HLSP Institute

Malaria in the Asia Pacific region: setting the scene for global health and development?

Sean Hewitt

May 2014

This paper aims to understand the new malaria initiatives in the Asia Pacific region in context.

Despite an overall improvement in the malaria situation, the burden of disease remains unacceptably high. Control and elimination efforts face a daunting array of challenges, from technical and programmatic issues, political and economic constraints, to the rapidly evolving donor and partner landscape, and environmental changes.

In response to these challenges a new, regionally-led response to malaria has emerged. Although focussed on a specific disease, these developments offer some insight into how the global aid architecture may evolve in future.

HRF Health Resource Facility for Australia's Aid Program

HLSP

HLSP Institute 10 Fleet Place | London EC4M 7RB | United Kingdom
T +44 (0) 20 7651 0302 | E institute@hlsp.org | W www.hlsp.org/institute

About the Health Resource Facility

The Health Resource Facility is an Australian Government funded Initiative managed by Mott MacDonald (Mott MacDonald Australia Pty Ltd)

Email: helpdesk@australianaidhrf.com.au

Tel: +61 (0) 2 6198 4100

Physical address:
The Health Resource Facility for Australia's Aid Program
Mott MacDonald (Mott MacDonald Australia Pty Ltd)
15 Barry Drive
Turner
ACT
2612
Australia

Postal address:
The Health Resource Facility for Australia's Aid Program
Mott MacDonald (Mott MacDonald Australia Pty Ltd)
GPO Box 320
Canberra City
2601
Australia

Acknowledgments

This paper is based on an Australian Government Department of Foreign Affairs and Trade (DFAT) funded report summarising the evidence base to support investing in malaria control and elimination in the Asia Pacific region (Palmer et al, 2013). The report was further developed into this paper by Sean Hewitt and Rebecca Dodd, formerly a member of the Health Resource Facility team.

Introduction

Over the last two years malaria has become an increasingly important priority of health development efforts in the Asia Pacific region. High-level political interest has been sparked by renewed hopes of elimination in some countries and the challenge of resistance to artemisinin, the key ingredient of modern malaria drugs, in others. Significant new regional funding for the disease has been announced from the Global Fund, the Asian Development Bank and the Australian Government. And no fewer than four new regional malaria initiatives are in the process of being established.

These rapid developments provide some insight into the health aid agenda in the post-MDG world, both in terms of which health issues will remain priorities, and how the aid model may be changing. The newly-established Asia Pacific Leadership for Malaria Alliance for example, involves 'recipient' countries as equal partners alongside donor countries in co-ordinating the malaria response. While there remains some uncertainty about how the new initiatives will be co-ordinated (with each other and with global efforts), the establishment of a distinct Asia Pacific response to malaria is a clear sign of the region's increasingly prominent role in determining the global development agenda.

This paper aims to understand the new malaria initiatives in the Asia Pacific region in context. It looks at the burden of malaria in the region and its impact, provides a summary of the evidence on the effectiveness of malaria prevention and control intervention in the region, looks at regionally-specific challenges and threats, and provides an overview of regional financing for the disease. It then summarises the latest developments in relation to the four new regional initiatives at the time of writing this paper, although it should be noted that that these are evolving and changing rapidly. The paper then makes a tentative effort to tease out the implications for global health development.

The impact of malaria in the Asia Pacific

Health impact

Over half the world's population is considered to be at risk of malaria. In 2010, it was the eleventh most significant cause of death (Lozano et al, 2012) and the cause of the seventh highest number of disability adjusted life years globally (Murray et al, 2012). According to the estimates in the World Malaria Report 2013 there were 207 million malaria cases and 627,000 malaria-related deaths in 2012 (WHO, 2013).

Children under-five are most at risk, accounting for around 77% of malaria deaths in 2012 (WHO, 2013). Pregnant women are also particularly vulnerable as pregnancy reduces immunity, increasing susceptibility to infection and increasing the risk of illness, severe anaemia and death (Rijken et al, 2012). Maternal malaria also heightens the risk of spontaneous abortion, stillbirth, premature delivery and low birth weight.

the World Health Organization (WHO) estimates that In the Asia Pacific region in 2012 there were around 28 million malaria cases and 45,500 malaria related deaths, nearly one third of which were in children under the age of five. The highest numbers of malaria cases (presumed and confirmed) were estimated to be in Pakistan (4.3 million), followed by Indonesia, India and Papua New Guinea (PNG). While the total number of cases is typically higher in the high-population Asian countries, the incidence of malaria per 1,000 population is often highest in the Pacific (see Table 1), with Vanuatu, Solomon Islands and PNG reporting the highest incidence in the region.

Table 1: Malaria statistics from 22 countries in the region[1] in 2012 as reported in the World Malaria Report 2013

	Population (millions)	Presumed and confirmed malaria cases (2012)	Incidence of malaria (/1000)	Country classification phase
Afghanistan	29.8	391,365	13.1	Control
Bangladesh	154.7	29,518	0.2	Control
Bhutan	0.7	82	0.1	Pre-elimination
Cambodia	14.9	45,553	3.1	Control
China	1337.1	2,718	0.0	Control
DPR Korea	24.8	21,850	0.9	Pre-elimination
India	1236.7	1,067,824	0.9	Control
Indonesia	246.9	2,051,425	8.3	Control
Korea (South)	49	555	0.0	Elimination
Lao PDR	6,645,827	46,819	7.0	Control
Malaysia	29.2	4,725	0.2	Pre-elimination
Myanmar	52.3	480,586	9.1	Control
Nepal	27.5	70,272	2.6	Control
Pakistan	179.1	4,285,449	23.9	Control
PNG	7.2	643,214	89.7	Control
Philippines	96.7	7,133	0.1	Control
Solomon Islands	0.5	57,296	104.3	Control
Sri Lanka	21.1	93	0.0	Elimination
Thailand	66.8	32,569	0.5	Control
Timor Leste	1.1	6,148	5.5	Control
Vanuatu	0.2	36,708	148.5	Control
Vietnam	90.8	43,717	0.5	Control
Totals	3,904.2	9,326,619	2.5	

Source: WHO 2013.

Economic impact

The direct and indirect costs associated with malaria are a substantial burden for poorer households (Russell, 2004). Reducing the malaria burden results in improved living standards and increased household income (as demonstrated in Vietnam by Laxminarayan, 2004).

The macro-economic impact of the disease at country level can also be significant. Malaria is responsible for an estimated average annual reduction of 1.3% in economic growth in countries with the

[1] This review is based on background research commissioned by the Australian Government in preparation for and follow up to the *Malaria 2012* conference http://malaria2012conference.com/. The conference considered data and information from 22 countries, which also constitute 'the region' in this paper: Afghanistan, Bangladesh, Bhutan, Cambodia, China, DPR Korea, India, Indonesia, South Korea, Laos, Malaysia, Myanmar, Nepal, Pakistan, PNG, the Philippines, Solomon Islands, Sri Lanka, Thailand, Timor Leste, Vanuatu and Vietnam.

highest burden (Gallup and Sachs, 2001). Several studies have found that eliminating malaria has a profound effect not just on health, but also on education and productivity. For example, a study that investigated the malaria elimination campaigns in the US in the 1920s and in Brazil, Columbia and Mexico in the 1950s concluded that "persistent childhood malaria infection reduces adult income by 40-60%" (Bleakley, 2006). Another study In India found that males who benefited from malaria elimination in early childhood enjoyed higher per capita household consumption as adults (Cutler et al, 2010).

Box 1: Epidemiology of malaria in Asia Pacific and populations at risk

There are two main types of malaria affecting humans: falciparum malaria and vivax malaria. Globally, similar numbers of people are at risk of contracting each (2.5 billion for falciparium and 2.6 billion for vivax in 2010) however 91% of all malaria cases are falciparum, (WHO, 2012 and Guerra et al, 2006a) and falciparum is associated with a higher mortality rate than vivax malaria.[2]

The epidemiology of malaria in the Asia Pacific is highly complex. Vivax malaria extends further north than falciparum malaria, into areas of central China and the Korean Peninsula (as a result of the vivax parasite's ability to survive cooler temperatures than the falciparum parasite during its mosquito-borne life-cycle stages). Elsewhere in the region falciparum tends to dominate, although this situation is gradually changing because falciparum malaria is more amenable to control than vivax. Vivax malaria is thus becoming the dominant strain in areas where malaria control measures are being implemented successfully. Falciparum malaria remains more of a problem in the least accessible areas where control efforts are less effective and access to medicines is poor. As a result malaria related mortality tends to disproportionately affect the most marginalised population groups (Meek, 1988).

In many **tropical areas** the primary malaria vectors cannot survive without dense shade and high humidity (Cui et al, 2011a) so intense transmission is largely restricted to forested areas. Transmission tends to be perennial with seasonal or periodic peaks associated with rainfall or sometimes linked to population movements. Transmission may occur in less densely forested areas as a result of secondary vectors, but generally it is much less intense. In forested regions, epidemics tend to be localised. Five main categories of people are affected in these areas: ethnic minority groups practicing slash and burn agriculture (all age groups are exposed but the disease burden in highest in children, as adults have high levels of immunity); forest fringe inhabitants (adult males visiting the forest and staying overnight to collect timber, hunt or collect forest products are most at risk); rubber plantation workers (exposure is highest among adult males who start work well before dawn); temporary migrants and seasonal workers (generally adults and predominantly adult males are most at risk); and new forest settlers (all age groups are affected but risk diminishes as forest is cleared).

In endemic areas in the **north of the region**, malaria vectors live in open countryside. The speed of development of malaria parasites in their mosquito vectors is temperature dependent and at lower temperatures development stops altogether. As a result, transmission is markedly seasonal in temperate areas and in the most northerly extent of malaria's range, in central China and the Korean Peninsula, there is only a very short transmission season. These northern areas are however prone to large-scale epidemics. In central China all age groups in affected rural communities are at risk. In South Korea transmission takes place mainly along the border with the People's Democratic Republic of (DPR) Korea and therefore primarily affects soldiers.

In **tropical coastal areas** the primary malaria vectors are associated with brackish water. In these areas malaria transmission tends to be intense and perennial. Both rural and semiurban communities are affected; all age groups are at risk but immunity develops with age.

Even within the diversity described above, the epidemiology varies considerably from one population group to another. Substantial variations are found not only along broad environmental gradients, but also between villages only a few kilometres apart and even between different clusters of houses within the same villages. In many cases the different situations require different malaria control strategies, adapted to risk group and vector behaviour, local health infrastructure and environmental conditions.

[2] This is due to differences in the geographical range of each species of Plasmodium (related to protective traits in some human populations and differences in the life-cycle and temperature tolerance of each parasite species) and due to differences in the seasonality of transmission and the vectorial capacity of mosquitos in different geographical settings.

Malaria control: lessons from the Asia Pacific

Despite the challenging and varied epidemiology of malaria described in Box 1, significant progress is being made across the region. A dramatic increase in funding since 2000 (see Section 6) has supported the progressive roll out of malaria control interventions across the region, leading to significant reductions in the malaria burden. In the WHO Western Pacific Region for example, between 2000 and 2012 the estimated number of malaria cases fell by 33%, while the estimated number malaria deaths fell by nearly 50%. During the same period in the WHO South East Asia Region the estimated number of malaria cases fell by 13% and malaria deaths fell by 14% (WHO, 2013).

Strong political commitment, technical expertise and increased resources have been key elements in the success of control programmes (WHO, 2010). In addition, a range of innovative approaches to service delivery have been developed to get key interventions to target populations. These include: provision of diagnosis and treatment for malaria at community level in remote areas; increased engagement with the private sector to improve the quality of their service provision; modelling strategies to improve quantification of commodity requirements; and application of mobile communications technology to improve the speed and accuracy of reporting (Zhao et al, 2011; Tatem et al, 2011; Meankaew et al, 2011).

Box 2: Malaria control and elimination

Malaria **control** is defined as reducing malaria morbidity and mortality to levels which are locally acceptable through the use of interventions to prevent and cure the disease. Globally, of the 101 countries or territories with malaria, 78 are classified as being in the control stage as are 17 of the 22 countries included in this report (see Table 1).

Malaria **elimination** is defined as reducing the number of new cases of locally acquired malaria infection within a specific geographic area to zero through the use of deliberate interventions.

Malaria **eradication** is the reduction of the number of new malaria cases globally to zero through progressive elimination in countries where it is feasible.

Sources: Roll Back Malaria Partnership, 2008; WHO, 2013.

While the improved quality and coverage of malaria control interventions has undoubtedly had a substantial impact on the malaria burden, malaria control efforts cannot take all of the credit. Deforestation has played a significant role in reducing transmission in specific areas (Colwell et al, 2011; Guerra et al, 2006b; Walsh et al, 1993) while socioeconomic development has contributed to the decline of malaria more generally, although this is not well documented (Worrall et al, 2005).

The key interventions to control malaria in the region are both effective and affordable: **long lasting insecticidal nets** (LLINs), **indoor residual spraying** (IRS), **early diagnosis and appropriate treatment** (EDAT).

The following section provides a summary of the evidence on the effectiveness of these interventions in the Asia Pacific region, the extent to which they are being implemented, and an overview of approaches to surveillance.

Prevention

Insecticide treated bednets (ITNs), which form the core of malaria prevention efforts in the region, have been shown to reduce malaria morbidity and mortality by as much as 50% and 17% respectively among children in parts of Sub-Saharan Africa. The evidence base supporting the use of ITNs in the Asia Pacific region is not as robust as that from Africa. However a number of randomised control trials in Pakistan and in the Greater Mekong sub region (Thailand, Myanmar and Cambodia) have demonstrated good protective effect (Lengeler, 2004a) (See Annex, p. 14).

There is a strong tradition of bednet use in South-East Asia for privacy, and also protection against nuisance mosquitoes. ITNs, which were introduced in the 1990s, have now been superseded by LLINs

and all but one country in the region has adopted WHO's bednet coverage targets (WHO, 2012) i.e. that ITNs/LLINs should be distributed to all those at risk of malaria infection, not just women and children.

Bednet ownership has been scaled up through periodic free mass distributions targeting all endemic areas. As a result, LLIN coverage has increased dramatically in some countries, although in others it remains unacceptably low and there are still areas of high malaria risk where vulnerable populations remain unprotected. Further, those areas that have achieved high levels of distribution need to maintain it, ideally by integrating distribution into ante-natal care services, health facilities, EPI (immunisation) campaigns etc. Disruptions to Global Fund funding, resulting from its restructuring, threaten the replacement of expiring LLINs. Given the three-year lifespan attributed to most LLINs there is a risk that current coverage levels could fall dramatically in a very short space of time.

Indoor residual spraying (IRS) is the application of long-acting insecticides to the walls and ceilings of houses and animal sheds in order to kill adult vector mosquitoes that land and rest on these surfaces. IRS reduces the lifespan of vector mosquitoes so that they do not have time to transmit malaria parasites from one person to another, and reduces the population of vector mosquitoes. Some insecticides also repel mosquitoes and so reduce the number of mosquitoes entering a sprayed room.

IRS is recommended by WHO's Global Malaria Programme as a major means of malaria vector control. IRS has helped to eliminate malaria from parts of Asia (Chareonviriyaphap et al, 2000), Russia, Europe, and Latin America (Schiff, 2002; Lengeler and Sharp, 2003; Roberts et al, 2004) and is still used to control malaria on a large scale in sub-Saharan Africa. (Further evidence is provided in the Annex).

National Malaria Control Programmes use IRS in two ways. Mass preventive IRS is a routine response in areas of consistently high annual malaria incidence. Focal responsive IRS is an emergency response to malaria outbreaks in endemic areas or to confirmed foci of malaria transmission in areas targeted for elimination (or for containment of artemisinin resistance).

Of the 22 countries covered by this review, 18 reported having IRS as a primary vector control intervention during 2013 (WHO, 2013).

Diagnosis and treatment

Efforts to prevent mosquito biting can only ever be partially successful. **Early diagnosis and appropriate treatment** (EDAT) of malaria infections is an essential element of control efforts.

Malaria microscopy remains the gold standard for malaria **diagnosis** and the diagnostic method of choice for larger health facilities especially in areas targeting elimination. In skilled hands microscopy can differentiate malaria species and quantify the level of parasites in the blood, allowing better-tailored clinical management. Rapid diagnostic tests (RDTs) also provide parasite-based diagnosis, and can be done at peripheral health facilities where there are no microscopists, at community level and in the private sector (Wongsrichanala et al, 2007). RDTs also provide a useful backup diagnostic method if, for example, a facility's microscopist is absent or if there is a power failure. Their development has been a very major advance in malaria control efforts.

The current global target for diagnosis of malaria is that all suspected cases receive a confirmatory test (either with microscopy or RDT). Some national strategic plans reflect this target, but most aim for 80% coverage or higher. Over the last 10 years RDTs have been progressively rolled out to most endemic areas in the region, greatly increasing overall diagnostic capacity (WHO, 2009a). Thirteen of the 22 countries in this review report rates of confirmatory diagnosis for malaria which are over 50%, although rates vary among countries, with diagnostic coverage is as low as 3% in Nepal (WHO, 2013).

The drugs traditionally used to **treat** uncomplicated falciparum malaria (chloroquine and sulphadoxine-pyrimethamine) have become ineffective in many parts of the world due to the development of drug resistance, so WHO now recommends Artemisinin-based Combination Therapies (ACTs). ACTs are highly effective at treating falciparum malaria in most places and they are thought to be relatively safe with few serious side effects (Sinclair et al, 2009). However, resistance to artemisinin has now also been detected (see section 5); this represents a major threat to global and regional malaria control efforts. All 22 countries covered in this review have now adopted an ACT as first-line treatment for uncomplicated falciparum malaria and most have now banned the use and sale of oral artemisinin-

based monotherapies (in order to minimise the risk of artemisinin resistance). In some places chloroquine is still being used to treat vivax malaria but it too is increasingly being treated with ACTs.

Although EDAT has tended to be provided primarily through static health facilities, recently access has been substantially improved in some countries through a variety of community-based initiatives (Yeung et al, 2011 and Service, 1993). Community-based delivery of EDAT has had particularly high impact on those marginalised populations bearing the greatest burden of malaria.

The private sector also plays a key role in the delivery of malaria treatment in many countries. Even so, in most of these very little is known about the role, reach, quality or affordability of treatments by private providers. Greater engagement with the private sector is thus key to the success of national malaria control efforts.

Communication

Utilisation of services is key to effective malaria control: it is generally accepted that at least 80% of people must sleep under their ITNs in order to achieve a 'community effect' (Howard et al, 2000); people must cooperate fully with spray-teams in order for IRS campaigns to achieve the coverage required; and people must promptly seek diagnosis and treatment for fever if EDAT services are to be effective. Altering the behaviour of target populations through effective communication and education can increase coverage considerably and thereby increase the cost-effectiveness and impact of interventions (Rimal et al, 2009).

All countries in the region support communication measures to maximise utilisation of their malaria prevention and case management services. As funding for malaria has increased in recent years, communication efforts have shifted from the traditional leaflet/poster based approach to Information, Education and Communication (IEC) and Behaviour Change Communication (BCC) for example through the use of mass media, music, song, dance and drama. However it should be noted that the impact of these interventions is not yet well documented.

Surveillance

Surveillance is central and critical to malaria control, underpinning the delivery of interventions. During the 'control phase' of operations, surveillance is used to target and assess the impact of interventions. In this phase surveillance does not need to be perfect but should be sufficiently robust to provide an overview of the epidemiological situation.

When programmes move into the 'elimination phase' (see below) cases occur more sporadically or in distinct foci and imported cases may comprise a significant proportion of all cases. In this setting surveillance is used to stop local transmission. Case reporting needs to be as rapid and accurate as possible with all malaria infections including asymptomatic cases being detected and treated to prevent onward transmission. This is accomplished by first identifying all suspected transmission foci using data from public and private sector health facilities, then investigating whether the case was locally acquired, and finally, if local transmission is confirmed, carrying out intensified surveillance (to detect symptomatic and asymptomatic cases) and implementing control activities until the focus of transmission is eliminated.

Although completeness of reporting from health facilities is relatively high in Asia (74%) and the Pacific (78%) (WHO, 2013), the quality of data is variable and timeliness is often poor, as many health information systems need upgrading. However, there has been significant progress in some countries, notably Thailand, Cambodia and China (see Annex). A key shortcoming is that malaria surveillance in the region does not currently incorporate data from the private sector.

New push towards elimination

In recent years, following the success of control efforts, elimination has become a real possibility for many countries in the region. It has thus become something of a rallying point for global malaria control efforts, attracting new financing, political support and attention.

In 2007 the Bill and Melinda Gates Foundation launched a new push towards malaria eradication, with the support of WHO and ministries of health in malaria endemic countries. A Global Malaria Action Plan (GMAP) was developed, with the long-term goal of malaria eradication and a shorter-term goal of elimination. Of the 22 countries covered in this review 16 have adopted malaria elimination as their eventual goal (Lynch and Hewitt, 2012).

The current elimination effort is much better placed to succeed than previous efforts. There are new insecticides, drugs and diagnostic tools as well as new technologies. Even so, the evidence base on what works to achieve elimination is much less robust than for other aspects of malaria control, and there are also significant challenges to overcome. Asymptomatic malaria cases for example present a significant barrier: there is no large-scale operationally feasible method for detecting these individuals, who act as parasite reservoirs and a source of continued transmission (Sullivan, 2010). Various methods including mass drug administration (MDA), mass screening, treatment and follow-up (MSAT), and focal screening, treatment and follow-up (FSAT) have been tried but with mixed results (WHO, 2010 and WHO, 2009b). Malaria textbooks recommend MDA but only in a very few instances has the required level of coverage and compliance been attained for it to have a long lasting impact. Similarly MSAT and FSAT have turned out to be so costly and labour intensive that few programmes can afford to implement them.

Even when elimination efforts are successful, there will always be potential for re-introduction of malaria from areas of continuing transmission (until global eradication is achieved). Yet there is limited information on the scale, rate and impact of human migration on malaria transmission. Understanding and identifying networks of human transit and migration within the Asia Pacific region will thus be particularly important in the future, especially in light of emerging resistance to key antimalarial drugs (WHO, 2011).

Finally, the level of effort required to achieve and then sustain elimination is commonly underestimated by countries (Mills et al, 2008). A considerable strengthening of health systems is needed to ensure any new case is detected (Mendis et al, 2009). Also it is notoriously difficult to sustain political commitment and maintain funding as elimination moves from the ‘pre-elimination’ to the ‘elimination’ and ‘prevention of reintroduction’ phases. There are several well-documented cases of reduced malaria burden leading to political complacency, withdrawal of funding and ultimately major resurgence of disease. In Vietnam for example, reduced emphasis on the National Malaria Elimination Programme following political changes in the late 1980s led to a major epidemic in 1991, which claimed almost 5,000 lives. Similar problems occurred in Sri Lanka in the 1970s (Feachem et al, 2010). Strenuous efforts are thus required to secure continued funding once the malaria situation starts to improve.

Emerging threats: resistance and vivax

Control and elimination efforts in the region face a number of emerging threats including resistance to the insecticides used on bednets, resistance to the artemisinin-based components of ACTs and the problematic issues surrounding the radical treatment of vivax malaria.

Insecticide resistance. At present pyrethroid insecticides are the only insecticides suitable for use with LLINs. Use of pyrethroids for IRS is therefore a serious concern as it could accelerate the development of resistance and thereby jeopardise the future effectiveness of LLINs (WHO, 2013). Conversely, use of IRS with a non-pyrethroid could mitigate the development of resistance to pyrethroid. DDT is still by far the best insecticide for IRS in countries where vectors are DDT susceptible, being cheaper, longer-lasting and more effective than alternative insecticides (Walker, 2000). However for environmental and other reasons many countries have switched to less-effective pyrethroid insecticides. Use of pyrethroids in agriculture is also a concern as this too can lead to the development of resistance (Roberts and Andre, 1994). Improved multi-sectoral insecticide management systems need to be put in place region-wide in order to ensure safe use and to reduce the chances of resistance developing. There is also an

urgent need to develop new non-pyrethroid insecticides suitable for use with LLINs, and to improve monitoring of potential insecticide resistance (Magesa et al, 1994).

Artemisinin resistance. The single biggest obstacle to effective malaria control and eventual elimination is the presence and possible spread of resistance to artemisinin (Cui et al, 2011b). Artemisinin resistance was first suspected on the Thailand-Cambodia border in 2006 (Yeung et al, 2009) and since then has been noted in a number of sites in the Mekong region. Although there has been good progress over the last few years in reducing the incidence of falciparum malaria on the Thailand-Cambodia border, resistance is no longer limited to this area. It is now also present on the Myanmar-Thailand border (Na-Bangchang et al, 2010) and in parts of southern and central Vietnam (Thanh et al, 2010). It is not known whether the resistant strains in these areas have spread from an original focus or have arisen independently.

Experts agree that there is a limited window of opportunity to contain or eliminate the resistant parasites before they spread to areas of higher transmission, putting at risk recent progress in malaria control (WHO, 2012). There are no other practical antimalarial medicines available that offer the same level of efficacy and tolerability as ACTs, and there are few promising alternatives in the immediate research and development pipeline (Muregi et al, 2011). Efforts to contain and prevent artemisinin resistance at global, regional, national and local levels thus need to be expanded, intensified and better coordinated.

Vivax malaria. It is widely believed that vivax malaria is a much less serious infection than falciparum and that it can be effectively treated with readily available affordable drugs (indeed for a long time it was referred to as “benign tertian malaria”). This dogma has led to its neglect. In fact vivax malaria is a larger and more serious threat than generally appreciated, particularly in areas where it is resistant to chloroquine (Baird, 2007). Recent studies have demonstrated that it can result in a severe disease resembling the cerebral malaria normally associated with falciparum (Woitsch, 2004).

The population at risk of vivax malaria is particularly high in Asia and, as efforts to control falciparium progress, it is increasingly becoming the predominant species of malaria in many areas. A key challenge is that primaquine, the only practical drug available for the radical treatment of vivax malaria, can cause a severe haemolytic reaction in patients who are deficient in the enzyme ‘glucose 6-phosphate dehydrogenase’ (G6PD). G6PD deficiency, which is common in some populations in Asia, requires a laboratory-based diagnostic test for identification (Price et al, 2011). Although primaquine is widely available in the public sector, health staff who do not have access to G6PD testing are understandably reluctant to use it. The vast majority of vivax malaria cases thus never receive radical treatment.

Point-of-care G6PD tests are currently in the late stages of development (Domingo et al, 2013) and it is hoped that as this new technology is rolled-out it will gradually lead to a very significant increase in the proportion of vivax patients receiving radical treatment and in a correspondingly significant reduction in vivax incidence.

Partner support to malaria in the Asia Pacific region

For all the reasons discussed so far, malaria remains a major public health threat in the region, and one that requires a co-ordinated response between countries, not least to address the emergence of drug resistance in border areas.

Financing

Globally, development assistance for malaria has increased dramatically since 2000, particularly in endemic countries, linked in part to the establishment of the (then) new funding mechanisms such as the Global Fund. According to WHO (2013), in 2013 international disbursements to malaria endemic countries were estimated to be nearly $2 bn. The Global Fund accounted for an estimated 50% of total external funding for malaria, while DFID, the President’s Malaria Initiative, the World Bank and other donors accounted for the rest.

Although the Global Fund Round 11 was cancelled in November 2011 due to financial difficulties, the end of 2013 saw the largest Global Fund replenishment yet, with donors pledging $12 bn of which 32% is expected to be allocated for malaria. A new funding model has also been announced by the Global

Fund whereby an indicative amount of funding is assigned to countries based on their malaria burden and ability to pay for malaria control. What these changes will mean for the Asia Pacific region however is not yet clear, but it seems that if funding commitments from all donors are honoured, there will be $2.3 bn available for malaria control globally per year between 2014 and 2016.
Traditionally, the Asia Pacific region has received a relatively small share of global resources, in part because of the lower burden of mortality associated with vivax malaria relative to falciparum, and because of donor focus on high burden countries in Sub-Saharan Africa (Baird, 2077). With the exception of PNG, international support for malaria in the region has not increased significantly since 2007. Further, approximately two thirds of funding for malaria in the region comes from governments, compared to less than 15% for Africa (Snow et al, 2010). GMAP estimated that the shortfall in funding required to achieve MDG 6(c), to have halted by 2015 and begun to reverse the incidence of malaria and other major diseases, was higher in the Asia Pacific region than in any other region: an estimated $2.5 bn for the period 2011-2020.

New initiatives

The relative neglect of malaria in the Asia Pacific region has catalysed a regionally-led focus on the disease, which has intensified over the last 12-18 months. Beginning with a major regional conference hosted by Australia in November 2012 ('Malaria 2012'), work has since begun on the development of four new initiatives.

1. **A Financing Partnership Facility:** In 2013, the Asian Development Bank (ADB) established a regional Malaria and Other Communicable Disease Threats Trust Fund. In the longer term this is envisaged as a fund for communicable disease; however in the short term the focus will be "*full support to malaria elimination and containment of artemisinin resistant malaria*" (ADB, 2013). Australia is providing $16.3 m and the UK $19.4 m to the trust fund, although additional contributions are being sought from other development agencies, the private sector and foundations (Lynch, 2014).

2. The Facility is linked to and will support the secretariat of the **Asia Pacific Leaders Malaria Alliance (APLMA)**, established at the 2013 East Asia Summit and co-chaired by the prime ministers of Vietnam and Australia. APLMA has some similarities to the African Leaders' Malaria Alliance, established in 2009 and convened by the African Union. APLMA's aim is to "*foster cooperation among governments and development partners for long-term response to malaria and communicable diseases in the region. It will support the process of securing long-term commitments for expanded coverage of key interventions and closing the financing gap for malaria and other communicable diseases"* (ADB, 2013). In other words, to mobilise resources and political commitment for malaria from *within* the Asia Pacific region.

3. **Emergency Response to Artemisinin Resistance (ERAR)**, a regional framework developed by WHO to guide the response to artemisinin resistance in the greater Mekong sub-region. The ERAR established a hub in Cambodia (based in the WHO office) to provide technical guidance to efforts to respond to artemisinin resistance in the sub-region, and technical assistance to countries with a focus on improving coordination between countries. The aim of the ERAR is to eliminate artemisinin resistant parasites from the Greater Mekong sub-Region by 2015 (Lynch, 2014).

4. **Global Fund Regional Artemisinin Initiative (RAI)**. A US$100 m grant from the Global Fund was signed in February 2014. This is expected to accelerate the implementation of the ERAR. It will channel funds according to Global Fund rules, i.e., through a regional principal recipient (UNOPS) to sub-recipients at country level. The RAI will have its own regional steering committee, which will provide oversight of grant implementation, monitor performance and co-ordinate with the ERAR.

Each of the four initiatives has a distinct role: APLMA on mobilising political support and leadership for broader malaria control and elimination efforts across the entire region, backed up by financing through the ADB Financing Facility; WHO's ERAR on technical leadership for tackling artemisinin resistance, in the defined geographic sub-region of the Greater Mekong; and the Global Fund providing resources to accelerate ERAR implementation. Nevertheless, there is potential for duplication, fragmentation, and high transaction costs for countries. For example, the aims of the ADB fund extend to artemisinin resistance; and the governance arrangements and mandates of the RAI's steering committee, APLMA and the WHO are likely to overlap. These issues will need to be carefully monitored and managed in the future.

Conclusions

Although there has recently been an overall improvement in the malaria situation in the region, the burden of disease remains unacceptably high. Highly endemic foci can still be found in many countries and in Myanmar, Papua New Guinea and Timor Leste the situation is particularly serious. Furthermore, the risk of a significant resurgence of malaria remains very real in several areas (Gosling and Chandramohan, 2008). Malaria control and elimination efforts in the region still face a daunting array of challenges relating to technical and programmatic issues, political and economic constraints, the rapidly evolving donor and partner landscape and environmental changes. The new and long overdue emphasis on improving the quality of malaria diagnostic and treatment services provided by the private sector presents a specific and significant challenge requiring further attention.

In response to these challenges a new, regionally-led response to malaria has emerged. Although focussed on a specific disease, these developments may provide some insight into how the global aid architecture may evolve in future. Weaker economies in the traditional aid-giving countries coupled with strong economic performance in Asia may mean that development resources for the region are increasingly mobilised from within the region. Indeed, the emergence of new regional donors, such as China and Korea, and the corresponding decrease in influence of European development agencies, suggest this may already be happening. This leads to questions on how the mandates of regional bodies overlap with global multilaterals, such as the UN agencies. In the post-MDG, post-global financial crisis world, these are likely to be critical questions, and keeping track of developments in malaria in the Asia Pacific region may provide some answers.

References

Asian Development Bank (2013). Strengthening regional response to Malaria, Artemisinin Resistance Malaria and other Communicable Diseases. Draft Schedule 16 August.

Baird JK (2007). Neglect of Plasmodium vivax malaria. Trends Parasitol. 23:533-9.

Bleakley H (2006). Malaria in the Americas: a retrospective analysis of childhood exposure. Documentos CEDE 003185, Universidad de los Andes, Bogota.

Chareonviriyaphap T, Bangs MJ, Ratanatham S (2000). Status of malaria in Thailand. Southeast Asian J Trop Med Public Health. 31(2):225-37.

Colwell DD, Dantas-Torres F, Otranto D (2011). Vector-borne parasitic zoonoses: emerging scenarios and new perspectives. Vet Parasitol. 182:14-21.

Cui L et al (2011a). Malaria in the Greater Mekong Subregion: Heterogeneity and complexity. Acta Trop.

Cui L et al (2011b). Challenges and prospects for malaria elimination in the Greater Mekong Subregion. Acta Trop.

Cutler D et al (2010). Early-life malaria exposure and adult outcomes: evidence from malaria eradication in India. American Economic Journal: Applied Economics 2: 72-94.

Domingo GJ et al (2013). G6PD testing in support of treatment and elimination of malaria: recommendations for evaluation of G6PD tests. Malar Journal. 12(1):391. [Epub ahead of print]

Feachem RG et al (2010). Shrinking the malaria map: progress and prospects. Lancet. 376:1566-78.

Gallup JL and Sachs JD (2001). The economic burden of malaria. Am J Trop Med Hyg. 64:85-96.

Gosling RD, Chandramohan D (2008). Tackling malaria today: Beware resurgence of malaria where incidence has fallen. 2008; 337:a1592.

Guerra CA, Snow RW, Hay SI (2006a). Mapping the global extent of malaria in 2005. Trends Parasitol. 22:353-8.

Guerra CA, Snow RW, Hay SI (2006b). A global assessment of closed forests, deforestation and malaria risk. Ann Trop Med Parasitol. 100:189-204.

Howard SC et al (2000). Evidence for a mass community effect of insecticide-treated bednets on the incidence of malaria on the Kenyan coast. Trans R Soc Trop Med Hyg. 94:357-60.

Kamol-Ratanakul P, Prasittisuk C (1992). The effectiveness of permethrin-impregnated bed nets against malaria for migrant workers in eastern Thailand. Am J Trop Med Hyg. 47:305-9.

Laxminarayan R (2004). Does reducing malaria improve household living standards? Trop Med Int Health. 9:267-72.

Lengeler C, Sharp B. Indoor residual spraying and insecticide- treated nets. In: Murphy C, Ringheim K, Woldehanna S, Volmink J editor(s). Reducing malaria's burden: evidence of effectiveness for decision makers. Washington: Global Health Council, 2003:17–24.

Lozano R. et al (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, vol. 380.

Luxemburger C et al (1994). Permethrin-impregnated bed nets for the prevention of malaria in schoolchildren on the Thai-Burmese border. Trans R Soc Trop Med Hyg. 88:155-9.

Lynch C, Hewitt S (2012) Malaria in the Asia-Pacific: Burden, success and challenges. Malaria 2012, Paper 1.

Lynch C (2014). Asia-Pacific Burden, Success and Challenges 2014. Prepared for the Access to Quality Medicines and Other Technologies Task Force meeting in Sydney 12-13 March 2014.

Magesa SM, Aina O, Curtis CF (1994). Detection of pyrethroid resistance in Anopheles mosquitos. Bull World Health Organ. 72:737-40.

Meankaew P et al (2010). Application of mobile-technology for disease and treatment monitoring of malaria in the "Better Border Healthcare Programme". Malar J. 9:237.

Meek SR (1988). Epidemiology of malaria in displaced Khmers on the Thai-Kampuchean border. Southeast Asian J Trop Med Public Health. 19:243-52.

Mendis K et al (2009). From malaria control to eradication: The WHO perspective. Trop Med Int Health. 14:802-9.

Mills A, Lubell Y, Hanson K (2008). Malaria eradication: the economic, financial and institutional challenge. Malar J. 7 Suppl 1:S11.

Misra SP et al (1999). Malaria control: bednets or spraying? Spray versus treated nets using deltamethrin: a community randomized trial in India. Trans R Soc Trop Med Hyg. 93(5): 456-7.

Muregi FW, Kirira PG, Ishih A (2011). Novel rational drug design strategies with potential to revolutionize malaria chemotherapy. Curr Med Chem. 18:113-43.

Murray CJ et al (2012). Global malaria mortality between 1980 and 2010: a systematic analysis. Lancet. 379:413-31.

Na-Bangchang K et al (2010). Declining in efficacy of a three-day combination regimen of mefloquine-artesunate in a multi-drug resistance area along the Thai-Myanmar border. Malar J. 9:273.

Palmer K, Hewitt S, Kelley J, Ormond L. (2013). Evidence base to support investing in malaria control and elimination in the Asia-Pacific Region. AusAID Health Resource Facility.

Pluess B et al (2010). Indoor residual spraying for preventing malaria (Review). The Cochrane Library, Issue 4.

Price RN et al (2011) Plasmodium vivax treatments: what are we looking for? Curr Opin Infect Dis. 2011; 24:578-85.

Rijken MJ et al (2012). Malaria in pregnancy in the Asia-Pacific region. Lancet Infect Dis. 12:75-88.

Rimal RN, Lapinski MK (2009). Why health communication is important in public health. Bull World Health Organ 87: 247-247. doi: 10.2471/BLT.08.056713

Roberts DR, Andre RG (1994). Insecticide resistance issues in vector-borne disease control. Am J Trop Med Hyg. 50:21-34.

Roberts D et al (2004). Malaria control and public health. Emerging Infectious Diseases; 10(6): 1170–1.

Roll Back Malaria (2008) Global Malaria Action Plan.

Rowland M et al (2000). Indoor residual spraying with alphacypermethrin controls malaria in Pakistan: a community-randomized trial. Trop Med Int Health 5(7):472-481.

Russell S (2004). The economic burden of illness for households in developing countries: a review of studies focusing on malaria, tuberculosis, and human immunodeficiency virus/acquired immunodeficiency syndrome. Am J Trop Med Hyg. 71:147-55.

Service MW (1993). Community participation in vector-borne disease control. Ann Trop Med Parasitol. 87:223-34.

Shiff C (2002). Integrated approach to malaria control. Clinical Microbiological Review, 15(2):278-93.

Sinclair D et al (2009). Artemisinin-based combination therapy for treating uncomplicated malaria. Cochrane Database of Systematic Reviews , Issue 3. Art. No.: CD007483. DOI: 10.1002/14651858.CD007483.pub2.

Snow RW et al (2010). Equity and adequacy of international donor assistance for global malaria control: an analysis of populations at risk and external funding commitments. Lancet. 376:1409-16.

Sochantha T et al (2006). Insecticide-treated bednets for the prevention of Plasmodium falciparum malaria in Cambodia: a cluster-randomized trial. Trop Med Int Health, 11 (8).

Tatem AJ et al (2011). The effects of spatial population dataset choice on estimates of population at risk of disease. Popul Health Metr. 9:4.

Thanh NV et al (2010). Monitoring for Plasmodium falciparum drug resistance to artemisinin and artesunate in Binh Phuoc Province, Vietnam: 1998-2009. Malar J. 9:181.

Walker K (2000). Cost-comparison of DDT and alternative insecticides for malaria control. Med Vet Entomol. 14:345-54.

Walsh JF, Molyneux DH, Birley MH (1993). Deforestation: effects on vector-borne disease. Parasitology. 106 Suppl:S55-75.

Wongsrichanalai C et al (2007). A review of malaria diagnostic tools: microscopy and rapid diagnostic test (RDT). Am J Trop Med Hyg. 77:119-27.

Worrall E, Basu S, Hanson K (2005). Is malaria a disease of poverty? A review of the literature. Trop Med Int Health. 10:1047-59.

World Health Organization (2009a). Malaria Microscopy Quality Assurance Manual.

World Health Organization (2009b). Regional Action Plan for Malaria Control and Elimination in the Western Pacific (2010-2015).

World Health Organization (2011). Global Plan for Artemisinin Resistance Containment (GPARC).

World Health Organization (2012). World Malaria Report 2012.

World Health Organization (2013). World Malaria Report 2013.

Woitsch B et al (2004). Comparative study of the in vitro sensitivity of Plasmodium falciparum to artemisinin in two border areas of Thailand. Wien Klin Wochenschr. 116 Suppl 4:35-40.

Yeung S et al (2009). Artemisinin resistance on the Thai-Cambodian border. Lancet. 374:1418-9.

Yeung S et al (2011). Socially-marketed rapid diagnostic tests and ACT in the private sector: ten years of experience in Cambodia. Malar J. 10:243.

Zhao J et al (2011). Indicators measuring the performance of malaria programs supported by the global fund in Asia, progress and the way forward. PLoS One. 6:e28932.

Annex: Evidence from the Asia Pacific on the effectiveness of malaria control interventions

ITN use in the Greater Mekgon Sub-region
In a study on the Thailand-Myanmar border, children aged 4-15 (n=350) who were given ITNs had 41% fewer symptomatic episodes and a non-statistically significant 20% relative reduction in prevalence of P. falciparum compared to those with untreated bednets (Luxemburger et al, 1994). A study in eastern Thailand showed a 41% reduction in the incidence of mild clinical episodes of P. falciparum and P. vivax in migrant workers (n=261) provided with ITN compared to untreated bednets (Kamol-Ratanakul and Prasittisuk, 1992). A larger scale cluster-randomised trial in 34 villages in northeast Cambodia (population 10,726) revealed a non-statistically significant reduction of 28% in P. falciparum incidence overall and a 35% reduction in P. falciparum incidence in children under 5 years old in communities provided with ITNs compared with communities not provided with any bednets (Sochantha et al, 2006).

Despite important differences in vector behaviour, transmission intensity and malaria burden, these estimates of ITN effectiveness approach those seen in trials in Africa.

IRS
A recent review concluded that the evidence from comparisons of IRS versus no IRS in unstable malaria settings confirmed that IRS reduces malaria incidence and prevalence (Pluess et al, 2010). One randomised control trial in India demonstrated a protective efficacy of 31% in terms of incidence and 28% in terms of prevalence (Misra et al, 1999) while another in Pakistan demonstrated a protective efficacy of 88% (95% CI 69 to 96%) in terms of incidence and 76% in terms of prevalence (Rowland et al, 2000).

Surveillance
Thailand and Cambodia have both recently developed largely automated systems in order to allow real-time surveillance from village level. Thailand's system relies on data input by PDA (personal digital assistant) and is web based, while Cambodia has developed an SMS (Short Messaging Service) based reporting system for use by Village Malaria Workers supported by a local mobile phone network provider. China has also developed a sophisticated web-based multi-disease surveillance system which ensures prompt reporting of all malaria cases to decision makers at various levels in the health system.