Access to Quality Medicines and Other Technologies
Task Force

Asia-Pacific Burden, Success and Challenges 2014

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# Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADB</td>
<td>Asian Development Bank</td>
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<tr>
<td>ACTs</td>
<td>Artemisinin-based combination therapies</td>
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<td>APEC</td>
<td>Association for Economic Cooperation</td>
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<td>APLMA</td>
<td>Asia-Pacific Leaders Malaria Alliance</td>
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<td>AP-MEN</td>
<td>Asia-Pacific Malaria Elimination Network</td>
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<td>ASEAN</td>
<td>Association of Southeast Asian Nations</td>
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<td>ASEAN-NDI</td>
<td>ASEAN Network for Drugs, Diagnostics, Vaccines and Traditional Medicine Innovation</td>
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<td>BMGF</td>
<td>The Bill and Melinda Gates Foundation</td>
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<td>BRIC</td>
<td>Brazil, Russia, India and PRC</td>
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<td>EAS</td>
<td>East Asia Summit</td>
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<td>ERAR</td>
<td>Emergency Response to Artemisinin Resistance</td>
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<td>GMAP</td>
<td>Global Malaria Action Plan</td>
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<td>GPARC</td>
<td>Global Plan for Artemisinin Resistance Containment</td>
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<td>GMS</td>
<td>Greater Mekong Subregion</td>
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<td>HWG</td>
<td>Health Working Group</td>
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<td>IRS</td>
<td>Indoor residual spraying</td>
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<td>LLINs</td>
<td>Long Lasting Insecticidal Nets</td>
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<td>ITNs</td>
<td>Insecticide treated nets</td>
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<td>MDG</td>
<td>Millennium Development Goals</td>
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<td>MEG</td>
<td>Malaria Elimination Group</td>
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<td>NMCPs</td>
<td>National Malaria Control Programs</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>PDP</td>
<td>Product Development Partnership</td>
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<td>PMI</td>
<td>US President’s Malaria Initiative</td>
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<td>PPP</td>
<td>Public-Private Partnership</td>
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<td>RAI</td>
<td>Global Fund’s Regional Artemisinin Initiative</td>
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<td>RDT</td>
<td>Rapid Diagnostic Test</td>
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<td>SARS</td>
<td>Severe Acute Respiratory Syndrome</td>
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<td>WHA</td>
<td>World Health Assembly</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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# Executive summary

Since 2000, the number of malaria deaths in the Asia-Pacific region has fallen by 25 per cent. Yet malaria is still a major killer in the region with around 36 million cases and 49,000 deaths\(^1\) each year. This is despite malaria being a wholly preventable and treatable disease.

Neither the malaria parasite, nor its mosquito vector, is restricted by international boundaries. Increased migration throughout the region increases the risk of malaria spreading between countries. This puts all national malaria control efforts at risk, as one country’s failure to control malaria can nullify neighbouring countries’ efforts. Within the Asia-Pacific, the emergence of artemisinin resistance is a profound and immediate threat to all malaria control efforts given the potential for spill over to neighbouring countries. Modelling has shown that artemisinin resistance could cause global malaria mortality to increase by 25 per cent; and productivity losses during illness and following death may exceed US$4 billion annually.\(^2\)

A number of challenges are preventing a more significant reduction in the burden of malaria disease and potentially increasing the likelihood of the spread of artemisinin resistance. These include the presence of substandard or fake malaria drugs in a heavily utilised private sector, high levels of labour mobility, low access to treatment or malaria commodities because of high prices, changing infrastructure and environmental conditions leading to new transmission pathways and difficulty in delivering interventions to hard-to-reach populations.

In addition, the role of external support in financing malaria control in the Asia-Pacific region is likely to decline in the future, which will require an increasing share to be met domestically. Between 2003-2009, external funding in the region represented on average 70 per cent of the total spend on malaria control and elimination.\(^3\) For many countries in the region overseas development aid represents a low and diminishing share of health expenditure, with a growing emphasis on domestic resources for malaria control. Any significant shortfalls in funding could leave the region vulnerable to resurgences in malaria, spread of artemisinin resistance and related to those, significant economic loss.

Malaria control activities can be addressed more effectively and efficiently at a regional level, potentially leading to better health outcomes than those achievable through national efforts alone. There are significant opportunities to address these issues regionally and ensure that coverage of and access to malaria treatment and commodities, as a regional public good, are increased to reach regional targets.

It is suggested that the Access to Quality Medicine and Technology Task Force (of the Asia Pacific Leaders Malaria Alliance) consider the following recommendations:

- **Generate and maintain high political commitment for intensified malaria control towards regional elimination.** The highly impressive gains that the region has made in reducing the burden of malaria are fragile. It is essential to design mechanisms within integrated health systems to

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retain vigilance and responsiveness to malaria resurgence. In particular, we cannot afford to allow the progress in responding to artemisinin resistance to slip. The potential economic and health gains of reduction in malaria burden in the region and the prospect of eventual elimination are strong arguments for an advocacy strategy in which regional leaders take the initiative to hold themselves accountable for progress.

- **Ensure regional ownership.** The need for regional ownership of malaria control and elimination is crucial. Moving from a donor-led activity to an integrated and regionally managed response will serve to protect gains made in malaria, and ensure stable funding which would also ensure that markets are clear about what demands will be made of them for antimalarials and other commodities.

- **Strengthen regional regulatory capacity to ensure good quality medicines and commodities.** Despite the World Health Organisation’s guidelines on combatting counterfeit medicines, most countries in the Asia-Pacific region do not have the infrastructure or financial resources to implement or enforce controls.

- **Strengthen regional Product Development and Public-Private Partnerships (PDPs and PPPs) for increased innovation.** Significant opportunities exist to engage with the private sector through Public-Private and Product Development Partnerships at regional level through pooled research and development (R&D) funds to develop innovative tools. Examples include improved treatment for *P. vivax* malaria and prevention of outdoor mosquito biting.

- **Strengthen regional manufacturing capacity.** The Asia-Pacific region is already a major manufacturer of malaria medicines and other technologies. 80 per cent of the global supply of the plant source of artemisinin is produced in the region, mainly in PRC and Viet Nam. Even so, much untapped potential remains: both the volume and the quality of production could be increased, bringing economic and health benefits to the region.
1. Burden of malaria in Asia-Pacific – epidemiology of the disease

Regional importance of malaria

Malaria is the ninth largest cause of death and disability globally. Despite recent gains, malaria is still a major killer and cause of economic loss in the Asia-Pacific region\(^4,5,6\) despite it being a wholly preventable and treatable disease. Malaria episodes lead to direct costs to patients and families associated with seeking healthcare and indirect costs due to lost income and school days missed by children. Research has shown that countries with intensive malaria grew 1.3 per cent less per person per year.\(^7\) Malaria also has a direct impact on four of the eight Millennium Development Goals (MDGs).\(^8\)

Neither the malaria parasite, nor its mosquito vector, is restricted by international boundaries. Increased migration throughout the region increases the risk of malaria spreading between countries. This puts all national malaria control efforts at risk, as one country’s failure to control malaria can nullify neighbouring countries’ efforts. Within the Asia-Pacific, the emergence of artemisinin resistance is a profound threat to all malaria control efforts given the potential for spill over to neighbouring countries. As such, malaria control activities are a regional public good, which, if tackled through a regional level coordinated approach, could lead to better health, economic and development outcomes than those achievable through national efforts alone.

Investment in malaria has the potential to deliver much more in terms of its contribution to broader development outcomes. Investing in malaria control and elimination represents very good value for money, offering some of the most cost effective health interventions available. It is estimated that the value of the benefits achieved through investment in malaria control globally exceed the costs by a factor of between 1.9 to 4.7.\(^9\) A summary of the available tools and interventions for malaria control is at Annex 1.

The current burden in the Asia-Pacific Region

The total population of the 22 malaria endemic countries of the Asia-Pacific region\(^10\) is 3.7 billion\(^11\) of whom approximately 62 per cent are at risk of being infected with malaria. According to the World Health Organisation (WHO) World Malaria Report 2013, there were an estimated 28 million malaria cases and 45,500 deaths in 2012 in the two WHO regions, South East Asia and Western Pacific regions (which are

\(^10\) In this paper, unless otherwise stated, the region refers to the following countries in Asia: Afghanistan, Bangladesh, Bhutan, Cambodia, China, DPR Korea, Timor Leste, India, Indonesia, Malaysia, Myanmar, Lao PDR, Nepal, Pakistan, Philippines, Republic of Korea, Sri Lanka, Thailand and Vietnam and the following countries in the Pacific: Papua New Guinea, Solomon Islands and Vanuatu.
the 22 countries minus Afghanistan and Pakistan). Other estimates and models have put the figures somewhat higher at 36 million cases and 49,000 deaths for all 22 countries combined.\textsuperscript{12}

According to modelled data prepared for Malaria 2012, the highest number of cases in 2010 occurred in India, Indonesia, Pakistan and Myanmar, which combined accounted for 91 per cent of cases in the region. The highest numbers of deaths occurred in India (54 per cent of total malaria deaths in the region), Indonesia (21 per cent) and Myanmar (7 per cent). When malaria cases are taken as a proportion of the population, however, the incidence of malaria in Asia is highest in Timor Leste, Myanmar, Cambodia, Indonesia and Afghanistan. Populations in the Pacific are at higher risk of being infected with malaria than those in Asia. Of the 7.96 million people in PNG, Solomon Islands and Vanuatu, 99.9 per cent are estimated to be at risk of malaria.\textsuperscript{13}

Since 2000, the rates of reported malaria cases and deaths have decreased significantly across the region as a whole. Over one quarter of countries in the region have achieved more than a 75 per cent reduction in malaria cases, while one-fifth have achieved a reduction of between 50 and 75 per cent. While it is difficult to attribute these significant reductions in malaria deaths and cases to any one factor, it is thought that the dramatic increase in coverage of key interventions – such as the distribution of mosquito nets, indoor residual spraying (IRS) and provision of improved diagnosis and appropriate treatment – are major drivers behind the downward trend.

Figure 1: Malaria cases for 2001 and 2011 for 10 Asia-Pacific countries with highest incidence

Source: http://www.unescap.org/stat/data/syb2013/B.4-Malaria-tuberculosis.asp

Geographical distribution of malaria

The distribution of malaria in the Asia-Pacific region is complex. Large differences in the malaria burden can occur within the same country, region, village or population group. Pockets, or ‘foci’, of relatively high transmission can be found along a landscape of generally low transmission. In Indonesia the highest malaria burden is in the easternmost provinces. In Thailand a large proportion of the burden is concentrated in border areas, while larger countries such as India and PRC have regions that are totally malaria-free.14

This variation happens because the transmission of malaria in any geographic locality depends on a number of factors such as temperature, rainfall and relative humidity, that affect mosquito breeding, lifespan, contact between humans and mosquitoes and the survival of the parasites within humans. Other factors, such as population distribution, land use, physical structure of houses, use of control and prevention measures and drug resistance also affect the amount of interaction between the vector, parasite and human.

To achieve a substantial reduction in malaria cases, interventions are required that prevent mosquitoes from biting humans in addition to use of drugs for effective treatment. These interventions must be based

on a sound understanding of the local characteristics of mosquitoes.\textsuperscript{15} The Asia-Pacific region has a high diversity of vector (mosquito) species incomparable to anywhere else globally.\textsuperscript{16} Currently, 16 dominant malaria vectors have been identified throughout the region, each with different characteristics affecting their ability to transmit malaria and our ability to control them. Biting times, breeding sites, preferred source of blood (human and animal) and resting preferences are important.\textsuperscript{17} More information on the distribution of malaria within the region is in Annex 2.

2. What are the regional dimensions of the problem?
A number of challenges are preventing a more significant reduction in the burden of malaria disease and potentially increasing the likelihood of the spread of artemisinin resistance. These include:

- the presence of substandard or fake malaria drugs in a strong, heavily utilised private sector;
- high levels of labour mobility;
- low access to treatment or malaria commodities because of high prices;
- changing infrastructure and environmental conditions leading to new transmission pathways and;
- difficulty in delivering interventions to hard-to-reach populations.

**Artemisinin resistance**
Artemisinin resistance is an urgent challenge for the region as a whole (see Figures 2 and 3), and specifically for the Greater Mekong Subregion where artemisinin resistance was first detected. The situation is critical. Resistance to previous antimalarial treatments is believed to have resulted in considerable excess mortality.\textsuperscript{18,19}

**Artemisinin resistance and preventing the spread of untreatable malaria**
Artemisinin resistance is a profound challenge currently unique to the Asia-Pacific region. Artemisinin-based medicines are the basis for artemisinin-based combination therapies (ACTs). ACTs are the most effective treatment for \textit{P. falciparum} malaria and used as first-line treatment throughout the world. When oral artemisinin derivatives are used alone (monotherapy), they contribute to speeding the development of drug resistance.

Malaria experts believe that it is possible to prevent the spread of artemisinin resistance to new locations but only by local complete elimination of \textit{P. falciparum} in areas of known resistance. A strategic plan, the Global Plan for Artemisinin Resistance Containment (GPARC), was agreed in 2011 and is being

\begin{footnotesize}\begin{enumerate}
\item Sinka, M. E. \textit{et al.} (2011).
\end{enumerate}\end{footnotesize}
implemented in the affected areas of the region. The GPARC provides guidance on how to protect ACTs as an effective treatment for *P. falciparum* malaria.

We have seen the first signs of resistance to artemisinin in the Greater Mekong Subregion, initially on the Thailand-Cambodia border and subsequently in neighbouring countries. Historical data on the spread of chloroquine resistance suggests that Myanmar was the gateway for the spread of antimalarial resistant parasites to Bangladesh and/or India and subsequently to Africa.\(^\text{20,21}\) If artemisinin resistance spreads, there is a risk of a dramatic resurgence of malaria cases and overall increase in transmission, which would lead to more malaria cases and more malaria deaths. This would be a major regional and global setback to progress in malaria control efforts over the last decade. The health and economic impacts of widespread artemisinin and ACT resistance are likely to be substantial. Global malaria mortality could increase by 25 per cent; productivity losses during illness and following death may exceed US$4 billion annually; and the direct medical costs associated with re-treatment and a rising number of cases of severe malaria (due to the spread of resistance) is likely to be over US$30 million annually. Costs of the introduction of an alternative treatment could exceed US$120 million for the policy change alone, while alternative therapies, once available, will likely cost in excess of US$100 million annually for each $ increase in unit cost over current ACT prices.\(^\text{22}\)

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\(^\text{22}\) White, L. et al. (2012).
WHO classifies regions into three tiers in relation to artemisinin resistance, with Tier 1 referring to areas for which there is credible evidence of artemisinin resistance, Tier II to areas with significant inflows of mobile and migrant populations from Tier I areas or shared borders, and Tier III to P. falciparum endemic areas which have no evidence of artemisinin resistance and limited contact with tier I areas. Figure 2 shows the distribution of these tiers in the Greater Mekong Subregion while Figure 3 shows the percentage treatment failure of different ACTs in the Greater Mekong Subregion (2006-2014).

Source: WHO Status report on artemisinin resistance
Attempts to contain artemisinin resistance first started in 2008 on the Cambodia-Thailand border. The 2012 Joint Needs Assessment of Artemisinin Resistance, funded by the Australian Government, brought much needed attention to the issue of resistance. Since then, a more vigorous international response has been mounted as reflected in increased funding and scale-up of coordination and activities in the Greater Mekong Subregion (GMS). See section 3 for further discussion. Further emergence and spread of artemisinin resistance is a real and immediate threat. Labour mobility in the region is high and will increase as the regional economic ties continue to strengthen. Substandard and fake antimalarials could drive further emergence of resistance and thus need to be curtailed urgently throughout the region.

**Weak private sector regulation and engagement**

The private sector plays an important role in the prevention, diagnosis and treatment of malaria in many countries in the Asia-Pacific region, both through the formal and informal sectors. Most money for malaria control comes directly from users at point-of-sale. This financing model favours those producing cheap and often substandard antimalarials and is considered a ‘market failure’. Governments in the region have poor capacity to regulate the private sector. As a result there is patchy availability of good quality medicines for malaria, the proliferation of substandard or fake medicines, poor prescribing practices and high prices in the private sector.

**Increased development resulting in a changing malaria landscape**

Population movements and changes in land use are two critical factors which are changing the pattern of malaria risk in the region. Migrants leaving low transmission areas to work in places of high transmission are at high risk of contracting malaria and potentially becoming ‘active transmitters’ on their return home. Rapid economic growth and the establishment of new economic corridors between countries, as well as persisting conflicts within countries in the region, have resulted in new migration routes. This increased connectivity makes malaria epidemiology even more complex. The creation of the economic free zone, planned by the Association of Southeast Asian Nations (ASEAN) in 2015, will further increase labour
mobility in the region. Changes in land use as a result of growing hydroelectric, petroleum, mining and rubber plantation sectors in some countries draws migrant labour and can also have an enormous effect on the distribution of mosquitoes, and thus malaria cases.

**Hard-to-reach and mobile populations**

People who become ill with malaria need access to health services that provide prompt and effective diagnosis and treatment. This is essential if targets for universal coverage of malaria interventions are to be met. Improved road networks and the introduction of community level diagnosis and treatment have increased accessibility to efficacious malaria care. However, a significant proportion of those suffering from malaria still cannot access care. This is a result of poor supply and delivery challenges to more remote areas, and within mobile populations, leaving people there at higher risk for malaria. A large proportion of malaria cases are thus treated at home. Many also seek care in the private sector, where the quality of care can be inadequate, and where better regulation is needed.

**Health systems and health information systems**

Malaria control and elimination activities rely on well-functioning health systems to deliver interventions and ensure access to diagnosis and treatment. Weak supply chains, poor regulation of the quality of antimalarials and other malaria technologies, and fragmented information systems all undermine malaria control and elimination efforts. Past experience, for instance from smallpox and yaws, has shown that strong health systems are a pre-requisite to the success of any disease elimination agenda. As such, investment in health systems is key to malaria control.

Monitoring and evaluation of malaria control programs has been strengthened considerably in most countries in the region in recent years, largely as a result of the Global Fund’s focus on performance-based funding. Yet, crucial gaps in information remain which make it difficult to get a sense of the current malaria situation beyond the overall trends of malaria cases and deaths. Added to this is the challenge of detecting and monitoring malaria infections and cases in a rapidly changing environment, including in the context of population mobility, changes in land use and climate change. Health information systems in the region are in urgent need of strengthening, prompting many malaria control and elimination programs to establish parallel malaria information systems to generate the epidemiological and operational data needed for planning and implementation. PRC is one notable exception to this trend.

**3. What is being done?**

**Political will and commitment**

Since 2000 there has been a significant reduction in the annual number of deaths and cases attributed to malaria in the region. These gains that have resulted from improvements in availability of Long Lasting Insecticidal Nets (LLINs), appropriate IRS and improved access to diagnosis and treatment (see Annex 3). Multiple factors have led to this reduction including political commitment, and increased investment.
In 2000, the United Nations Millennium Declaration set a target to halt and begin to reverse the global incidence of malaria by 2015. This goal was reinforced in 2005, and again in 2007 at the World Health Assembly (WHA) where countries were urged to establish policies and operational plans to “ensure that at least 80 per cent of people at risk of, or suffering from, malaria benefit by 2010 from major preventive and curative interventions, so as to ensure a reduction in the burden of malaria of at least 50 per cent by 2010 and 75 per cent by 2015”. These targets are reflected in the Roll Back Malaria Partnership Global Strategic Plan 2005-2015 and have been incorporated into National Malaria Control Programs (NMCPs) across the region.

Regional strategies from the Eastern Mediterranean (2011-2015) and South East Asian (2006-2010) regions of WHO include the target of reducing malaria illness by 50 per cent and deaths by 75 per cent by 2015, compared to a 2000 baseline. The Western Pacific Region Action Plan for Malaria Control and Elimination (2010-2015) proposes to reduce malaria deaths and illness by 50 per cent by 2015 compared with 2007, and to achieve the interruption of malaria transmission in targeted areas in at least seven countries.

In 2007, Bill and Melinda Gates put forward the idea of malaria elimination and eradication and were supported by WHO and Ministries of Health in malaria endemic countries. A Global Malaria Action Plan (GMAP) was developed and the Malaria Elimination Group (MEG) was formed. A ‘Three Part Strategy’ for elimination was subsequently developed which outlines a plan to: reduce the burden of malaria through aggressive control in the malaria heartland; progressively eliminate malaria from the endemic margins; and conduct research to bring forward new malaria control tools. In order to meet the ambitious targets for the region, ‘universal coverage’ (100 per cent of all people requiring interventions receive them) needs to be achieved with all core interventions (LLINs, diagnosis and treatment). See Annex 1 for a list of core interventions.

Three countries in the region, Malaysia, Republic of Korea, and Sri Lanka, have entered the pre-elimination phase which means that they have reduced malaria to very low levels (less than 5 per cent of all fever cases are confirmed as malaria). In these countries there is strong political will and commitment to elimination and surveillance systems are strong enough to detect very low numbers of malaria cases. The remaining 18 countries of the region are in the control phase, and the majority of these have been scaling up to achieve universal coverage since 2008. Fifteen countries have committed to elimination either at a national or sub-national level, expressing a goal of elimination in their national strategic plans, all of which are members of the Asia-Pacific Malaria Elimination Network (APMEN).

In 2011, the World Health Assembly urged its Member States, WHO and international partners to agree to a series of actions to sustain gains that have been made in malaria control – among others, to take immediate action to combat resistance to artemisinin-based medicines. Malaria 2012 in Sydney galvanised support for sustained malaria control, elimination and artemisinin containment in the region.

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as reflected in the final consensus statement. In 2012, during regional meetings, ASEAN and ASEAN+3 health ministers recognised the importance of artemisinin resistance and the impact it could have on malaria elimination region wide. Further, the declaration of the 7th East Asia Summit on regional responses to malaria control and addressing resistance to antimalarial medicines was endorsed by all East Asia Summit (EAS) Heads of Government. This political commitment was translated into the establishment of the Asia-Pacific Leaders Malaria Alliance (APLMA) described below.

Regional architecture for health and malaria in the Asia-Pacific

Asia-Pacific has been growing in terms of its economic influence in the world since the 1960s. A number of regional bodies exist including the ASEAN, the Association for Economic Cooperation (APEC), the Asian Regional Forum and the ASEAN +3 all of which reflect the desire to buttress regional strength financially. In 2003, as a result of the emergence of regional and global health epidemics, such as Severe Acute Respiratory Syndrome (SARS) and Avian influenza, APEC established a Health Technical Forum, subsequently upgraded to the Health Working Group (HWG). The HWG, which first met in April 2013, addresses health-related threats to economies’ trade and security, focusing mainly on emerging infectious diseases.

In addition to the APEC HWG, ASEAN countries acknowledge and prioritise healthcare as a priority in the region. Since 1980, ASEAN Health Ministers have met every two years to discuss and engage with issues that the entire ASEAN community must confront and resolve. One of the most recent issues highlighted by the ASEAN Health Ministers Meeting was the regulation of medical devices as part of the ASEAN Medical Device Directive. In 2009, the ASEAN Network for Drugs, Diagnostics, Vaccines, and Traditional Medicine Innovation (ASEAN-NDI) was proposed during the 40th Meeting of the ASEAN Subcommittee on Biotechnology. This initiative aims to standardise drugs and vaccines, lower the cost of clinical trials, and catalyse more innovation and discovery.

Since the Malaria 2012 meeting in Sydney, momentum has gathered for a regional architecture through which countries can channel funding and advocate for political commitment as well as technical assistance. In doing so, the region can begin to safeguard the investments and gains made in malaria control and elimination over the previous ten years and ensure that the region, as a whole, can move to elimination while also actively managing threats such as artemisinin resistance.

Asia-Pacific Leaders Malaria Alliance (APLMA)

In 2013, leaders attending the annual East Asia Summit endorsed the creation of the APLMA. The purpose of APLMA is to act as a high level advocacy platform, supported by two taskforces: the first is on access to quality medicines and other technologies, and the second on regional financing for malaria.

APLMA is committed to reduce malaria cases and deaths by 75 per cent by 2015 and to contain the spread of drug resistant forms of the parasite. It aims to do this by expanding the fight against the illness beyond

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27 Asia-Pacific Economic Cooperation: Steering Committee on Economic and Technical Cooperation.
the health sector into the arenas of regional trade, transportation, migration, and rural industries such as agriculture, mining and forestry.

Emergency Response to Artemisinin Resistance (ERAR)

In 2013, the ERAR framework was established by the WHO to guide a coordinated technical and scientific response to artemisinin resistance in the GMS. This is an initiative mechanism involving WHO Regions for South-East Asia and the Western Pacific working with a regional hub in Cambodia. The aim is to eliminate artemisinin resistant parasites from the GMS by 2015. The main activities of ERAR are to ensure coordination between countries through alignment of national level planning, bring partners together to find common ways to resolve issues and to ensure strong monitoring and data collection systems. The ERAR is also collaborating throughout the region to assess drug efficacy in order to quickly identify the emergence of resistance beyond the current containment areas.

Where is the money for malaria control and elimination in the Asia-Pacific coming from?

Most funding of malaria interventions comes directly from users as out of pocket expenditures at point-of-sale.

The role of external support in financing malaria control in the Asia-Pacific region is likely to decline in the future, which will require an increasing share to be met domestically. Between 2003-2009, external funding in the region represented on average 70 per cent of the total spend on malaria control and elimination. For many countries in the region overseas development aid represents a low and diminishing share of health expenditure and the contribution of domestic funding is critical. Any significant shortfalls in funding could leave the region vulnerable to resurgences in malaria, spread of artemisinin resistance and related to those, significant economic loss.

Currently, the major international financiers of malaria control in the region are the Global Fund to Fight AIDS, Tuberculosis and Malaria, the US President’s Malaria Initiative (PMI), the Bill & Melinda Gates Foundation and the governments of Japan, Australia and the United Kingdom.

Co-investing countries in the Asia-Pacific Region

Globally, emerging economies, such as India and PRC, are contributing towards global health in significant ways and playing a more important role in financing malaria control. These include the BRIC countries (Brazil, Russia, India and PRC) and East Asian countries including South Korea, Brunei and Malaysia. As such, these are potentially untapped sources with considerable funding potential though investments are likely to align to geo political interests and initial funding from these governments may be small and unpredictable. Some examples of regional partners’ contributions to global health include:

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The **Indian Government’s** 2010 budget allocated US$536 million for financial contributions and loans to other governments, including US$126 million to international organisations.\(^{31}\) Within the Asia-Pacific region, India is building public health capacity in Nepal and Afghanistan.\(^{32}\) Some of India’s health aid ventures piggyback on the country’s successful industries, such as pharmaceuticals. It currently exports US$8.3 billion in drugs and services. These exports constitute a significant portion of its cooperation with other BRIC nations on health issues.

The **Republic of Korea Government** prioritises global health, diverting nearly 15 per cent of its aid budget to health and medical services.\(^{33}\) Through its aid program, Seoul has agreed to donate 1000 Korean won (about US$1) for each airline passenger departing from Korea, to help treat and prevent HIV/AIDS and Malaria in the African continent. This program is expected to annually generate revenues of around US$20 million. The Republic of Korea Government has also established partnerships with key developing countries, for example with Cambodia, to develop medical professionals’ capacity.

**The Asian Development Bank (ADB) hosted Trust Fund**

In 2013, the ADB established the Regional Malaria and Other Communicable Disease Threats Trust Fund to support countries in Asia and the Pacific attain malaria control and elimination targets and to contain artemisinin resistance, particularly in the Mekong region. The Fund has garnered cornerstone financing from the Government of Australia through the Department of Foreign Affairs and Trade (US$16.3 million) and the UK Government (US$19.4 million). Additional contributions are being sought from development partners, the private sector and foundations and importantly, given the regional public goods nature of malaria control, regional countries.

In this initial phase, the Malaria Trust Fund aims to add value by strengthening regional cooperation as needed to address gaps, including:

- The design of a funding mechanism with regional buy-in for sustained financing of the gap between national and global (e.g., Global Fund) resources;
- Improved management of artemisinin efficacy as a regional good, for example, by working with the pharmaceutical industry and national regulatory authorities to reduce the level of counterfeit and substandard antimalarials, and to eliminate use of artemisinin oral monotherapies;
- Establishing a regional ‘knowledge hub’ and scorecard system to improve transparency and use of information and data, similar to the regional AIDS data hub housed at UNAIDS in Bangkok;
- Piloting Results-Based activities for quick response to identified threats; and

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\(^{31}\) Bliss, K. *Key Players in Global Health: How Brazil, Russia, India, China, and South Africa are Influencing the Game*. 63 (CSIS, 2010). at <http://books.google.com/books?id=NSCT_JN--9MC&pgis=1>

\(^{32}\) Bliss, K. (CSIS, 2010).

\(^{33}\) Bliss, K. (CSIS, 2010).
• Strengthening health impact/Social analysis Assessments used by development agencies and national authorities to better identify and mitigate potential impacts of private and public sector infrastructure activities on malaria transmission.

The Global Fund to Fight AIDS, Tuberculosis and Malaria - Regional Artemisinin Initiative (RAI)

The majority of countries in the Asia-Pacific region have received significant funding from the Global Fund. In addition, to this country-level support, in 2013 the Global Fund committed US$100 million over three years to a regional grant in the GMS to combat artemisinin resistance in five countries. The Global Fund’s Regional Artemisinin Initiative (RAI) is the result of a collaborative effort between multiple partners and the Ministries of Health in Thailand, Viet Nam, Myanmar, Lao PDR and Cambodia. The initiative aims to achieve elimination of *P. falciparum* malaria by 2016. It recognises that an accelerated national response and a multi-country approach is necessary.

The main interventions supported through the RAI initiative include long-lasting insecticide treated nets and targeted IRS, as well as case management in areas where there was evidence of delayed response to ACTs or at risk of spread of resistant parasites. There is also special focus on migrant populations living and working in border areas. The grant is also aimed at helping to halt the marketing and sale of oral artemisinin mono-therapies, which threaten the long-term usefulness of ACTs. It will also set up a rigorous surveillance system linked to control of outbreaks and therapeuic efficacy studies in sentinel sites. PRC will provide technical support to RAI by sharing experience and best practices.

**Australian Government**

Australia is committed to contributing to a coordinated and regionally owned response to malaria in the Asia-Pacific region. This is demonstrated at the highest political level with the Australian Prime Minister co-chairing the APLMA and significant representation on its two supporting taskforces, addressing access to quality medicines and regional financing. Australia’s bilateral and multilateral investments, including through the Global Fund, support country and regional programs to contribute to these goals.

The malaria portfolio spans investment in the Asian Development Bank’s Regional Malaria and Other Communicable Disease Threats Trust Fund, supporting the WHO to coordinate a regional framework to respond to artemisinin resistance in the GMS, investing in research and development, supporting neighbouring countries to intensify their malaria programs as well as their underlying health systems and working with emerging co-investing countries such as PRC to collaborate on shared priorities, for example malaria in the Pacific and Mekong regions.

**The Japanese Government** has been a key political partner in the development of Asia’s regional focus. Funding for malaria from the Japanese government has varied year-on-year and has focussed mainly on The Solomon Islands, Thailand, Viet Nam and Myanmar.

**The United States Government** has supported antimalarial drug resistance monitoring and drug quality surveillance and strategic information in the GMS since 2000. The PMI focuses in areas of known or emerging artemisinin resistance, including activities to reduce malaria transmission in cross-border areas.
Proposed PMI activities are aligned with the national malaria control program strategies and seek to complement contributions from other donors.

The **United Kingdom Government** has committed £11.8 million (estimated $19.4 million) to the newly established Regional Malaria and Other Communicable Disease Threats Trust Fund and is committed to reducing the spread of drug resistant malaria in the GMS. In addition, the UK has invested in the Tracking Artemisinin Resistance Collaboration which is investigating the spread of parasite resistance to artemisinin-based therapies across different sites in Asia. More broadly, a global health support program has been established with the Chinese government (2012-2017) to support PRC’s aim of improving its overseas health programmes. At the country level the UK, in collaboration with Gates, has supported the displacement of oral artemisinin monotherapies in Myanmar.

The **Bill & Melinda Gates Foundation (BMGF)** plays a key role in promoting progress towards global targets for malaria elimination especially by building evidence around strategies for malaria elimination. Examples of areas operational research include the mobility and the spread of artemisinin resistance, the identification of an artemisinin resistance marker and ACT watch studies (that seek to fill evidence gaps on malaria diagnostics, antimalarial medicines and fever case management in the private and public sectors).

The BMGF are also supporting the coordination and mobilisation for containment and elimination of artemisinin resistance. At the country level, BMFG has supported the replacement of artemisinin monotherapy. While BMGF focus in the Asia-Pacific has primarily been on the GMS, and the elimination of falciparum Artemisinin resistant parasites, it has also supported antimalarial efficacy studies beyond GMS throughout the Asia-Pacific.

**The Asia-Pacific Economic Cooperation**

The private sector has an important role to play in malaria control as new economic activity. For example the opening of a mine or roads often involves new population movements and can affect the local environment. This has an impact on malaria transmission and development of drug resistance. Public sector agencies can lead the way in setting standards for good corporate practices that support malaria control activities. No standardised protocols or recommendations exist for assessing the potential impact of infrastructural and environmental changes brought about by private sector or development activities on malaria control, elimination and spread of artemisinin-resistant parasites. The concept of Corporate Social Responsibility is strong, and growing in the APEC region. True public private partnerships are needed that tackle the issue and foster mutual accountability.

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4. What more is needed?

Economic integration and high levels of labour mobility mean that regional solutions are needed: drug resistant parasites do not respect borders, and the cost of technologies in one country can have an impact on supply in its neighbour. It is suggested that the Access to Quality Medicine and Technology Task Force consider the following priorities for action:

**Generate and maintain high political commitment for intensified malaria control towards regional elimination.** The highly impressive gains that the region has made in reducing the burden of malaria are fragile. It is essential to design mechanisms within integrated health systems to retain vigilance and responsiveness to malaria resurgence. In particular, we cannot afford to allow the progress in responding to artemisinin resistance to slip.

The potential economic and health gains of a reduction in the malaria burden in the region, and the prospect of eventual elimination, are strong arguments for an advocacy strategy in which regional leaders take the initiative to hold themselves accountable for progress. A similar approach in Africa, in which countries maintain and share a scorecard on progress, has been a powerful tool.

**Ensure regional ownership.** Further emergence and spread of artemisinin resistance is a real and immediate threat for the Asia-Pacific region. Malaria control and artemisinin resistance can only be addressed through a regional approach based on strong regional ownership and collaboration. Resources, leadership and governance all need to be sourced from within the region, with strong support from the regional architecture. Any global funding needs to support an integrated and regionally managed response that will serve to protect the gains made in malaria, and ensure stable funding. Such stability will mean that markets are clear about what demands will be made of them for antimalarials and other commodities. Pooled funding and procurement are potential options to increase regional ownership, ensure availability of stocks through advance market commitments and take advantage of economies of scale.

**Strengthen regional regulatory capacity to ensure good quality medicines and commodities.** Despite the World Health Organisation’s guidelines on combatting counterfeit medicines, most countries in the Asia-Pacific region do not have the infrastructure or financial resources to implement or enforce controls.

**Strengthen regional Product Development and Public-Private Partnerships (PDPs and PPPs) for increased innovation.** Significant opportunities exist to engage with the private sector through Public-Private and Product Development Partnerships at regional level through pooled R&D funds to develop innovative tools needed to further advance malaria control in the region. Examples are treatments for *P. vivax* and prevention of outdoor mosquito biting. New innovations can be brought to market by leveraging regional strength to make greater use of financial incentives such as grants, subsidies, tax incentives, manufacturer-based subsidies and in-kind support to influence private provision.
Strengthen regional manufacturing capacity. The Asia-Pacific region is already a major manufacturer of malaria medicines and other technologies. 80 per cent of the global supply of the plant source of artemisinin is produced in the region, mainly in PRC and Viet Nam. Even so, much untapped potential remains: both the volume and the quality of production could be increased, bringing economic and health benefits to the region. Options for doing this include; the use, where appropriate, of market-based incentives, public-private partnerships to address production standards and private sector performance-based supply chain models similar to the Informed-Push Model used at national level in Senegal.
Annex 1: What tools are available to control and eliminate malaria?

As a result of the burden of malaria globally, and potential economic gains as a result of its control and elimination, a Global Malaria Action Plan (GMAP) was developed in 2012 which outlines interventions and targets for each region in terms of control. The aim of the GMAP is for countries to achieve universal coverage with all vector control, diagnostics and treatment interventions.

**Long Lasting Insecticidal Nets (LLINs)** are mosquito nets that are impregnated with a long-lasting formulation of insecticide during the manufacturing process; the insecticide remains in the net for 20 to 30 washes without the need for re-treatment. WHO also recommend the use of technologies such as long lasting insecticide treated hammock nets (LLIHNs) for special populations such as forest workers. Long lasting nets differ from conventional insecticide treated nets (ITNs) which require re-treatment every six months.

**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 those surfaces. The primary effects of IRS are to reduce the overall population of vector mosquitoes and to reduce their lifespan so that they do not live long enough to transmit malaria parasites from one person to another. Some insecticides used for IRS also repel mosquitoes and so reduce the number of mosquitoes entering the sprayed room, again reducing human-vector contact. Indoor resting mosquitoes are readily controlled by indoor spraying with residual insecticides. Dominant mosquitoes in the Pacific and Mekong areas tend to feed outside in the early evening before people go inside their nets, or insecticide sprayed houses. To minimise transmission people also need protection from vector mosquitoes during this period.

**Controlling outdoor biting:** Some tools currently being explored are: spatial and topical repellents, baited traps for malaria vectors, insecticide treated clothing, insecticide treated face nets and outdoor treated nets.

**Larval control:** There may be some instances where some species of vectors may be controlled through the destruction of breeding sites if these are few, fixed and findable.

**Insecticide treated livestock:** In areas where the primary vectors have a tendency to feed on cattle, treating livestock with insecticide has shown some promise as a means of malaria control.

**Early detection and treatment in different transmission settings**

**Diagnosis** The use of parasitological diagnosis is recommended for all populations at risk of contracting malaria. Properly performed malaria microscopy remains the gold standard for malaria diagnosis and the diagnostic method of choice for larger health facilities (in skilled hands microscopy is more sensitive than rapid diagnostic tests as it allows for the identification of different malaria species, and the quantity of parasites present and thus more appropriate treatment). However, microscopy is not possible in all settings, and weak capacity for quality assurance means it is not always performed well. Over the last ten years Rapid Diagnostic Tests (RDTs) have become established as an essential diagnostic method. RDTs now go to most health facilities, even those with microscopy, and are used for example when no microscopist is on shift, power failures, or when testing needs to be very fast for whatever reason.
Treatment Artemisinin-based combination therapies (ACTs) are the recommended first line treatment against P. falciparum and have been adopted by all countries in the Asia-Pacific Region. ACTs are recommended because the artemisinin component very quickly reduces the parasite load so the partner drug has to clean up less parasites, which is faster and means there is less chance of mutation. Provided that both medicines are efficacious at the outset, they help to protect one another’s efficacy by preventing or delaying the development of drug resistance in parasites.

Chloroquine combined with 14 days treatment with primaquine is recommended for P. vivax malaria in places where there is no proven resistance to chloroquine. In regions where P. falciparum and P. vivax coexist and mixed infections occur, treatment is as for P. falciparum using an ACT (plus primaquine if P. vivax is definitely present). Primaquine, however, is contraindicated in pregnant women and in certain other medical conditions.
Annex 2: Distribution of Malaria and Mosquito Species within the Asia-Pacific region

There are five species of malaria parasites (Plasmodium) that infect humans of which two, *Plasmodium falciparum* and *Plasmodium vivax*, are most prevalent in the region. The most serious malaria infections are caused by *P. falciparum*, which can lead to severe illness, anaemia, low birth weight in babies born to infected mothers, cerebral malaria and death. According to the 2011 World Malaria Report, 82 per cent of reported malaria cases in the region were due to *P. falciparum*. *Plasmodium knowlesi* (a Simian or “monkey malaria”) was recently documented as a fifth species that can cause malaria in humans in Cambodia, Indonesia, Malaysia, Myanmar, the Philippines Thailand and Viet Nam. It is unknown how many cases are due to this species, but this illustrates the threats of malaria with changing environments.

*P. vivax* is a larger and more serious threat than previously appreciated, particularly in areas where it is resistant to chloroquine. Recent studies have shown that *P. vivax* can cause severe disease that resembles cerebral malaria caused by *P. falciparum*. In addition, the lifecycle of *P. vivax* parasites includes a dormant stage that is difficult to detect and treat. An estimated 42 per cent of the global population at risk of *P. vivax* transmission is located in India. Eight out of ten countries with the highest populations at risk of *P. vivax* are in Asia (PRC, Indonesia, Myanmar, Pakistan, the Philippines, Thailand and Viet Nam).

Differences in the biology of each malaria species result in differences in their distribution. For example, *P. vivax* parasites can develop at lower temperatures than *P. falciparum* parasites. As a result *P. vivax* malaria extends further north into central PRC and the Korean Peninsula and is the most prevalent parasite in northern Pakistan, Nepal and central Afghanistan. *P. vivax* malaria is more difficult to control than *P. falciparum* malaria and gradually becomes the dominant species where malaria control measures have been implemented and *P. falciparum* prevalence has decreased.

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Malaria does not affect people equally: some age groups and some populations are at more risk of infection than others. In areas with high malaria risk, individuals frequently bitten by infected mosquitoes tend to develop some immunity to malaria at a young age. In lower transmission settings, which include most areas in the region, individuals are exposed to fewer mosquito bites, develop less immunity and have a higher risk of falling ill at any age. In all areas, pregnant women and children under age five are most vulnerable to the effects of the disease. Where there is variable transmission, the groups at highest risk are those whose behaviour means that they come into more contact with mosquitoes; for example people who work in forests.47,48

Annex 3: What we have achieved within the Asia-Pacific region

**Long Lasting Insecticidal Nets** are distributed in all countries in the region. With the exception of Indonesia, LLINs are distributed free of charge to all age groups. However, as of 2010, based on household survey results, most countries had not achieved the 100 per cent LLIN coverage target. Two countries (Solomon Islands and Vanuatu) achieved 100 per cent coverage, Nepal and Indonesia achieved between 60-70 per cent and the remaining countries between 1 and 45 per cent coverage. Average LLIN ownership in the Pacific region is much higher than in Asia (100 per cent versus 19 per cent). Models of LLIN coverage between 2008 and 2012 based on the number of mosquito nets procured and distributed are more optimistic. These models suggest that LLIN ownership in the region peaked at 72 per cent in 2010 but then declined to 63 per cent in 2011. While coverage with LLINs has increased dramatically in recent years it is still unacceptably low in high risk populations, as in the region as a whole.

Because of the importance of the GMS, specific indicators for ITN and LLIN use are described in Table 1 below.

**Table 1: LLIN coverage in Greater Mekong Subregion**

<table>
<thead>
<tr>
<th></th>
<th>Myanmar</th>
<th>Cambodia</th>
<th>Thailand</th>
<th>Lao</th>
<th>Viet Nam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Households with at least one net</td>
<td>97.4</td>
<td>99.4</td>
<td>-</td>
<td>90</td>
<td>99</td>
</tr>
<tr>
<td>Households with at least one Insecticide Treated Net</td>
<td>35.1</td>
<td>74.7</td>
<td>36</td>
<td>90</td>
<td>19</td>
</tr>
<tr>
<td>Persons who slept under an Insecticide Treated Net the previous night</td>
<td>15.9</td>
<td>52.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Children who slept under an Insecticide Treated Net the previous night</td>
<td>19.4</td>
<td>56.3</td>
<td>-</td>
<td>81</td>
<td>5</td>
</tr>
<tr>
<td>Pregnant women who slept under an Insecticide Treated Net the previous night</td>
<td>20.3</td>
<td>56.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Indoor Residual Spraying** In 2010, 16 countries in the region recommended the use of IRS in their national strategic plans. Of those, in 2009, seven countries reported populations covered by IRS (PRC, Malaysia, Papua New Guinea, the Philippines, Solomon Islands, Thailand and Viet Nam). IRS coverage across the

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50 *Myanmar Artemisinin Resistance Containment Project.*
51 Cambodia Malaria Survey. (2010).
52 *Bednet study, Lao PDR.* (2009).
53 *Bednet study, Lao PDR.* (2009).
region is generally low as IRS is targeted at pockets of high transmission or used in response to malaria outbreaks, rather than used in routine control activities.

**Diagnosis** The revised global target for diagnostic coverage is 100 per cent, that is all suspected malaria cases should receive a confirmatory test using either RDTs or microscopy. Some strategic plans in the region reflect this target, but the majority currently aim for diagnostic coverage of 80 per cent or more. The roll-out of RDTs across the region has increased diagnostic capacity. In 2010, on average 59 per cent of reported cases in the public sector in the region were confirmed with microscopy. All but four countries in the region use RDTs both at health facility and community levels. Where RDTs have not been installed at community level, they are being piloted with a view to expansion, which should further increase diagnostic coverage. There are limited initial efforts to promote parasitological diagnosis in the private sector, which is an important source of care in some countries.

**Treatment** Every country in the region has adopted an ACT as first-line treatment for uncomplicated *P. falciparum* malaria and most retain chloroquine and primaquine for *P. vivax* cases. Data on access to ACTs, either in the public or private sectors, are limited and show wide variations between countries. In the public sector, between 9 per cent and 100 per cent of patients receive ACT treatment for *P. falciparum* malaria. However, not everybody accesses public health facilities. Indeed, WHO estimates that just 58 per cent of the population in Asia access public health services in the event of fever, 19 per cent access private sector services and 22 per cent treat fever at home, with data for Pacific countries quite similar.
Access to Quality Medicines and Other Technologies Task Force