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Vector Control in the Indo-Pacific: A Summary of Technical, Regulatory and Market Access Landscapes

INNOVATIVE VECTOR CONTROL CONSORTIUM

November 2019

Summary of key challenges and opportunities

TECHNICAL

Malaria:

- Outdoor and residual transmission, especially forest-related transmission ecologies.
- Suboptimal delivery of indoor interventions.
- Opportunity for several potential tools, including:
  - Repellents
  - Treated materials
  - Attractive Targeted Sugar Baits
  - Improved indoor control tools
  - Application equipment

***Aedes*-borne diseases:**

- Growing threat due to proliferation of larval habitats, population movement and climate change.
- Opportunities include:
  - Development of spatial repellents
  - Trapping
  - Outdoor residual spraying
  - ATSBs
  - Treated materials
  - Improved larvicide applications

Surveillance and information management:

- Often antiquated systems for both *Aedes* and *Anopheles* and not used for program decision making.
- Opportunities include:
  - Improved trapping
  - Use of information management
  - Mobile communications
  - GIS and remote sensing for risk-area stratification
  - Technologies for mosquito identification and analysis

Operational:

- Lack of insecticide resistance data, especially for *Aedes* species
- Difficult to collect malaria vectors like *An. dirus* and *An. minimus*
- Lack of widespread capacity to conduct laboratory and semi-field trials
- Opportunities include:
  - Working with regional partners to fill insecticide resistance information gaps.
  - Draw on existing, and develop new capacity for high throughput lab and semi-field testing of vector control tools.

MARKET ACCESS:

- Highly fragmented retail market with products of variable quality and effectiveness.
- Opportunities to influence market drivers through public awareness, legislation and other market shaping interventions to find synergies with public sector investments.
- Several strong potential implementing partners in both public and private sectors. e.g. public health campaigns and manufacturers to leverage for market access.

REGULATORY:

- Many national regulatory frameworks based on agricultural, not public health pesticides.
- Often fragmented registration processes with lack of standardized guidelines, demand for local bio-efficacy trials, lengthy registration processes and lack of enforcement.
- Opportunities to improve national regulatory authority capacities and regional harmonization through regional networks advocating to prioritize essential public health pesticide products.

Background

> Mosquito-borne diseases continue to cause high morbidity and mortality rates and threaten health security across the Indo-Pacific region. In 2017, there were over 13 million malaria cases, with 23,000 malaria deaths. While many countries are making progress toward elimination, malaria transmission persists in high-risk areas and populations where new tools are desperately needed. For *Aedes*-borne diseases, between 2010 and 2017, there were over a million dengue cases reported (and the majority of cases are not reported). Chikungunya, Zika and other arboviruses, lymphatic filariasis, leishmaniasis and Japanese encephalitis are also of concern in many areas.

Recognising vector-borne disease threats to regional health security, the Australia Department of Foreign Affairs and Trade (DFAT) provided the Innovative Vector Control Consortium (IVCC) with a five-year grant in 2018 to support the development of a Vector Control Product Toolbox for the Indo-Pacific region.

As a first step, IVCC commissioned three landscaping studies: a Technical Landscape conducted by the University of California, San Francisco (UCSF) Malaria Elimination Initiative; a Market Access Landscape by the company FutureBridge; and a Regulatory Landscape by the consultant John Vasanthan Paul. These were conducted between September 2018 and May 2019, and included:

- a desk review of 19 countries
- in-depth consultations and key informant interviews with governments and partners in focus countries Cambodia, Indonesia, Malaysia, Myanmar, Papua New Guinea (PNG) and Vietnam
- consultations with over 20 industry partners.

While there is a wide range of malaria transmission ecologies – stretching from South Asia through to the Pacific Islands – common themes emerged:

- Outdoor transmission is a key challenge necessitating innovation and access to vector control tools for outdoor protection.
- 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. Limited testing in PNG indicates that pyrethroid susceptibility remains high.
- Most national programmes rely almost exclusively on mass distribution of long-lasting insecticide treated nets (LLINs), with the exception of Pakistan and India, which implement wide-scale indoor residual spraying (IRS).

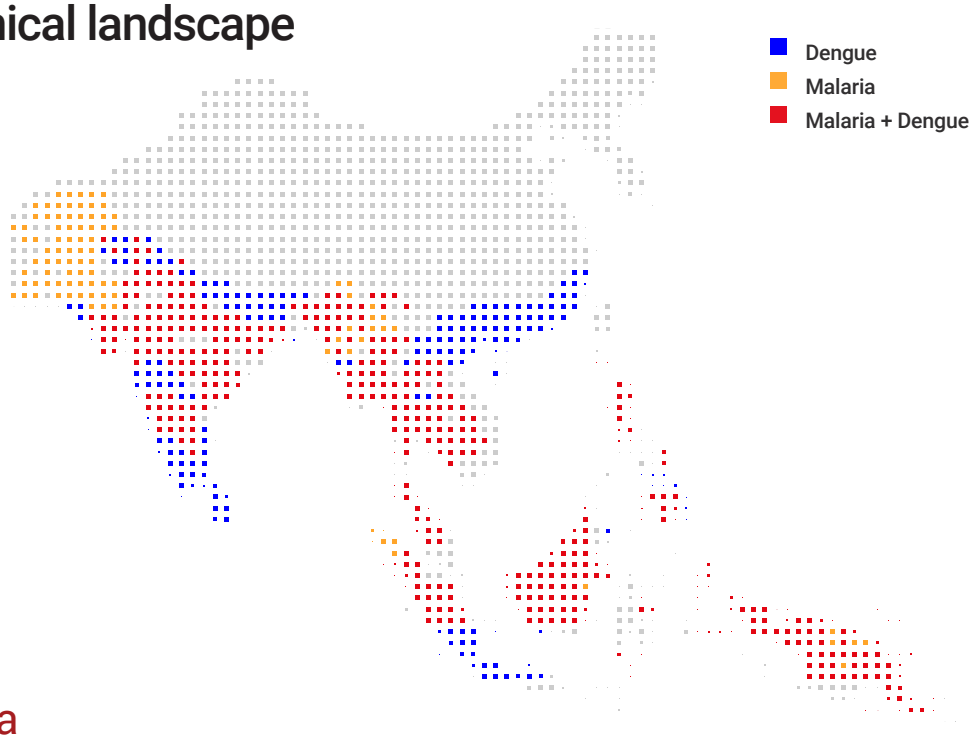
Aedes-borne diseases are on the rise as *Ae. aegypti* and *Ae. albopictus* populations continue to proliferate with increasing occurrences of dengue outbreaks and often inadequate diagnostic capacity to detect chikungunya and Zika viruses.

- There are some countries with relatively strong *Aedes* control programmes, but most lack capacity, 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 (IHR) for health security varies significantly, with most countries lacking adequate tools and resources.

IVCC is uniquely positioned to address these challenges in collaboration with national programmes and research, implementation and industry partners.

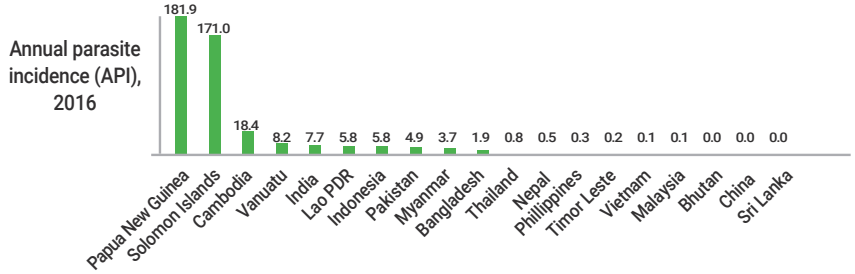
Potential solutions fit into IVCC's integrated vector management (IVM) portfolio of work, because rather than a single product, it is likely to be an integrated package of tools and approaches that, driven by improved, high-quality data and implementation, can sustainably reduce mosquito-borne diseases in the region.

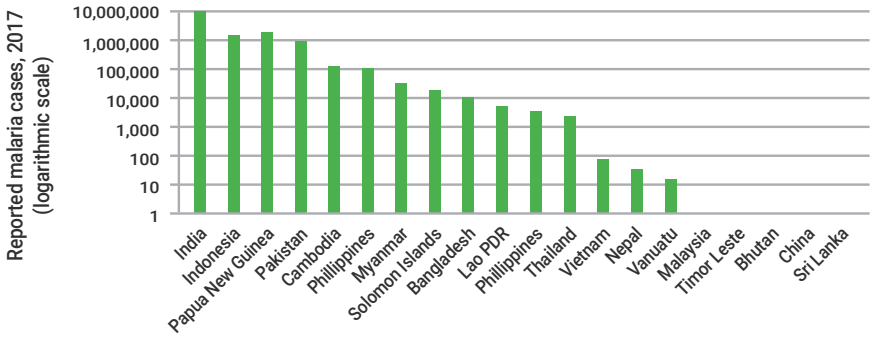
Technical landscape



Malaria

In 2017, there were an estimated 23,320 malaria deaths and 13.147m malaria cases in the Asia-Pacific. While malaria declined from 17 cases per 1,000 population at risk to 7 cases per 1,000 population in the WHO South East Asia region between 2010 and 2017, malaria cases have plateaued at 2.5 cases per 1,000 population at risk in the Western Pacific Region (although cases increased by over threefold in PNG and Solomon Islands during those years), and multi-drug resistance in malaria parasites remains a threat to elimination in the GMS.[1,2] Twenty-two countries have committed to the goal of malaria elimination by 2030.





[1] World Health Organization. World Malaria Report 2018. Geneva: Global Malaria Programme.

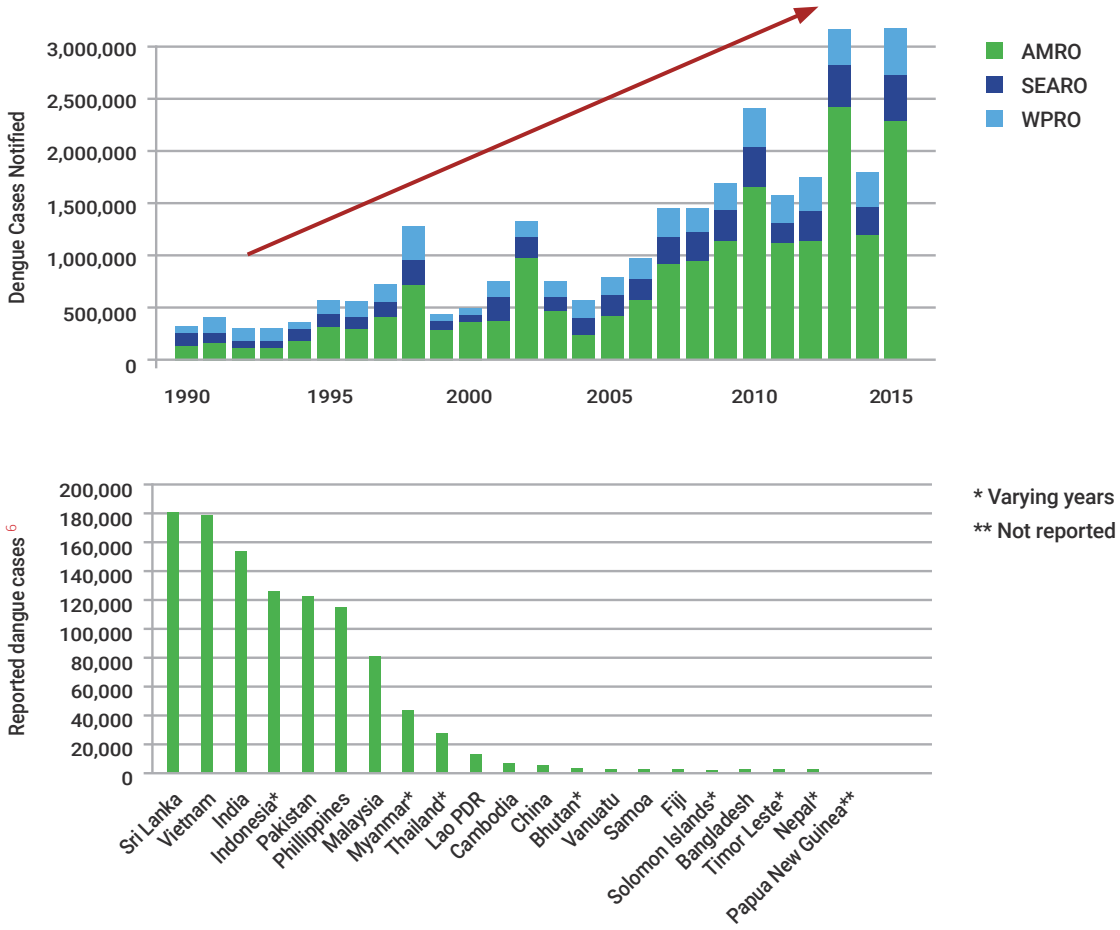
[2] Imwong M, Suwannasin K, Kunasol C, Sutawong K, Mayxay M, Rekol H, et al. The spread of artemisinin-resistant Plasmodium falciparum in the Greater Mekong subregion: a molecular epidemiology observational study. Lancet Infect Dis. 2017; 17(5):491–497.

Dengue, Zika, and chikungunya

Over the past 50 years, global dengue incidence has increased 30-fold. In the Asia-Pacific region, there is a dearth of dengue incidence data, but over a million cases were reported in 2017 (this is probably an underestimate and the true figure could be as high as 23m[3].) Sri Lanka, Vietnam, India, Indonesia, Pakistan and the Philippines report the highest numbers of cases. Dengue in PNG is 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.[4] Chikungunya is also not well documented, as symptoms resemble dengue and are misdiagnosed and under-reported. Additionally, chikungunya epidemics exhibit fluctuating and cyclical trends; such epidemics are marked by severe outbreaks interspersed by silent periods spanning from several years to a few decades.[5] Indonesia, Sri Lanka, India and Bangladesh report the highest numbers. Zika epidemiology is categorised based on reports of transmission, with only a handful of cases reported across the region, although Zika may also be under-diagnosed and under-reported. According to the last update by the WHO in March 2018, Samoa and Solomon Islands reported new introduction or reintroduction of cases, and 12 other countries in the region reported ongoing virus transmission.

Other vector-borne diseases considered in the technical landscape include lymphatic filariasis, leishmaniasis and Japanese encephalitis.

Dengue Cases per year for the 3 WHO regions which report regularly to the Secretariat



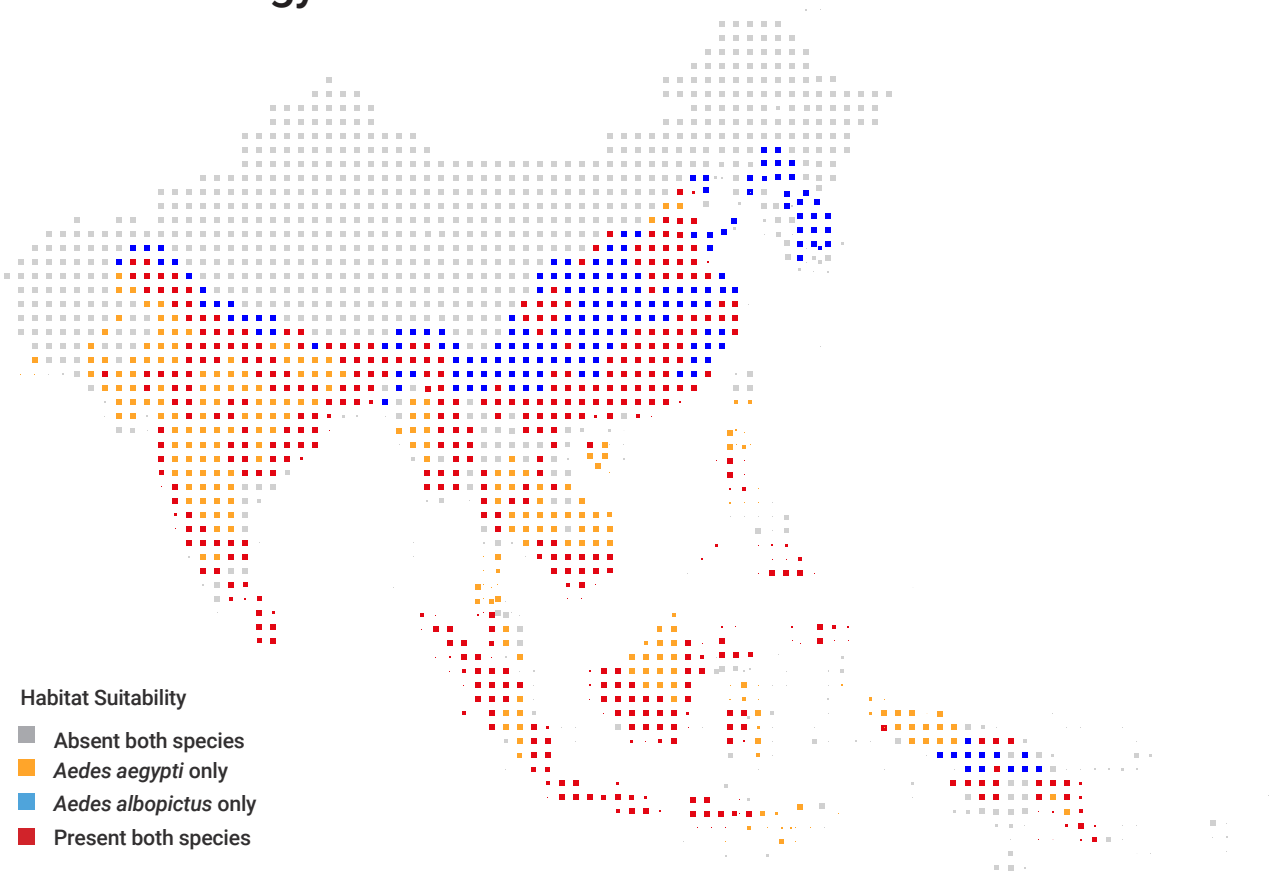
[3] Shepard DS, Undurraga EA, Halasa YA, Stanaway JD. The global economic burden of dengue: a systematic analysis. Lancet Infectious Diseases. 2016; 16:935–941. Appendix, page 15.

[4] Senn N, Luang-Suarkia D, Manong D, Siba PM, McBride WJ. Contribution of dengue fever to the burden of acute febrile illnesses in Papua New Guinea: an age-specific prospective study. Am J Trop Med Hyg. 2011; 85(1):132–137. doi:10.4269/ajtmh.2011.10-0482v.

[5] WHO. Guidelines for Prevention & Control of Chikungunya Fever. 2009.

[6] Default year for countries is 2017. For those marked with * the years are: Indonesia (2004-2010 average), Myanmar (2015), Thailand (2012), Bhutan (2010), Solomon Islands (2016), Timor Leste (2010) and Nepal (2012).

Vector ecology



Anopheles

Outdoor transmission driven by early evening and outdoor vector biting continues to pose the biggest challenge to malaria elimination in the Asia-Pacific.[6] Vector species are highly diverse in the region, with over 19 dominant vector species and many more secondary vectors. Many of the vectors are naturally exophilic and exophagic, while others have become more so over time, largely due to behavioural 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*).

Aedes

Ae. aegypti is the primary vector of dengue, and, although it is commonly reported as a daytime biter with peaks in early morning and before dusk, feeding continues throughout the night in PNG and Solomon Islands. *Ae. albopictus* is usually a secondary vector of dengue but can be very competent for chikungunya. *Ae. albopictus* is increasing in relative proportion as the spatial distribution spreads north and south. There are other *Aedes* species that have been incriminated as dengue vectors, although they are geographically limited. 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 urbanisation, and the presence of suitable climate.[7] 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.

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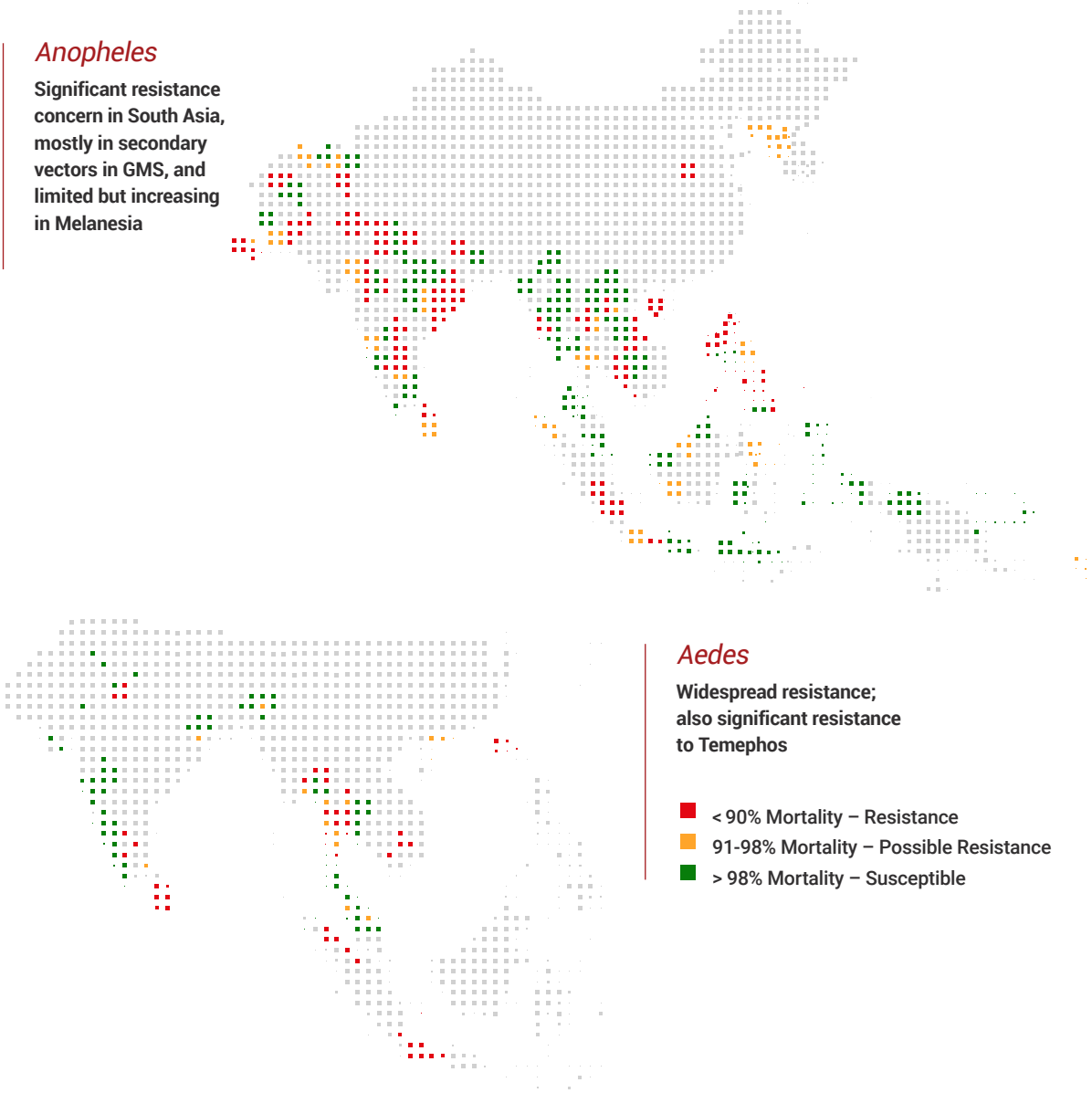
[6] Malaria vector control in the Greater Mekong Sub-region: an independent situation analysis and suggestions for improvement. 21 September 2018. Prepared by Sean Hewitt PhD VBDC Consulting Ltd, http://www.vbdc-consulting.com/files/180920.pdf.

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

Insecticide resistance

Anopheles

Significant resistance concern in South Asia, mostly in secondary vectors in GMS, and limited but increasing in Melanesia



Aedes

Widespread resistance; also significant resistance to Temephos

- **< 90% Mortality – Resistance**
- **91-98% Mortality – Possible Resistance**
- **> 98% Mortality – Susceptible**

There is limited physiological insecticide resistance data reported, especially for the major vectors in the GMS.[8] 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. 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.

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.[9] Not shown on the map, due to lack of data published or reported to the WIN Network, are the high levels of pyrethroid resistance in *Aedes* in PNG[10] and reported high levels of pyrethroid and temephos resistance among several *Aedes* populations throughout Cambodia.[11]

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8 WHO. Global report on insecticide resistance in malaria vectors: 2010–2016. Global Malaria Programme. 2018.

9 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.

10 S Karl, personal communication.

11 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 4 March 2018.

Human behaviour and high-risk populations for malaria

In areas of higher transmission such as eastern Indonesia, PNG, 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 such as the GMS, transmission is highest among specific risk groups including forest-goers (for logging, hunting, forest-product gathering and agriculture); construction and mine workers; security personnel and forest rangers; and other seasonal workers. The majority of these populations are adult men, but in some contexts whole families are at risk. Given that much of the work is outdoors and often during peak *Anopheles* biting, there is a high risk of malaria infection for these workers. Other groups such as people displaced by conflict or disasters are also at elevated risk.

Technical challenges and potential solutions for vector control in the Indo-Pacific

Malaria

- Outdoor transmission where indoor vector control tools such as ITNs and IRS are not sufficient. Often an occupational disease for forest-goers (especially GMS, Malaysia) and for individuals engaged in small-scale farming activity in PNG.
- Suboptimal delivery of indoor interventions where needed. Strong net culture in many countries, very active consumer net market but for untreated nets; technically more efficacious LLINs may not be used for reasons of texture, size, mesh size.
- Urgency to address outdoor residual transmission due to multi-drug resistance in GMS.

Aedes-borne diseases

- Growing threat across region due to proliferation of *Aedes* larval habitats, population movement and climate change.
- Lack of effective surveillance and control tools; some countries with strong programmes, including IHR vector surveillance and control around ports of entry, but others with weak programmes.
- Gaps in insecticide resistance mapping; indications of pockets of strong pyrethroid and temephos resistance, but large data gaps.
- Large semi-regulated pest control sector in some countries (some others with well regulated and collaborative links with private sector). Often associated with tourism sector.

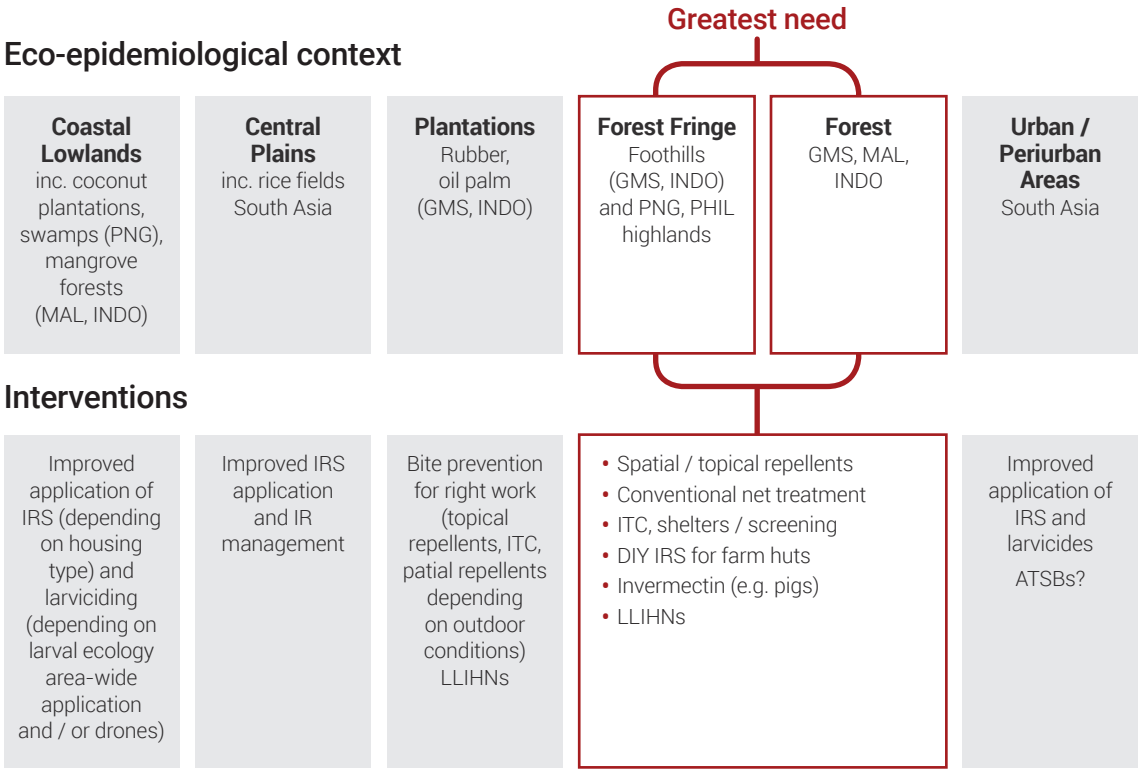
Surveillance, information management

- In many countries, antiquated systems for both *Aedes* and *Anopheles*. Entomological capacity and surveillance systems often not used for programme decision making.
- Insufficient use of information technology advances, including for information management, mobile communications, GIS and remote sensing for risk-area stratification.

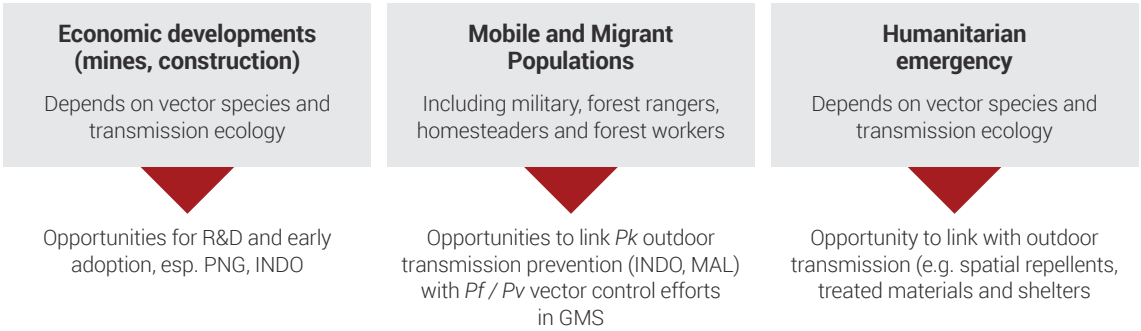
Operational

- Capacity to conduct laboratory and semi-field vector control product testing to inform product development and delivery strategies is severely lacking in most countries in the region.
- General lack of effective integrated vector management programmes driven by local evidence/data and tailored to local ecologies.
- Gap between research and operations in some countries. Potential for strong regional network of research and training institutions, but sometimes lack of coordination with control programmes.
- Lack of insecticide resistance data, especially for *Aedes* and for dominant, but difficult to collect malaria vectors such as *An. dirus* and *An. minimus*.

Potential solutions: *Anopheles*



Potential prioritisation: high-risk populations (malaria)

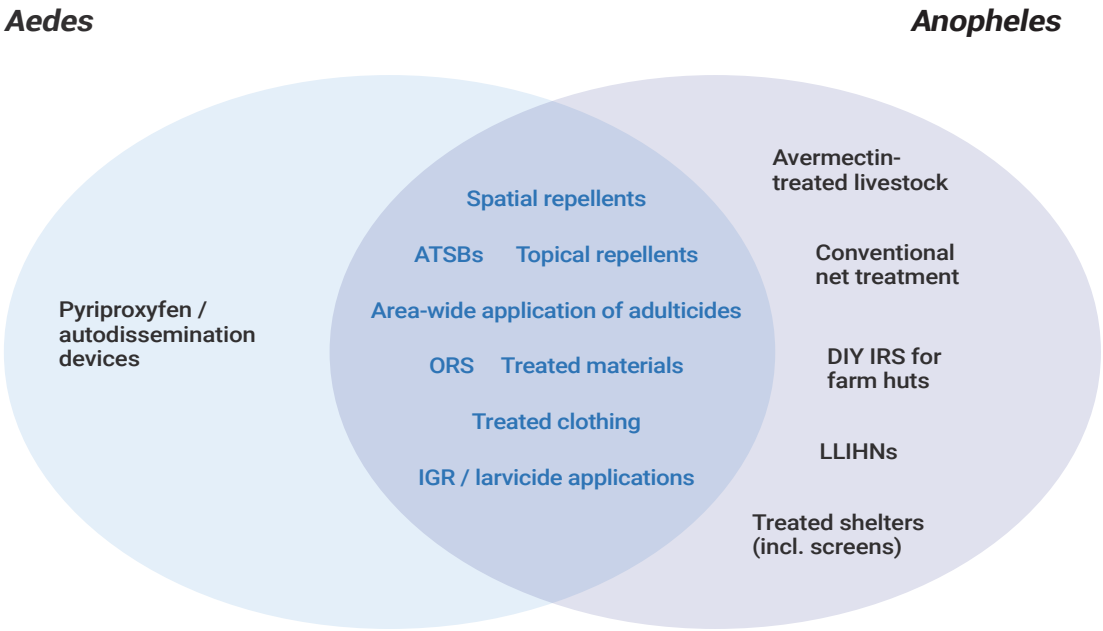


Potential solutions: *Aedes*

- Spatial repellents, both active and passive emanators.
- Peri-domestic targeted spraying (i.e. outdoor residual spraying – ORS), potentially in combination with trapping.
- Attractive Targeted Sugar Baits.
- Improved IGR/larvicide applications, including area-wide applications.
- Treated materials with pyriproxyfen/auto-dissemination devices.
- Improvements to *Aedes* and virus surveillance and risk analysis for better forecasting and targeting interventions.

(WMP Wolbachia initiative active in several countries; and SIT and GM initiatives are currently outside IVCC portfolio).

Potential solutions: outdoor biting



Potential solutions: surveillance

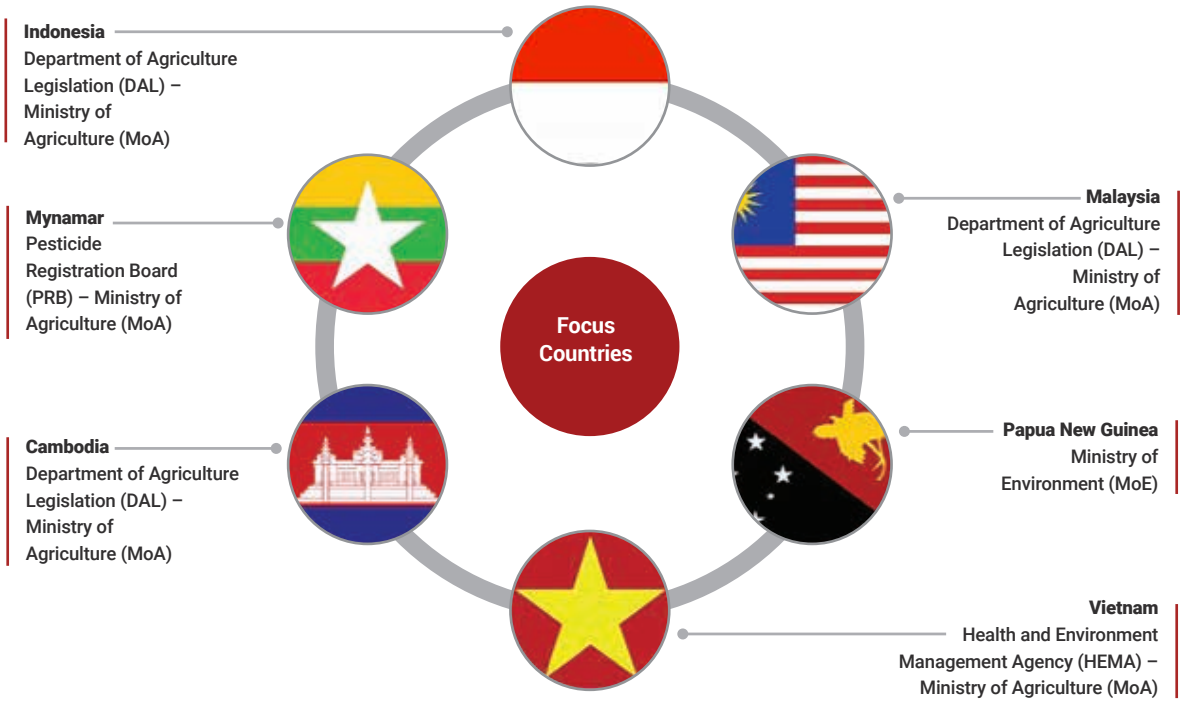
- Improved trapping for both *Aedes* and *Anopheles*, especially for outdoor resting/biting and forested areas.
- Improved use of remote sensing, GIS and mobile technology (including *Aedes* "smart traps" and crowd sourcing) for targeting, M&E risk-area stratification and outbreak prediction.
- Improved technologies for mosquito identification and analysis – species identification, insecticide resistance status, parasite/virus detection, age grading.

Potential solutions: testing capacity

- Leverage semi-field test capacity in Thailand to evaluate products of potential relevance across the region.
- Improve capacity for high-throughput lab and semi-field testing of vector control tools and strategies across the region.

Regulatory landscape

Across the Indo-Pacific region, public health pesticides are usually regulated under the Ministry of Agriculture. There are a few exceptions: the Health and Environmental Agency in Vietnam; the Ministry of Environment in Singapore and PNG; the Food and Drug Administration in Thailand. While dossier requirements are generally similar, many countries have their own special requirements. Some insist on test reports from GLP labs or ISO 17025 accredited labs only, while others have no specific requirements. Many insist on in-country effectiveness trials and do not accept data available from other countries. Some countries in the region do not specify the appropriate evaluation process and leave it to the manufacturer or the testing institute to decide.



While WHO Pre-Qualification (PQ) listing is not mandatory for registration, it is often mandatory for international donor-funded programmes such as those run by the Global Fund. Many focus countries in the region are not aware of the change from WHOPES to WHO PQT-VC in terms of vector control product evaluation and should be made aware of this significant change.

Regulatory authorities in the focus countries do not have any cooperation with Stringent Regulatory Authorities (SRAs), such as the US EPA or the EU, nor have any collaborative registration process among each other. In addition to this, the regulatory authorities in this region, such as CIBRC (India), ICAMA (China), NEA (Singapore), APVMA (Australia) and MAFF (Japan), do not have any influence in expediting the registration of products in the focus countries.

Malaysia and Indonesia have robust training procedures for pest control operators, whereas in the other countries training and certification is not very structured.

In many countries, disposal plans are not properly framed and there are no clear guidelines provided. It is left to the discretion of the manufacturers as well as the end users.

Regulatory challenges and potential solutions

1. Synergies with retail market

The retail vector control market is very large but highly fragmented, with products of variable quality and effectiveness. Suboptimal low-cost products in market (including topical repellents, coils, aerosols and untreated nets) may make market-based consumer-focused approaches difficult. There are opportunities to influence market drivers through public awareness.

2. Fragmented registration processes

There are great differences between the countries' registration processes. Pesticide regulations are often framed for agriculture and do not accommodate public health needs. ASEAN harmonisation was initiated in 2018. There is also potential in the work of the newly established VCAP (Vector Control Platform for Asia-Pacific) jointly led by APLMA and Unitaid, working in close collaboration with APMEN.

3. Standardised guidelines and specifications

There are often no guidance documents for specific categories of vector control products. Ideally, each product category requires specific physical/chemical characteristics and specifications, as well as specific testing, toxicological, packaging and labelling requirements. In some countries, such as Vietnam, there are no guidelines for registration of microbial public health pesticides. There is often no legislation to allow waiving tests that are irrelevant for a particular type of pesticide. Regulatory authorities under the Ministry of Agriculture sometimes have less understanding of public health products and fit these into the regulatory template designed for agriculture. The WHO has guidelines for different use categories (i.e. specifications and study guidelines including risk assessments for mosquito coils, vaporisers, IRS, ITNs, space sprays and larvicides) that could be referred to in many countries.

4. Acceptance of regional trials

Malaysia and Singapore accept regional trial data, but Vietnam and Indonesia insist on local bio-efficacy trials. In Myanmar, due to the lack of efficacy-testing facilities, reports of trials conducted following international protocols are accepted. However, in-country chemical analysis of the end-use product is mandatory in all the countries. Harmonisation of guidelines and processes would help in countries accepting regional trials regardless of in which country the trials have been conducted.

5. Strengthening analytical and testing facilities

Countries in the region have varying capacity for testing vector control products. Some, such as Malaysia, have highly evolved facilities in terms of entomological and chemical testing. Several laboratories are ISO 17025 and GLP accredited in Malaysia. In Vietnam, many ISO 17025 accredited laboratories are available but very few are GLP accredited. In Indonesia, the testing is all to be done by government approved laboratories. Myanmar, Cambodia and PNG need to have their capacity improved. There is a general need for improving the equipment and facilities for testing, and for improving capacity of personnel in testing and evaluation of products.

6. Lengthy registration processes

Many of the countries in the region do not have any specific legislation to promote the registration of pesticides used for public health by providing special categories such as reduced risk or minor use pesticides. There should be legislation enacted wherein priority for evaluation and approval can be granted, especially for products to be used in mass distribution under malaria elimination programmes. This would help create a fast track regulatory mechanism and thereby improve access to newer and more innovative products to address the diversity of vector control challenges in the region.

7. Enforcement and implementation

There is often a lack of coordination among ministries within a country. Ministry of Agriculture regulations are often made without the cooperation of the Ministries of Health, Industry, Commerce, Environment, etc. There may be no proper enforcement or implementation of the legislation and no monitoring of pesticide imports, sale of unregistered pesticides, sale of counterfeit pesticides, and their use and disposal. The lack of enforcement could have a negative impact on the availability of good quality pesticides, as the manufacturers of high quality products are less incentivised to bring products to an unregulated market to compete with cheaper, low-quality products. There should be proper implementation of legislation, coordinated across the different ministries in a country. If there is seamless co-ordination between the ministries, enforcement legislation can be enacted properly, and regulatory processes will be able to be implemented as intended.

Market Access Landscape

Indo-Pacific has the largest continental economy by both GDP nominal and Purchasing Power Parity and is the fastest-growing economic region in the world. Factors contributing to the economic growth are the increasing GDP of several countries, improved internet access and coverage, improved access to healthcare services.

Regional Vector Control Funding

The major funding agencies across the Indo-Pacific region are The Global Fund, UNICEF, Unitaid, USAID, the World Bank, and the Bill & Melinda Gates Foundation, providing funds individually or in collaboration. In 2017, ~USD340 million was contributed by leading donors, including Global Fund, World Bank, and USAID; 20% of the donation by Global Fund was invested in the Indo-Pacific region. Out of the total funds allocated to Indo-Pacific, 32% were invested for malaria prevention and control activities.

Public and Private Sector Procurement Channels

Procurement channels for donor products include national government bodies, Non-Governmental Organizations (NGOs), and community health services. Distribution channels for the retail market include grocery stores, supermarkets, convenience stores, hypermarkets, e-commerce, general stores, and hawkers. Donors such as The Global Fund provide funds to national Procurement Service Agencies (PSA), which procure vector control products from manufacturers. Another funding model involves global donors allocating funds to a country's government, which will procure vector control products from manufacturers and distribute them to the local government, and later to end users via community services or hospital/health service agencies.

Vector Control Products in the Indo-Pacific

Various vector control products (donor products and retail products) are used in the Indo-Pacific region to help prevent and control malaria. Mosquito coils account for the highest retail market share due to their affordability and increased utilization in rural areas. Insecticide-Treated Nets/Long Lasting Insecticidal Nets (ITNs/ LLINs) were introduced in this region, as an effective means of preventing mosquito bites and malaria transmission. ITNs/LLINs in Asia are distributed for free in support of the WHO's recommendation. A total of USD3 billion is required annually to achieve malaria elimination during 2018-2020 in the Indo-Pacific region. The current annual funding is projected to be USD0.5 billion during 2018-2020. Therefore, the anticipated financing gap is likely to be 80% during the above-mentioned time period.

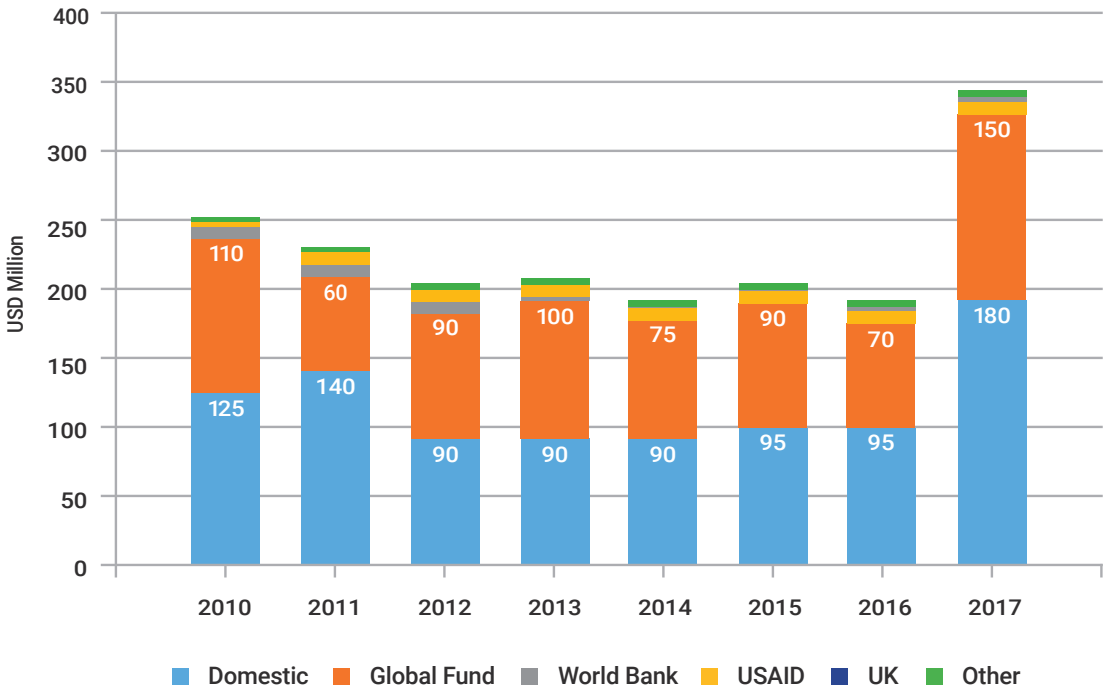
Regional retail market size and projected growth

The Indo-Pacific retail market for vector control products was estimated to be ~USD5.5 billion in 2018. The retail market is highly fragmented and is influenced by climate conditions. Retail sale of products such as coils, repellents, mats, lotions, and others is ubiquitous compared to LLINs or bed nets. While there is a large market for untreated mosquito bednets in several countries, LLINs are usually accessed through public sector mass campaigns that usually take place once every three years. The vector control market in the Indo-Pacific region is growing, due to factors such as the enhancement of cross-border and regional collaborations, as well as the strategic partnership across all sectors encouraging a smooth functioning of vector control and prevention activities.

Economic burden and investments for control

Dengue exerts significant economic burden in the Indo-Pacific region. Shephard et al have published a series of studies, including in 2013 where they estimated that between 2001 and 2010, there was an annual average of 2.9m dengue episodes and 5,906 deaths, with an annual economic burden of US$950m or about US$1.65 per capita. The annual number of disability-adjusted life years was 214,000 (120,000–299,000), which is equivalent to 372 DALYs per million inhabitants.[12] The most recent study for India estimates US$5.71bn in economic costs for the 2016 outbreak.[13] Region-wide estimates for malaria burden and costs of elimination are currently being investigated.[14] From 2012 to 2018, countries in the Asia-Pacific region increased their domestic financing for malaria by 44%, and it is estimated that it will increase by an additional 40% during 2018–2020.

FUNDING BY SOURCES FOR MALARIA PREVENTION & CONTROL IN ASIA-PACIFIC, 2010–2017[15]



[12] Shepard DS, Undurraga EA, Halasa YA. Economic and disease burden of dengue in Southeast Asia. PLoS Negl Trop Dis.; 7(2):e2055. doi:10.1371/journal.pntd.0002055.

[13] Hariharan, Dhwani et al. Economic burden of dengue illness in India from 2013 to 2016: A systematic analysis. International Journal of Infectious Diseases, in press (accessed 11 June 2019).

[14s] Shretta R, Silal S, White LJ, Maude RJ. Predicting the cost of malaria elimination in the Asia-Pacific. Wellcome Open Res. 2019; 4:73. Published 24 April 2019. doi:10.12688/wellcomeopenres.15166.1.

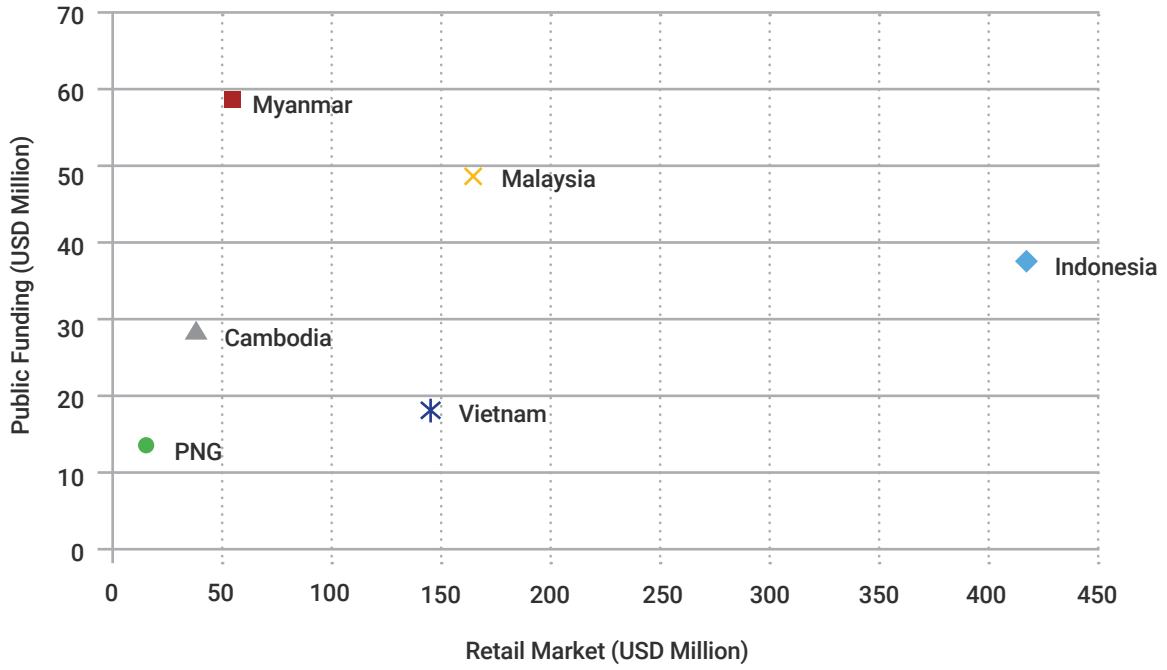
[15] WHO World Malaria Report 2018.

Retail market

The Indo-Pacific has a very large retail market for vector control products, including direct purchase of coils, vaporising mats, aerosols and repellents. For example, in Vietnam, sprays/aerosol sales are US$115m and coils US$30m per year. When comparing the retail market against public funding for malaria, the retail market in Indonesia and Vietnam comprises around 90% of the overall spending on vector control activities.

Although the retail market in the region is highly fragmented and made up of products with variable quality and effectiveness, the potential synergies between public/donor investment and this significant market must be explored to maximise the impact of any new products. In many countries, there are opportunities to leverage high-profile public awareness campaigns and to work with several strong implementing partners and initiatives.

PUBLIC FUNDING VS RETAIL MARKET (USD MILLION), 2017–2018



Conclusion

> The Technical Landscape, Market Access Landscape and Regulatory Landscape studies highlight several biological, ecological, technical, anthropological and economic challenges. There is a great diversity of vectors with rapidly changing and challenging transmission ecologies both for forest-related malaria vectors and the proliferation of *Aedes* larval habitats.

Technically, we do not yet have a good set of tools for outdoor and residual malaria transmission, or a set of tools and strategies to reduce *Aedes* and the growing threats of arboviral transmission. Many of our intervention strategies will rely on uptake and use at the individual, household and community levels, requiring tools developed with a focus on human- centred design, to bridge the gap between technical efficacy and community effectiveness.

There are also several operational, market and legislative challenges. Operationally, there is a dearth of field entomologists and product-testing capacity in many of the countries; and, while there is a vibrant market for mosquito-related products, we sometimes miss opportunities for synergies, for example with mosquito nets and spatial/topical repellents. Finally, there are regulatory challenges, particularly related to market access for effective existing and innovative products.

Fortunately, each challenge presents an opportunity. As outlined in Annex II, there is a wealth of research and training institutions throughout the region, and along with networks such as APMEN/APLMA and other DFAT investments in malaria and other vector-borne diseases, there are great opportunities for cross-learning and capacity development.

There are also several private and public sector partners active in the region, collaborating with governments and institutions to find solutions to these challenges. Through networks such as ZERO by 40, these initiatives can focus on both the immediate needs with existing tools, and longer-term needs in the development of new tools. Finally, in terms of legislation, regional heads of state have committed to malaria elimination by 2030, and most recognise and prioritise the threats of *Aedes*-borne diseases. The 'Landscape Reports' have described human resource, market access and regulatory challenges, but there is a strong political will to solve these problems.

IVCC will not address all these issues alone. Working in concert with national governments, implementing partners and regional structures, IVCC will endeavour to develop the necessary tools and processes, which can then be broadened region-wide to reduce the threats of vector-borne diseases and improve health security in the Indo-Pacific.

Selected country profiles, including disease burden, market access and regulatory landscape

CAMBODIA

- **Disease burden**

Malaria increased in 2017 and 2018; epicentre for drug resistance; forest-related with predominant outdoor/residual transmission. Strong "net culture" with interest in developing personal protection tools as part of "forest packs". Increasing dengue burden 14,000 cases p.a. and spreading to rural areas. Low MoH surveillance and control capacity. IHR capacity for VBD lacking.

- **Market access**

Heavy donor investment for malaria, almost none for dengue. Several strong R&D and implementation partners.

- **National public health pesticide regulations**

Agriculture pesticides regulated by Ministry of Agriculture, Fisheries and Forestry; no regulations for public health pesticides. Large, semi-regulated PCO sector (much related to tourism).

INDONESIA

- **Disease burden**

Malaria concentrated in eastern provinces (Papua, NTT). High occupational risk for forest workers and miners. LLIN usage high, IRS minimal. Strong private sector VC programmes.

Dengue hyperendemic in 400 of 497 districts; most vulnerable ASEAN country. Large World Mosquito Program investment for Wolbachia.

- **Market access**

GoI funding increase from 6% in 2011 to 52% in 2016; several major international donors. Large consumer market for pest control products. R&D and implementation partners (including for spatial repellents) with universities and private sector.

- **National public health pesticide regulations**

Regulated through Ministry for Agriculture; lengthy registration process; in-country trial requirement. Retail licensing required with OTC licence granted by MoH. PCO licence essential. Requires Free Sales Certificate and registration of trademark. Analytical test report from GLP accredited test lab in country is mandatory. Data from other countries is not acceptable.

MALAYSIA

- **Disease burden**

Malaria: 4,000 cases in 2017, 88% *P. knowlesi* (increase of 80% over 2016), most among forest-goers and forest-fringe habitations, especially Sabah. Reliance on free LLIN distribution, IRS some larviciding and trial of ORS. Strong national programme

Dengue endemic in 2017: 84,000 cases, 180 deaths. Strong national programme including GoM-supported community-based programmes.

- **Market access**

GoM funds 100% VBDC programmes (malaria US$48m in 2017), including research grants for P.k. Strong partnership among MoH, universities and research institutes. Large MSc entomologist cadre posted to States. Some joint programmes with private sector for *Aedes*.

- **National public health pesticide regulations**

Ministry of Agriculture Pesticides Board responsible. Efficacy trials by USM and IMR in collaboration with MoH. Retail licence required; need permit for advertising. PCO sector well monitored, including training and certification. Strong Pest Control Association of Malaysia collaboration with MoH and municipal vector control programmes. Regional test reports are accepted if done following internationally accepted test protocols. Regional testing should be done in countries which have similar pest profile and climatic conditions.

MYANMAR

- **Disease burden**

Major malaria decline in recent years, down to just 85,000 cases in 2017, mostly forest-related mobile and migrant populations. Risk of spread of multi-drug-resistant *P falciparum* outside the GMS through India and Bangladesh. Strong net culture. Reliance on free LLIN distribution, some IRS; reviewing forest packs and recent trials on topical repellents. Surveillance and control capacity needs strengthening.

- **Market access**

Malaria control funded largely by major international donors, Global Fund and PMI, but large out-of-pocket expenditures for prevention and treatment in private sector. Good government and implementing partner collaboration, including some with R&D infrastructure. Entomology posts exist, but there are many vacancies, resulting in low capacity. *Aedes* programmes need strengthening.

- **National public health pesticide regulations**

Ministry of Agriculture, Pesticides Registration Board responsible for regulation. Efficacy trials capacity for public health pesticides not available; reports from other countries accepted. Chemical analysis can be conducted. Retail licence for household pesticides has no fee. Need licence to advertise. Lengthy process for innovative products, but local NGO recently registered Insecticide Treated Clothing in collaboration with international manufacturer.

PAPUA NEW GUINEA

- **Disease burden**

More than 90% of population reported in "high malaria transmission" areas, with 500,000 cases reported in 2017. LLINs are the primary intervention (75% coverage, 50% usage). IRS has been halted. Dengue often undiagnosed and unreported, but *Aedes* prevalent in urban areas.

- **Market access**

Most funding from Global Fund through Rotarians Against Malaria, DFAT and private sector, especially the mining and extraction sector, where there are several private vector control initiatives.

- **National public health pesticide regulations**

Ministry of Environment requires import permit for pesticides, but there are no regulations or guidelines for public health pesticides and a lack of testing capacity.

VIETNAM

- **Disease burden**

Malaria becoming increasingly focal. In 2015, 211 communes had an API > 1, compared to 488 in 2011. Malaria deaths decreased from 20 in 2007 to 3 in 2016. Between August 2016 and July 2017, just six out of 63 provinces accounted for 66% of total confirmed malaria cases and 81% of confirmed *P. falciparum*. Binh Phuoc alone accounted for 39% of confirmed *P. falciparum*. As elsewhere in the GMS, increasingly malaria is becoming an occupational disease predominantly affecting men. Insecticide resistance has been detected in secondary malaria vectors including *An. epiroticus, An. sinensis and An. vagus. An. minimus* has shown pyrethroid resistance in Northern Vietnam, and there are indications of possible pyrethroid resistance in *An. dirus* in Central Vietnam. Dengue continues to exert a very high health and economic cost in Vietnam, with all four serotypes circulating. Pyrethroid resistance among *Ae. aegypti* populations is prevalent, especially in the south, where greater volumes of pyrethroid insecticides have been used. There is a lot of work on *Wolbachia*, with the World Mosquito Program Asia Regional Hub, based in Ho Chi Minh City.

- **Market access**

LLINs and Hammock Nets (popular among forest-goers in Vietnam and Cambodia) are procured through Global Fund. As in the other GMS countries, there is a very high ownership and use of untreated nets from the market. Uniquely, Vietnam continues to successfully conduct community re-treatment programmes with products including the ICON 2.5CS, approved by WHOPES in 1999. IRS continues, with about a half million population protected in 2016. Vietnam has a very strong network of training and research institutions working with both malaria and *Aedes*-borne diseases, and significant malaria initiatives working with at-risk groups including military and forest rangers.

- **National public health pesticide regulations**

Requires Free Sales Certificate. All documents should be translated into Vietnamese. Analytical test report should be from an ISO 17025 accredited lab. In-country evaluation of public health pesticides is mandatory. Would be complex, as VC products regulated under Animal or Human Health Directorate.

Research capacity in selected countries, not including implementing partners

CAMBODIA	Armed Forces Research Institute of Medical Sciences (AFRIMS) Institute Pasteur/Cambodia (IP/C) Institute of Tropical Medicine (ITM) Antwerp Malaria Consortium (MC) Médecins Sans Frontiéres (MSF) University of South Florida (USF) US National Institutes of Health (NIH) US Naval Medical Research Unit-2 (NAMRU-2) US President's Malaria Initiative (PMI)
CHINA	Chinese Center for Disease Control and Prevention (iCDC) Beijing Institute of Microbiology and Epidemiology Jiangsu Institute of Parasitic Diseases (JIPD)
INDONESIA	Eijkman Institute for Molecular Biology Gadjah Mada University Litbangkes, Ministry of Health Research Institute Universitas Hasanuddin University of Notre Dame (UND) University of California, San Francisco (UCSF)
MALAYSIA	Institute for Medical Research, Ministry of Health (IMR) University of Malaya (UM) University of Malaysia, Sabah (UMS) Universiti Sains Malaysia (USM), Penang
MYANMAR	Department of Medical Research, Ministry of Health and Sports (DMR) Duke University Japan International Cooperation Agency (JICA) US President's Malaria Initiative (PMI)
PAPUA NEW GUINEA	Australian Defence Force Malaria and Infectious Disease Institute Burnet Institute James Cook University (JCU) Papua New Guinea Institute of Medical Research (IMR) University of Queensland (UQ)
SRI LANKA	MoH Anti Malaria Campaign (AMC) and National Dengue Unit University of Kelaniya University of Notre Dame (UND)
THAILAND	Armed Forces Research Institute of Medical Sciences (AFRIMS) Kasetsart University (KU) Mahidol Oxford Research Unit (MORU) Shoklo Malaria Research Unit (SMRU)
VANUATU	Australian Defence Force Malaria and Infectious Disease Institute
VIETNAM	Institute of Malariology, Parasitology, and Entomology Quy Nhon (IMPE-QN), Ministry of Health Institute of Tropical Medicine (ITM) Antwerp National Institute of Malariology, Parasitology and Entomology (NIMPE), Ministry of Health Oxford University Clinical Research Unit (OUCRU) University of California, San Francisco (UCSF) University of Massachusetts, Amherst

Registration complexity of different vector control product types

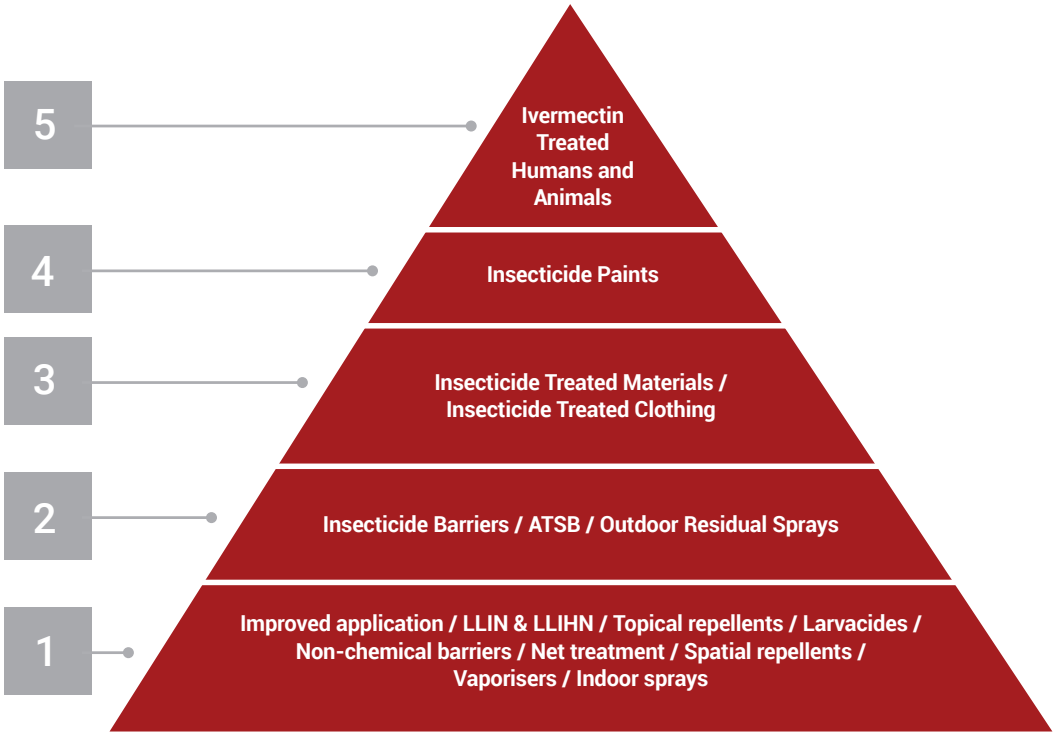
(5) Most complex, as it would be regulated under Animal or Human Health Directorate.

(4) Needs extensive testing with specifications and data requirements to be finalised.

(3) No categories, but some have been approved for military use. MoH should help MoA understand the importance of these newer products.

(2) Can be considered with some minimal data generated. ORS needs additional environmental safety evaluation. Net barriers would be a label extension of ITNs, but this too would need some additional data generated.

(1) Registered as recommended public health products in several countries.



Complexity in registration

It is important that the regulatory processes in the countries create legislation to fast-track certain low-risk products or use extensions of certain existing product categories.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