Pac. Surveill. Response J.* 4, 46–50

51 Kumar, N.P. *et al.* (2011) Chikungunya virus outbreak in Kerala, India, 2007: a seroprevalence study. *Mem. Inst. Oswaldo Cruz* 106, 912–916

52 Gubler, D.J. (2002) Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century. *Trends Microbiol.* 10, 100–103

53 Sachs, J. and Malaney, P. (2002) The economic and social burden of malaria. *Nature* 415, 680–685

54 Gupta, I. and Chowdhury, S. (2014) Economic burden of malaria in India: the need for effective spending. *WHO South East Asia J. Public Health* 3, 95–102

55 Stahl, H.C. *et al.* (2013) Cost of dengue outbreaks: literature review and country case studies. *BMC Public Health* 13, 1048

56 World Health Organization (2012) *Handbook for Integrated Vector Management*, WHO

57 Guyant, P. *et al.* (2015) Past and new challenges for malaria control and elimination: the role of operational research for innovation in designing interventions. *Malar. J.* 14, 279

58 Killeen, G. (2014) Characterizing, controlling and eliminating residual malaria transmission. *Malar. J.* 13, 330

59 Erlanger, T.E. *et al.* (2008) Effect of dengue vector control interventions on entomological parameters in developing countries: a systematic review and meta-analysis. *Med. Vet. Entomol.* 22, 203–221

60 Corbel, V. and N'Guessan, R. (2013) Distribution, mechanisms, impact and management of insecticide resistance in malaria vectors: a pragmatic review. In *Anopheles Mosquitoes – New Insights into Malaria Vectors* (Manguin, S., ed.), InTech

61 Tusting, L.S. *et al.* (2015) The evidence for improving housing to reduce malaria: a systematic review and meta-analysis. *Malar J.* 14, e209

62 Ogoma, S.B. *et al.* (2010) Screening mosquito house entry points as a potential method for integrated control of endophagic filariasis, arbovirus and malaria vectors. *PLoS Negl. Trop. Dis.* 4, e773

63 Lenhart, A. *et al.* (2013) A cluster-randomized trial of insecticide-treated curtains for dengue vector control in Thailand. *Am. J. Trop. Med. Hyg.* 88, 254–259

64 Hill, N. *et al.* (2014) A household randomized, controlled trial of the efficacy of 0.03% transfluthrin coils alone and in combination with long-lasting insecticidal nets on the incidence of *Plasmodium falciparum* and *Plasmodium vivax* malaria in Western Yunnan Province, China. *Malar. J.* 13, 208

65 Kawada, H. *et al.* (2006) Field evaluation of spatial repellency of metofluthrin-impregnated latticework plastic strips against *Aedes aegypti* (l.) and analysis of environmental factors affecting its efficacy in My Tho City, Tien Giang, Vietnam. *Am. J. Trop. Med. Hyg.* 75, 1153–1157

66 Achee, N. *et al.* (2012) Spatial repellents: from discovery and development to evidence-based validation. *Malar. J.* 11, 164

67 Syafruddin, D. *et al.* (2014) Impact of a spatial repellent on malaria incidence in two villages in Sumba, Indonesia. *Am. J. Trop. Med. Hyg.* 91, 1079–087

68 Curtis, C.F. *et al.* (1990) Natural and synthetic repellents. In *Appropriate Technology in Vector Control* (Raton, B., ed.), pp. 75–92, CRC

69 Sathantriphop, S. *et al.* (2014) Comparative behavioral responses of pyrethroid-susceptible and -resistant *Aedes aegypti* (diptera: Culicidae) populations to citronella and eucalyptus oils. *J. Med. Entomol.* 51, 1182–1191

70 Wilson, A.L. *et al.* (2014) Are topical insect repellents effective against malaria in endemic populations? A systematic review and meta-analysis. *Malar. J.* 13, 446

71 Gryseels, C. *et al.* (2015) Factors influencing the use of topical repellents: implications for the effectiveness of malaria elimination strategies. *Sci. Rep.* 5, 16847

72 Murray, N. *et al.* (2014) Acceptability of impregnated school uniforms for dengue control in Thailand: a mixed methods approach. *Glob. Health Action* 7, 24887

73 Banks, S.D. *et al.* (2014) Insecticide-treated clothes for the control of vector-borne diseases: a review on effectiveness and safety. *Med. Vet. Entomol.* 28, 14–25

74 DeRaedt Banks, S. *et al.* (2015) Permethrin-treated clothing as protection against the dengue vector, *Aedes aegypt*i: extent and duration of protection. *PLoS Negl. Trop. Dis.* 9, e0004109

75 Schreck, C.E. and McGovern, T.P. (1989) Repellents and other personal protection strategies against *Aedes albopictus*. *J. Am. Mosq. Control Assoc.* 5, 247–250

76 Pennetier, C. *et al.* (2010) New protective battle-dress impregnated against mosquito vector bites. *Parasit. Vectors* 3, 81

77 Xue, R.D. *et al.* (2012) Field evaluation of the Off! clip-on mosquito repellent (metofluthrin) against *Aedes albopictus* and *Aedes taeniorhynchus* (Diptera: Culicidae) in northeastern Florida. *J. Med. Entomol.* 49, 652–655

78 Keiser, J. *et al.* (2005) Reducing the burden of malaria in different eco-epidemiological settings with environmental management: a systematic review. *Lancet Infect. Dis.* 5, 695–708

79 Sahu, S.S. *et al.* (2014) Environmental management through sluice gated bed-dam: a revived strategy for the control of *Anopheles fluviatilis* breeding in streams. *Indian J. Med. Res.* 140, 296–301

80 Wijaya, T. (2013) The effect of rain guard on reducing latex loss. *J. Mater. Sci. Eng.* 3, 564–568

81 Hiscox, A. *et al.* (2013) Risk factors for the presence of *Stegomyia aegypti* and *Stegomyia albopicta* in domestic water-holding containers in areas impacted by the Nam Theun 2 hydroelectric project, Laos. *Am. J. Trop. Med. Hyg.* 88, 1070–1078

82 World Health Organization (2013) *Larval Source Management: A Supplementary Measure for Malaria Vector Control: An Operational Manual*, WHO

83 Kay, B. and Nam, V.S. (2005) New strategy against *Aedes aegypti* in Vietnam. *Lancet* 365, 613–617

84 Walshe, D.P. *et al.* (2013) Larvivorous fish for preventing malaria transmission. *Cochrane Database Syst. Rev.* 12, CD008090

85 Miyagi, I. *et al.* (1992) Biological control of container-breeding mosquitoes, *Aedes albopictus* and *Culex quinquefasciatus*, in a Japanese island by release of *Toxorhynchites splendens* adults. *Med. Vet. Entomol.* 6, 290–300

86 Baldacchino, F. *et al.* (2015) Control methods against invasive *Aedes* mosquitoes in Europe: a review. *Pest Manag. Sci.* 71, 1471–1485

87 Gabrieli, P. *et al.* (2014) Engineering the control of mosquito-borne infectious diseases. *Genome Biol.* 15, 535

88 Alphey, L. (2014) Genetic control of mosquitoes. *Annu. Rev. Entomol.* 59, 205–224

89 Cui, L. *et al.* (2012) Malaria in the Greater Mekong subregion: heterogeneity and complexity. *Acta Trop.* 121, 227–239

90 Manguin, S. *et al.* (2008) Bionomics, taxonomy, and distribution of the major malaria vector taxa of *Anopheles* subgenus *Cellia* in Southeast Asia: an updated review. *Infect. Genet. Evol.* 8, 489–503

91 Yu, G. *et al.* (2013) The *Anopheles* community and the role of *Anopheles minimus* on malaria transmission on the China–Myanmar border. *Parasit. Vectors* 6, 264

92 Tisgratog, R. *et al.* (2012) Host feeding patterns and preference of *Anopheles minimus* (Diptera: Culicidae) in a malaria endemic area of western Thailand: baseline site description. *Parasit. Vectors* 5, 114

93 Baimai, V. *et al.* (1988) Geographic distribution and biting behaviour of four species of the *Anopheles dirus* complex (Diptera: Culicidae) in Thailand. *Southeast Asian J. Trop. Med. Public Health* 19, 151–161

94 Muenworn, V. *et al.* (2009) Biting activity and host preference of the malaria vectors *Anopheles maculatus* and *Anopheles sawadwongporni* (Diptera: Culicidae) in Thailand. *J. Vector Ecol.* 34, 62–69

95 Upatham, E.S. *et al.* (1988) Bionomics of *Anopheles maculatus* complex and their role in malaria transmission in Thailand. *Southeast Asian J. Trop. Med. Public Health* 19, 259–269

96 Oo, T.T. *et al.* (2002) Studies on the bionomics of *Anopheles dirus* (Culicidae: Diptera) in Mudon, Mon State, Myanmar. *J. Vector Ecol.* 27, 44–54

97 Hawley, W.A. (1988) The biology of *Aedes albopictus*. *J. Am. Mosq. Control Assoc. Suppl.* 1, 1–39

98 Sivan, A. *et al.* (2015) Host-feeding pattern of *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) in heterogeneous landscapes of South Andaman, Andaman and Nicobar Islands, India. *Parasitol. Res.* 114, 3539–3546

Glossary

Anthropophilic: vectors attracted to people.

Artemisinin-based combination therapy (ACT): recommended by the WHO for treatment of uncomplicated *falciparum* malaria.

Chikungunya: a disease caused by the chikungunya virus from the family *Togaviridae*, transmitted by the mosquitoes *Aedes albopictus* and *Aedes aegypti*.

Community protection using vector control: mosquito control using methods that reduce mosquito numbers in an area and/or the survival of the vector population, thus providing greater protection than can be achieved by deploying vector control at an individual level (vs individual protection).

Dengue: a febrile illness caused by the dengue virus from the family *Flaviviridae*, transmitted by *Ae. aegypti* and *Ae. albopictus*.

Emerging infectious diseases: a group of infectious diseases that have emerged, increased in incidence, or spread in geographical area.

Endophagic: having a tendency to blood feed indoors.

Exophagic: having a tendency to blood feed outdoors.

Exophilic: having a preference for resting outdoors.

Genetic control: controlling mosquitoes by releasing sterile males or genetically modified mosquitoes into an area.

Integrated vector management (IVM): adaptive, evidence-based vector management that draws on vector control measures from both within and outside the health sector.

Larval source management (LSM): management of immature mosquito life stages using environmental management, larvicides, and biological control.

Latex: a white, milky suspension of rubber polymers released from the *Hevea brasiliensis* tree after tissue injury.

Malaria: an infectious disease caused by parasitic protozoans of the genus *Plasmodium*, transmitted by *Anopheles* mosquitoes.

Mosquito-borne disease: transmission of pathogens from human and animals to humans and animals by a mosquito vector.

Natural rubber: latex from *H. brasiliensis* trees processed into rubber (vs **synthetic rubber**).

Personal protection (vector control): mosquito control using methods like repellents and protective clothing to reduce mosquito biting exposure of individuals (vs community protection).

Rubber plantation: an artificial forest where *H. brasiliensis* trees are grown for commercial purposes.

Southeast Asia (SEA): according to the Association of Southeast Asian Nations (ASEAN), this comprises Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, and Viet Nam.

Synthetic rubber: a mixture of polymers made from artificial elastomers synthesised from petroleum byproducts (vs natural rubber).

Vector: an organism that transmits pathogens from one host to another.

Vector control: all methods (i.e., chemical, biological, environmental, and genetic) aiming to reduce vector longevity, vector density, and/or host–vector contact.

Zoophilic: vectors attracted to animals.

Box 1. Rubber Tree Cultivation in Southeast Asia

Hevea brasiliensis is a tropical softwood tree that produces nearly all of the world's natural rubber. Since the tree is of economic importance, many clones have been developed that vary in latex production, wood productivity, disease resistance, and soil-nutrient adaptation (http://lad.nafri.org.la). Rubber trees are grown in a nursery and planted in the plantation when they are 1–2 m high. Fungicides, herbicides, and fertilisers are used to increase their development rate and protect them from tree blight. To our knowledge insecticides are not used in the plantations. Tapping starts after the tree is 7 years old or when 70% of the trees in the plantation have a circumference of >50 cm (Figure I). In SEA, tapping is conducted during the rainy season from June to November when rubber trees are physiologically active. Latex, the milky suspension of rubber particles, is present outside the phloem in the latex vessels of the bark. These vessels are curved at a 30° angle up the tree in a right-handed spiral. This spiral makes tapping latex difficult and requires skill from the rubber tappers. A series of thin slices of bark are cut in half of a spiral around the trunk without damaging the growing layer (Figure II). The latex seeps out of the cut into a gutter and is collected in a collecting cup (Figure III). The latex slowly coagulates within 3 h of tapping and the flow stops. Tapping in SEA is done typically from 21.00 to 05.00 h, when phloem flow is highest. On average every worker taps 750 trees per night, equivalent to 1.5 ha of rubber plantation [8]. The frequency of tapping is dependent on the country, but in general trees are tapped every 2 days. When one tapping panel has no bark left, a new panel is made, until all areas of the tree have been used. If tapping has been done carefully the same area of bark can be tapped again after a few years. Latex can be tapped for up to 30 years, after which the trees are felled and sold as tropical softwood. The latex from the cups is collected in large buckets. Depending on the facilities, the latex is left liquid by

adding ammonium or coagulated by adding 94% formic acid. Liquid latex is filtered and

processed into smoked sheets. Solid latex can be processed in many ways, with the quality of the

rubber depending on the method.

Table 1. Land-Use Development with the Resulting Change in Dominant Vectors and Disease Risk

Change in Land Use	Primary and Secondary Forest	Bare Land	Immature Rubber Plantation	Mature Rubber Plantation
Dominant Vectors	*Anopheles dirus sensu lato* *Anopheles minimus sensu lato* *Aedes albopictus*	*Anopheles maculates sensu lato*	*Ae. albopictus* *An. maculatus s.l.*	*An. dirus s.l.* *An. minimus s.l.* *Ae. albopictus*

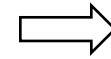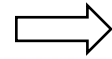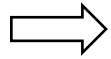|			
Malaria Risk	High	Low	Low	Medium
Dengue Risk	Medium	Low	Low	High
Emerging Disease Risk	High	Low	Low	Medium

Table 2. Main Malaria and Dengue Vectors of SEA

Vector-Borne Disease	Vector	Habitat Preference	Habitat Larvae	Biting Peak	Behaviour	Flight Range (m)	Seasonality	Refs
Malaria	*Anopheles minimus sensu lato*	Forest with high canopy coverage	Clear, unpolluted water along shaded grassy edges of slow-moving streams	After 22.00 h, throughout the night until 05.00/06.00 h	Anthropophilic and zoophilic **Endophagic** and **exophagic**	1500–3000	Dry season	[30,31,89–92]
	Anopheles dirus sensu	Forest with high canopy coverage	Temporary waters and stagnant/slow-moving	Early morning	- Anthropophi	1500–3000	Rainy season	[22,29,30,89,90,93]

Disease	Species	Habitat	Breeding site	Biting time	Feeding behaviour	Flight range	Season	References
	lato	and forest fringe	shaded water in forests	and 18.00–01.00 h	lic Endophagic and exophagic			
	Anopheles maculatus sensu lato	Low tree-canopy coverage	Sunlit streams and ground pools	Early morning and 20.00–23.00h	Anthropophilic and zoophilic **Exophagic**	1500–3000	Dry and rainy season	[22,29,30,90,94–96]
Dengue	Aedes albopictus	Urban and rural habitats	Artificial or natural containers outdoors	06.00–11.00 h, 16.00–19.00 h	Anthropophilic Exophagic	200–1000	Rainy season	[39,97,98]
	Aedes aegypti	Urban habitats, becoming more common in rural areas	Artificial containers with no reliable water supply indoors	All day	Anthropophilic Endophagic and exophagic	200–1000	Rainy season	[81,97,98]

Figure 1. Disease Distribution Maps in Southeast Asia. (**A**) Malaria cases in 2010. (**B**) Dengue cases in 2010. (**C**) Rubber production in 2010. Data collected from [1] (http://www.anrpc.org; http://data.worldbank.org; http://www.searo.who.int). Images made using © CartoDB.

Figure 2. Personal Protection Methods. (**A**) Topically applied repellent. (**B**) Permethrin-treated work clothing. (**C**) Metofluthrin emanator worn on a belt. (**D**) Pyrethroid mosquito coil worn on a belt.
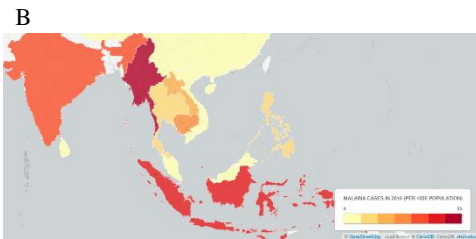
Box 1

Figure I. Rubber Plantation.

Figure II. Rubber Worker Tapping Latex.

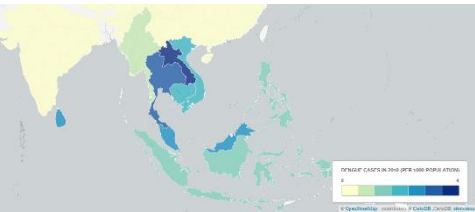Figure III. Rubber Tree with Latex Cup.

fig 1A, B & C showing positions

B

C

fig 2A-D showing positions

Fig I for box 1

Fig II for box 1

Fig III for box 1