Vector Control in the Indo-Pacific: Technical Landscape

INNOVATIVE VECTOR CONTROL CONSORTIUM

NOVEMBER 2019

Asia Pacific Vector Control Technical Landscape Analysis

Report prepared for the Innovative Vector Control Consortium (IVCC) by the University of California, San Francisco (UCSF) Global Health Group's Malaria Elimination Initiative.

With funding from the Department of Foreign Affairs and Trade (DFAT), Australia

Research team:

Allison Tatarsky, UCSF Malaria Elimination Initiative

Michael Macdonald, Consultant

Neil Lobo, UCSF Malaria Elimination Initiative and University of Notre Dame

Elodie Vajda, UCSF Malaria Elimination Initiative

Tom Burkot, James Cook University

A special thanks to Alemayehu Midekisa, Chris Cotter, and Saehee Lee from the UCSF Malaria Elimination Initiative for their contributions to this work, as well as Catherine Moyes and Marianne Sinka from the University of Oxford for sharing published and unpublished data on disease distribution and vector habitat suitability, and for constructing binary maps of occurrence for this report. The research team would also like to thank the many key informants who participated in this landscape analysis and provided valuable insights.

Contents

Acronyms

APLMA	Asia Pacific Malaria Leaders Alliance
APMEN	Asia Pacific Malaria Elimination Network
ATSB	Attractive toxic sugar bait
BMGF	Bill & Melinda Gates Foundation
CRCT	Cluster randomized controlled trial
DIY	Do It Yourself
DFAT	Department of Foreign Affairs and Trade (Australia)
GMS	Greater Mekong Subregion
HRP	High risk population
IRS	Insecticide residual spraying
ITC	Insecticide treated clothing
ITM	Insecticide treated material
ITN	Insecticide treated net
IVM	Integrated vector management
IVCC	Innovative Vector Control Consortium
JE	Japanese encephalitis
LF	Lymphatic filariasis
LLIHN	Long last insecticide treated hammock net
LLIN	Long lasting insecticide treated net
LSM	Larval source management
MAP	Malaria Atlas Project
MOH	Ministry of Health
ORS	Outdoor residual spraying
PCO	Pest control operator
PMI	President's Malaria Initiative (US)
PQ	Pre-Qualification (WHO)
RIDL	Release of Insects with Dominant Lethal
SEARO	South East Asia Regional Office (WHO)
SIT	Sterile Insect Technique
UCSF	University of California, San Francisco
ULV	Ultra-low volume (spraying)
VCAG	Vector Control Advisory Group (WHO)
VL	Visceral leishmaniasis
WHO	World Health Organization
WPRO	Western Pacific Regional Office (WHO)

Executive summary

Mosquito-borne diseases continue to cause high morbidity and mortality and threaten health security across the Asia Pacific region. In 2017, there were over 13 million malaria cases, with 23,000 malaria deaths, and while many countries are making progress toward elimination, malaria transmission persists in high risk areas and among high risk populations where new tools are desperately needed. Between 2010 and 2017, there were over 1 million dengue cases reported, although this is widely believed to be significantly underestimated and underreported. Chikungunya, Zika, lymphatic filariasis and Japanese encephalitis are of concern in many areas and require an integrated vector control approach to leverage a broader mosquito-control toolbox, efforts, and resources.

The Innovative Vector Control Consortium (IVCC) commissioned the University of California, San Francisco (UCSF) Malaria Elimination Initiative to conduct this vector control technical landscape analysis to guide research and development of new vector control tools for the Asia Pacific region in support of country efforts to control and eliminate mosquito-borne disease and enhance regional health security, with a primary focus on malaria and *Aedes*-borne diseases. The landscape analysis was conducted between September 2018 and February 2019 and included a desk review of 19 countries and visits to eight of these countries for in-depth consultations and key informant interviews with governments and partners in Cambodia, China, Indonesia, Malaysia, Myanmar, Papua New Guinea, Sri Lanka, and Vietnam, as well as consultations with over 20 industry partners.

While there is a wide range of malaria transmission ecologies stretching from South Asia, through the Greater Mekong Subregion (GMS), Malaysia, Indonesia and the Western Pacific, common themes emerged. Outdoor transmission is the key technical and biological challenge expressed by every national malaria program and partner consulted, necessitating innovation and access to vector control tools for outdoor protection, including against *P. knowlesi*, an emerging concern in the region. Despite a lack of insecticide resistance data in many parts of the region, insecticide resistance among dominant *Anopheles* vectors is widespread in South Asia, and there are indications that pyrethroid resistance is increasing in the GMS (a subregion also confronting multi-drug resistant parasites) and elsewhere. Most national programs rely almost exclusively on mass distribution of long lasting insecticide-treated nets (LLINs), with the exception of a small handful of countries who implement widescale indoor residual spraying (IRS) as their primary vector control intervention. There are several partner efforts to understand and address the entomological and anthropological aspects of outdoor malaria transmission in the region, and there have been attempts to develop coordinated strategies both at the national and sub-regional levels, but there has been no effective, acceptable, affordable, and scalable tool or package of tools to address existing gaps in protection. Small volumes make product development and procurement challenging, but when considering markets in Africa and Latin America for outdoor tools, *Aedes* control, and mosquito-borne disease prevention in humanitarian emergencies, the opportunity may be more substantial.

Aedes-borne diseases are on the rise as *Aedes aegypti* and *Ae. albopictus* populations continue to proliferate with increasing occurrences of dengue outbreaks and often inadequate diagnostic capacity to detect chikungunya and Zika. There are some countries with relatively strong *Aedes* control programs, but most lack capacity and accessible and effective surveillance and control options. Insecticide resistance among *Aedes*, both pyrethroid adulticides and temephos larvicide, is very severe in some countries. Capacity for emergency response and implementation of International Health Regulations for health security varies significantly, with most countries lacking adequate tools and resources.

IVCC is uniquely positioned to address these challenges in collaboration with country governments and research, implementation, and industry partners. Potential solutions fit into the IVCC's integrated vector management (IVM) portfolio of work, as it will not be one new product that will turn the tide, but an integrated package of tools and approaches that – driven by improved, high quality data and implementation – can sustainably reduce mosquito-borne diseases in the Asia Pacific.

Opportunities identified from this landscape analysis include:

- Develop longer-lasting, portable, acceptable, scalable, bite prevention products, which could include repellent self-treatment or an optimized concept for the "forest packs," and expand the evidence base of these products for public health impact.
- Improve application equipment for adulticides and larvicides, including exploring new application technologies for targeted indoor residual spraying (TIRS) and area-wide larviciding.
- Optimize long lasting insecticide treated nets (LLINs) and long lasting insecticide treated hammocks (LLIHNs) to better fit consumer preference, as well as explore opportunities to subsidize sales through the private market and/or develop long lasting retreatment for preferred conventional nets and hammocks.
- Explore the effectiveness of attractive toxic sugar baits (ATSBs) for *Aedes* control in urban and peri-urban environments rather than *Anopheles* environments where multiple abundant competition for sugar sources exist.

This report provides a regional synthesis of diseases, vectors, biological challenges, and gaps in protection based on current vector control interventions. The report also summarizes evidence on the malaria and *Aedes*-borne disease control toolboxes and opportunities for IVCC intervention.

Background and objectives

In 2018, the IVCC received a five-year grant from the Australia Department of Foreign Affairs and Trade (DFAT) to develop and disseminate vector control technologies for malaria and other vector-borne diseases in the Asia Pacific region. As a first step of this project, IVCC commissioned the University of California, San Francisco, Global Health Group's Malaria Elimination Initiative (MEI) to conduct a vector control technical landscape analysis in the region.

Included in this analysis are the main mosquito-borne diseases in the Asia Pacific region, including malaria, lymphatic filariasis, dengue, chikungunya, Zika, and Japanese encephalitis, and their associated mosquito vectors, as well as a brief look at visceral leishmaniasis. Nineteen countries across the region are included in the desk review, eight of which were visited by a research team member for in-depth consultation, including: Cambodia, China, Indonesia, Malaysia, Myanmar, Papua New Guinea, Sri Lanka, and Vietnam.

The overarching aim of this landscape analysis as part of the larger project is to **guide development of new vector control tools for countries in the Asia Pacific region in support of country efforts to control and eliminate mosquito-borne diseases and enhance regional health security**.

Specific objectives of the landscape analysis include:

1. Describe mosquito-borne disease transmission ecology across the region and by country, including the biological challenges to controlling disease
2. Document ministry of health vector borne disease strategic and technical priorities and gaps, capacity, and emergency response
3. Gather information on vector control products available by market type and delivery pathways
4. Identify gaps in protection based on disease transmission and implemented intervention strategies
5. Develop broad target product profiles based on gaps in protection

Methods

The inclusion criteria for the analysis included three mosquito genera (*Anopheles*, *Aedes*, and *Culex*) and five mosquito-borne diseases (malaria, dengue, Zika, chikungunya, lymphatic filariasis, and Japanese encephalitis). We used a mixed-methods approach in a three-part analysis:

Disease landscape

We mapped and analyzed descriptive statistics of diseases and vectors across the region based on data from the Malaria Atlas Project, World Health Organization (WHO), and United States and European Centers for Disease Control and Prevention (CDC), country reports, and peer-reviewed literature.

Desk review

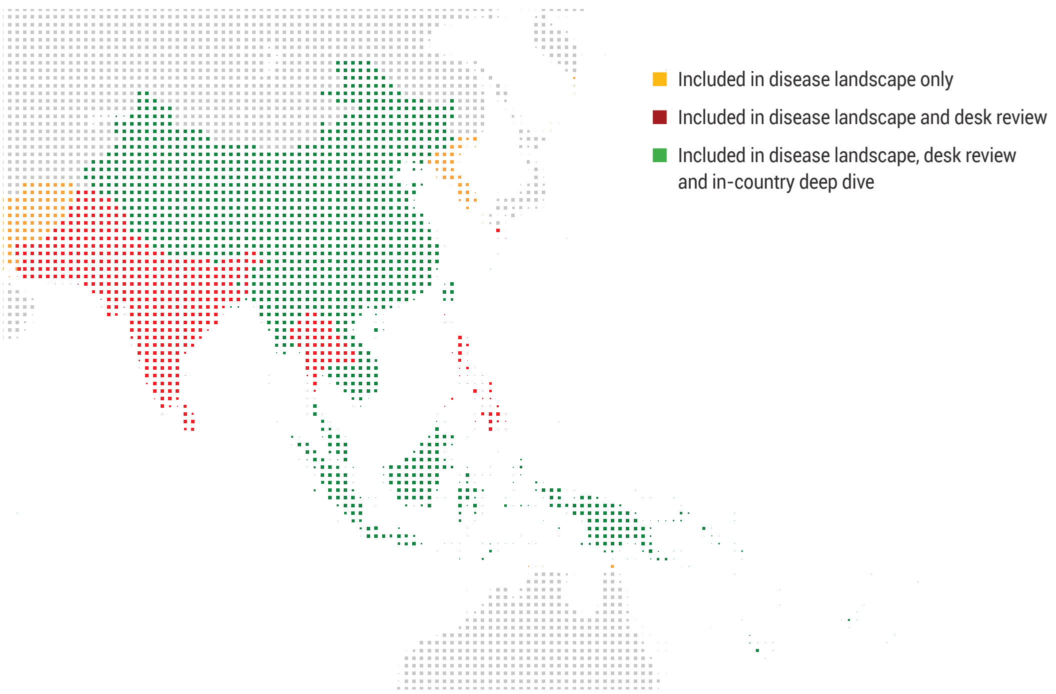
Grey and peer-reviewed literature were reviewed and remote and in-person consultations conducted with key stakeholders and subject matter experts. Grey literature included WHO regional reports and reviews and resources from WHO Pre-Qualification (PQ) and the Vector Control Advisory Group (VCAG); ministry of health (MOH) reports, including malaria program reviews, annual reports, presentations, and Global Fund concept notes; Asia Pacific Malaria Elimination Network (APMEN) reports; donor and partner reports; and Walter Reed Bioinformatics Unit (WRBU) reports, among others. Peer-reviewed literature was searched based on key information gaps, with a focus on systematic reviews of the vector control toolbox for malaria and *Aedes*-borne diseases. We conducted consultations with key stakeholders and subject matter experts at the American Society for Tropical Medicine and Hygiene (ASTMH) conference in October 2018 and Roll Back Malaria (RBM) Vector Control Working Group (VCWG) meeting in January 2019, as well as remotely by Skype.

In-country deep-dives

We traveled to select countries (based on consultation with IVCC and DFAT) to conduct comprehensive key informant interviews based on a semi-structured interview guide and made site visits to research facilities where possible. The interview guide included specific questionnaires by key informant category: government, research institution, NGO implementing partner, private sector implementing partner (e.g. extractives industry, pest control operator, etc.), retail vendor, and vector control manufacturer. We also collected additional relevant grey literature.

Twenty-four countries in the Asia Pacific region were included in the disease landscape, 19 countries in the desk review, and eight countries in the country deep-dives (Figure 1).[1]

FIGURE 1. COUNTRIES INCLUDED IN THIS TECHNICAL LANDSCAPE ANALYSIS



The next section summarizes epidemiology and entomology by disease across the Asia Pacific region to contextualize the scope and scale of mosquito-borne disease and the need for new vector control tools.

[1] Deep dives: Cambodia, China, Indonesia, Malaysia, Myanmar, Papua New Guinea, Sri Lanka, Vietnam; Additional countries for desk review: Bangladesh, Bhutan, India, Lao PDR, Nepal, Pakistan, Philippines, Solomon Islands, Thailand, Timor Leste, and Vanuatu. Additional countries only for disease landscaping: Afghanistan, Fiji, North Korea, Samoa, and South Korea.

Disease landscape

The epidemiology of malaria, dengue, chikungunya, Zika, lymphatic filariasis (LF), and Japanese encephalitis (JE) across the Asia Pacific region is described below. Figure 2 illustrates areas where four of the diseases are co-endemic, and Figure 3 illustrates countries where malaria, dengue, or malaria and dengue are present. These maps are modelled predictions based on data of infection occurrence (or, in the case of *P. falciparum* and *P. vivax*, infection prevalence).

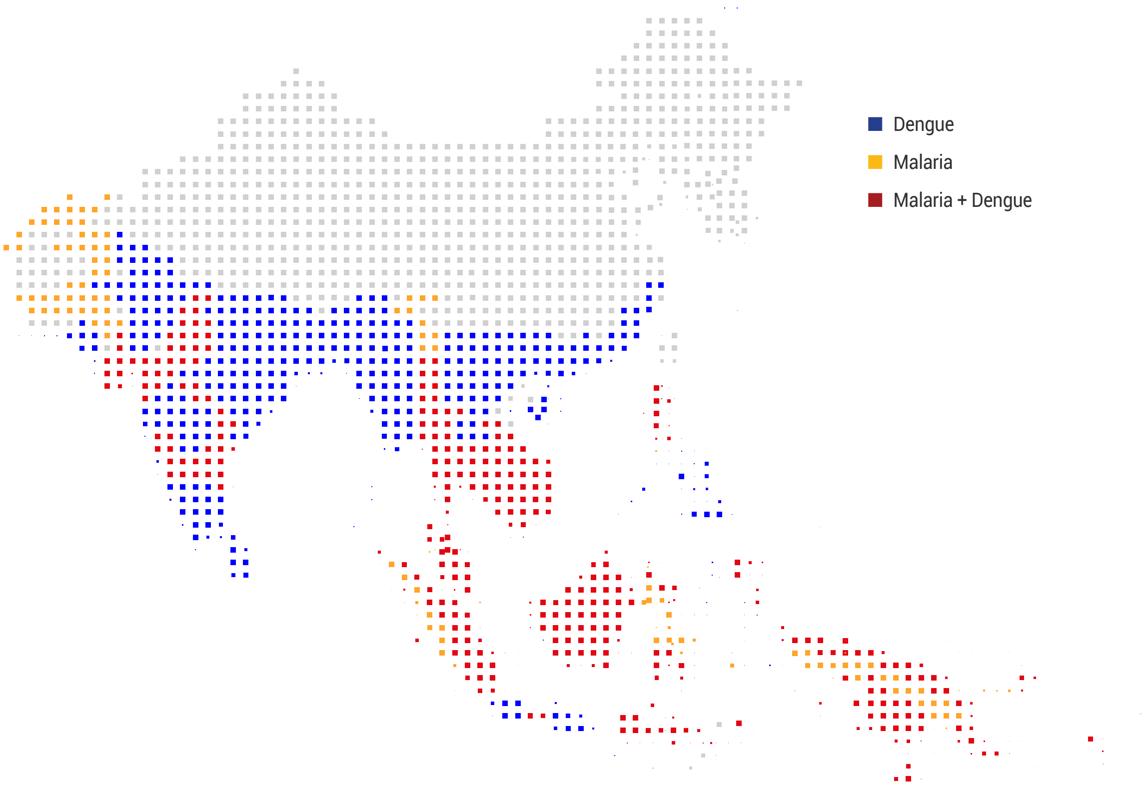
FIGURE 2. THE OVERLAP IN THE GEOSPATIAL DISTRIBUTIONS OF FOUR DISEASES: MALARIA (*P. FALCIPARUM*, *P. VIVAX*, AND *P. KNOWLESI*), DENGUE, CHIKUNGUNYA, AND LYMPHATIC FILARIASIS. [2]

There was no geospatial data available on JE occurrent at the time of writing this report. Therefore, the relative probability of occurrence for *Culex tritaeniorhynchus*, the main vector for JE, is used as a proxy for JE risk but is not included in this map (see Figure 6).

---

[2] Malaria data from https://map.ox.ac.uk/. Dengue, chikungunya, and LF data from Catherine Moyes, Marianne Sinka, Nick Golding, Josh Longbottom, Freya Shearer and Moritz Kraemer (University of Oxford). The binary map of LF infection occurrence was derived from Cano J, Rebollo MP, Golding N, et al. The global distribution and transmission limits of lymphatic filariasis: past and present. Parasites & Vectors. 2014; 7:466; https://doi.org/10.1186/s13071-014-0466-x as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of dengue infection occurrence was derived from Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature. 2013; 496:504-507; https://doi.org/10.1038/nature12060 as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of chikungunya infection occurrence was derived from Nsoesie EO, Kraemer MUG, Golding N, et al. Global distribution and environmental suitability for chikungunya virus, 1952 to 2015. Eurosurveillance. 2016; 21(20); https://doi.org/10.2807/1560-7917.ES.2016.21.20.30234 as detailed in Weetman D, Kamgang B, Badolo A, et al. *Aedes* mosquitoes and *Aedes*-borne arboviruses in Africa: Current and future threats. International Journal of Environmental Research and Public Health. 2018; 15(2), 220; https://doi.org/10.3390/ijerph15020220.

FIGURE 3. SPATIAL DISTRIBUTION OF DENGUE (ALONE), MALARIA (ALONE), AND MALARIA + DENGUE INFECTION OCCURRENCE.2 MALARIA INCLUDES *P. FALCIPARUM*, *P. VIVAX*, AND *P. KNOWLESI*.



Malaria

Epidemiology

In 2017, there were an estimated 23,320 malaria deaths and 13,147,000 malaria cases in the Asia Pacific region (Figures 4 and 5), 86% of which were reported from the WHO SEARO[3] region, of which 65% was *P. vivax*.[4] Despite this, the region is celebrating some successes, with Sri Lanka certified malaria free in 2016 and China and Malaysia reporting zero human malaria cases since 2017 and 2018, respectively. While malaria has declined from 17 cases per 1,000 population at risk to 7 cases per 1,000 population in the SEARO region between 2010 and 2017, malaria cases have plateaued at 2.5 cases per 1,000 population at risk in the WPRO[5] region (although cases increased by over 3-fold in Papua New Guinea and Solomon Islands during those years) and multi-drug resistance in malaria parasites remains a threat to elimination in the GMS.[6,7] Twenty-two countries have committed to the goal of malaria elimination by 2030, which is actively supported by the Asia Pacific Malaria Elimination Network (APMEN)[8] and the Asia Pacific Malaria Leaders Alliance (APLMA).[9]

3 Bangladesh, Bhutan, DPRK, India, Indonesia, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste (malaria at risk SEARO countries)

4 World Health Organization. World Malaria Report 2018. Geneva; Global Malaria Programme.

5 Cambodia, China, Lao PDR, Malaysia, Papua New Guinea, Philippines, Republic of Korea, Solomon Islands, Vanuatu, Vietnam (malaria at risk WPRO countries)

6 World Health Organization. World Malaria Report 2018. Geneva; Global Malaria Programme.

7 Imwong M, Suwannasin K, Kunasol C, Sutawong K, Mayxay M, Rekol H, et al. The spread of artemisinin-resistant Plasmodium falciparum in the Greater Mekong subregion: a molecular epidemiology observational study. Lancet Infect Dis. 2017; 17(5): 491-497.

8 APMEN http://www.apmen.org/

9 APLMA https://www.aplma.org/

FIGURE 4. ANNUAL MALARIA PARASITE INCIDENCE (API) (CASES PER 1,000 POPULATION AT RISK) FOR 2016 BY COUNTRY.[10]

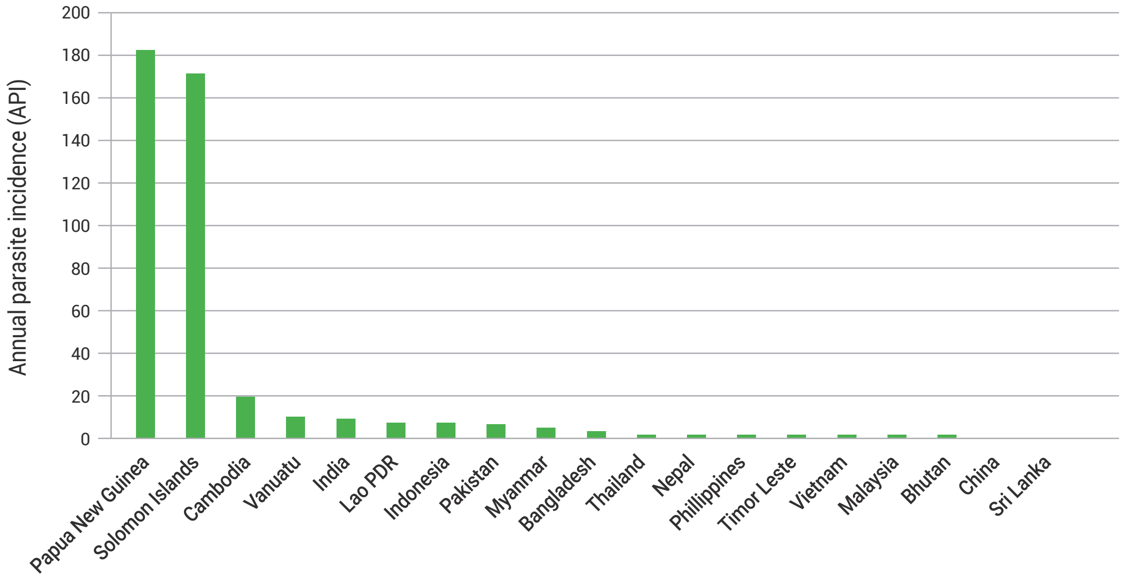
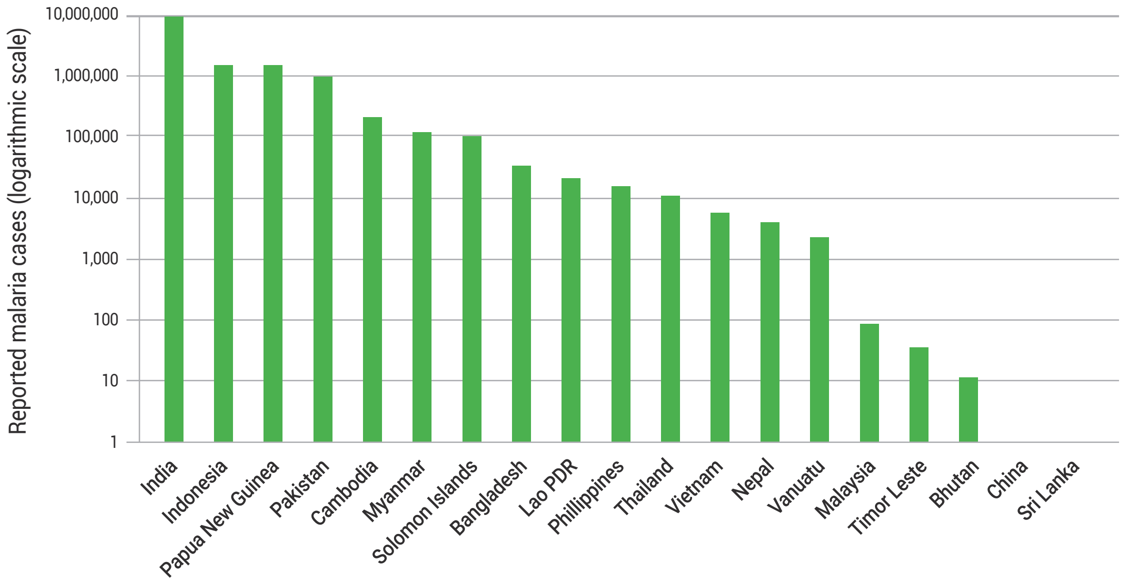


FIGURE 5. REPORTED MALARIA CASES (LOGARITHMIC SCALE) BY COUNTRY IN 2017.[11]



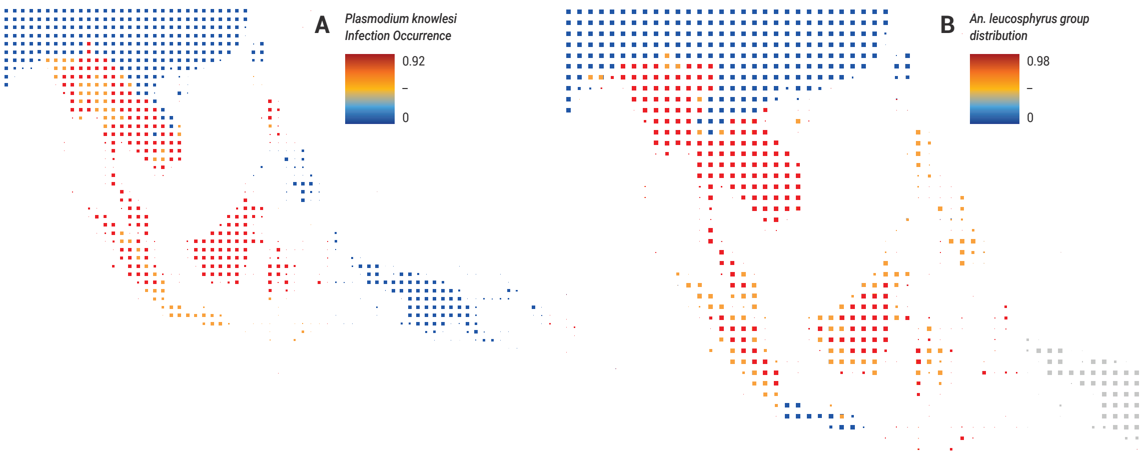
There are multiple drivers of malaria transmission across the Asia Pacific region, including vector and human behaviors, and insecticide resistance, which are described further below, that significantly impact the effectiveness of vector control interventions, as do the environment, climate, and changing landscape ecology, which are beyond the scope of this analysis.

[10] World Health Organization. World Malaria Report 2017. Geneva, Global Malaria Programme.

[11] World Health Organization. World Malaria Report 2018. Geneva, Global Malaria Programme.

Plasmodium knowlesi, a zoonotic malaria parasite, is now the most common Plasmodium species infecting humans in Malaysia where cases are confirmed by polymerase chain reaction (PCR). *P. knowlesi* has been reported from several other countries but is likely underreported due to misdiagnosis by microscopy as *P. falciparum* or *P. vivax*.[12] The rise of *P. knowlesi* is due in part to deforestation and land-use changes, prevalent throughout the region.[13] There are distinct parallels between *P. knowlesi* challenges and malaria in the GMS regarding the vectors (from the *An. leucosphyrus* group), transmission ecology, human ecology, and potential control strategies and tools. Moreover, there are operational research capacities in Malaysia that could be better linked to other regional efforts for control of "forest malaria." Estimates of *P. knowlesi* infection occurrence and distribution of the main vector group are mapped in Figure 6.

FIGURE 6. THE RELATIVE PROBABILITY OF OCCURRENCE OF (A) *P. KNOWLESI* INFECTION AND (B) AN. LEUCOSPHYRUS GROUP MOSQUITOES.[14]



13 Barber BE, Rajahram GS, Grigg MJ, William T, Anstey NM. World Malaria Report: time to acknowledge Plasmodium knowlesi malaria. *Malar J*. 2017;16(1):135. Published 2017 Mar 31. doi:10.1186/s12936-017-1787-y

14 Davidson, G., Chua, T.H., Cook, A. et al The Role of Ecological Linkage Mechanisms in Plasmodium knowlesi Transmission and Spread. EcoHealth (2019). https://doi.org/10.1007/s10393-019-01395-6

Vector ecology

Outdoor transmission driven by early evening and outdoor vector biting continues to pose the biggest challenge to malaria elimination in the Asia Pacific.[15] Vector species are highly diverse in the region, with over 19 dominant vector species and many more secondary vectors.[16] The distributions of *An. dirus* s.l., *An. punctulatus*, *An. subpictus*, and *An. flavirostris* are shown in Figure 7. Many of the vectors are naturally exophilic and exophagic, while others have become more so over time, largely due to behavioral resistance to avoid insecticides used in indoor interventions. While many of the efficient vectors are anthropophagic (e.g. *An. dirus* s.s., *An. baimai, An. minimus* s.s., and *An. punctulatus*), other important vectors are more zoophagic or opportunistic, and still contribute significantly to malaria transmission (e.g. *An. farauti, An. culicifaces*, and *An. stephensi*) (Table 1).

Some of the greatest malaria vector biodiversity occurs in the South-East Asia region.[17] The main vectors in this region are *Anopheles* dirus s.l., *An. minimus* s.l., and *An. sundaicus* s.l. Of the *An. dirus* s.l. species, *An. dirus* s.s. and *An. baimai* are dominant and considered forest and forest-fringe malaria vectors with anthropophilic and exophagic behaviors with larvae found in rain water pools and occasionally artificial containers, as well as in mono-agricultural environments. *An. minimus* s.l., including the two main vectors *An. minimus* and *An. harrisoni*, are widespread in hill forested areas, (with *An. harrisoni* more limited to the northern parts of the GMS and showing more exophagic and zoophilic behavior than *An. minimus* s.s.) and preferring slow running steams for larval habitats. Vectors in the *An. sundaicus*-related group are coastal; larvae prefer brackish water and adults exhibit both endo- and exophagy and anthropophagy behaviors. Note that *An. epiroticus*, usually reported on the Southeast Asia mainland, may also be found in Indonesia and is only distinguished by molecular methods.

In the Western Pacific region, the *An. punctulatus* complex dominates, including three primary vector species *An. farauti*, *An. punctulatus*, and *An. koliensis* and four secondary vectors.[18] *An. farauti* has the widest geographic distribution but is limited to coastal areas whose larvae are found in both brackish and fresh water swamps as well as temporary ground pools. *Anopheles* farauti adults are increasingly adapting to biting early and outdoors and to rest outdoors. *An. punctulatus* is mainly found in lowland regions and foothills, with larval habitats in temporary ground pools, rock pools, and pools in rivers and streambeds. *An. koliensis* is predominantly an inland species in the lowlands and river valley flood plains with larval habitats of wheel tracks, drains, swamps, and natural ground pools. Both *An. punctulatus* and *An. koliensis* feed indoors and outdoors but later at night than *An. farauti*. *Anopheles* koliensis may have been eliminated in the Solomon Islands by IRS.

In South Asia, *An. culicifacies*, found in a range of sun-lit larval habitats, from agricultural drainage canals and borrow-pits in Punjab to rock pools in dry-season river beds in Sri Lanka, is the principal vector of rural malaria while *An. stephensi* is the main vector in urban areas where it had adapted to water cisterns and other human-made larval habitats. In India specifically, An. fluviatilis in found in the hills and foothills while *An. dirus*, *An. minimus*, and An. nivipes are in the northeastern states.[19]

---

15 Malaria vector control in the Greater Mekong Sub-region: an independent situation analysis and suggestions for improvement 21 September 2018 Prepared by Sean Hewitt PhD VBDC Consulting Ltd http://www.vbdc-consulting.com/files/180920.pdf

16 Sinka ME, Bangs MJ, Manguin S, Chareonviriyaphap T, Patil AP, Temperley WH, et al. The dominant *Anopheles* vectors of human malaria in the Asia-Pacific region: occurrence data, distribution maps, and bionomics precis. Parasites & Vectors. 2011; 4(89).

17 Suwonkerd W, Ritthison W, Ngo CT, Tainchum K, Bangs MJ, Chareonviriyaphap T. Vector biology and malaria transmission in Southeast Asia. IntechOpen. 2013; 10:273-325.

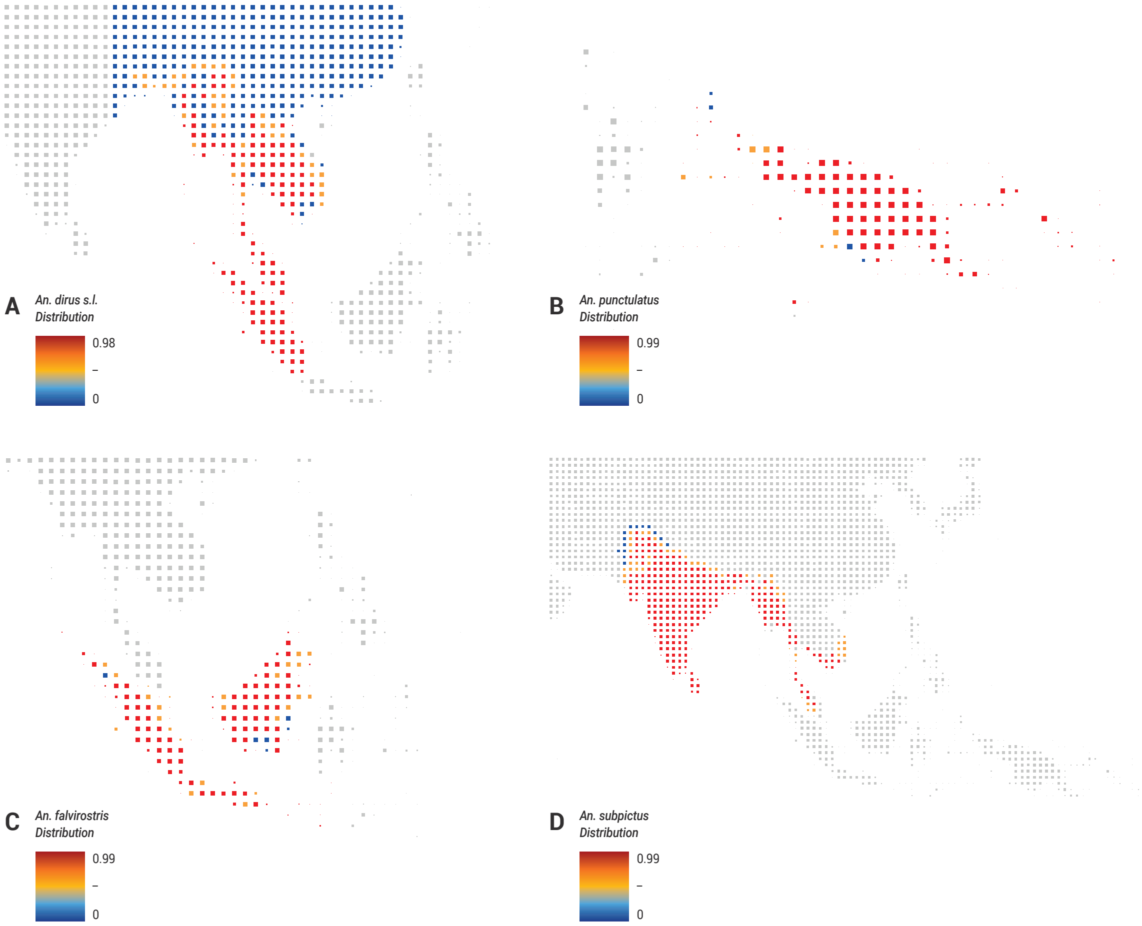
18 Beebe NW, Russell TL, Burkot TR, Lobo NF, Cooper RD. The Systematics and Bionomics of Malaria Vectors in the Southwest Pacific, *Anopheles* mosquitoes - New insights into malaria vectors, Prof. Sylvie Manguin (Ed.), ISBN: 978-953-51-1188-7, InTech. Available from: http://www.intechopen.com/books/anopheles-mosquitoes-new-insights-into-malaria-vectors/the-systematics-and-bionomics-of-malaria-vectors-in-the-southwest-pacific.

19 Kumar A, Chery L, Biswas C, Dubhashi N, Dutta P, Dua VK, et al. Malaria in South Asia: Prevalence and control. Acta Trop. 2012; 121(3).

TABLE 1. DOMINANT VECTOR SPECIES AND BIONOMICS FOR THREE KEY SUB-REGIONS IN THE ASIA PACIFIC

	Dominant species	Distribution	Human vs. animal preference	Feeding preference (indoors vs. outdoors)	Resting preference (indoors vs. outdoors)	Larval habitats
Southeast Asia (GMS, Indonesia, Malaysia, Philippines)	*An. dirus, An. balabacensis*	Forest, forest fringe, mature rubber plantations	Human (and An. balabacensis primate preference)	Outdoors	Both, now mostly outdoors	Shaded rain pools and occasionally artificial containers
	An. minimus, An. harrisoni, An. flavirostris	Forest hills, plantations	Both	Outdoors	Outdoors, with *An. minimus* preferring both	Slow running streams
	An. epiroticus, An. sundaicus	Coastal	Human	Both	Indoors	Brackish and fresh water
	An. vagus, An. aconitus	Agricultural areas	Both	Outdoors	Both	Rice fields, swamps
South Asia (Bangladesh, Bhutan, India, Nepal, Sri Lanka, Pakistan)	*An. culicifacies*	Rural, rice fields	Animal	Outdoors	Mostly indoors	Early rice, drainage canals
	An. stephensi	Urban, peri-urban	Human (urban) Animal (rural)	Both	Both	Man-made (urban); ponds, canals, streams, wide range (rural)
	An. subpictus	Rural, rice fields	Animal	Both	Indoors	Wide range
Western Pacific (Papua New Guinea, Solomon Islands, Vanuatu)	*An. farauti*	Coastal	Both	Both	Outdoors	Brackish and fresh water; permanent and temporary water pools
	An. koliensis	Lowlands and river valley flood plains	Both (but human preference)	Both	Outdoors	Wheel tracks, drains, natural ground pools
	An. punctulatus	Lowland regions, foothills	Both (but human preference)	Both	Outdoors	Rock pools, pools in rivers and streams

FIGURE 7. ESTIMATED SPATIAL DISTRIBUTION OF *AN. DIRUS* S.L. (A), *AN. PUNCTULATUS* (B), *AN. FLAVIROSTRIS* (C), *AN. SUBPICTUS* (D).[20]



Insecticide resistance

There is limited physiological insecticide resistance data reported for many Asia Pacific countries, especially for the major vectors in the GMS.[21] Despite this, trend analyses indicate that the frequency of pyrethroid resistance in *Anopheles* increased globally between 2010 and 2016. Similar trends are not yet observed for the other three classes of insecticide, although resistance to organophosphates and carbamates is more common in SEARO and WPRO. In 2017, 47 of 89 endemic countries reported data into the WHO Malaria Threats Map, and Figure 8 below is a snapshot of the Malaria Threats Map for the Asia Pacific region as of February 2019. Note that the lack of insecticide resistance data may be due not to the lack of regional tests being conducted for specific species but a failure to report results from resistance tests.

[20] Malaria Atlas Project https://map.ox.ac.uk/explorer/#/explorer.

[21] WHO. Global report on insecticide resistance in malaria vectors: 2010-2016. Global Malaria Programme. 2018.

FIGURE 8. ESTIMATES OF INSECTICIDE RESISTANCE AMONG *ANOPHELES* POPULATIONS IN THE ASIA PACIFIC TO THE FOUR INSECTICIDE CLASSES[22]

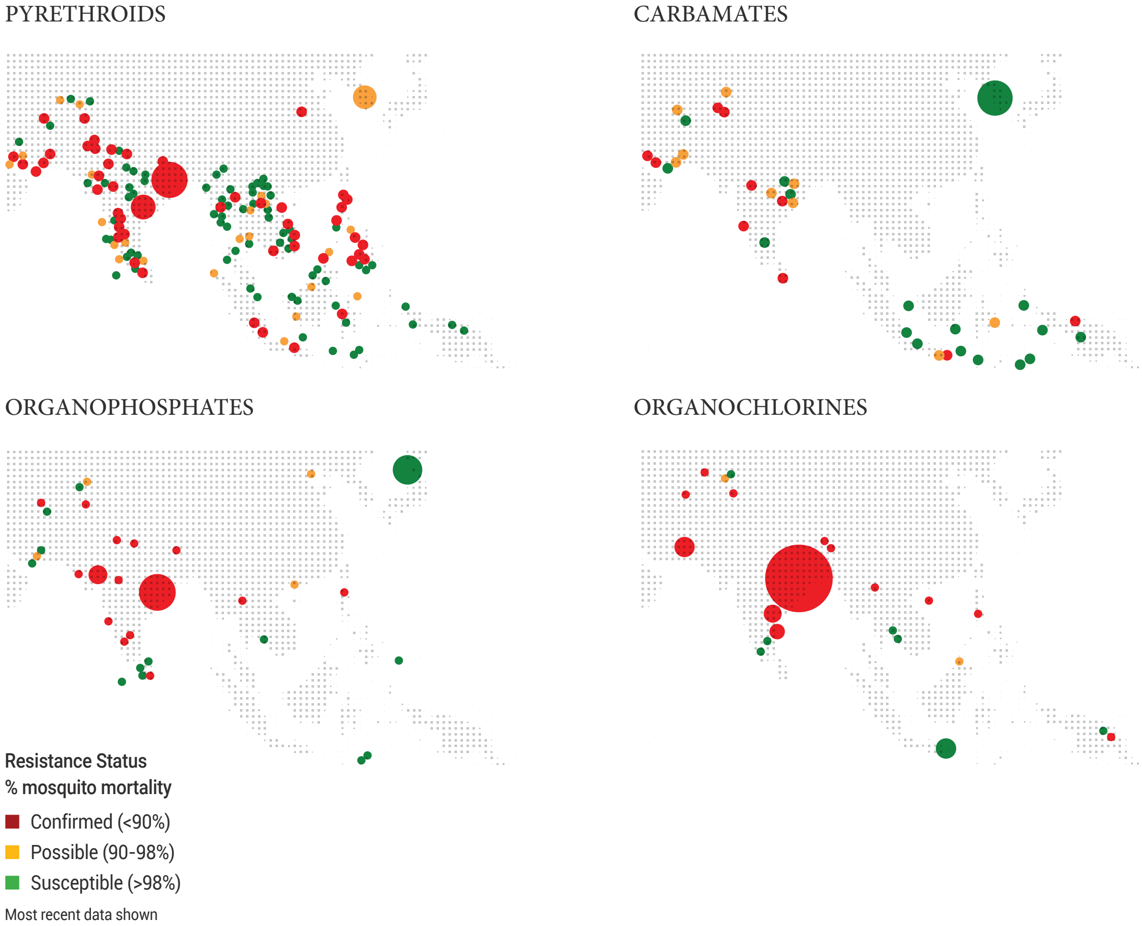


Table 2 below summarizes the physiological resistance data reported to the WHO between 2010 and 2016 across the Asia Pacific region by country, insecticide class, resistance mechanism, and vector species. Only a handful of countries monitored all four classes, and of those, China, India, Pakistan, and Myanmar reported resistance to at least three insecticides.

It is important to note that the resistance shown for the GMS is largely for secondary vectors like An. barbaristrosis, An. annularis and An. epioriticus, not *An. dirus* s.l. (except for an isolated report from Lao PDR[23] and An. balabacensis in Malaysia) and only rarely for *An. minimus* and *An. dirus* (northern Vietnam, southern China). While physiological insecticide resistance is a major challenge in South Asia, it does not appear to be significant concern at present for malaria elimination in the rest of the region, although resistance may be emerging and close monitoring is critical.

[22] WHO Malaria Threats Map. Accessed February 2019. http://apps.who.int/malaria/maps/threats/

[23] Marcombe S, Bobichon J, Somphong B, et al. Insecticide resistance status of malaria vectors in Lao PDR. *PLoS One*. 2017;12(4):e0175984. Published 2017 Apr 24. doi:10.1371/journal.pone.0175984

TABLE 2. PHYSIOLOGICAL RESISTANCE STATUS TO FOUR INSECTICIDE CLASSES AND RESISTANCE MECHANISMS TESTED OR DETECTED (OR BOTH) FOR ADULT MALARIA VECTORS, FOR 2010-2016.[24]

Country*	Resistance status				Resistance mechanisms							Species exhibiting resistance
					Metabolic			Target site				
	Pyrethroids	Organochlorines	Carbamates	Organophosphates	Monooxygenases	Esterases	GSTs	kdr L1014	kdr L1014S	kdr (unspecified)	Ace-1R	
Bangladesh	R	-	-	-	-	-	-	-	-	-	-	An. philippinensis, An. vagus
Bhutan	S	-	-	-	-	-	-	-	-	-	-	
Cambodia	R	R	-	-	-	-	-	-	-	-	-	An. barbirostris, An. maculatus s.l., An. vagus
China	R	R	R	R	-	-	-	D	-	-	D	An. minimus s.l., An. sinensis s.l., An. vagus
DPRK	S	S	S	S	-	-	-	-	-	-	-	
India	R	R	R	R	D	D	-	D	D	-	-	An. culicifacies s.l., An. fluviatilis, An. stephensi
Indonesia	R	S	R	S	-	-	-	-	-	-	-	An. aconitus, An. barbirostris, An. peditaeniatus, An. vagus
Lao PDR	R	R	-	-	-	-	-	-	-	-	-	An. aconitus, An. annularis, An. hyrcanus s.l., An. minimums s.l., An. peditaeniatus, An. philippinensis, An. sinensis s.l., An. vagus
Malaysia	S	-	-	-	-	-	-	-	-	-	-	
Myanmar	R	R	-	R	-	-	-	-	-	-	-	An. aconitus, An. annularis, An. hyrcanus s.l., An. minimums s.l., An. peditaeniatus, An. philippinensis, An. sinensis s.l., An. vagus
Nepal	-	R	S	S	-	-	-	-	-	-	-	An. annularis, An. culicifaces s.l.
Pakistan	R	R	-	R	-	-	-	-	-	-	-	
Papua New Guinea	S	-	-	-	-	-	-	-	-	-	-	An. farauti
Philippines	R	S	-	S	-	-	-	-	-	-	-	
Republic of Korea	-	-	-	-	-	-	-	D	D	-	D	An. sinensis s.l.
Solomon Islands	R	R	-	S	-	-	-	-	-	-	-	An. farauti s.l.
Thailand	R	-	-	-	-	-	-	-	-	-	-	An. barbirostris
Vanuatu	S	-	-	-	-	-	-	-	-	-	-	
Vietnam	R	S	-	-	-	-	-	-	-	-	-	An. aconitus, An. annularis, An. epiroticus, An. kochi, An. maculatus s.l., An. minimus s.l., An. nivipes, An. philippinensis, An. sinensis s.l., An. vagus

[24] WHO. Global report on insecticide resistance in malaria vectors: 2010-2016. Global Malaria Programme. 2018.

Human behavior and high-risk populations for malaria

In areas of higher transmission such as eastern Indonesia, Papua New Guinea, Solomon Islands, and central-east India, nearly the entire population is at risk for malaria. These populations are often in remote villages where access to health services is more limited. To some extent in these areas and to a large extent in other areas like the GMS, transmission is highest among specific risk groups characterized to varying extents by ministries of health and partners. Broadly, this risk is often associated with occupation, including 1) forest-goers (for logging, rubber tapping, etc.), 2) construction and mine workers, 3) security personnel, 4) border crossers, and 5) seasonal workers.[25] The majority of these populations are men between the ages of 15 and 60, as evidenced by malaria case data across the region. Given that much of the work is outdoors and often during peak *Anopheles* biting, individuals have a higher risk of malaria infection. Other groups such as people displaced by conflict or disasters are also at elevated risk and often includes families.

In considering a "precision vector control" approach in the Asia Pacific, understanding human behavior and its intersection with vector behavior is critical. We therefore considered high risk populations (HRPs) and their behaviors from the perspective of mosquito-borne disease prevention and control in Table 3 below that summarizes use cases for new tools.

In this context, it is important to understand perceived risk among these HRPs. A recently published systematic review by Nofal et al. of qualitative literature on interventions for forest-goers in the GMS acknowledges that individuals' understanding of malaria and perceived risk is critical to designing intervention packages.[26] In some areas, going into the forest is perceived to increase risk of contracting malaria (e.g. in Myanmar, malaria was referred to as "forest-sickness"), but individuals take the risk because they need income. In other settings, malaria was perceived as an insignificant risk since mosquitoes in the forest were not seen as malaria vectors. Nuisance biting was often the driver of use of personal protection measures.

Rudimentary protection measures, including wearing long shirts and trousers, were used but were often impractical because of the strenuous nature of forest work, although preferences vary by setting. Burning leaves to repel mosquitoes was popular but was recognized as inadequate and potentially harmful. The strong smell and high cost of repellents were reasons that they weren't readily used. Authors concluded that current vector control tools have limitations and that human-centered approaches should be used to design appropriate vector control tools for these populations; authors also recommended further research on chemoprophylaxis as a potential alternative.

25 WHO, IOM. Population mobility and malaria. 2017.

26 Nofal SF, Peto TJ, Adhikari B, Tripura R, Callery J, Bui TM, et al. How can interventions that target forest-goers be tailored to accelerate malaria elimination in the Greater Mekong Subregion? A systematic review of the qualitative literature. Malaria Journal. 2019; 18(32).

TABLE 3. SUMMARY OF USE CASES FOR NEW TOOLS

Movement	Target human population	Risk profile	Indoor exposure to mosquito biting	Outdoor exposure to mosquito biting	Existing vector control tools (use/ uptake is variable)	Potential new tools and approaches
More static	Village-based, accessible	All ages (in higher transmission areas), adult men (lower transmission areas)	Generally higher coverage of interventions; exposure outside protection of LLINs	Cooking, studying, gathering during peak biting times; overnight fishing	LLINs, focal IRS, community-based LSM	Spatial repellents, ivermectin-treated livestock, insecticide-treated paints, conventional net retreatment and improved application of adulticides (IRS, ORS), larviciding (including area-wide application), house improvements (e.g. screening, barrier fences)
	Village-based, remote/ tribal/ conflict areas	All ages (in higher transmission areas), adult men (lower transmission areas)	Generally lower coverage of interventions	Cooking, studying, gathering; overnight fishing	LLINs	Spatial repellents, house improvements (e.g. screening, barrier fences), insecticide-treated paints, DIY IRS, DIY repellent treatment kit
	Forest/ farm-based (seasonal), semi-permanent structures*	Adult men, sometimes families	Open structures; exposure outside protection of LLINs and/or LLIHNs	Work activities at peak biting times	LLINs, LLIHNs, topical repellents (limited)	Spatial repellents (if more closed structure), DIY IRS (farm huts that are more closed), longer-lasting topical repellents, bite proof clothing/ITC, DIY repellent treatment kit, ITM (e.g. blankets, mats)
	Internally displaced populations	All ages	Generally higher coverage of interventions; exposure outside protection of LLINs and/or ITM	Cooking, studying, gathering during peak biting times	LLINs, ITM	Spatial repellents, ATSBs,[27] area-wide adulticiding and larviciding, improved ITM (e.g. shelters, blankets)
	Long-term, formal project-based (construction, mines, dams)	Adult men, sometimes families	Generally higher coverage of interventions; exposure outside protection of LLINs, screening, and other interventions	Gathering during peak biting times	LLINs, focal IRS, small-scale LSM, space spraying, improved housing	Spatial repellents, ATSBs, area-wide adulticiding and larviciding
	Security, defense force, and forest ranger camps	All ages	Generally higher coverage of interventions; exposure outside protection of LLINs and/or IRS	Cooking, studying, gathering during peak biting times	LLINs, IRS	Spatial repellents, LLIHNs, improved application of adulticiding (IRS, ORS, area-wide) and larviciding
More mobile	Frequent movement between village and forest/ farm and/ or informal/ illegal mines*	Adult men	Often sleeping/ working outdoors in forest; if indoors, LLINs are often left in villages so no protection in forest/ farm/ mines	Sleeping and/ or working outdoors	LLINs, LLIHNs	Spatial repellents (if in enclosed area), long-lasting topical repellents, bite proof clothing/ITC, ITM (shelters, mats, blankets), DIY repellent treatment kit
	Security and defense force personnel and forest rangers	Adult men	Often working overnight	Working during peak biting hours	Topical repellents, bite proof clothing, LLITH	Longer lasting topical repellents, bite proof clothing/ITC, DIY repellent treatment kit, ITM
	Border crossers	Adult men	Generally sleeping outdoors and/or in temporary shelters	Outdoors during peak biting hours	IEC	Longer lasting, low cost topical repellents through consumer market, LLIHNs

*Delivery/distribution often at the village, at nearby towns, and/or along main roads

DIY=do it yourself; IEC=information, education, communication; ITC=insecticide treated clothing; ITM=insecticide-treated materials (e.g. blankets, tarpaulins); LLIHN=long lasting insecticide treated hammocks

The focus in this analysis is vector control. Given this, other existing and important interventions and potential gaps in protection related to access to quality and effective diagnosis and treatment and other preventive interventions (e.g. chemoprophylaxis) are not included.

Accurately determining drivers of transmission, and therefore the appropriate response, requires a deeper, site-specific analysis.

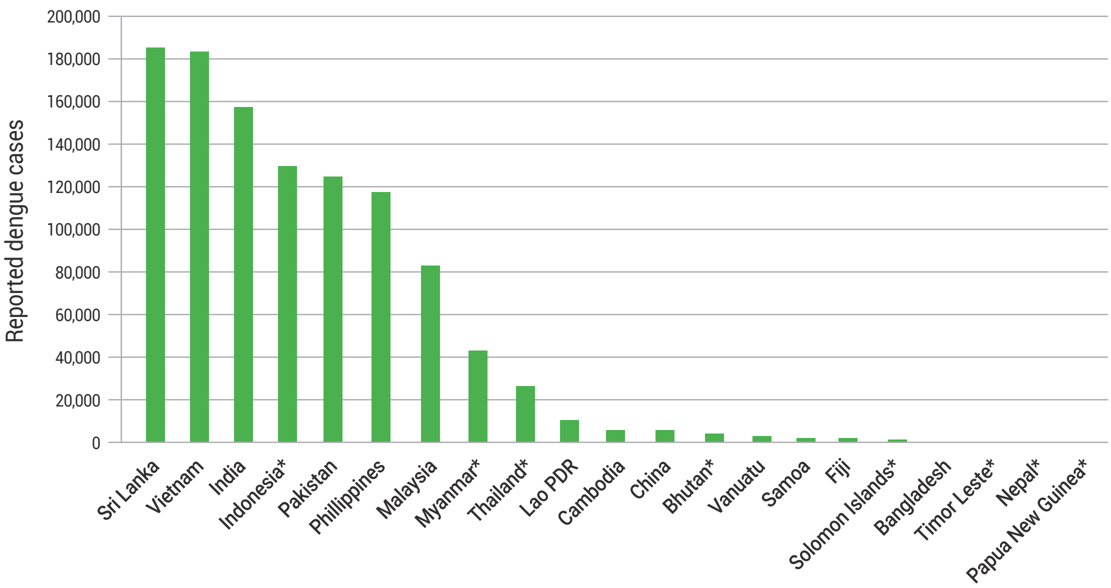
[27] ATSBs: early consensus from this landscape analysis was that most malarious areas offered too many alternative sugar sources for ATSBs to be effective against *Anopheles*. The exceptions may be displaced persons camps, some development projects (e.g. mines), or in urban areas (for *Aedes*).

Dengue, Zika, and chikungunya

Epidemiology

Over the past five decades, the global dengue incidence has increased 30-fold.[28] As many as 400M people are infected annually, with 40% of the world's population at risk in more than 100 endemic countries, with further spread to previously unaffected areas.[29] Each year, there are an estimated 20,000 deaths and 264 DALYs lost per million population.[30] In the Asia Pacific region, there is a dearth of consolidated data on dengue incidence, but based on the analysis for this report, over 1M cases were reported in 2017 or preceding years (between 2010 and 2016), although we believe this to be widely underestimated and underreported, particularly due to asymptomatic infections. A systematic analysis of the global economic burden of dengue by Shepard and colleagues (2016) compiled reported dengue episodes and projected nearly a 20-fold increase in estimated true burden in 2013, with an estimate of 22.85 million dengue cases in South Asia (39.1% of cases globally) and 23.21 million dengue cases in Southeast Asia, East Asia, and Oceania (39.7% of cases globally).[31] Of reported dengue episodes (not modeled and likely a significant underestimate), Sri Lanka, Vietnam, India, Indonesia, Pakistan, and the Philippines have recorded some of the highest numbers of dengue in the region (Figure 9). See Annex 1 for the detailed statistics and maps of dengue infection occurrence in Figures 2, 3 and 10.

FIGURE 9. REPORTED DENGUE CASES, 2017 (DATA SOURCES IN ANNEX 2). AS NOTED ABOVE, TRUE BURDEN IS ESTIMATED TO BE MUCH HIGHER.



*Data from other years (preceding 2017)

**Dengue cases in Papua New Guinea are rarely reported, but a study published by Senn et al (2011) indicates a seroprevalence of 8% among patients presenting to Madang clinics with acute febrile illness. According to Luang-Sarkia et al (2018), dengue surveillance is generally not undertaken and patients with acute febrile illness not regularly tested for dengue.

28 WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

29 CDC. Dengue. Accessed February 2019. https://www.cdc.gov/dengue/index.html

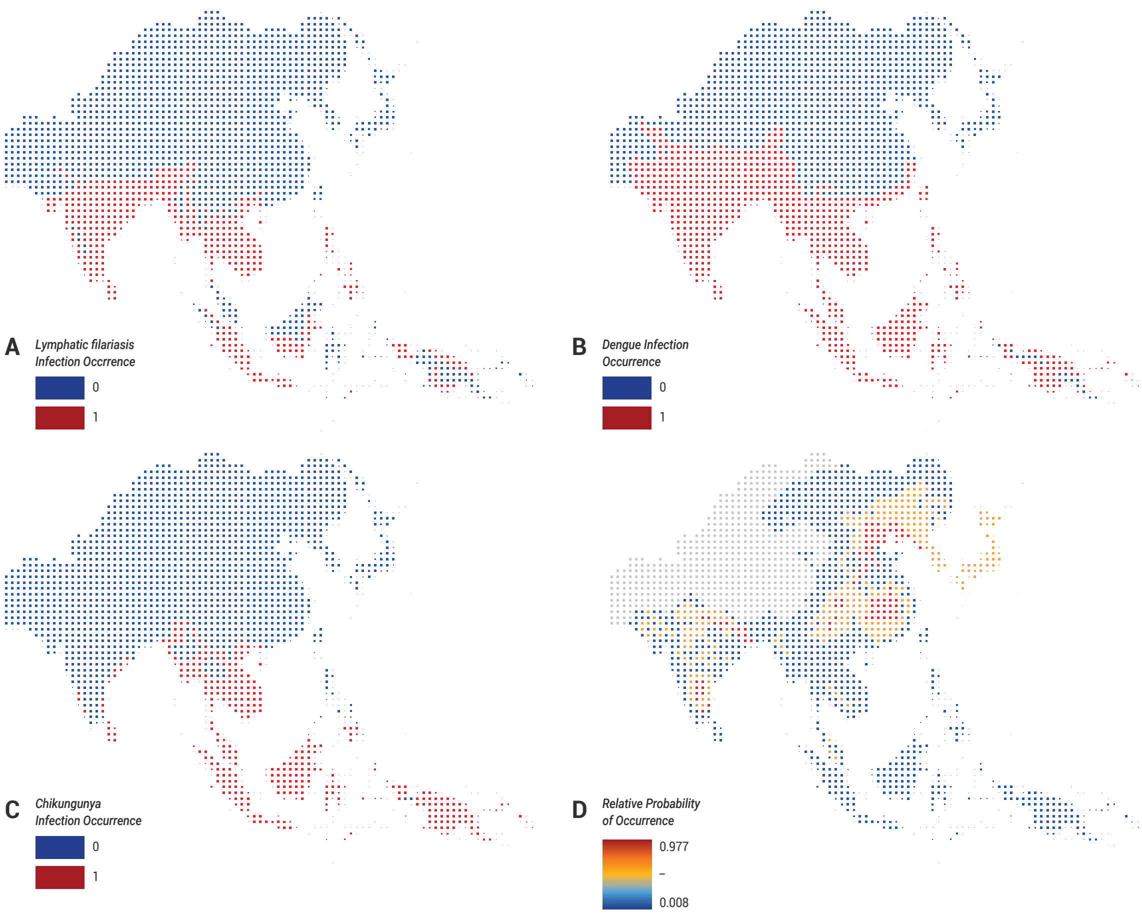
30 WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

31 Shepard DS, Undurraga EA, Halasa YA, Stanaway JD. The global economic burden of dengue: a systematic analysis. Lancet Infectious Diseases. 2016; 16:935-941. Appendix, page 15.

Chikungunya is similarly not well documented, often because the symptoms resemble dengue and co-infection with dengue is common so chikungunya goes misdiagnosed and underreported. Additionally, chikungunya epidemics exhibit fluctuating and cyclical trends; such epidemics are marked by severe outbreaks interspersed by silent periods spanning several years to a few decades.[32] According to our analysis, there were over 184,000 cases of chikungunya reported over the last several years in the Asia Pacific (Figure 10), although it is likely a significant underestimate for the reasons mentioned above. Indonesia, Sri Lanka, India, and Bangladesh have reported some of the highest numbers of chikungunya in the region (Annex 1).

As described in Annex 1, Zika epidemiology is categorized based on reports of transmission with only a handful of cases reported across the region, although Zika may also be underdiagnosed and underreported. According to the last update by the WHO in March 2018, Samoa and Solomon Islands reported new introduction or reintroduction of cases (Category 1) and 12 other countries in the region reported ongoing virus transmission (Category 2).

FIGURE 10. PREDICTED RELATIVE PROBABILITY OF OCCURRENT OF INFECTION FOR LF (A), DENGUE (B), AND CHIKUNGUNYA (C). MAP D IS THE RELATIVE PROBABILITY OF *CULEX TRITAENIORHYNCHUS* OCCURRENCE WITHIN THE JE ENDEMIC ZONE, USED AS A PROXY FOR JE RISK.[33]



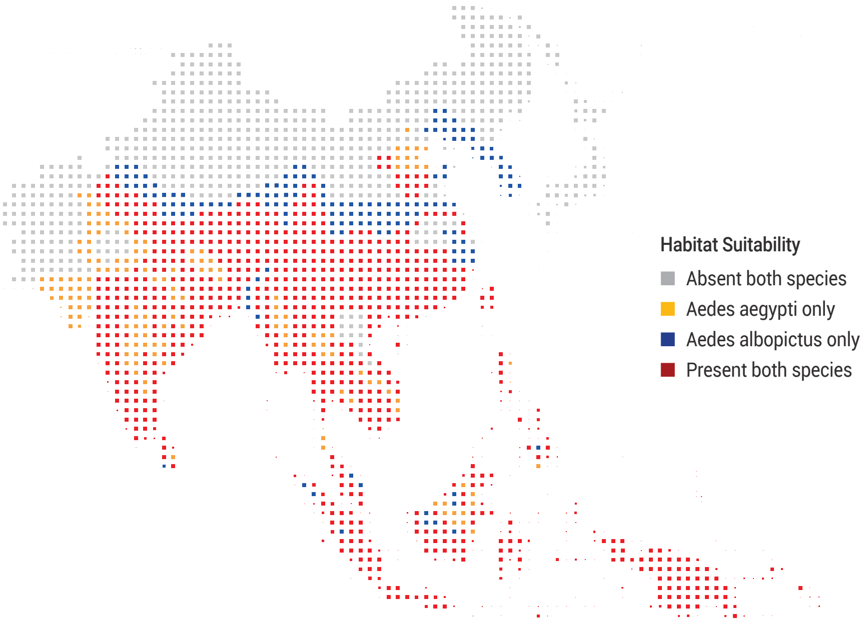
32 WHO. Guidelines for Prevention & Control of Chikungunya Fever. 20093

33 The binary map of LF infection occurrence was derived from Cano J, Rebollo MP, Golding N, et al. The global distribution and transmission limits of lymphatic filariasis: past and present. 2014; 7:466; https://doi.org/10.1186/s13071-014-0466-x as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of dengue infection occurrence was derived from Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature. 2013; 496:504-507; https://doi.org/10.1038/nature12060 as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of chikungunya infection occurrence was derived from Nsoesie EO, Kraemer MUG, Golding N, et al. Global distribution and environmental suitability for chikungunya virus, 1952 to 2015. Eurosurveillance. 21(20); https://doi.org/10.2807/1560-7917.ES.2016.21.20.30234 as detailed in Weetman D, Kamang B, Badolo A, et al. *Aedes* mosuqitoes and *Aedes*-borne arboviruses in Africa: current and future threats. International Journal of Environmental Research and Public Health. 2018; 15(2): 220; https://doi.org/10.3390/ijerph15020220. The relative probability of *Cx tritaeniorhynchus* occurrence within the JE endemic zone is detailed in Longbottom J, Browne AJ, Pigott DM, et el. Mapping the spatial distribution of the Japanese encephalitis vector, *Culex tritaeniorhynchus* Giles, 1901 (Diptera: Culicidae) within areas of Japanese encephalitis risk. Parasite & Vectors. 2017; 10:148; https://doi.org/10.1186/s13071-017-2086-8.

Vector ecology

Aedes aegypti is the primary vector of dengue and has evolved to mate, feed, rest and lay eggs in and around human habitation.[34] Although Ae. aegypti is commonly reported as a daytime biter with peaks early morning and before dusk, feeding continues throughout the night in Papua New Guinea and the Solomon Islands (C Butafa, unpublished data). *Ae. albopictus* is usually a secondary vector of dengue but can be very competent for chikungunya. Concerningly, *Ae. albopictus* is increasing in relative proportion as the spatial distribution spreads north and south (Figure 11). There are other *Aedes* species that have been incriminated as dengue vectors, although they are geographically limited. Habitat suitability estimates for Ae. aegypti and *Ae. albopictus* are provided in Figure 11.

FIGURE 11. HABITAT SUITABILITY ESTIMATES FOR AE. AEGYPTI, AE, *ALBOPICTUS*, AND BOTH COMBINED.[35] (WHILE DIFFICULT TO SEE IN THE MAP, IT SHOULD BE NOTED THAT AE. AEGYPTI AND *AE. ALBOPICTUS* ARE COMMON MOSQUITOES THROUGHOUT THE SOLOMON ISLANDS.)



Kraemer et al. (2019) recently released an analysis on the future spatial distribution of Ae. aegypti and *Ae. albopictus*, which concludes that spread is occurring in combination with human movement, including urbanization, and the presence of suitable climate.[36] Authors note that, even under current climate conditions and population density, both vector species will continue to spread globally, posing a significant risk to human health and global health security.

Insecticide resistance

Globally, insecticide resistance to all four classes of insecticides, including temephos, has been on the rise in Ae. aegypti while the levels of resistance in *Ae. albopictus* is relatively low, although resistance is expected to increase.[37] Figure 12 describes point data for pyrethroid resistance detected in Ae. aegypti populations across the Asia Pacific region in 2017. Not shown on the map due to lack of data published or reported to the WIN Network is high levels of pyrethroid resistance in *Aedes* in Papua New Guinea (S Karl, personal communication) and reported high levels of pyrethroid and temephos resistance among several *Aedes* populations throughout Cambodia.[38]

---

[34] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

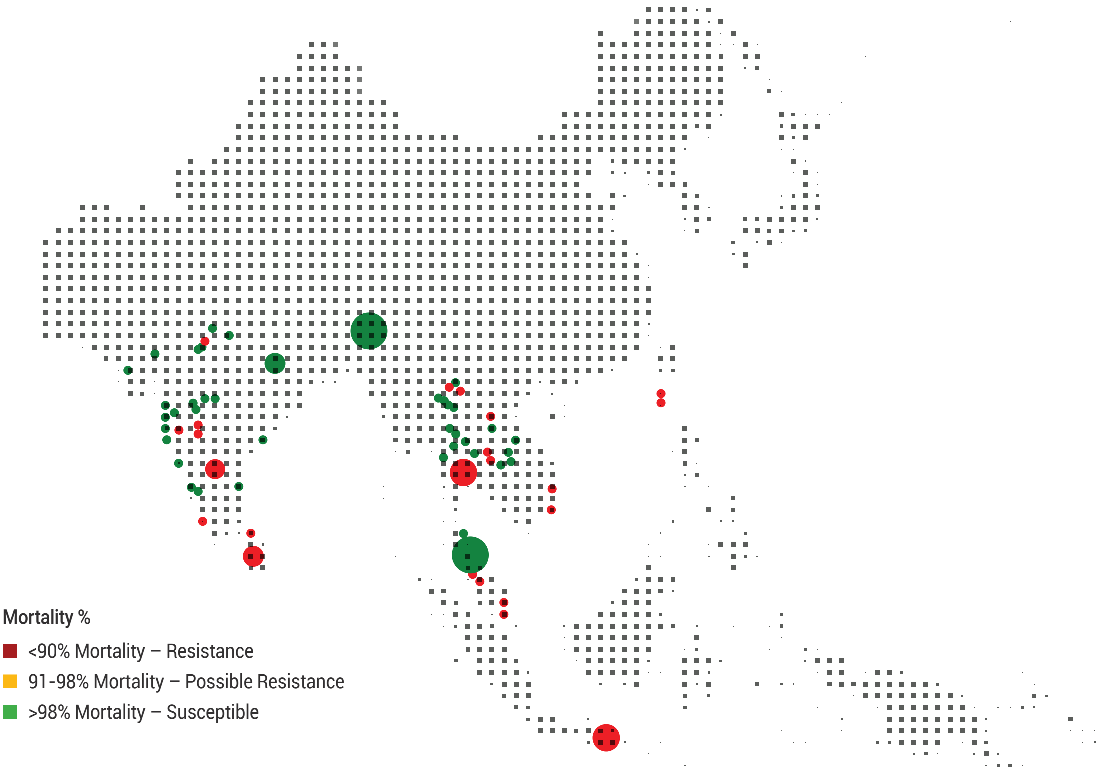
[35] Kraemer MUG, Sinka ME, Duda KA, et al. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. eLIFE. 2015; 4:e08347; https://doi.org/10/7554/eLife.08347.

[36] Kraemer MUG, Reiner Jr RC, Brady OJ, Messina JP, Gilbert M, Pigott DM, et al. Past and future spread of the arbovirus vectors *Aedes aegypti* and *Aedes albopictus*. Nature Microbiology. 2019.

[37] Vontas J, Kioulos E, Pavlidi N, Morou E, della Torre A, Ranson H. Insecticide resistance in the major dengue vectors *Aedes albopictus* and *Aedes aegypti*. Pesticide Biochemistry and Physiology. 2012; 104(2):126-131.

[38] Boyer S, et al Resistance of *Aedes aegypti* (Diptera: Culicidae) Populations to Deltamethrin, Permethrin, and Temephos in Cambodia. Asia Pac J Public Health. 2018 Mar;30(2):158-166. doi: 10.1177/1010539517753876. Epub 2018 Mar 4.

FIGURE 12. GEOGRAPHIC DISTRIBUTION OF PYRETHROID RESISTANCE IN *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* IN THE ASIA PACIFIC.[39] DATA INCLUDES ALL STANDARD TESTS, DOSAGES, AND MOSQUITO LIFE STAGES (BOTH LARVAE AND ADULTS).



Other mosquito-borne diseases

Lymphatic filariasis

An estimated 120 million people in 81 countries are infected currently with lymphatic filariasis (LF), caused by parasitic worms transmitted by mosquito vectors, and 1.34 billion people live in areas where filariasis is endemic and are at risk of infection.[40] Of all filariasis infections, 90% are caused by Wuchereria bancrofti and the remaining caused by Brugia malayi and B. timori worms.

In 2000, the WHO established the Global Programme to Eliminate Lymphatic Filariasis, which has a stated goal of eliminating LF as a public health problem by 2020. The strategy includes 1) interrupting transmission using combinations of albendazole and diethylcarbamazine (DEC) delivered through mass drug administration (MDA) and 2) alleviate suffering and disability by introducing basic measures, such as improved hygiene and skin care to people living with disabling clinical manifestations of the disease.

Approximately 55.7% of the 1.34 billion people at risk globally are in the Asia Pacific where LF is caused by W. bancrofti and B. malayi. The genera of vectors responsible for transmission vary by geographic area with *Culex quinquefasciatus* and *Anopheles* dominating in Asia and Papua New Guinea, respectively, with some contributions from Mansonia and *Aedes* vectors and B. timori transmitted by Cx. quinquefasciatus.[41,42] According to this analysis, LF is still endemic in Bangladesh, India, Indonesia, Lao PDR, Malaysia, Myanmar, Papua New Guinea, Philippines, and Timor Leste (Figure 10). A number of countries have eliminated LF in the region.

---

[39] Moyes CL, Vontas J, Martins AJ, et al. Contemporary status of insecticide resistance in the major *Aedes* vectors of arboviruses infecting humans. PLoS NTD. 2017. https://doi.org/10.1371/journal.pntd.0005625.

[40] WHO. Lymphatic filariasis progress report 2000-2009 and strategic plan 2010-2020. WHO Global Programme to Eliminate Lymphatic Filariasis. 2010.

[41] Sudomo M, Chayabejara S, Duong S, Hernandex L, Wu WP, Bergguist R. Elimination of lymphatic filariasis in Southeast Asia. Adv Parasitol. 2019;72:205-33.

[42] Dickson BFR, Graves PM, McBride WJ. Lymphatic filariasis in mainland Southeast Asia: a systematic review and meta-analysis of prevalence and disease burden. Trop med and Infect Dis. 2017; 2(32).

Japanese encephalitis

Japanese encephalitis (JE) is the leading cause of vaccine-preventable encephalitis in the Asia Pacific region [43] and causes an estimated 68,000 clinical cases in the region each year with a case-fatality rate as high as 30%, although less than 1% of people infected with JE develop clinical illness.[44] JE is a flavivirus, related to West Nile and St. Louis encephalitis viruses, and is transmitted by Cx. tritaeniorhynchus to humans through a transmission cycle between mosquitoes and non-human hosts, including pigs and birds. Humans do not usually develop sufficient viremia to infect mosquitoes. JE transmission occurs primarily in rural agricultural areas associated with rice production and flooding irrigation. Because these settings are the primary larval habitats for Cx. tritaeniorhynchus, the spatial distribution of the vector is used as a proxy for JE risk across the region (Figure 10, D).

The WHO reports 24 countries in the WHO SEARO and WPRO regions have endemic JE virus, with more than 3 billion at risk of infection (Figure 10, D). According to this analysis, there were an estimated 4,652 cases of JE reported in the Asia Pacific region with the highest reports from India, China, Myanmar, Philippines, Indonesia and Vietnam (Annex 2).

Recommended prevention tools include repellents, insecticide treated clothing, and a vaccine. The WHO recommends that JE vaccination be integrated into national immunization schedules in all areas where JE disease is recognized as a public health issue.[45]

Summary of vector control evidence, opportunities, and recommendations

WHO recommendations, evidence on the *Anopheles* and *Aedes* control toolboxes, a summary of interventions in use across the Asia Pacific region, and recommendations from this landscape analysis are summarized below.

WHO recommendations for control for *Anopheles* and *Aedes* vectors

For *Anopheles* control, the WHO recommends ITNs and IRS as the core vector control methods, as detailed in the new Guidelines for Malaria Vector Control released in February 2019.[46] In specific settings and circumstances, the core interventions can be supplemented by other measures including larval source management and scale-up of personal protection measures.

For *Aedes* control, the WHO recommends larval source management through chemical control, biological control, and/or environmental management and recommends additional interventions for individual and household protection; including bite-proof clothing; repellents; ITNs for people sleeping during the day; indoor coils, aerosols, and vaporizers; and household fixtures including window and door screening and air-conditioning. The effectiveness of IRS for *Aedes* control is not well documented according to WHO.[47] It should be noted that increasing reports of night-time biting *Aedes* makes use of ITNs and IRS more relevant.

---

[43] CDC. Japanese encephalitis. Accessed February 2019. https://www.cdc.gov/japaneseencephalitis/transmission/index.html

[44] WHO. Japanese encephalitis. 2015. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis

[45] WHO. Japanese encephalitis. 2015. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis

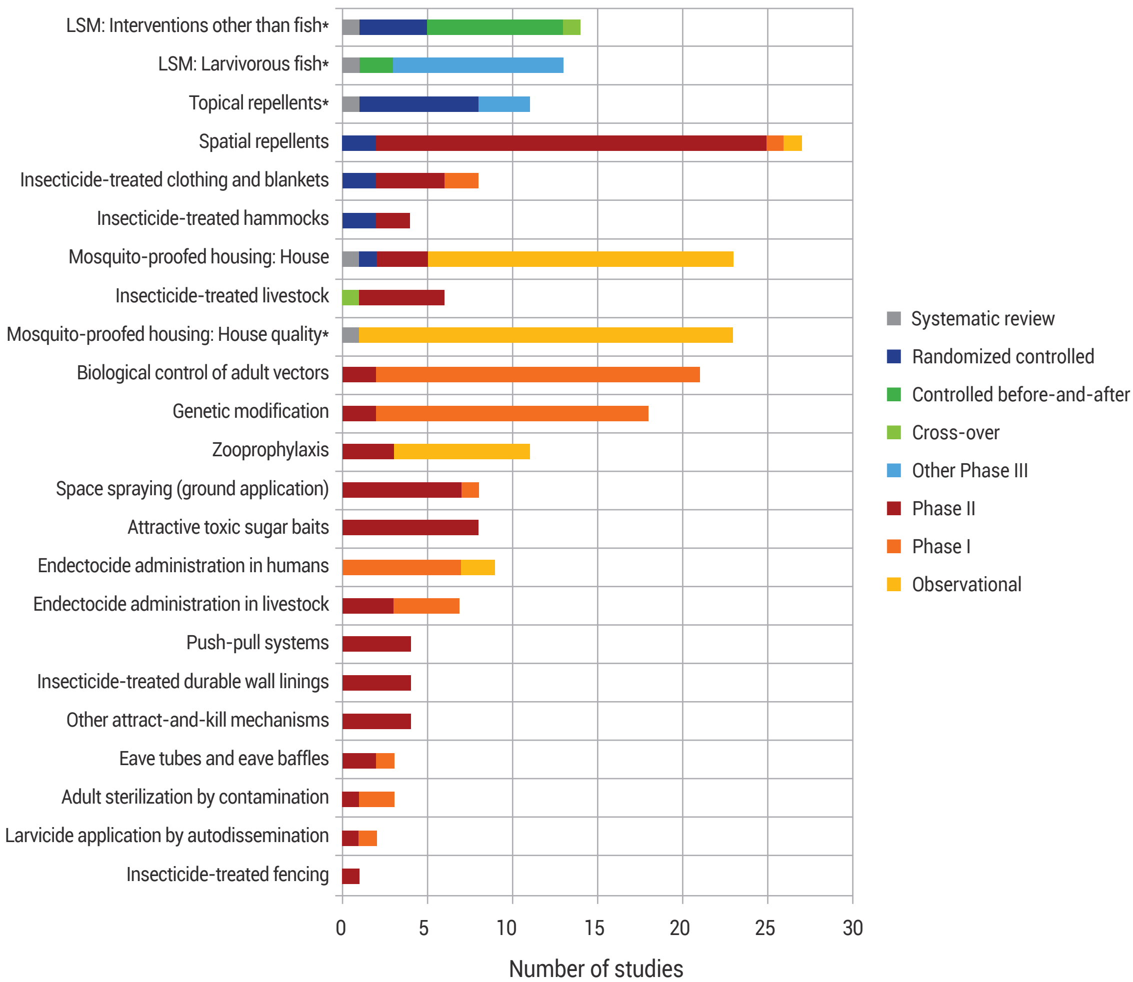
[46] WHO. Guidelines for Malaria Vector Control. Global Malaria Programme. 2019.

[47] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

Evidence synthesis of the malaria vector control toolbox

In 2015, the UCSF Malaria Elimination Initiative conducted a systematic review of the availability and quality of evidence for 21 malaria vector control tools, excluding ITNs and IRS, describing an expanding pipeline of research on supplementary tools while identifying important gaps in the evidence base.[48] Of 17,912 studies screened, 155 were eligible for inclusion in the review. Of 21 vector control tools, only seven had at least one Phase III community-level evaluation (Figure 13).[49] Phase III trials were conducted on LSM, mosquito proofed housing, topical repellents, spatial repellents, insecticide-treated clothing and blankets, insecticide treated hammocks, and insecticide-treated livestock, all with varying impact on malaria transmission.[50] Systematic reviews of LSM and mosquito-proofed housing concluded that both interventions can offer population level protection from malaria while the systematic review and meta-analysis on topical repellents concluded that topical repellents are unlikely to provide effective population level protection against malaria. Two insecticide-treated hammock Phase III trials in Venezuela and Vietnam and one trial of insecticide-treated livestock in Pakistan reduced malaria incidence and prevalence, while two Phase III trials of insecticide-treated blankets and clothing had variable results. Spatial repellent Phase III trials included one in Indonesia using metofluthrin coils and another in China using transfluthrin coils, both demonstrating reductions in malaria prevalence. The remaining 14 tools were supported by at least one Phase II or Phase I evaluation. A meta-analysis was not possible due to the heterogeneity of the studies.

FIGURE 13. FREQUENCY OF ELIGIBLE STUDIES FOR 21 VECTOR CONTROL TOOLS, STRATIFIED BY STUDY DESIGN (FROM WILLIAMS AND TUSTING, 2018). *STUDIES WITHIN THE SYSTEMATIC REVIEWS ARE DESCRIBED HERE.



[48] Williams YA, Tusting L, Hocini S, Graves PM, Killeen GF, Kleinschmidt, et al. Expanding the vector control toolbox for malaria elimination: a systematic review of the evidence. Adv in Parasit. 2018; 99:345-379.

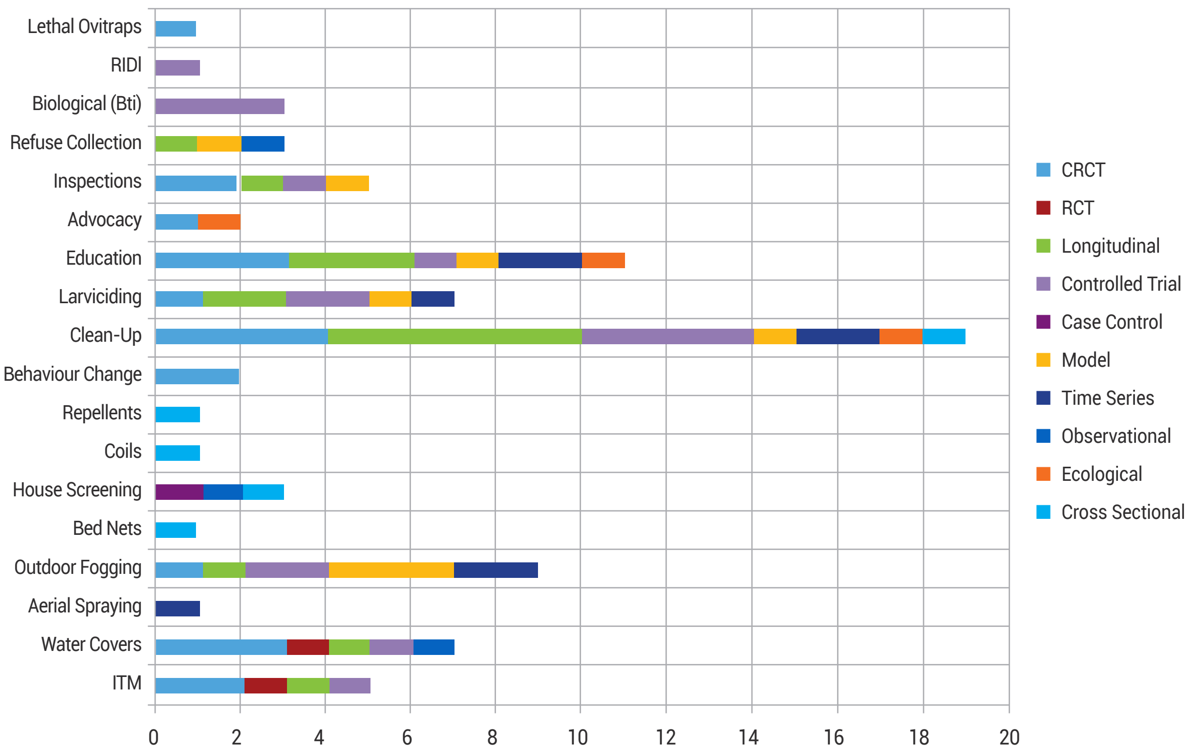
[49] The level of evidence required for WHO policy recommendation is evidence of efficacy on malaria cases from two or more Phase III randomized control trials.

[50] Note: several tools listed are not currently recommended for public health use but are endorsed by WHO for personal protection (e.g. topical repellents and insecticide treated clothing).

Evidence synthesis of the *Aedes*-borne disease vector control toolbox

Bowman and colleagues from the University of Liverpool and Liverpool School of Tropical Medicine conducted a systematic review and meta-analysis of dengue vector control.[51] A total of 960 potentially relevant studies were identified, 41 studies were included in the final review, and 19 were included in the meta-analysis. Figure 14 illustrates the tools and approaches under review, stratified by study design. There were five Phase III studies, although none of them were randomized controlled trials. House screening was shown to significantly reduce the odds of dengue incidence, as did the combination of community-based environmental management with the use of water container covers. Indoor residual spraying reduced the odds of infection, but the results were not significant. The analysis found that there was no evidence that mosquito repellents, bed nets, or mosquito traps reduced the odds of dengue infection. The use of knockdown sprays and mosquito coils were both significantly associated with an increased odds of dengue infection (implying increased use was a response to *Aedes* nuisance and dengue, not a cause of increased infection).

FIGURE 14. FREQUENCY OF ELIGIBLE STUDIES FOR *AEDES*-BORNE DISEASE VECTOR CONTROL TOOLS, STRATIFIED BY STUDY DESIGN (FROM BOWMAN, 2016)



CRCT=cluster randomized controlled trial, RCT=randomized controlled trial. Ecological studies are studies in which the unit of observation is the population or community. Disease rates and exposures are measured in each of a series of populations and their relation is examined.[52]

[51] Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence?: Systematic review and meta-analysis. PLoS Negl Trop Dis. 2016; 10(3).

[52] The BMJ. Chapter 6: Ecological studies. (n.d.). Retrieved from https://www.bmj.com/about-bmj/resources-readers/publications/epidemiology-uninitiated/6-ecological-studies

Achee and colleagues reviewed alternative strategies for mosquito-borne arbovirus control, including traps, attractive toxic sugar baits (ATSB), insecticide-treated materials, classical sterile insect technique (SIT), release of insects with dominant lethality (RIDL), *Wolbachia*, and gene drives.[53]

Another systematic review and meta-analysis of cluster randomized controlled trials (CRCTs) for *Aedes aegypti* control was conducted by Alvarado-Castro and colleagues.[54] Eighteen studies met the inclusion criteria, and ten papers were included in the meta-analysis based on entomological indices. Community mobilization (n=4 studies) was consistently effective based on entomological outcomes, one CRCT of biological control (copepods and *Bti*) showed a small impact, and the five studies of chemical control did not show a significant impact based on entomological outcomes. One CRCT of community mobilization measured the impact on dengue infection in Nicaragua and Mexico and found a significant impact on childhood dengue infection.[55]

Country reports summary

Table 4 includes a summary of interventions and tools used in the Asia Pacific region, as well as tools under evaluation by country. For malaria, nearly all programs rely on universal distribution of LLINs. Hammock culture is variable but some countries have started to scale up long-lasting insecticide treated hammocks with donor funding. IRS is in many national strategies, often for focal or outbreak response but is implemented at small scale, if implemented at all. Outdoor residual spraying (ORS) is increasingly being evaluated for both *Anopheles* and *Aedes* control but is not implemented at large scale by any program. Space spray, both indoors and outdoors, is commonly part of national dengue strategies, most often for outbreak response, but implementation is variable. LSM is widespread and often decentralized to districts and communities; larviciding is the main LSM intervention with some small-scale use of larvivorous fish and environmental management. The most common use of bite prevention tools for public health is through "forest packs" being delivered and evaluated by national malaria programs and partners in the GMS, which include a combination of topical repellents, hammocks, LLINs, and/or long sleeve clothing. There is other ongoing research, as described below.

---

53 Achee NL, Grieco JP, Vatandoost H, Seixas G, Pinto J, Ching-NG L, et al. Alternative strategies for mosquito-borne arbovirus control. PLoS Negl Trop Dis. 2019;13(1).

54 Alvarado-Castro V, Solis-Paredes S, Nava-Aguilera E, Morales-Perez A, Alarcon-Morales L, Balderas-Vargas NA, et al. Assessing the effects of interventions for *Aedes aegypti* control: systematic review and meta-analysis of cluster randomized controlled trials. BMC Public Health. 2017;17(sup 1):384.

55 Andersson N, Nava-Aguilera E, Arostegul J, Morales-Perez A, Suaso-Laguna H, Legorreta-Soberanis J, et al. Evidence based community mobilization for dengue prevention in Nicaragua and Mexico (Camino Verde, the Green Way): cluster randomized controlled trial. BMJ. 2015;351:h3267.

TABLE 4. SUMMARY OF INTERVENTIONS USED ACROSS THE ASIA PACIFIC REGION BY MARKET AND DISEASE, ALSO NOTING INTERVENTIONS UNDER EVALUATION BY COUNTRY (NOT EXHAUSTIVE)

Tool	Public health		Community		Consumer	Military / forest rangers	Econ. dev zones	PCOs	Under evaluation	
	Malaria	Other VBD	Malaria	Other VBD	Non-specific	Non-specific	Non-specific	Nuisance	Malaria	Other VBD
LLIN	■						■		IDN	
Untreated nets					■	■				
ITH/LLITH	■								VNM	
Untreated hammocks					■	■				
Targeted IRS and / or IRS for foci and / or outbreak response	■	■				■				
Forest packs*	■								MMR, KHM, VNM	
Targeted larviciding and/or for outbreak response	■	■	■	■			■	■		
Small scale environmental management	■	■	■	■			■			
Targeted ORS	■	■							IDN, MMR	MYS
Small scale use of larvivorous fish	■	■		■				■		
Topical repellents (not including forest packs)		■			■	■	■		VNM	
ITC/bite-proof clothing (not included in forest packs)						■			MMR	
Space spray		■					■	■		
Community education and clean-up programs		■	■	■						
Coils					■					
Aerosols					■					
Candles					■				VNM, KHM	
Untreated house screens					■					
Controlled fires for smoke (as repellent)					■					
Waste management					■					
Lethal ovitraps					■					
Spatial repellents					■				IDN	LKA
Ivermectin in humans					■				THA, SLB	
Ivermectin in livestock					■				VNM	
Insecticide treated fencing/tarpaulins					■				IDN, VNM, KHM	
Wolbachia					■					IDN, MYS, LKA, MMR
Autodissemination traps					■					MYS
ULV adulticide and larvicide					■					MYS
Sterile insect technique					■					MYS, LKA
Insecticide treated paint					■					MYS

IDN=Indonesia, KHM=Cambodia, LKA=Sri Lanka, MYS=Malaysia, MMR=Myanmar, SLB=Solomon Islands, THA=Thailand, VNM=Vietnam
*Forest packs include topical repellents and/or LLINs and/or long sleeve shirts and/or LLIHNs

Challenges for vector control in the Asia Pacific

Below is a summary of key challenges collated from the key informant interviews.

Malaria elimination

- Outdoor malaria transmission is the primary concern for most countries, including difficulty in accessing and providing appropriate, user-friendly malaria prevention tools for high risk populations, both in village settings with early/outdoor biting as well as among mobile and migrant populations, a highly heterogenous at risk population across the Asia Pacific.
- There is limited attention to consumer preference for LLINs and LLIHNs, causing limited uptake in some areas and preference for conventional nets and hammocks. There is generally weak follow-up after distribution and weak quality control of large procurements.
- *P. knowlesi* transmission is increasing in some countries, raising new concerns about controlling this zoonotic malaria that parallels transmission of *P. falciparum* and *P. vivax* in the GMS.
- IRS is included in many national strategic plans, especially for foci and outbreak response, but its implementation is very limited with the exception of a few countries such as India where IRS is the primary vector control intervention.
- There is a lack of evidence on and resources for integrated vector control strategies, which is what will be required for elimination in the region.
- Global normative guidance is seen to hinder the ability of national malaria programs in the Asia Pacific to incorporate supplemental vector control tools into national malaria strategy based on local transmission dynamics.

***Aedes*-borne disease control**

- *Aedes* control (where present) is stalling in the wake of increasing dengue and other *Aedes*-borne disease transmission, including spread to more rural areas. There is a lack of suitable tools with heavy reliance on decades-old *stegomyia* indices and temephos-based strategies. Poor municipal waste management systems lead to larval habitat proliferation.
- There are large gaps in *Aedes* insecticide resistance monitoring and mapping, although pyrethroid resistance appears to be extensive in many countries.
- The *Aedes* control market is very different from the *Anopheles* control market, including some countries with large semi-regulated PCO sectors.

Surveillance, information management and targeting

- *Aedes* and *Anopheles* surveillance systems are antiquated in many countries, and data is often not being used for decision-making. This is often due to a lack of resources and capacity.
- Rapidly changing environments and transmission ecology in many countries is affecting both *Anopheles* and *Aedes* distribution and behavior. This combined with a lack of efficient vector surveillance results in suboptimal targeting and risk-area stratification.
- There is insufficient use of rapidly evolving information technology, including integrated electronic databases, mobile technology, GIS, remote sensing and 'big data' to monitor, target, and develop interventions. The lack of central databases for central decision-making may also contribute to less evidence-based decision-making. Conversely, the reliance and expectation of partners and donors on large databases and advanced decision-making tools may not match national or local capacity.

Operational

- Vector-borne disease control programs and strategies are often disparate or siloed, also with large gaps between control programs and national research institutions working in parallel with limited true collaboration in some settings.
- Some decision-makers require training in vector biology and transmission ecology to better adapt strategies to heterogenous and complex contexts.
- Vector control is often multi-sectoral involving agriculture, public works, and other ministries and also decentralized to district and/or community level, making accountability and measuring of impact difficult.
- There are inadequate resistance management plans, a lack of insecticide resistance data, and lack of registered alternate products for resistance prevention or management.
- Sub-optimal, low-cost products are available on retail and professional pest control markets in many places, disincentivizing companies to introduce higher quality yet higher cost products.
- Sluggish and challenging regulatory and policy processes exist with a reliance from key procurers on policy recommendations. The WHO is in the process of establishing new regulatory and policy processes that aims to address these challenges.
- There are significant challenges with national pesticide product registration, including
    - Reliance on WHO regulatory and policy guidelines/recommendations in some countries;
    - Very slow registration of new products;
    - Insecticides not considered medical in nature so there is a need to re-categorize for health; and
    - Low volumes and/or unstable markets.

Vector control recommendations from this landscape analysis

Broadly, IVCC can capitalize on its IVM portfolio to develop a vector control toolbox for the Asia Pacific region with a focus on malaria elimination, *Aedes*-borne disease control, and regional health security. Outdoor transmission is considered the most pressing challenge by stakeholders and experts. It's important to note that, while the epidemiology of malaria in the Asia Pacific is different from that in Africa, outdoor transmission – long understood as a challenge in the Asia Pacific – is increasing in relative importance in sub-Saharan Africa so this report and consideration of IVCC's program of work in this space should consider the potential demand in Africa.[56,57] Similarly, there may be synergies between tool development for vector control in humanitarian emergencies, i.e. for displaced families in situations where traditional LLINs and IRS are not practical and where tools are needed for outdoor transmission.[58]

As shown in Figure 15, we describe tools by those that function outdoors versus indoors and by those that require area wide (i.e. community) application versus individual use for bite prevention. There is a growing toolbox for mosquito control, but each tool has both limitations and opportunities for development and optimization by IVCC and other partners, as noted in Figure 15. Given the small size in this document, this figure is also attached as Annex 2 to this report.

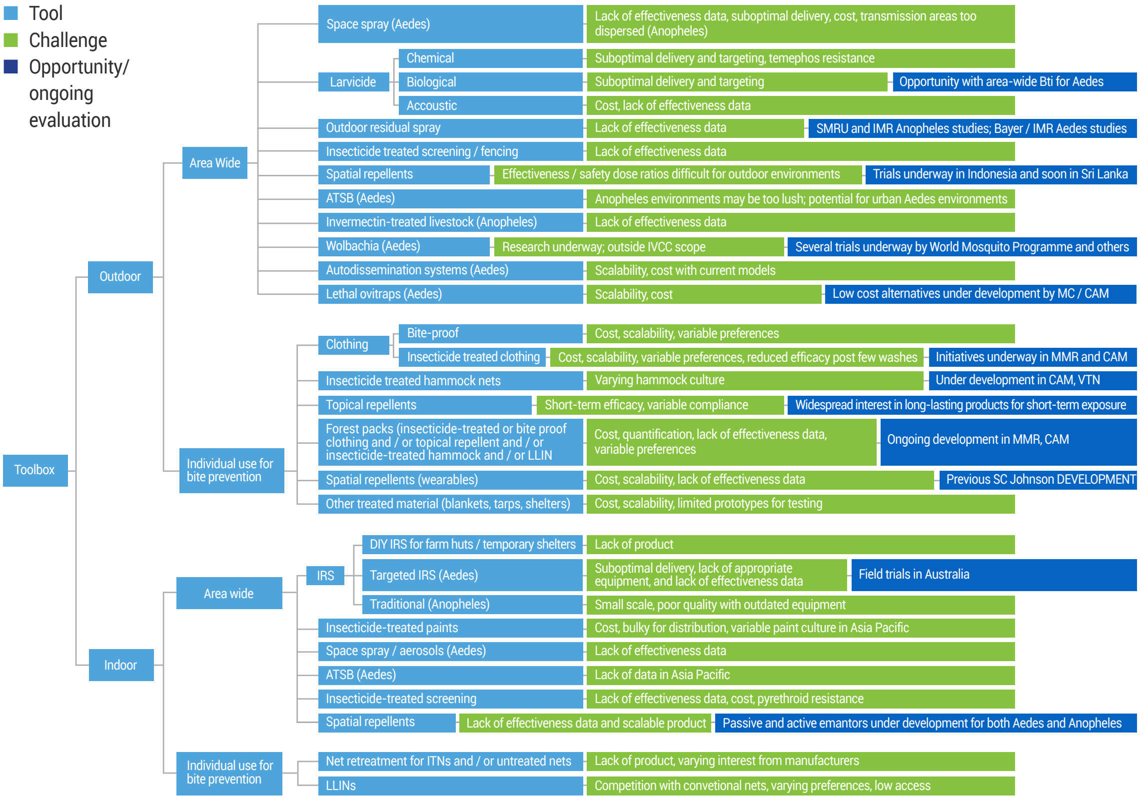
---

[56] Durnez L, Coosemans M. Residual transmission of malaria: an old issue for new approaches. Chapter 21, *Anopheles* mosquitoes – New insights into malaria vectors. IntechOpen. 2013; 671-704.

[57] Bier JC, Wilke ABB, Benelli G. Newer approaches for malaria vector control and challenges of outdoor transmission. Toward Malaria Elimination – A Leap Forward, IntechOpen. 2018

[58] https://endmalaria.org/sites/default/files/Vector-Control-Humanitarian-Emergency-meeting-report-.pdf

FIGURE 15. MIND MAP OF VECTOR CONTROL TOOLS FOR *ANOPHELES* AND *AEDES* CONTROL (SEE ATTACHMENT FOR FULL SIZE)



Below is a summary of our recommendations based on the desk review and key informant interviews, along with our consultations with industry and innovation partners.

LLINs. LLINs work on specific susceptible mosquito bionomic traits, including an overlap between mosquito time and place of biting and LLIN use (usually indoors) and susceptibility to the insecticide on the net. LLINs also provide a physical protective barrier against biting.

There is a strong net culture in the Asia Pacific region, especially the GMS. LLIN access and coverage continue to be challenges, especially for families that have multiple living spaces (i.e. village and farm/forest) and populations that live in remote areas. There is also competition with conventional nets in many places where individuals prefer the colors, designs, and shapes of the conventional nets accessible through local shops. The disruption of the private market for ITNs with LLINs only distributed through public health mass campaigns has reduced access in some areas; continuous/routine distribution has helped fill gaps, and subsidized sales of nets may help fill gaps in more peri-urban settings where individuals seek out products from local shops. Community retreatment activities are still popular in some countries (e.g. Vietnam) where demand for retreatment kits remains strong. Until there is more insecticide resistance data from the Asia Pacific, we would not yet recommend consideration of PBO or dual-AI[59] LLINs. Applicability of nets to migrant and mobile populations depends on housing consideration, with outdoor transmission incurring a gap in protective coverage from mosquito bites.

---

[59] PBO=piperonyl butoxide, a synergist (enhancing the functionality of insecticides) ; dual-AI=dual active ingredient

IVCC opportunity: explore market opportunities for long lasting retreatment strategies and subsidized sales of LLINs through the private sector to improve access to quality and effective products.

IRS, ORS, and outdoor space spraying. IRS functions best on indoor resting mosquitoes susceptible to the active ingredient. ORS and outdoor space spraying effectiveness relies on contact between the active ingredient, susceptibility to the active ingredient, and an overlap between the mosquito (presence or resting behavior) and the space sprayed.

Across these interventions, there is a lack of epidemiological effectiveness data for both *Aedes*- and *Anopheles*-borne diseases. In many countries, IRS is in national strategies but is either not implemented, or is implemented at small scale, with the exception of India and Pakistan, and to a lesser extent in Vietnam. In India, given widespread insecticide resistance, innovation in IRS insecticide and application technology may have a significant impact on malaria, *Aedes*-borne diseases, and visceral leishmaniasis. Where IRS infrastructure exists, evidence should be generated on 1) targeted IRS for *Aedes* control and 2) IRS in malaria foci and for malaria outbreak response. For enclosed and semi-enclosed farm huts and semi-permanent structures, do-it-yourself (DIY) IRS could be effective depending on the local vector species.

There is increasing interest in ORS for malaria elimination across the Asia Pacific. In Malaysia and Indonesia, ongoing entomological field evaluations of ORS targeting *P. knowlesi* vectors are funded by the MOHs. In Myanmar, a phase II entomological study of residual effect of ORS and knockdown from different insecticides is being funded by the Bill & Melinda Gates Foundation. None of the studies are looking at epidemiological impact[60] (which, at present, will be required for a WHO policy recommendation).

Space spraying is often conducted without appropriate planning and monitoring, and the new WHO malaria vector control guidelines include a recommendation *against* space spraying given the very limited evidence; a similar lack of epidemiological evidence exists for *Aedes*-borne disease. Efforts are required to optimize the intervention (timing, frequency) with robust monitoring and evidence of effectiveness.

IVCC opportunity: generate epidemiological evidence on these interventions as part of an IVM approach based on local transmission dynamics and vector bionomics and explore product development for DIY IRS and application equipment.

ATSB. ATSB effectiveness is based on mosquito sugar feeding, which can occur at all times in a gonotrophic cycle. Access to the ATSB device is based on the abundance of alternative sugar sources will impact efficacy. There is significant interest and expanding research in ATSB for both *Aedes* and *Anopheles* control; epidemiological evidence of impact is lacking, although large clinical trials are underway. Several industry partners consulted as part of this landscape analysis noted an interest in developing attractants. The entomological impact of ATSBs are highly variable based on climate, alternative food-sources (i.e. local flora including plant species and flowering state), active ingredient, and the physiological state of the mosquitoes.[61] Given that most of the Asia Pacific is tropical and lush, appropriateness of ATSB outdoors for *Anopheles* control may be limited, while *Aedes* environments may be much more suitable to ATSB.[62]

60 Although the Myanmar study by the Shoklo Malaria Research Unit may include an evaluation of the SG6-P1 biomarker of human exposure to *Anopheles* saliva for monitoring the vector-control intervention.

61 Florenzano JM, Koehler PG, Xue RD. Attractive toxic sugar bait (ATSB) for control of mosquitoes and its impact on non-target organisms: a review. Int J Environ Res Public Health. 2017; 14(4): 398.

62 Sissoko F, Junnila A, Traore SF, Doumbia S, Dembele SM, Schlein Y, et al. Frequent sugar feeding behavior by *Aedes aegypti* in Bamako, Mali, makes them ideal candidates for control with attractive toxic sugar baits (ATSB). PLoS NTD. In review.

IVCC opportunity: develop and demonstrate impact of ATSB indoors for *Aedes*-borne disease control and malaria elimination in urban and peri-urban environments and in displaced persons camps.

Bite prevention. For the purposes of this report, bite prevention strategies are interventions that prevent vector-host contact and include spatial repellents, both area wide and wearables, topical repellents, insecticide treated hammocks, insecticide treated clothing, bite-proof clothing, other insecticide treated materials (blankets, sheeting, tarps, tents), and LLINs (summarized above). All these tools require individual use and compliance, and all offer protection outdoors, which is the most significant gap in protection in the Asia Pacific region, especially for malaria but also other mosquito-borne diseases. Spatial repellents, insecticide treated blankets, and LLINs can also be used indoors. Long lasting insecticide treated hammocks are the only products that have been procured and distributed through the public health sector to high risk populations in the GMS (Vietnam and, to a lesser extent, Cambodia). While hammock culture is variable across the region, there is a significant opportunity in optimizing and scaling hammock products following acceptability studies.

The key limitations of tools in the bite prevention space include compliance, longevity of effect, frequency of application/use required, delivery challenges, market size, low-cost competition in the consumer market, and lack of entomological and epidemiological evidence. Longer-lasting products (topical and spatial repellents) can help address compliance and delivery challenges related to replacement. Ensuring products are portable and designed to fit local needs and preferences will also improve compliance. Leveraging subsidized sales to the consumer market for free distribution through the public health sector, as well as leveraging the humanitarian, African, and Latin American markets increases the potential market size for these tools.

Other key gaps include consensus on testing guidelines and standardized screening methods, epidemiological evidence for various target product profiles and use cases, and identifying and developing new active ingredients.[63,64] There is interest from several industry partners in exploring product development with existing active ingredients and also in exploring new active ingredients.

There is increasing research and development in the bite prevention space, with significant opportunity for impact.[65] One approach is through forest packs, which are starting to gain traction in the GMS with funding from the Global Fund and PMI. These packs vary in specific products, but generally include a topical repellent, insecticide treated hammock, long sleeves and pants, and/or LLINs, alongside a flashlight and rucksack for transport. Another approach is through do-it-yourself (DIY) repellent treatment kit for various materials (e.g. blankets, eave ribbons, etc.) A kit could be adapted to setting and textile, making it highly versatile.

IVCC opportunity: building on the Outdoor Bite Prevention Innovation Workshop convened by IVCC in April 2017,[66] consolidate and manage the bite prevention roadmap; identify and further develop and evaluate key tools, including hammocks, longer lasting topical repellents, spatial repellents, DIY treatment kit, and clothing following more detailed review of the market landscape and product opportunities.

---

63 Arctec. Report for IVCC: an expert review of spatial repellents for mosquito control. 2018. LSHTM.

64 Richardson J. Presentation at RBM VCWG February 2019. Bite prevention tools roadmap: spatial protection with volatile pyrethroids.

65 Moore S. Presentation at RBM VCWG February 2019.

66 Systematic Inventive Thinking UK (SIT-UK). Outdoor Bite Prevention – Innovation Workshop. Report for IVCC. April 2017.

Other:

- Insecticide treated paints. Similar to IRS, insecticide treated paints rely on a mosquito resting on a painted surface and susceptibility to the active ingredient. Although epidemiological data is lacking for insecticide treated paints, entomological data is increasingly positive. Besides lack of evidence on public health impact, key limitations to scale up have been cost, bulkiness of the products, and pyrethroid resistance in some areas (relevant for the pyrethroid-only paints). Residual efficacy of the paints are about three years so as long as householders do not resurface/repaint the walls of their homes (as is customary in some Asia Pacific countries), then paints have a much longer durability than IRS. **IVCC opportunity: expand the evidence base for insecticide treated paints for *Aedes*-borne disease control and explore cost structures by leveraging the consumer and professional markets for the public health market**.
- Chemical, biological, and acoustic larvicides. Though there is considerable regional interest and a WHO recommendation for larviciding as a supplemental intervention, there is limited evidence on effectiveness in the Asia Pacific region and lack of implementation resources (funding, manpower, know-how) for *Anopheles* control. For *Aedes* control, there is widespread use of larviciding, often decentralized to district levels and to communities, thus making measuring impact difficult. New application technology may improve the scale of impact of larviciding, such as ULV spraying of *Bti* and other larvicides for *Aedes* control, currently being evaluated in Malaysia and elsewhere, and drone spraying of larviciding for *Anopheles* control. There is also increasing research on the use of drone and satellite remote sensing to map *Anopheles* larval habitats for LSM targeting. Acoustic larvicide technology is being used across the US and increasingly among private pest control operators in the Asia Pacific region. At present, there is a lack of data on disease impact. **IVCC opportunity: explore novel application methods for chemical and biological larvicides and increase the evidence base on effectiveness and best practices for implementation across the region.**
- Insecticide treated screening/barriers: There are clear use cases for insecticide treated screens and barriers around villages and farm huts but further research is needed on entomological and epidemiological impact, as well more research to understand the impact of this tool on resistant vectors and in areas of pyrethroid resistance. **IVCC opportunity: expand the evidence on effectiveness of insecticide treated screening and barriers, which could play an important role in an integrated vector management approach.**
- Ivermectin-treated livestock. The efficacy of this intervention is based on the proportion of mosquitoes that will feed on treated animals. Evidence is still limited for this intervention but there is growing interest across Africa and the Asia Pacific for malaria control (with ivermectin as well as other endectocides, including eprinomectin and fipronil). With a small-scale trial ongoing in Vietnam treating water buffalo with ivermectin for impact on *Anopheles*, this approach could be explored across the GMS, Papua New Guinea and elsewhere for pigs, as an example, which are very common across many communities in the region. **IVCC opportunity: expand the evidence base on livestock treated with ivermectin in areas with important exophagic and zoophagic vectors.**

Conclusion

This report offers a snapshot of mosquito-borne diseases and opportunities for vector control product research, development, and access in the Asia Pacific region. With the right set of tools targeted to the right populations at the right time in the right place, mosquito-borne diseases can be controlled and eliminated, improving health outcomes and health security for all.

Annex 1. Reported disease statistics by country, ranked from highest to lowest burden or risk per disease
(top three highest burden countries by disease highlighted in red)

Country	Malaria API (2016)	Country	Malaria cases (2017)	Country	Dengue cases (2017)	Country	Chikungunya cases*	Country	Zika risk (last update Mar 2018)	Country	Pop covered by LF MDA*	Country	Japanese encephalitis (2017)
Papua New Guinea	181.9	India	9,590,000	Sri Lanka	185,000	Indonesia	83,756	Samoa	Cat 1	India	419,112,086	India	2,043
Solomon Islands	171.0	Indonesia	1,530,566	Vietnam	183,287	Sri Lanka	37,000	Solomon Islands	Cat 1	Indonesia	50,785,500	China	1,147
Cambodia	18.4	Papua New Guinea	1,500,657	India	157,000	India	30,121	Bangladesh	Cat 2	Myanmar	34,016,081	Myanmar	442
Vanuatu	8.2	Pakistan	956,280	Indonesia*	129,435	Bangladesh	14,160	Cambodia	Cat 2	Nepal	11,207,367	Philippines	361
India	7.7	Cambodia	208,273	Pakistan	125,000	Pakistan	8,387	Fiji	Cat 2	Philippines	7,000,897	Indonesia	281
Lao PDR	5.8	Myanmar	116,772	Philippines	117,654	Lao PDR	4,638	India	Cat 2	Papua New Guinea	5,602,188	Vietnam	200
Indonesia	5.8	Solomon Islands	103,482	Malaysia	82,840	Samoa	2,500	Indonesia	Cat 2	Timor Leste	1,279,948	Nepal	63
Pakistan	4.9	Bangladesh	32,924	Myanmar*	42,913	Papua New Guinea	1,590	Lao PDR	Cat 2	Lao PDR	149,801	Thailand	28
Myanmar	3.7	Lao PDR	20,712	Thailand*	26,616	Cambodia	1,500	Malaysia	Cat 2	Fiji	78,862	Sri Lanka	23
Bangladesh	1.9	Philippines	15,253	Lao PDR	11,039	Thailand	453	Myanmar	Cat 2	Samoa	61,325	Malaysia	20
Thailand	0.8	Thailand	11,043	Cambodia	6,372	Philippines	282	Papua New Guinea	Cat 2	Malaysia	30,642	Bangladesh	19
Nepal	0.5	Vietnam	5,481	China	5,900	China	173	Philippines	Cat 2	Bangladesh	0	Lao PDR	9
Philippines	0.3	Nepal	3,829	Bhutan*	4,700	Bhutan	68	Thailand	Cat 2	Bhutan	0	Timor-Leste	7
Timor Leste	0.2	Vanuatu	2,270	Vanuatu	3,000	Malaysia	30	Vietnam	Cat 2	Cambodia	0	Cambodia	5
Vietnam	0.1	Malaysia	85	Samoa	2,466	Nepal	3	Vanuatu	Cat 3	China	0	Bhutan	3
Malaysia	0.1	Timor Leste	36	Fiji	2,200	Fiji	1	Bhutan	Cat 4	Pakistan	0	Papua New Guinea	1
Bhutan	0.02	Bhutan	11	Solomon Islands*	1,212	Myanmar	0	Nepal	Cat 4	Solomon Islands	0	Pakistan	0
China	0	China	0	Bangladesh	876	Solomon Islands	0	Sri Lanka	Cat 4	Sri Lanka	0	Samoa	0
Fiji	0	Fiji	0	Timor Leste*	278	Timor Leste	0	Timor Leste	Cat 4	Thailand	0	Fiji	Not available
Samoa	0	Samoa	0	Nepal*	183	Vanuatu	0	China	Not available	Vanuatu	0	Solomon Islands	Not available
Sri Lanka	0	Sri Lanka	0	Papua New Guinea**	0	Vietnam	0	Pakistan	Not available	Vietnam	0	Vanuatu	Not available
Source: WHO WMR 2017.		Source: WHO WMR 2018. Estimated cases (point value).		*Data from other years (preceding 2017). Sources: ECDC, WHO, MOH. ** DENV cases in PNG rarely reported, but study published by Senn et al (2011) indicates a seroprevalence of 8% amongst patients presenting to Madang clinics with acute febrile illness. According to Luang-Sarkia et al (2018), DENV surveillance not undertaken, patients with acute febrile illness not regularly tested.		*Various years. Sources: ECDC, MOH, WHO, peer-reviewed literature.		Sources: WHO, CDC, ECDC. Cat 1: Area with new introduction or re-introduction with ongoing transmission. Cat 2: Areas with virus transmission following previous virus circulation. Cat 3: Areas with interrupted transmission and with potential for future transmission. Cat 4: Area with established competent vector but no known documented past or current transmission.		*Various years; proxy for populations at risk for F. Sources: Graves et al (2013), MOH, WHO.		ource: WHO Global Data Observatory.	