MALARIA CONTROL IN THE GREATER MEKONG SUBREGION: AN OVERVIEW OF THE CURRENT RESPONSE AND ITS LIMITATIONS

Abstract. The malaria burden in the Greater Mekong Subregion has been dramatically reduced over the last 20 years but the disease remains an important public health issue in all six countries. This chapter introduces the standard tools for malaria control (long lasting insecticidal nets; indoor residual spraying; early diagnosis and appropriate treatment; epidemic surveillance and response; and, communication) and presents the evidence base supporting the use of each of these tools in the Subregion. Targeting approaches and delivery mechanisms for these tools are presented and discussed country by country. The technical limitations of these standard tools and delivery mechanisms are then discussed in the context of local variations in the epidemiology of the disease. The challenges presented by the feeding and resting habits of local vectors, by the characteristics and behavior of different human population groups, and by particular species and drug resistant strains of malaria parasites are considered.

A range of innovative tools and delivery mechanism that have been developed to address these problems are presented and moves to bring these various innovations together to provide a comprehensive package of malaria control services for each risk group are discussed. Implementation arrangements are introduced and an overview of the stakeholder landscape at regional and country level is provided. Finally, remaining programmatic gaps (which include limited coverage, declining funds, drug resistance, weak surveillance and weak health systems) are highlighted and areas in need of further action (including the need for continued innovation) are discussed.

Keywords: malaria control, standard tools, case management, current innovation, technical limitation, GMS

INTRODUCTION

The malaria burden in the Greater Mekong Subregion (GMS) has been dramatically reduced over the last 20 years (see Chapter 2). During this period malaria control activities have been scaled-up very significantly as a result of increased political and financial support from both domestic and international sources. The Global Fund alone has provided USD353M for malaria control in the six countries of the GMS since 2002 (Global Fund, 2012a). The impact of this scale-up has been very pronounced with reductions in malaria mortality of more than 50% in most countries during the last 10 years (see Chapter 2). Interventions such as the provision of free insecticide treated bednets (ITNs) (and more recently long-lasting insecticide treated bednets (LLINs)) and the use of rapid diagnostic tests (RDTs) and atemisinin-based combination therapies (ACTs) are generally considered to have played an important part in this success.

Nevertheless, malaria remains an important public health issue throughout the region and national malaria control programs (NMCPs) generally continue to receive strong political support.

Malaria is now largely concentrated in remote areas with low population densities and limited services and infrastructure, especially in and near forested areas which often lie close to international borders. The epidemiology of the disease is particularly complex and varied in the GMS. In many places, the population groups most affected are ethnic minorities, and within these groups cultural and linguistic barriers often constrain malaria control efforts. In some areas the malaria situation is made worse by armed conflict affecting access to malaria control services. Population movements are a key feature in the GMS and this further complicates the epidemiology and control of the disease (see Chapter 4). The rapid increase in the number of large infrastructure and agricultural development projects in the region is also having a significant impact on the epidemiology of communicable diseases in general and malaria in particular (see Chapter 1).

Perhaps the most serious problem that the GMS faces at present is artemisinin resistant falciparum malaria which threatens to undermine global malaria control efforts unless it can be quickly eliminated (see Chapter 5). A large number of partners are now working together with NMCPs in an effort to address these challenges. Priorities vary from one country to the next depending on the epidemiological situation and on their artemisinin resistance status. National program priorities, impact level targets and elimination goals, which are presented in detail in Chapter 2, are summarized in Table 1.

METHODOLOGY

This chapter introduces the standard tools for malaria control as set-out in the Global

Table 1
Summary of national program priorities, impact level targets and elimination goals in the GMS.

Country	Cambodia	China (Yunnan)	Lao PDR	Myanmar	Thailand	Viet Nam
Priorities	Malaria control, containment of artemisinin resistance and province-wise move towards elimination	Prevention of importation of malaria by Chinese economic migrants returning from highly endemic areas of Myanmar and preventing local transmission in the few remaining endemic foci.	Malaria control with a gradual province-wise move towards elimination.	Massive rapid scale-up of malaria control effort and containment of artemisinin resistance.	Containment of artemisinin resistant falciparum malaria along borders with Cambodia and Myanmar, and malaria control moving towards elimination elsewhere. Impact of malaria on tourism is a key concern.	Containment of artemisinin resistant falciparum malaria in four provinces in the Central Highlands and malaria control moving towards elimination elsewhere.
Impact targets - mortality	Annual probable and confirmed malaria deaths reported in public health facilities down to less than 1 per 100,000 by 2015 and down to zero by 2020.		Annual malaria deaths (as reported by hospitals) down to 0.2 per 100,000 by 2015.	To reduce malaria mortality by at least 50% by 2015 compared to baseline data in 2007.	Malaria mortality rate down to 0.05 per 100,000 in 2016.	Malaria mortality rate below 0.02 per 100,000 by 2020.
Impact targets - morbidity	Annual probable and confirmed malaria cases reported in public health facilities down to less than 2 per 1,000 by 2015.	By 2015, zero malaria case in all 55 type 3 counties; by 2015, no locally transmitted malaria in all 55 type 2 counties and in 2 type 1 counties; by 2015, 17 type 1 counties are below 0.1/1000 API.	Annual parasite incidence down to 2 per 1,000 by 2015.	To reduce malaria morbidity at least 50% by 2015 compared to baseline data in 2007.	Annual parasite incidence down to 0.2 per 1,000 by 2016.	Annual parasite incidence below 0.15 per 1,000 by 2020.
Elimination targets	Pf by 2020; all species by 2025.	All species by 2020 in Yunnan (by 2015 elsewhere).	No timeline yet formalized.	To prevent or at minimum significantly delay the spread of artemisinin resistant falciparum parasites within country and beyond its border.	Interruption of malaria transmission (no indigenous cases for 3 years) in 60% of districts by 2016 and 80% by 2020.	By 2020 no hyperendemic provinces; 40 provinces with no local transmission; 15 provinces in elimination mode and 8 provinces in pre-elimination mode.

Malaria Action Plan (GMAP) and then presents the evidence base supporting the use of each of these tools in the GMS. Targeting approaches and delivery mechanisms for these standard tools are presented and discussed country by country. The technical and funding limitations of these standard tools and delivery mechanisms are then discussed in the context of local variations in the epidemiology of the disease in the GMS. A range of innovative tools and delivery mechanism that have been piloted and developed to address these limitations are presented. Implementation arrangements are introduced and an overview of the stakeholder landscape at regional and country level is provided. Finally, remaining programmatic gaps are highlighted and areas in need of further action are discussed.

The information presented in this chapter is based on a review of published literature, international reports and documents from national malaria control programs (including national strategic plans, program reviews, funding applications, grant agreements and grant performance reports - most of which are available online). Findings were corroborated with feedback from national program staff and from WHO country staff.

FINDINGS

1. Standard tools for malaria prevention and case management

The key malaria control interventions outlined in the Global Malaria Action Plan (GMAP) are long lasting insecticidal nets (LLINs), indoor residual spraying (IRS), early diagnosis and treatment (EDAT) and communication (RBM, 2008). The targets set out in the GMAP are for universal coverage – that is 100% ownership and at least 80% utilization of LLINs and 100% of patients receiving locally appropriate case management.

Insecticide treated bednets (ITNs) form the core of malaria prevention efforts in all six countries in the GMS. All six countries also use IRS as an emergency response to outbreaks and most use it on a very limited scale for routine malaria prevention (specifically targeting high transmission areas with low ITN coverage). EDAT through static public sector health facilities forms the foundation of malaria case management services throughout the region. All countries also support communication measures to maximize utilization of malaria prevention and case management services by target populations in order to boost program impact.

1.1 Insecticide Treated Bednets

Insecticide Treated Bednets (ITNs) have been shown to be highly effective in reducing malaria morbidity and mortality by as much as 50% and 17%, respectively among children in areas of stable transmission in sub-Saharan Africa (Lengeler, 2004). The evidence base supporting the use of ITNs in the GMS is not as robust as that supporting their use in the majority of African countries. Nevertheless, a number of randomized controlled trials in the region have

found significant improvements in malaria outcomes as a result of ITNs. 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-randomized 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 behavior, transmission intensity and malaria burden, these estimates of ITN effectiveness approach those seen in trials in Africa.

ITNs are primarily a personal protection measure, however, there is some evidence from trials in Africa that high coverage rates also provide a 'community effect' reducing overall transmission so that people without nets gain some level of protection (Howard *et al,* 2000).

There is a strong culture of bednet use in the GMS where they have been used traditionally for many years for privacy and protection against nuisance mosquitoes. ITNs have been in increasingly widespread use by NMCPs since the 1990s. In the GMS, conventional ITNs have recently been superseded by LLINs everywhere except in Viet Nam (see FINDINGS section 3.2.1) (Global Fund, 2012b; Okell *et al*, 2012). LLINs differ from ITNs in that they either have insecticide incorporated into, or securely attached on to the surface of the yarn. As a result the residual efficacy of the insecticide is much longer than on conventional ITNs and they also withstand washing far better (Guillet *et al*, 2001).

Delivery approach. Different countries in the region have adopted different approaches to bednet delivery but all provide their core bednet services free of charge for all those residing in target areas. Most strategies are now based on periodic mass distribution campaigns (directed by NMCPs, managed by local health services and supported by community volunteers), the frequency of which depend on the estimated viable life of the LLINs used. These mass distributions are sometimes supplemented by ongoing topping-up to maintain coverage. Topping-up operations aim to replace lost or damaged nets and provide nets for pregnant women and new settlers, with delivery through health facilities, antenatal services and special campaigns as appropriate. An Africa-focused model developed recently indicates that in high transmission settings, supplementing a universal mass campaign with extra ANC delivery should achieve a 1.4 times higher mortality reduction than campaign delivery alone (Okell *et al*, 2012).

Private ownership of untreated bednets is high in many parts of the region (Global Fund, 2012b; Malaria Consortium, 2010) and so most NMCPs provide bednet-dipping services during bednet distribution campaigns whereby members of the target population who prefer to use their own conventional bednets can have their nets treated with insecticide (usually a long-lasting formulation) free of charge.

Bednet strategies differ considerably between countries (and sometimes within countries) in a number of different ways making some inter-country comparisons difficult. Until recently most NMCPs in the GMS targeted vector control operations based on proxy indicators of endemicity such as proximity to forest or on some more complex stratification of risk taking into account ecological and entomological factors as well as epidemiological ones. Now all countries target ITN operations based on recent history of local transmission but they still use different thresholds for inclusion despite the existence of standard thresholds/milestones recommended by WHO (2007a). The sizes of the target units (village, commune or district) may also differ, potentially having a profound affect on the cost effectiveness and impact of interventions in different countries. Target coverage (nets per person), netting material, insecticide, insecticide formulation and method of attachment to the netting fibers, and net size may also vary between countries.

Some countries organize mass distributions of LLINs nationwide every few years, others organize mass distributions in different areas each year on a cyclical basis depending on logistical constraints. With LLINs and long-lasting insecticide for treating conventional bednets, the timing of distribution or dipping is not as critical as it is with conventional ITNs (with insecticide of short residual efficacy) and this is a major advantage as it removes the operational demands associated with rapid deployment.

Quantification of requirements. Different countries use different models and different assumptions within those models to quantify their bednet requirements. For example the LLIN attrition rates used may differ from one country to the next for similar net types and this affects the frequency of the periodic mass distribution campaigns and the scale of topping-up operations and therefore the cost effectiveness of the overall approach. These assumptions have generally not been validated.

Large-scale unforseen population movements may sometimes undermine quantification of bednet requirements and well-set plans for LLIN distribution campaigns are frequently thrown off course by funding and procurement bottlenecks.

Implementation of ITNs/LLINs in the GMS. Key features of national ITN/LLIN strategies are presented in Table 2.

In **Cambodia** LLINs are currently provided to all those living in or within 2 km of the forest at a rate of 1 net per 2 people and privately owned conventional bednets in target communities

Table 2
Country wise comparison of key features of bednet strategies in the GMS.

Country	Cambodia	China (Yunnan)	Lao PDR	Myanmar	Thailand	Viet Nam[a]
Primary focus of programme ITNs or LLINs:	ITNs or LLINs	LLINs	LLINs	LLINs	LLINs	ITNs
Cost of service to end user:	Free	Free	Free	Free	Free	Free
Targetting approach for mass distribbution:	All those living in or within 2 km of the forest.	All natural villages with an incidence greater than or equal to 1% in the previous year.	Based on a village level stratification of malaria risk derived from reported incidence between 2006 and 2008.	Based on village level stratification of malaria risk and on accessibility (some very remote areas and areas with ongoing security concerns are underserved).	All villages where transmission has been reported during the previous 3 years.	Based on a commune level stratification of malaria risk. ITNs (LLINs since 2011) only given to poorer members of target communities in stratum 5 (incidence ≥ 10/1,000).
Type of net:	Olyset or Permanet (under GF)	Terylene	WHOPES-agreed (polyethylene or polyester) brand names under GF	Yorkool (GF) and Permanet under MARC.	Permanet or Royal sentry or Yorkool (under GF).	Permanet.
Effective lifespan attributed to LLIN.	3 years	5 years	3 years irrespective of brand name	3 years	Annually (based on family needs).	NA
Frequency of mass distribution:	Depending on donors' support and delay in procurement	N/A	depending on donors' support.	Every 3-year	Every 3-year.	Annual (replacing 1/3 of bednets based on records).
Target coverage	1 net per 2 people	1 net per 2 people	1 net per 1.5 people	Two LLINs per household except in MARC areas (1 LLIN per 2 people)	1 net per 2 people (but 1 net per person in artemisinin resistance containment areas - 22 provinces).	1 net per 2 people
Treat privately owned conventional bednets:	Yes	Yes	Yes	Yes	Yes	Yes
Insecticide for treating conventional bednets longlasting or conventional:	Longlasting	Conventional	Longlasting	Conventional	Longlasting (once a year) but still conventional in use.	Conventional
Targetting approach for retreatment:	As for mass distribution.	All natural villages with at least one reported case the previous year, but with an incidence of less than 1%.	As for mass distribution.	Based on ITNs ownership and stratification.	Based on ITNs ownership in endemic areas.	Based on a commune level stratification of malaria risk targeting strata 3, 4 and 5 (incidence greater than 0).
Frequency of treatment/retreatment of conventional bednets:	Annually	As required	Annually	As required	Annually	Annually
ITN coverage achieved in 2010:	38%[b]	42%[b]	73%	19.9% (2011 survey)	92.5%[c]	68%[d]

[a]Vietnam's bednet policy has however recently been updated and the National Strategic Plan for 2011-2015 stipulates providing LLINs to all those in need in 'high' endemic areas [zone 5] (irrespective of means); treating privately owned conventional bednets in 'low', 'medium' and 'high' endemic areas [zone 3-5] with long-lasting insecticide; and providing conventional bednets treated with long-lasting insecticide for poor people in 'low' and 'medium' endemic areas [zones 3 and 4]; However this change in policy has yet to be implemented as funds are not currently available. [b]ITN coverage refers to survey based estimates of '% of people sleeping under an ITN the previous night'. [c]ITN coverage refers to % of impregnated nets/total number of nets from survey in 43 provinces where pockets of transmission are documented (out of a total of 77 provinces). [d]ITN coverage based on distribution and dipping records.

are treated annually with a long-lasting insecticide.

In **Yunnan Province** the targeting of bednets changed in 2010 from a malaria risk-stratification based approach to a responsive incidence based approach (MOH China-NIPD, 2010). All natural villages with an incidence greater than or equal to 1% in the previous year are now targeted for free distribution of LLIN to achieve 100% coverage based on a delivery rate of 1 net per 2 people (taking existing coverage into consideration). All 'natural villages' with at least one reported case the previous year, but with an incidence of less than 1% are targeted to receive free annual retreatment of all existing conventional bednets (China does not use a long lasting insecticide formulation for retreatment at present).

In **Lao PDR** bednets are targeted based on a village level stratification of malaria risk derived from reported incidence between 2006 and 2008. LLINs are provided at a rate of 1 net per 1.5 people (up from 1 net per 2.4 people prior to 2011) to all those living in 'high' and 'medium' transmission areas ('stratum 3' and 'stratum 2', respectively) as well as in the 623 remote villages not yet classified according to malaria risk. Privately owned conventional bednets in 'low' transmission areas (stratum 1) and conventional bednets used by military and police personnel in strata 2 and 3 are all treated annually with a long-lasting insecticide.

In **Myanmar** bednets are targeted based on village level stratification of malaria risk and on accessibility (some segments of the population are hard to reach due to geographical isolation or ongoing security concerns, mainly in border areas). In recent years Myanmar's NMCP has been severely constrained by lack of funds and this has led to very low ITN coverage amongst the population at risk (less than 6% in 2008). Current efforts are targeting 'high' and 'moderate' risk villages. Two LLINs will be provided per household and an estimated 8 million privately owned conventional bednets will be treated with a long-lasting insecticide every two years.

In **Thailand** bednets are targeted based on a village level stratification of malaria risk. LLINs are distributed in all villages where transmission has been reported during the previous 3 years. Three-yearly mass distributions target all residents and generally aim to achieve a coverage rate of 1 net per 2 people but 1 net per person in containment tier 1 (in-line with the recommendations of the International Task Force for the Containment of Artemisinin Resistance). Privately owned conventional bednets are treated or re-treated at the same time. Thailand is just starting to use lasting insecticide formulations for retreatment.

Viet Nam is the only country that still implements a bednet program based primarily on conventional ITNs. Interventions are targeted on the basis of a commune-level stratification of malaria risk. In order to maximize cost effectiveness the NMCP has in the past opted for a policy of treating privately owned conventional bednets annually with standard lifespan formulations of synthetic pyrethroids, only providing free ITNs (LLINs since 2011) to poorer members

of target communities. These free bednets are provided at a rate of one per 2 people and thereafter replaced at a rate of one-third each year. The bednet policy has however recently been updated and the National Strategic Plan for 2011-2015 stipulates providing LLINs to all those in need (irrespective of means) in 'high' endemic areas [zone 5]; treating privately owned conventional bednets in 'low', 'medium' and 'high' endemic areas [zone 3-5] with long-lasting insecticide; and providing conventional bednets treated with long-lasting insecticide for poor people in 'low' and 'medium' endemic areas [zones 3 and 4]; However this change in policy has yet to be implemented as funds are not currently available.

LLIN/ITN coverage. Over the last decade LLIN/ITN coverage has increased dramatically in all countries but it still remains inadequate. Latest figures for estimated coverage are presented in Table 2. It should be noted that these coverage estimates are sometimes based on the proportion of people who slept under an ITN/LLIN 'last night' (from household level malaria indicator surveys) and sometimes on estimated ownership (based on distribution records). Bednet ownership does not however equate to utilization. In Cambodia the national malaria survey conducted in 2010 indicated that ITN ownership had risen to 75% in target areas (compared with 43% in 2007). However, in households with an ITN, only 53% of all respondents reported sleeping under an ITN the previous night (Malaria Consortium, 2010). Furthermore the denominator for coverage estimates is the target population, the definition of which varies significantly from one country to another (see Table 2). Standardization of approach would help funding partners to allocate support more equitably.

It should be noted that ITN/LLIN coverage can fall rapidly depending on distribution strategy and supply.

1.2 Indoor residual spraying (IRS)

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. The primary effects of IRS are to reduce the lifespan of vector mosquitoes so that they do not have time to transmit malaria parasites (from becoming *infected* it generally takes at least 9 days for a mosquito to become *infective* to humans, longer at lower temperatures) from one person to another, and to reduce the population of vector mosquitoes. Some insecticides also repel mosquitoes and so reduce the number of mosquitoes entering the sprayed room thereby reducing human-vector contact. All of these effects result in reduced vectorial capacity.

Depending on local vector behavior and availability of funds, IRS can prove effective instead of or as an adjunct to ITNs (Pluess *et al*, 2010). Historical and programmatic documentation has clearly established the impact of IRS, which has helped to eliminate malaria from parts of Asia (Chareonviriyaphap *et al*, 2000), Russia, Europe, and Latin America (Schiff, 2002; Lengeler

et al, 2003; Roberts *et al*, 2004). It is still used to control malaria on a large scale especially in sub-Saharan Africa and it is recommended by WHO's Global Malaria Programme as a major means of malaria vector control. 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 randomized 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 69-96%) in terms of incidence and 76% in terms of prevalence (Rowland *et al,* 2000). The review team also found that some limited data suggested that ITNs give better protection than IRS in unstable areas, but concluded that more trials would be needed to compare the effects of ITNs with IRS, as well as to quantify their combined effects (Pluess *et al*, 2010).

Delivery mechanisms. IRS can be broadly divided into two types of strategic implementation in the GMS: 'mass preventive' or 'focal responsive'. Mass preventive IRS is a routine response in areas of consistently high annual incidence. Spraying is generally carried out at regular intervals of six or twelve months depending on the length of the transmission season and the residual efficacy of the insecticide used. In contrast, 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). Focal responsive IRS normally relies on a single round of spraying. In the case of malaria outbreaks, all households in the outbreak community are usually targeted, whereas in the case of confirmed transmission foci, spraying is usually restricted to households within a given distance of each confirmed case.

Mass preventive IRS can result in the development of insecticide resistance and assuming pyrethroids are used this could undermine the effectiveness of ITN campaigns. Limited responsive IRS in known transmission foci is in contrast very unlikely to result in the development of insecticide resistance. Rigorous monitoring of the insecticide susceptibility status of primary vectors is therefore particularly important where mass preventive IRS is in use.

The residual efficacy of IRS varies from around two to twelve months, depending on the insecticide used and the type of surface treated (depending on dosage and substrate the residual efficacy of various public health insecticides can be expected to fall in the following ranges: DDT – 6 to 12 months; pyrethroids – 4 to 6 months; organophosphates and carbamates – 2 to 6 months), so to ensure maximum effect campaigns should be carried-out before the peak malaria transmission season.

IRS requires strong management for planning, organization and implementation. For maximum impact it is also heavily dependent on community acceptance. Householders are required to remove furniture and belongings from their homes prior to spraying and must allow spray teams full access to their properties.

IRS programs aim to achieve coverage in excess of 80% in an effort to maximize effect.

Implementation of IRS in the GMS. According to national strategic plans Lao PDR, Myanmar, Thailand and Viet Nam all conduct mass preventive indoor residual spraying (IRS) once or twice a year (depending on the duration of the transmission season) in endemic areas, generally targeting residents in communities not covered by Global Fund supported bednets. In fact the coverage of mass preventive IRS is generally very low, with all countries placing much greater emphasis on ITNs. In theory, all six GMS countries conduct responsive focal IRS either in the event of 'outbreaks' in more endemic areas or when 'transmission foci' are identified as a result of active case investigation in less endemic containment areas. Details are summarized in Table 5. In fact, the use of focal responsive IRS is also very limited and in most GMS countries technical capacity is sub-optimal, standard operating procedures are not clearly set up and thresholds for implementation are not well defined. The entomological issues surrounding the use of IRS in this region are discussed in detail in Chapter 3.

1.3 Early diagnosis and appropriate treatment

Efforts to prevent mosquito biting can only ever be partially successful. Early diagnosis and appropriate treatment (EDAT) of malaria infections is thus an essential element of malaria control efforts. EDAT reduces the burden of malaria by shortening and reducing the severity of clinical episodes and preventing deaths at the individual patient level, but it also has an impact at the population-level by reducing the parasite reservoir and the infectivity of parasites to mosquitoes, thereby reducing transmission.

Diagnosis. Malaria microscopy remains the gold standard for malaria diagnosis and the diagnostic method of choice for larger health facilities especially in areas targeting elimination (WHO, 2007a). In skilled hands microscopy is more sensitive than RDTs as it can differentiate malaria species more fully, and quantify parasites allowing better-tailored clinical management and follow-up of individual case outcomes (Wongsrichanalai *et al*, 2007).

RDTs enable parasite-based diagnosis to take place at peripheral health facilities where there are no microscopists. RDTs also provide a useful backup diagnostic method if for example a health facility's microscopist is absent or if there is a power failure preventing the use of microscopy. Their development has been a very major advance. Over the last 10 years RDTs have been progressively rolled-out to most endemic areas in the Region (WHO, 2009).

The WHO recommends parasitological diagnosis for all persons with suspected malaria to ensure that only confirmed cases receive treatment with an ACT (WHO, 2010a).

P. vivax and *P. falciparum* are both common in the GMS and so countries are now replacing falciparum specific RDTs with newer 'combo-RDTs' capable of detecting *P. falciparum* specific antigens and non-specific Plasmodia antigens (and of distinguishing between the two). The

sensitivity and specificity of these tests is sub-optimal at present but improving as the technology is developed (WHO, 2012a).

Treatment of falciparum malaria. The drugs traditionally used to treat uncomplicated falciparum malaria have become ineffective in many parts of the world due to the development of drug resistance. The World Health Organization now recommends Artemisinin-based Combination Therapies (ACTs) for treating uncomplicated falciparum malaria world-wide.

ACTs combine an artemisinin-derivative (a relatively new group of drugs which are very effective) with another longer-lasting drug with a different mode of action and a different biochemical target in the parasite. The rationale is twofold: i) the combination is often more effective; and ii) in the very rare event that a mutant parasite resistant to one of the medicines arises *de novo* during the course of the infection, this resistant parasite will be killed by the other antimalarial medicine. This mutual protection is thought to prevent or to delay the emergence of resistance. To realize the two advantages, the partner medicines in a combination must independently be sufficiently efficacious in treating malaria (WHO, 2010a).

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). All six countries in the GMS recommend ACTs as the first-line treatment of *P. falciparum* infections. The addition of a single dose of primaquine is also recommended to quickly kill gametocytes (the parasite stages that are infective to vector mosquitoes) and thereby reduce the risk of onward transmission especially in suspected and confirmed areas of artemisinin resistance.

Treatment of vivax malaria. WHO recommends oral chloroquine for the treatment of vivax malaria where parasites are susceptible. This is effective and well tolerated. Vivax malaria can also be treated with ACTs and this is the norm where parasites exhibit resistance to chloroquine (as is now the case in Cambodia – see Chapter 5). ACTs can also be used in preference to chloroquine to ease the logistical difficulties associated with supplying different antimalarials to the same area (as is the case in Lao PDR).

With both chloroquine and ACTs additional treatment is required to cure the patient completely. This is because the *P. vivax* parasite can lie dormant in the liver for months or years before becoming active again. ACTs may help to delay these relapses but to achieve a radical cure, patients must be treated with primaquine for 14 days (Sinclair *et al*, 2009). Primaquine should not however be used for treating pregnant women, children under 4 years old or patients with a severe form of a relatively common enzyme deficiency (see G6PD deficiency below).

The other three less prevalent species of Plasmodia, *P. ovale*, *P. malariae* and *P. knowlesi* are successfully treated with chloroquine at 25 mg/kg however, like *P. vivax, P. ovale* also has a dormant liver stage and so primaquine is required for radical cure.

Table 3
Country-wise summary of malaria diagnosis and treatment in the GMS.

	Country					
	Cambodia	China	Lao PDR	Myanmar	Thailand	Viet Nam
Diagnosis:	Microscopy in hospitals and healthcare facilities - combo-RDTs in health centers and health posts with no microscope and in villages where VMWs are in operation.	Microscopy at county level	Microscopy in hospitals - combo-RDTs elsewhere	Microscopy and combo tests in hospitals and healthcare facilities - combo-RDTs in remote villages.	Microscopy everywhere except in 460 remote villages (Combo RDTs).	Microscopy in healthcare facilities till commune level - combo-RDTs in remote villages.
First-line treatment for falciparum malaria:	DHA-PIP AP (Pailin Province only).	DHA-PIP	AL	AL, AS+MQ, DHA-PIP	AS+MQ, AP (Trat and Chantaburi Provinces only).	DHA-PIP
PQ single dose with ACT (Pf)	No	No	No	45 mg	30 mg	30 mg
Second-line treatment for falciparum malaria:	Q+T	None	Q+D	AS+D, AS+T	Q+D	Q+D, Q+C
Treatment for severe malaria:	AS+DHA-PIP	AM, AS, PYR	AS+AL	AM, AS, Q	AS, Q	AS, Q
Treatment for vivax malaria:	DHA+PIP	CQ	AL	CQ	CQ	CQ+PQ
PQ in addition to CQ or ACT	No	22.5 mg per day during 8d	No	15 mg per day during 14d	15 mg per day during 14d	15 mg per day during 14d

RDT, rapid diagnostic test; DHA, dihydroartemisinin; PIP, piperaquine; PQ, primaquine; ACT, artemisinin-based combination therapy; Q, quinine; T, tetracycline; AM, artemether; AS, artesunate; PYR, pyronaridine; CQ, chloroquine; AL, artemether-lumefantrine; D, doxycycline; MQ, mefloquine; AP, atovaquone-proguanil; C, clindamycin

For the initial treatment of severe malaria all countries in the GMS now use either parenteral artesunate or artemether. WHO currently recommends that parenteral treatment with artesunate (preferably intravenous), artemether or quinine (in order of preference) be followed by a complete course of either an ACT, or quinine plus either clindamycin or doxycyclin (WHO, 2010a) because in some parts of the GMS the use of artemisinin-based drugs is already compromised by the existence of parasites resistant to artemisinin derivatives (Phyo *et al*, 2012; Chapter 5). Not all countries in the GMS adhere to this recommendation at present. A country-wise summary of treatment guidelines is presented in Table 3.

Treatment and prevention of malaria during pregnancy. Pregnant women are particularly vulnerable to the effects of malaria as pregnancy reduces immunity, increasing susceptibility to infection and increasing the risk of illness, severe anemia and death (Ahmed *et al*, 2007; McGready and Nosten, 2008; Mueller *et al*, 2008; Seal *et al*, 2010; Rijken *et al*, 2012). For the unborn child, maternal malaria increases the risk of spontaneous abortion, stillbirth, premature delivery and low birth weight - a leading cause of child mortality. Routine intermittent preventive treatment during pregnancy (IPTp) with sulphadoxine-pyrimethamine significantly reduces neonatal mortality due to malaria and in highly endemic areas the benefits outweigh the risks (Mubyazi *et al*, 2008; Mueller, *et al*, 2008; Gosling *et al*, 2010; Oyibo and Agomo, 2011). IPTp has not however been widely implemented in the GMS. The reasons for this are discussed under DISCUSSION section 1.6.5.

Quantification of requirements. As with commodities associated with prevention, different countries use different models and different assumptions within those models to quantify their RDT and drug supply requirements. With the exception of Viet Nam, all countries in the GMS use ACTs in age-group specific packaging. This complicates forecasting of requirements (as these age groups are not reflected in the routine surveillance system) and commonly results in stock-outs of drugs for specific age categories.

Epidemics of non-malaria febrile illnesses can result in large numbers of RDTs being used for differential diagnosis (Acestor *et al*, 2012; FIND, 2012) and this can undermine the quantification of RDT requirements.

1.4 Epidemic surveillance and response

Many less endemic areas in the GMS are prone to malaria outbreaks, which left unaddressed can develop into large-scale epidemics (Ettling, 2002; Konchom *et al*, 2005). Outbreaks are commonly associated with mass population movements resulting from civil unrest (Konchom *et al*, 2005) or large-scale agricultural or infrastructure development projects (Cui *et al*, 2012; Deyer, personal communication) both of which are key issues in the region. All countries include measures for detection, investigation, response and follow-up of outbreaks and epidemics in

their national strategic plans however capacity is variable. In some countries staff in peripheral health facilities are expected to detect outbreaks using simple charts showing outbreak thresholds based on mean malaria incidence over several preceding years (CIMPE *et al*, 2010a). In others this function is automated through real-time health information systems (Wang *et al*, 2008; Malaria Consortium, 2011; Khamsiriwatchara *et al*, 2012). To date there has been no systematic review of overall outbreak response capability in the GMS.

1.5 Communication

Utilization 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 for the ITNs to have a 'community effect'; people must cooperate fully with spray-teams in order for IRS campaigns to achieve the coverage required; and, people must urgently seek diagnosis and treatment for fever for EDAT services to be fully effective. For each of these standard interventions a certain level of coverage can be achieved by simply providing the service free of charge or at minimal cost. However, altering the behavior of target populations through effective communication and education can increase coverage considerably and thereby increase cost-effectiveness and impact (Rimal and Lapinski, 2009).

As mentioned above, all countries support communication measures to maximize utilization of their malaria prevention and case management services. It is an area that has traditionally been weak within malaria control programs but in recent years, as funding has increased, more emphasis has been placed on 'information, education and communication' (IEC) and 'behavior change communication' (BCC) and the quality of interventions has improved. Rather than relying solely on the traditional leaflet/poster-based approach there has been increased emphasis on the use of mass media and on the use of music, song, dance and drama at community level as well as on 'interpersonal communication' by health workers and volunteers during patient consultations. However, it should be noted that the actual impact or outcomes of IEC/BCC strategies have not yet been well documented due to the persistent lack of indicators to effectively measure IEC/BCC interventions in the region (WHO, 2011d).

Recently there has been increased interest in a modern variant of IEC/BCC, 'communication for behavioral impact' (COMBI) and methods looking at 'positive deviance' used during the Cambodia-Thailand containment project (CNM *et al*, 2011; WHO *et al*, 2012b)). The key to effective COMBI is an integrated approach that uses a variety of communication actions appropriate to the behavioral outcome desired. Effective management of COMBI requires a high level of expertise and commitment. It has worked in some places, but not in others and it seems that more emphasis will need to be placed on recruitment and training of specialist staff if it is to become more broadly effective (Palmer K, personal communication).

Much more remains to be done in the field of behavior change but with funding short, emphasis seems likely to be placed on essential prevention and treatment activities (as evidenced by the restricted scope of Global Fund's Transitional Funding Mechanism (Global Fund, 2011).

2. Limitations of standard tools for malaria prevention and case management in the Greater Mekong Subregion (GMS)

With the notable exception of IPTp the basic preventive and curative interventions described above are being rolled-out successfully across the region but often malaria continues to be a serious problem even where coverage of recommended interventions is high. The epidemiology of malaria in the GMS is such that the standard tools for disease prevention and case management have a number of serious limitations. These can be broadly divided in to three groups according to their origins:

1. Issues relating to the **vectors** of malaria:

- Early biting outdoors by vectors undermines the impact of ITNs.
- Outdoor resting by vectors limits the effect of IRS;

2. Issues relating to the **human hosts**:

- The characteristics of certain population groups leave them unprotected by standard preventive interventions and unable to access case management services promptly;
- People's tendency to seek treatment in the generally unregulated private sector increases their risk of not being diagnosed and receiving inappropriate treatment and potentially increases the genetic pressure for selection of drug resistant parasites;
- The relatively high prevalence of an enzyme (G6PD) deficiency amongst certain population groups in the GMS prevents the use of primaquine (which is necessary for the radical cure of vivax malaria and for killing falciparum gametocytes) (Gametocytes are the parasite stages in the blood that are responsible for infecting vector mosquitoes).

3. Issues relating the **parasites** themselves:

- The growing proportion of *P. vivax* infections in the GMS and the difficulties associated with detecting and killing its dormant liver stages hampers the control of this species of malaria and undermines the broader malaria elimination effort.
- The recent evolution of artemisinin resistant *P. falciparum* parasites is a particularly critical issue as it threatens to undermine control and elimination efforts in the region and beyond.

Each of these issues is discussed in more detail below.

2.1 Limitations relating to the vectors of malaria in the GMS

2.1.1 Early biting and outdoor resting vectors. The behavior of *Anopheles* species largely determines their vector status, and insights into their behavior help to evaluate the appropriateness of various vector control measures (Trung *et al*, 2005). *Anopheles* mosquitoes are mainly nocturnal, but precise biting periodicity can vary through the course of the night according to a wide range of extrinsic factors (see below). Some species prefer to feed indoors (endophagic) while others prefer to feed outdoors (exophagic). Some prefer to rest indoors after taking a blood meal (endophilic) while others prefer to rest outdoors (exophilic). Malaria transmission caused by late-biting endophagic vectors can be markedly reduced through the use of ITNs/LLINs or through improved housing construction to prevent mosquito entry (*eg*, window screens). Indoor spraying with residual insecticides readily controls endophilic mosquitoes. In contrast, exophagic and exophilic vectors may be best controlled through source reduction (destruction of the breeding sites) if breeding sites are accessible and limited in size and number.

An. dirus and *An. minimus* are the main vectors of malaria in the GMS (both are species complexes made up of several closely related species). *An. dirus* is generally long-lived, highly anthropophagic and exophagic making it a particularly efficient vector even at low population densities (Chareonviriyaphap *et al*, 2000). The open construction of most houses in the forest present little barrier to biting even for exophagic mosquitoes (Obsomer *et al*, 2007). *An. dirus* is by far the most efficient vector of malaria in the GMS, but the fact that its distribution is closely linked to dense forest cover means that its relative importance as a vector is diminishing as deforestation continues. Overall, *An. minimus* has been reported as more zoophilic, exophilic, and exophagic than *An. dirus* making it a less efficient vector (Chareonviriyaphap *et al*, 2000). However, *An. minimus* requires less shade than *An. dirus* and so is less vulnerable to the effects of deforestation. As deforestation continues in the region the relative importance of *An. minimus* as a malaria vector can therefore be expected to grow.

An. maculatus (also a species complex) has been implicated as an important secondary vector of malaria in the GMS (Chareonviriyaphap *et al*, 2000). It is often present at the margins of hilly forest zones and in rubber plantations. Studies in the region have shown that *An. maculatus* is relatively zoophilic and exophagic when compared with *An. dirus* and *An. minimus* which accounts for its lower vectorial capacity (Muenworn *et al*, 2009).

For all of these species complexes the behavior and vectorial capacity can vary considerably between and within sibling species. Major differences may also occur from one place to another according to a multifarious range of interactions between host and vector. A recent review of published studies on the biting periodicity of *An. dirus* failed to classify this species as either a late or an early biter due to the remarkable variation in findings. The phase of the moon, the season and the weather were each identified as key influencing factors. This is likely

to hold true for both *An. minimus* and *An. maculatus*.

Studies in the region do however confirm that under certain circumstances biting by vectors does occur early in the evening before most people with bednets would be using them. A recent unpublished study of *An. minimus* in Cambodia demonstrated a marked shift in behavior towards early biting in November and December coinciding with the period of peak malaria transmission (Sochanta, 2002). The majority of infected mosquitoes detected in this study were captured before villagers were under their nets (4/11 before 08:00 PM and 7/11 before 10.00 PM).

Early biting can clearly be expected to reduce the effectiveness of ITNs but the extent of this reduction is not known. What is clear is that despite these limitations the protective efficacy of ITNs is sufficiently high to make them a key tool for malaria prevention in the GMS (Kamol-Ratanakul and Prasittisuk, 1992; Luxemburger *et al,* 1994; Sochantha *et al,* 2006).

IRS has been shown to result in a greater tendency of vectors to bite outdoors (Ismail *et al*, 1974; Suthas *et al*, 1986). Similarly, the use of bednets might be expected to select for earlier biting but this has yet to be conclusively demonstrated.

2.2 Limitations relating to the human hosts of malaria in the GMS

2.2.1. Groups underserved by standard tools and delivery mechanisms. Some key risk groups are still not adequately protected by standard preventive interventions, are unable to access case management services promptly and lack information on malaria because the provision of these services is not well suited to their specific situations or needs.

As described in Chapter 2, there are five broad categories of people affected by malaria in the GMS: forest fringe inhabitants, ethnic minority groups, rubber plantation workers, temporary migrants and seasonal workers, and new forest settlers. The epidemiology of the disease varies considerably from one group to another, as do their specific needs in terms of malaria prevention and case management.

In remote ethnic minority communities, seasonal migration from relatively accessible villages to inaccessible and scattered forest-fields limits access to malaria control services. Recent rapid growth in the hydroelectric, mining and rubber plantation sectors and road construction associated with the development of new economic corridors are all resulting in increased population movements locally (often as a result of forced resettlement) as well as large-scale occupational migration, placing people (who often have no immunity) in malaria endemic areas with poor health service coverage (see Chapters 1 and 4). Persisting civil unrest in southern Thailand and eastern and northern states in Myanmar and the recent Thai-Cambodia border conflict have all contributed to internal and cross-border population displacements and have hampered the provision of health services in affected areas. The increased connectivity between populations

(often across borders) may increase the complexity of the malaria problem by increasing the movement of drug resistant parasites.

Due to their high mobility and due to the frequently isolated nature of their work, effective malaria surveillance and control efforts targeting these vulnerable groups (described in box 1 of Chapter 2) have proved difficult. Most undocumented international migrants lack access to appropriate health care services while abroad and remain extremely vulnerable to malaria (Malaria Consortium, 2008). In these settings, cross-border collaboration becomes all the more important; mobile and migrant populations often cluster near provincial or national borders and this presents unique challenges for implementation and coordination. Neighboring countries may be unwilling or unable to cooperate due to political tensions, cross-border conflicts, competing priorities, unbalanced economic situations, or lack of resources, infrastructure or capacity. In order to address these pressing issues, there is a real need in all GMS countries to establish and harmonize policies and cross-border activities with a multi-sectoral approach and with the involvement of ministries of health, interior, defense, foreign affairs and labor (WHO, 2012b). The already difficult task is further hampered by the fact that ministries sometimes have conflicting priorities and agendas.

2.2.2 Problems associated with treatment seeking practices. People's tendency to seek treatment for fever outside the public sector puts them at considerable risk of receiving inappropriate diagnosis and treatment and misleading information. This is particularly the case when and where the private sector is flourishing without proper guidance on good practices and without regulation and supervision. The lack of pharmaceutical regulation is a problem in most GMS countries and the presence of counterfeit and substandard drugs (including artemisinin-based monotherapies) is widespread outside the public sector. The Mekong drug quality monitoring study, which ran from 2003 to 2007, revealed that 20% of artesunate treatments in Cambodia and 29% in Lao PDR were fake. *Ad hoc* studies throughout the region between 1996 and 2009 have reported the failure of antimalarial drugs to reach standard specifications. Most recently there have been reports of a high proportion of substandard anti-malarials in Cambodia and a significant number of counterfeit forms of artesunate in Lao PDR (Lon *et al*, 2006; Sengaloundeth *et al*, 2009). It is of great concern that the vast majority of these counterfeits contained subtherapeutic doses of active ingredient designed to deceive basic quality assurance measures, as this is likely to accelerate genetic pressure for the selection of resistant parasites (WHO, 2008).

2.2.3 'G6PD' enzyme deficiency and the routine use of 8-aminoquinolines. Malaria patients with a congenital deficiency in the enzyme glucose-6-phosphate dehydrogenase (G6PD) are at risk of hemolysis (bursting of the red blood cells) if treated with 8-aminoquinolines like primaquine. Unfortunately the prevalence of G6PD deficiency is particularly high and patchy in the GMS, especially amongst certain ethnic groups. Although national treatment guidelines recommend

the use of primaquine for patients who do not have *severe* G6PD deficiency, screening for G6PD deficiency is not generally available outside of hospitals and clinicians therefore rarely prescribe the drug. Rapid tests for G6PD deficiency for field use are under development but current versions are not yet sufficiently sensitive and specific to make the use of primaquine completely safe (Kim *et al*, 2011). Clinicians are unlikely to scale-up the prescription of 8-aminoquinolines until this situation has been resolved.

It is unclear yet if a single dose primaquine is reducing the transmission of falciparum malaria when combined with ACT but in individual patients it reduces gametocyte prevalence and density (Graves *et al*, 2012). The systematic use of a single 15 mg dose of primaquine together with ACT is considered efficacious and safe for the treatment of falciparum gametocytes in adults (WHO, 2012c).

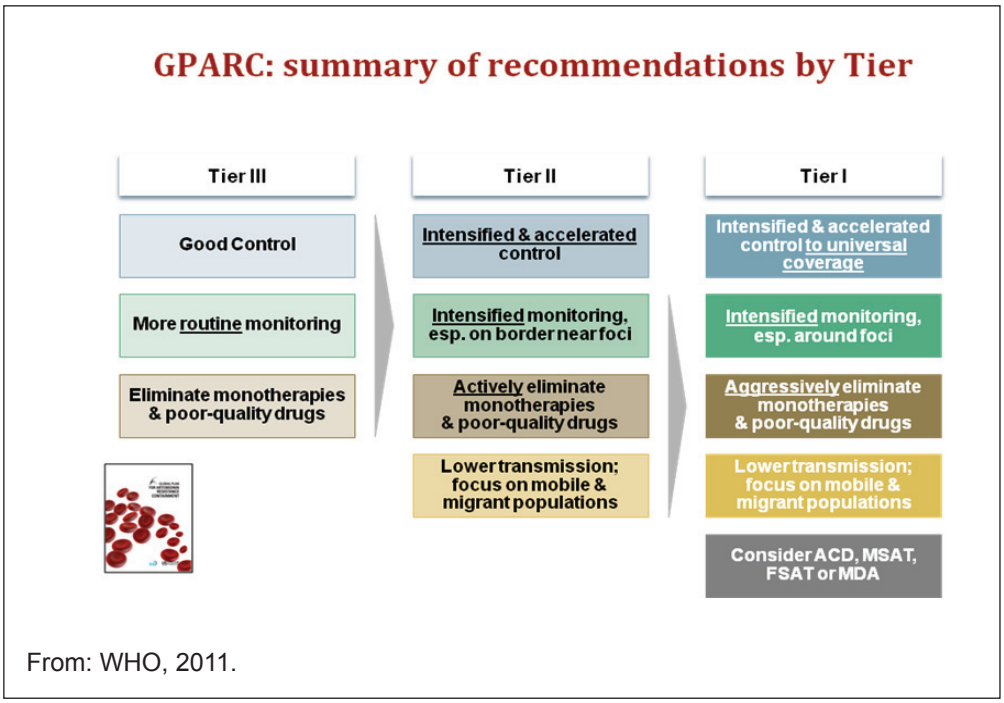
2.3 Limitations relating to the malaria parasites in the GMS

2.3.1 The growing importance of artemisinin resistant *P. falciparum.* The recent evolution of artemisinin resistant *P. falciparum* parasites is a particularly critical issue as it threatens to undermine control and elimination efforts in the GMS and beyond. As described in Chapter 5, artemisinin resistance has now been confirmed at sites in Cambodia and Thailand and suspected artemisinin resistance has been identified at sites in Viet Nam and Myanmar. The need for action on top of routine control interventions is urgent as evidenced by the rapid evolution of artemisinin resistance on the Thailand-Cambodia border. The Global Plan for Artemisinin Resistance Containment (GPARC) was established in 2011 to protect ACTs as an effective treatment for *falciparum* malaria. By the end of 2011 there had been a massive reduction of malaria cases and deaths in target areas but that same year the ACT dihydroartemisinin-piperaquine failed in western Cambodia due to resistance to piperaquine forcing a change to the non-artemisinin based combination therapy atovaquone-proguanil.

Current containment efforts (outlined in box 1 and presented in detail in the GPARC document (WHO, 2011) are mainly constrained by a lack of human and financial resources (especially in Viet Nam and Myanmar) and by poor managerial performance and coordination, and fall far short of what is recommended by WHO (WHO and AusAID, 2012). Coverage with essential malaria prevention and treatment interventions has not reached targeted levels in some of the 'hotspots' of artemisinin resistance. In part this is due to most hotspots being in remote areas underserved by health services and inhabited by hard to reach and in some cases highly mobile populations (WHO, 2011).

It is not clear exactly how the situation will develop. An expert group recently concluded that the worst-case scenario based on no further investment in ARC was that hopes of elimination would be lost and malaria control would be set back by 30 years leading to thousands

Box 1



From: WHO, 2011.

of additional deaths each year. At the same time they predicted that an immediate adequate investment in ARC would mean that long-term savings would balance the additional costs involved (WHO, 2012c).

2.3.2 Difficulties detecting and treating vivax malaria. In the past vivax malaria was thought of as a relatively benign condition and this has led to its serious neglect in terms of research and development. Vivax malaria is far more serious than generally thought and it often manifests itself as a severe disease (Rogerson and Carter, 2008). The relative abundance of *P. vivax* in the GMS and the difficulties associated with detecting and killing its dormant liver stages hamper its control and undermine the broader malaria elimination effort. The fact that it is more difficult to control vivax than falciparum malaria means that as malaria control efforts progress towards elimination, it is increasingly becoming the predominant species of *Plasmodium* in many areas (as described in Chapter 2).

3. Current innovations to address the limitations of standard tools

WHO's regional offices have worked with NMCPs to develop strategies that address many of the limitations associated with the standard tools and delivery mechanisms described in a FINDINGS Section 2 above. The 'SEARO Malaria Control and Elimination Strategy for the

South-East Asia Region (2011-2016)' (*in preparation*) and the 'WPRO Regional Action Plan for Malaria Control and Elimination in the Western Pacific (2010-2015)' (WHO, 2009) promote the use of innovative approaches in order to maximize the utilization of appropriate malaria prevention and case management services by communities and key risk groups as well as to strengthen community-based surveillance towards malaria elimination.

3.1 Innovations to address early biting and outdoor resting by vector mosquitoes

3.1.1 Repellents. Use of topical repellents can provide personal protection against malaria but their large-scale effectiveness in real conditions remains questionable. MOPH-BVBD in Thailand has promoted the use of repellents during the artemisinin resistance containment project but without investing in the assessment of that tool (WHO, 2011). Efficacy studies have demonstrated that repellents work well but they require regular application (Killeen *et al*, 2011). A large-scale effectiveness study is currently being carried out in Cambodia in collaboration with the Antwerp Institute of Tropical Medicine (RBM-VCWG, 2011, 2012; Coosemans M, personal communication).

3.1.2 'Source reduction'. Source reduction involves the destruction or modification of vector breeding sites by physical, chemical or biological means in order to interrupt mosquito production. Source reduction has been one of the positive side effects of the widespread deforestation across the region. The options for source reduction in the GMS are limited by the breeding habits of the main vectors of malaria. *An. dirus* breeds in small, temporary groundwater collections or slow-moving perennial streams, *An. minimus* selects the quiet edges of slow moving streams and *An. maculatus* prefers puddles. All three species require shade. In forested areas these habitats are generally very abundant and often hard to reach. Short of continued deforestation, source reduction is therefore not a viable option for controlling any of these three vectors. Habitat modification, whereby adult vectors are discouraged from entering villages, may however have a role in highly endemic communities in future. Habitat modification is discussed under DISCUSSION section 1.6.1 and in Chapter 3.

3.2 Innovations to address the needs of key risk groups

In the last decade emphasis on addressing the needs of vulnerable populations in the region has increased considerably. Between 2000 and 2007 the Asian Development Bank (ADB) and WPRO supported a project to assist in the development of a comprehensive package of malaria control interventions for ethnic minority groups (EMGs) and to raise awareness of the issues surrounding communicable disease control in remote communities in the GMS (ADB, 2005). The results suggest that malaria intervention packages for marginalized communities need to be comprehensive, free and tailored to the specific requirements of each group (Schratz *et al*, 2010; WHO, 2010b). Project outputs included a draft regional communication strategy targeting

EMGs, the mainstreaming of malaria control for EMGs and the effective promotion of regional collaboration for malaria control.

Increased emphasis is also now being placed on mobile and migrant populations. Key innovative interventions in use at present include smaller LLINs that can be deployed in the cramped conditions often found in EMG field huts and in the temporary structures erected for shelter by migrants, long-lasting insecticide treated hammock nets (LLIHNs) and hammocks, and home based management of malaria through village based and mobile volunteers, all supported by targeted communication programs (WHO and ADB, 2008).

3.2.1 Country-wise innovations to standard delivery of ITNs/LLINs. In Cambodia supplementary LLINs and LLIHNs are provided to mobile/migrant populations (including cross-border migrants), forest goers, seasonal workers, new settlers and soldiers, police and other official groups working in forested areas along the Thai-Cambodia border. Additional communities are targeted in containment hotspots in tiers 1 and 2 aiming at reaching an average of 1 LLIN per person (WHO, 2011). Distribution campaigns are directed by CNM (or NGO partners where present) and managed by provincial, district and commune level health staff in collaboration with village-based volunteers and in cooperation with other members of the target communities. Seasonal migrants involved in agricultural work on large farms in endemic areas are protected through LLIN loan schemes managed by NGO partners with the cooperation of farm managers. In addition Population Services International (PSI) is working directly with the private sector to bundle free long-lasting insecticide treatment kits with commercially available conventional mosquito nets (PSI, 2011). PSI aims to cover 70% of the estimated 900,000 family-sized bednets and hammock nets imported into Cambodia each year. However, given the focal nature of malaria transmission in Cambodia the cost effectiveness of this approach is a concern.

In **China**, as well as providing preventive services for those living in Yunnan's most endemic communities the NMCP places a heavy emphasis on preventing malaria amongst Chinese migrants visiting Myanmar as most of Yunnan's malaria cases are imported from Myanmar (63% in 2009) (GFATM, 2010a). Under phase 1 of China's GF R10 malaria grant the Yunnan Institute of Parasitic Diseases (part of China CDC) is providing LLINs to Chinese workers migrating to Myanmar through border malaria posts. Under the same grant the NGO Health Poverty Action (HPA) is providing LLINs to Chinese workers based in Myanmar (through annual mass distributions coordinated with the employers of large migrant groups). HPA is also providing LLINs to residents of the most endemic villages in the five Special Regions of Myanmar where 95% of Yunnan's imported cases are thought to originate (Myanmar's Kechi Special Region I, Kechi Special Region II, Kanggong Special Region, Shan Special Region II and Shan Special Region IV). In addition HPA is working with traditional birth attendants to provide extra LLINs to pregnant women in the target villages.

In **Lao PDR** conventional bednets used by military and police personnel in strata 2 and 3 (malaria incidence >1/10,000) are all treated annually with a long-lasting insecticide. Supplementary single LLINs are provided to the estimated 30% of pregnant women attending antenatal care services (including those provided by traditional birth attendants) and to the estimated 20% of the population making regular visits to the forest or their forest farms. Mass distribution campaigns are implemented under the direction of the 'Vector Control Unit' at the 'Centre for Malariology, Parasitology and Entomology', the 'Vector Control and Epidemiology Unit' at provincial level and by the 'Epidemiology and Entomology Unit' at district level in collaboration with community members and NGO partners (where present) (MOH-CIMPE, 2010a).

As soon as funds can be secured there are plans to expand the coverage and scope of Lao PDR's bednet program with provision of supplementary LLINs for seasonal agricultural workers in stratum 3, for workers and their families involved in infrastructure development projects in strata 2 and 3, for new settlers in strata 2 and 3 and for official groups involved in the protection of forests and wildlife in stratum 3. Treatment of privately owned conventional bednets with a long-lasting insecticide will be introduced in strata 2 and 3 but dropped in stratum 1 (MOH-CIMPE, 2010a).

In **Thailand** the three-yearly mass bednet distributions described in FINDINGS section 1.1 above target not only Thai residents but also military personnel and registered migrant populations. It aims to achieve a coverage rate of 1 impregnated bednet for 2 persons in documented endemic villages countrywide (MOPH-BVBD, 2010; WHO, 2012d) except in artemisinin resistance hotspots in tiers 1 and 2 where the aim is to achieve a coverage of 1 net per resident and mobile person in-line with the recommendations of the National and International Task Force for the Containment of Artemisinin Resistance. Supplementary hammocks and hammock-nets treated with long-lasting insecticides and repellents are provided to mobile populations and forest goers as appropriate.

Unregistered migrants are also targeted through the provision of LLINs to all fever cases tested at Malaria Posts as well as through special operations conducted by NGO partners (Institute of Migration, Raks Thai Foundation and American Refugee Committee). LLINs and bed mats are also provided for all refugees in camps along the Thailand-Myanmar border.

In addition, the routine preventive IRS carried out twice a year in endemic areas ['A1 and A2'] targets not only residents but also M1 migrants not covered by GF bednets. However, there is a plan to phase out routine preventive IRS over the next five years. IRS as part of the response to malaria foci will continue (WHO, 2012d). Routine preventive IRS is also carried out in all refugee camps (GFATM, 2010b).

In **Viet Nam** supplementary single LLINs or hammocks and hammock-nets treated with

long-lasting insecticides are now provided to mobile populations and forest goers during routine ITN distribution campaigns at a rate of one per household, but so far the geographical coverage of these supplementary nets remains very limited.

Rubber tappers are another high-risk group in southern and central Viet Nam. They work in the rubber plantations at night and very early in the morning and this greatly increases their contact with vector mosquitoes. The NMCP has therefore developed 'face-nets' treated with long-lasting insecticide to protect them from malaria.

3.2.2 Innovations to the standard delivery of EDAT

3.2.2.1 Community-based management of malaria. Although the coverage of public sector health facility-based services has increased slightly in many countries during the last decade the major improvement in access to diagnosis and treatment for malaria has been as a result of the introduction and expansion of community-based services. Following a successful pilot project in Cambodia in 2001 (Oum *et al*, 2005), village-based provision of diagnosis and treatment for malaria - the 'Village Malaria Worker (VMW) Project' - was adopted by Cambodia's MoH to reach highly-endemic communities without reasonable access to health care facilities. In addition to VMWs, mobile malaria workers (MMWs) have since been introduced in some areas to address the needs of recognized groups active in remote endemic areas (WHO, 2012e). The role of VMWs has also been expanded to provide essential surveillance support for artemisinin resistance containment operations in containment tiers 1 and 2. The project now covers 1,400 villages and treats around 50,000 confirmed malaria cases each year (almost half of the malaria cases identified by Cambodia's public sector – see also Chapter 2) at a cost of just over USD2 million per year (WHO, 2012e). Add-on interventions for children with diarrhea and acute respiratory tract infections have been shown to be viable and to improve the cost effectiveness of the VMW scheme still further and these have been introduced in some communities but additional funding is required for continued expansion of these services (WHO, 2012e; WHO and UNICEF, 2012). Following extensive lobbying by WHO and with financial support from the Global Fund, community-based diagnosis and treatment has since been adopted and introduced throughout the GMS and beyond. This new delivery mechanism has greatly improved access to early diagnosis and appropriate treatment especially for those in remote places bearing the greatest burden of malaria (WHO, 2012e).

Cool chain for home based management of malaria. Low cost low-tech 'cooler-boxes' (which operate by simple evaporation of water and require no electricity) have been developed for VMWs and outlying facilities to maximize the shelf-life and quality of RDTs and antimalarials (Chanthap *et al*, 2010). However the design of the current version is not sufficiently robust and they rapidly deteriorate to a point where they cease functioning effectively. A tougher model is

urgently needed before coverage is increased (WHO, 2012e).

3.2.2.2 Standby treatment. In Viet Nam ACT-based standby treatment for malaria is provided on request to individuals travelling to endemic areas whereas elsewhere in the region use of standby treatments is rare (MOH Viet Nam-NIMPE, 2011). Use in Viet Nam is currently excessive (NIMPE *et al*, 2010) but properly regulated, and possibly linked to the use of RDTs, it offers promise as a means of ensuring early access to treatment for hard to reach individuals in remote high-risk areas (NIMPE *et al*, 2010).

3.3 Innovations to address the problems associated with treatment seeking in the private sector

As discussed in DISCUSSION section 2.2 people's tendency to seek treatment for fever outside the public sector puts them at considerable risk of inappropriate treatment. Malaria control programs in the GMS have adopted a number of strategies to address this issue and promote rationale use of medicines including: increasing the coverage and strengthening the performance of public sector healthcare services; strengthening pharmaceutical regulation, quality assurance monitoring and enforcement; and, strengthening private sector healthcare services.

3.3.1 Strengthening public sector healthcare services. All of the countries in the region are working to strengthen the quality and where appropriate the coverage of facility-based healthcare services provided by the public sector. In addition countries are expanding the coverage of public sector healthcare provision through the expansion of community based case management services (see FINDINGS section 3.2.2 above).

3.3.2 Strengthening pharmaceutical regulation, monitoring and enforcement. Efforts are underway to strengthen pharmaceutical regulation, monitoring and enforcement. Following a resolution issued by the World Health Assembly in 2007 (WHO, 2007a) all GMS countries have now banned the use of artemisinin based monotherapies but some countries still produce them for export (WHO, 2012b). In Thailand the sale of antimalarials is banned altogether in the private sector.

Monitoring of drug quality has been introduced in all countries in collaboration with specialized international partners. The quality and coverage of this monitoring remains variable however and the sampling approach would benefit from inter-country and inter-study standardization since results vary greatly with the method used. In response to mounting evidence of fake and poor quality antimalarials an antimalarial drug quality database has been created under the Asian Network of Excellence in Quality Assurance of Medicines (ANEQAM), assisting efforts to track down and prevent the production of counterfeit anti-malarials. In addition a forum for 'Building Regional Expertise in Medicines Regulation, Information Sharing, Joint Investiga-

Table 4
Key risk groups by country and summary of special supplementary malaria control measures underway for each country in the GMS.

Country	Cambodia	China (Yunnan)	Lao PDR	Myanmar	Thailand	Viet Nam
Risk group/situation						
Ethnic minority groups.	Community based Rx/Dx, additional LLIHN/single LLINs for field use & culturally adjusted IEC/BCC.		Community based Rx/Dx & special IEC/BCC.	Community based Rx/Dx & special IEC/BCC.	Community-based Rx/Dx - additional LLINs and culturally adjusted IEC/BCC	Community based Rx/Dx, [additional LLIHN/single LLINs for field use] & special IEC/BCC.
Forest goers.	LLIHN/single LLINs.				LLIHN & repellents.	LLINs & Standby treatment.
Seasonal agricultural workers.	LLIN loan scheme for big farms, taxi advertised helpline & mobile volunteers providing Rx/Dx.				screening in outreach facilities (by microscopy) on a voluntary basis - LLINs / LLIHN	
Rubber plantation workers.					LLIHN & Repellents	Insecticide treated face nets
Economic migrants (new settlers to forest areas).	LLINs.		LLINs.			LLINs.
Infrastructure development projects.			LLINs, [IRS] & community based Rx/Dx.			
Army.	ITNs [& repellents].		ITNs.	ITNs.	ITNs & repellents.	ITNs.
Conflict areas.				Cross-border support from China based INGO for 5 northern States including community based Rx/Dx & LLINs.	Same services provided but using local staff only who are familiar with local security context	
Emmigrant workers.		Chinese nationals working in Myanmar provided LLINs on departure, LLINs and community based Rx/Dx at settlements in Myanmar and screening on return.			LLIN & LLIHN & repelents	
Registered immigrant workers.			See infrastructure development projects (above).		Similar services as for residents. Workplace screening and special IEC/BCC (such as malaria corner) - provision of LLINs	
Unregistered immigrant workers.					Rx/Dx through malaria posts with LLINs for all patients with fever including migrants	
Refugees / displaced people.					LLINs, LLIHNs, repellents, IRS, community based Rx/Dx & special IEC/BCC.	
Frequent short-term border crossers.					Same as for unregistered migrant workers	Standby treatment
Standby treatment.						
All risk groups.	subsidised RDTs and ACT to private sector by PSI.				LLINs, LLIHNs, repellents, IRS, community based Rx/Dx & special IEC/BCC.	

Rx, diagnosis; Dx, treatment

tion and Enforcement' (BREMERE) has recently been established in Bangkok to support joint investigations and promote collective enforcement actions within and among countries in the region (Phanouvong *et al,* 2010).

Countries are increasingly working towards stricter enforcement of regulations. In 2007 Operation Jupiter (an international collaboration between scientists, public health workers and police) had a major breakthrough leading to the seizure of fake artesunate and a number of arrests in China. However, overall the capacity of national regulatory authorities to sample and test for fake, sub-standard and possibly degraded anti-malarials across the region is variable and generally insufficient (WHO *et al*, 2012).

3.3.3 Strengthening private sector healthcare services. Some countries have worked closely with the private sector to improve the quality of the healthcare services they provide. In Cambodia in 2003 the NMCP launched the 'Malarine Project', which pioneered the sale of subsidised RDTs and ACTs through the private sector (Littrell *et al*, 2011). This innovative project provided important lessons on private sector engagement that informed the development of the Affordable Medicines Facility (malaria)(AMFm), which was launched in 2010 to pilot the delivery of heavily subsidised ACTs to the public, private and NGO sectors in a number of African countries and in Cambodia. The AMFm pilot in Cambodia has been severely hampered by delays in the procurement of ACTs (WHO, 2012f) and many challenges remain to be addressed in this field (MOH-CNM Cambodia and MOH-CIMPE Lao PDR, 2011 unpublished reports; Littrell *et al*, 2012).

3.4 Innovations to address the problem of artemisinin resistance

Recent Global Fund grants to Cambodia and Thailand aim to support a continuation and expansion of the bi-country artemisinin resistance containment project initiated in 2009 (GFATM, 2010a,c). A recent joint review by technical partners in the region concluded that:

'…*a good, if delayed, start has been made to addressing artemisinin resistance in the GMS. In some areas the impact has already been impressive. In general the approach to containment as outlined in the Global Plan for Artemisinin Resistance Containment (GPARC) and several associated national level strategies and plans is appropriate. It is acknowledged that national strategies are, with the exception of those of Cambodia and Thailand, in their early stages of implementation. However, overall the assessment is sobering. It is impossible to avoid the conclusion that not enough is yet being done, with enough intensity, coverage and quality, to contain a problem that could not only slow future progress but also undo the gains already made in malaria control worldwide'*.

Appropriate strategies for the containment of artemisinin resistance are presented in the GPARC - the 'Global Plan for Artemisinin Resistance Containment' - (developed by WHO with

Table 5
Country-wise summary of key points associated with malaria control and elimination in the GMS.

Country	Cambodia	China (Yunnan)	Lao PDR	Myanmar	Thailand	Viet Nam
Provision of free LLIN.	Yes	Yes	Yes	Yes	Yes	Yes (only to poor)
Free insecticide treatment for privately owned bednets.	Yes	Yes	Yes	Yes	Yes	Yes
Private sector engagement for ITN.	Bundling with long-lasting insecticide at central level	No	No	Bundling with long-lasting insecticide through selected outlets (managed by PSI).	No	No
Mass preventive IRS.	No	No	Yes [limited coverage]	Yes [limited coverage]	Yes [limited coverage]	Yes [limited coverage]
Focal responsive IRS (outbreak).	Yes	Yes	Yes	Yes	Yes	Yes
Number of sentinel sites monitoring insecticide resistance.	4	3	None in 2010 (10 to be set up from 2012)	5 (additional 7 from 2012)	6	3 (but additional studies in 20 "moving" sites)
Treatment and diagnosis guidelines last updated.	2012	2009	2011	2008	2008	2009
Facility based diagnosis and treatment.	Nationwide	Nationwide	Nationwide	Nationwide but limited coverage in conflict areas.	Nationwide	Nationwide
Community based delivery of EDAT.	Complete (>95%)	N/A (village doctors)	Substantial (~80%)	Partial (but expanding)	Complete (malaria posts) (~100%).	Partial (expanding)
Status of private sector (PS) in diagnosis and treatment.	Substantial PS engaged through AMFm pilot.	Minor PS except village doctor network which is fully engaged.	Moderate and growing but little engagement.	Very substantial but limited engagement.	NIL (limited illegal activity).	Moderate in some provinces where no ban enforced.
Population seeking treatment outside public sector.	59-80	<5%	60-80	60	N/A	13-23
Private sector engagement for diagnosis and treatment.	Extensive	N/A	No	Limited	N/A	No
Number of sites monitoring antimalaria drug resistance (Pf or Pv or both).	5	3	3	9	9	5
Artemisinin resistance status.	Confirmed in Pailin	Suspected	None detected	Confirmed on the Myanmar-Thai border in Mae Sot District and Myawaddy Township.	Confirmed in 3 districts on the Cambodia-Thai border	Suspected
ARC program in tiers 1&2[a]	Operational	N/A	N/A	Planned but not fully funded.	Operational	Planned but partially funded
Communication for behavior change.	Yes	Yes	Yes	Yes	Yes	Yes

[a]ARC, artemisinin resistance containment.

partners in 2011). The key *'containment'* interventions, which are supplementary to routine malaria control interventions, are summarized in box 1. The intensity of the response required is graded geographically in to tiers one to three according to proximity to the focus of artemisinin resistance (with 'tier one' at the epicenter).

A number of innovative containment strategies have been piloted in tiers one and two including:

- Focused screening and treatment (FSAT): a PCR-based strategy to detect malaria parasite carriers and contain drug resistant *P. falciparum* in Pailin, Cambodia (Hoyer *et al*, 2012);
- Respondent-driven sampling (RDS): an innovative method for investigating migration pattern and behaviors in unrecorded mobile migrants (Khamsiriwatchara *et al*, 2012; Wang-roongsarb *et al*, 2011);
- Use of web-based malaria information systems to manage, monitor and map individual patients under treatment (Khamsiriwatchara *et al*, 2012; Satimai *et al*, 2012);
- Use of atovaquone-proguanil as first-line drug treatment in tier one areas (MOPH Thailand, 2011, unpublished data; MOH Cambodia, 2012, unpublished data);
- Innovative cross border Cambodia-Thailand IEC/BCC strategies (Malaria consortium, 2011; MOPH Thailand and MOH Cambodia, 2011, unpublished data).

3.5 Bringing the various interventions together to form a comprehensive package for each risk group

With the elimination of malaria and artemisinin resistant *P. falciparum* high on the regional agenda it is now a priority to ensure that the various interventions discussed above come together so that each of the risk groups is targeted with a comprehensive package of preventive and curative measures that are tailored to their specific needs. In order to achieve this it is useful to categorize the various population groups according to needs. A key consideration is whether the risk group is static or mobile as this determines the suitability of several standard interventions including large sized LLINs, IRS and facility-based case management services. The static and mobile groups can then be further categorized according to sub-group based on more specific needs. In Lao PDR the NMCP has developed a matrix that matches the various interventions available to the various risk groups present in the national malaria landscape (Table 6). As well as ensuring that the risk groups have the best cover possible with the tools and delivery strategies currently available, the matrix also helps to identify gaps in the national strategy. It should be noted that at present the Lao PDR matrix is just a planning instrument as the NMCP is currently in need of funding to enable it to implement the various interventions described.

This is an area that is under further development region-wide and WHO has recently

established a TWG to explore this further and develop an approach that is applicable throughout the GMS and beyond.

Integration of activities run by NMCPs is generally limited (Shigayeva *et al*, 2010) and valuable opportunities for synergy are often lost as a result. For example, diagnosis and treatment for malaria is now available at community level in many of the region's transmission hotspots, but children in these same communities do not generally have access to treatment for acute respiratory tract infections or diarrhea (Mayxay *et al*, 2007; Thang *et al*, 2009; Phommanivong *et al*, 2010; WHO, 2012e). Greater efforts are needed to develop practical mechanisms to effectively operationalize integration across health programs, in order to take full advantage of opportunities for life-saving synergies between malaria and other health initiatives and to strengthen health systems in general.

4. Partners involved in malaria control and elimination in the GMS

The successful implementation of national strategies depends on motivating many stakeholders at global, regional and national levels to support or conduct program activities. Gathering high-level political commitment and promoting inter-sectoral and multi-organizational action through regular meetings and coordination and advocacy events helps to strengthen regional and global exchange and cooperation. Countries in the GMS need to work together closely on cross-border issues and so sharing information between national programs is essential.

4.1 Partnerships at regional level

There are an increasing number of important stakeholders at regional level that support the six GMS countries technically and financially and help them to maintain broader region-wide and global perspectives. These include:

The World Health Organization (WHO). WHO provides technical guidance and support to the malaria control community throughout the region through its network of specialist staff at country and regional levels. WHO also provides specialist technical assistance as required and provides financial support for specific program activities where requested.

WHO's Mekong Malaria Programme (MMP). MMP aims to facilitate the implementation and monitoring of a comprehensive malaria strategy endorsed by national authorities and stakeholders to address common Mekong challenges in order to further impact malaria morbidity and mortality. Primarily funded by USAID, the MMP strategy was developed in-line with the WHO Western Pacific Regional Office's (WPRO) Regional Action Plan 2010-2015, WHO Southeast Asia Regional Office's (SEARO) Revised Malaria Control Strategy 2006-2010, and USAID indicators. The main malaria strengthening components of the strategy include policies and management, prevention, case management, IEC/BCC, vulnerable groups and strategic information. The main systems strengthening components of the strategy include regional

Table 6
Lao PDR planning-matrix illustrating targeting of malaria interventions (*eg*, vector control, personal protection and case management) by risk group as per National Malaria Strategy adopted in 2010[a].

	Static population					Mobile population	
	Villages	Pregnant women	Construction projects	Forest plantation workers	Soldiers and police.	workers involved in newly set up rubber, coffee plantations	People involved in seasonal labor/forest activity and longer term newly set up small and large project development activities
Risk strata based on last 3-year village incidence							
Stratum 1 (low risk, API: 0-0.1/1,000)	ITNs / LLINs: up to the population to buy from the market; Combo tests and ACT are available down to health centers. Mass media only. Integrated surveillance system is strengthened.						
Stratum 2 (moderate risk - API: 0.1 - 10/1,000)	Promotion of free bednet and diagnosis/treatment service.	1 extra large LLIN provided free by TBA/ANC clinic to every pregnant women as required. TBA/VMV and districts provided with stock of LLINs for pregnant women based on village population and rural pregnancy rate.	Advise on health related issues including requirements for prevention of malaria and other communicable diseases. NMCP has an agenda with the national infectious disease committee of the PM's office and is engaging with relevant ministries - *eg*, Ministry of planning and investment, labor etc.	Promotion of free bednet and diagnosis / treatment service.	Promotion of free bednet, diagnosis and treatment service.		
	Free re-impregnation of existing conventional bednets with long-lasting insecticide as required.		Construction companies will be held responsible by the Health Impact Assesment Committee for providing LLINs for all employees and their families at coverage rates recommended in national guidelines for Vector Control.	Free treatment of existing conventional bednets with longlasting insecticide as required.	Free re-impregnation treatment of existing conventional bednets with long lasting insecticide as required.		
	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks.		Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks.	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks.	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks.		

Stratum 3 (high risk API: >10/1,000)	Free LLINs provided through periodic mass distribution (periodicity depends on lifespan of LLIN: polyester - 3 years; polyethylene - 5 years). 1.5 people per extra large net or 1 person per single net.	1 extra large LLIN provided free by TBA/ANC clinic[b] to every pregnant women as required. TBA/VMV and districts provided with stock of LLINs for pregnant women based on village population and rural pregnancy rate.	Advise on health related issues including requirement for prevention of malaria and other communicable diseases. NMCP has an agenda with the national infectious disease committee of the PM's office and is engaging with relevant ministries - *eg*, Ministry of planning and investment, labor etc.	LLINs will be provided to employers at standard subsidized price.	Single LLINs will be provided to army and police forces according to requirements free of charge.	Additonal LLINs, hammock nets (LLIHN) for use in forest farms provided through routine periodic mass distribution.	Single LLINs , hammock nets (LLIHN) will be made available for sale at standard subsidized price through selected public/private sector providers (service advertised by billboards at key points of entry to forest and high risk agricultural areas.
	Annual replacement of lost/damaged nets during follow-up campaign (35% per annum for polyester; 20% per annum for polyethylene TBD. Not during mass distribution years.		Construction companies will be held responsible by the Health Impact Assesment Committee for providing LLINs for all employees and their families at coverage rates recommended in national guidelines for Vector Control.			Annual replacement of lost/damaged nets during follow-up campaign (35% per annum for polyester; 20% per annum for polyethylene TBD. Not during mass distribution years.	Construction companies will be held responsible by the Health Impact Assesment Committee for providing LLINs for all employees and their families at coverage rates recommended in national guidelines for Vector Control.
			Repellents will be provided at a subsidised price as required.	Repellents will be provided as required.	Repellents will be provided free of charge as required.		Repellents will be provided at a subsidised price through Private registered retailers.
	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks and in areas of intense transmission.		Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks and in areas of intense transmission.	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks and in areas of intense transmission.	Provide free indoor residual spraying (according to national vector control guidelines) in response to outbreaks and in areas of intense transmission.		Engaging private companies into indoor residual spraying operations (according to national vector control guidelines) in response to outbreaks and in areas of intense transmission. Companies procure insecticides and equipments with technical inputs and training provided by the national program.

[a]"free" interventions are depending on available funding and procurement performance; [b]TBA traditional birth attendant; ANC antenatal care

cooperation, public-private partnerships, integration and elimination (WHO and CDC, 2009).

USAID-Regional Development Mission - Asia. Launched as part of the RBM partnership in 1999, RDM-A is active in the control of malaria in the Mekong countries. Since 2010, the President Malaria Initiative (PMI) has put additional funds in malaria control in the GMS to reach USD 14 million in 2012.

Key areas of focus include:

- Monitoring and evaluation: The recently funded Regional Malaria Indicator Framework creates an updated Mekong-specific M&E framework that was developed through the joint efforts of the six Mekong NMCPs, WHO, USAID, United States Centers for Disease Control and Prevention (CDC), and MC with leadership from MEASURE Evaluation.

- Cross-border areas: Efforts to strengthen malaria control in areas with evidence of artemisinin resistance to achieve Mekong targets set by MMP and WPRO.

- Surveillance: Continued support to NMCPs to conduct therapeutic efficacy studies at 35 sites across the six Mekong countries. Also work with partners to determine vector transmission ecology in relation to current LLIN deployments.

- Operations research and training: Primaquine use guided by a second-generation point of care G6PD test and research into personal protection measures. Support regional training courses and field epidemiology programs [via Academy for Education Development (AED) group developing Mekong Infectious Disease BCC (MID-BCC) tools].

- Coordination: Regional coordination efforts for MMP programs in cross-border focus areas.

Asian Collaborative Training Network for Malaria (ACTMalaria). ACTMalaria, based in the Philippines, is a unique network controlled by its Member countries. It continues to grow after more than 10 years in operation. The network has 2 major objectives:

- Provide collaborative training for member countries to meet the needs of malaria control in Southeast Asia and Mekong Region.

- Improve communications among member countries on malaria problems affecting common borders.

It has been successful in organizing a series of training courses that target a wide range of participants particularly those that do not have the credentials to pursue university courses. Its training is needs-based and uses problem-based learning. One of its most important course offerings is the 'MMFO' (Managing Malaria Field Operations) that provides managers and field officers with the basic skills to effectively plan and manage malaria field operations.

Malaria Consortium (MC). MC opened an office in Thailand in 2007 based at the Faculty

Table 7

Summary of geographical coverage of major funding and technical partners involved in malaria related efforts in the GMS.

[Dark grey - continuing support; light grey - support phasing out; dark black - support phasing in].

	Cambodia	China (Yunnan)	Lao PDR	Myanmar	Thailand	Viet Nam	Mekong region
Major funding partners							
Global Fund							
USAID/PMI							
AusAID							
BMGF							
Clinton Foundation							
JICA							
DfID							
Major technical partners							
World Health Organization							
WPRO							
SEARO							
ACTMalaria							
Malaria Consortium							
APMEN							
PMI							

of Tropical Medicine, Mahidol University. It has designed and analysed large-scale malaria surveys in Cambodia (2004, 2007, and 2009), and supported the creation of ACTMalaria for regional training. MC is a partner for M&E and operational research in the MMP.

Asia Pacific Malaria Elimination Network (APMEN). APMEN was established in 2009 under the leadership of the University of California, San Francisco's 'Global Health Group' in partnership with the School of Population Health, University of Queensland, and in close collaboration with WHO, to bring attention and support to malaria elimination in the Asia-Pacific Region, with a particular focus on *Plasmodium vivax*. APMEN is composed of thirteen Asia Pacific countries that are pursuing malaria elimination (including Cambodia, China, Thailand and Viet Nam), as well as leaders and experts from key multilateral and academic agencies. APMEN aims to collaboratively address the unique challenges of malaria elimination in the region through leadership, advocacy, capacity building, knowledge exchange, and building the evidence base.

4.2 Partnerships at country level

Each of the six GMS countries has a government agency that is responsible for managing national malaria control and elimination efforts. Below central level the management structure varies from one country to another. In most countries there are also numerous stakeholders involved in funding, providing technical assistance or supporting implementation of activities. In some countries the recent increase in the number of partners has been so dramatic that it has led to serious coordination issues.

4.2.1 Cambodia. In **Cambodia** the national malaria control effort is led by the National Center for Malaria Control, Parasitology and Entomology ('CNM'). Management of implementation is largely decentralized through Provincial Health Departments and through Malaria Supervisors at Provincial level or sometimes at Operational District level.

Numerous international partners are involved in supporting Cambodia's malaria control effort to the extent that inter-agency coordination has become a critical issue.

Funding partners include:

- Global Fund (GF) – GF Round 6 (R6) and R9 grants consolidated into single stream funding (SSF) - implemented by the CNM and 16 partners targeting malaria control, containment and the move towards elimination, and a GF Affordable Medicines Facility for malaria (AMFm) grant implemented by CNM and 4 partners. Total GF support is expected to be USD56M between 2012 and 2015.

- United States Agency for International Development (USAID)/President's Malaria Initiative (PMI) – 'Greater Mekong Sub-Region Malaria Control Program (GMS-MCP)' project focusing on implementation of malaria control and containment of artemisinin resistance and

related operational research in selected sites in Myanmar, Thailand and Cambodia (Cambodia component worth USD0.9M in 2012 then USD1.4M annually). (PMI, 2012). GMS-MCP will be managed by a consortium led by University Research Co, LLC (which recently implemented a similar project in Cambodia). PMI also provides financial support for the US non-governmental organization (NGO) Family Health International (FHI).

- USAID – Support for technical assistance (TA) through the WHO amounting to USD0.35M annually.

- Clinton Foundation– Technical support for drug related issues including forecasting of antimalarial requirements.

Implementing partners include:

- Population Services International (PSI) – Supporting private sector subsidized ACTs and RDTs and conducting population-based surveillance surveys for ACTs and other drugs.

- Malaria Consortium (MC) – Providing technical support for M&E including management of periodic large-scale malaria indicator surveys, development of surveillance systems, operational research and BCC.

- Partners for Development (PfD) – Providing management support for malaria control activities in Kratie and Koh Kong Provinces.

- Health Poverty Action (HPA) (formerly Health Unlimited) – Providing management support for malaria control activities in Ratanakiri and Preah Vihear Provinces.

- Family Health International (FHI) – Providing management support for malaria control activities in 46 villages including village malaria workers (VMWs) and surveillance.

- University Research Co, LLC (URC) – Providing management support for VMWs in 240 villages and conducting operational research relating to the containment of artemisinin resistance (*eg*, scheme for loan of LLINs by farm managers to seasonal migrant workers).

4.2.2 China. In **China** the national malaria control effort is led at Central Level by the National Institute of Parasitic Diseases (NIPD) in Shanghai, part of the China's Centre for Disease Control (China- CDC). Implementation of activities is primarily through the Bureaus of Disease Control at County and District (City) levels, and through Township Hospitals and the network of Village Doctors. Technical support is provided by Provincial (Municipal), Prefecture, District (City) and County CDCs.

China's main external funding partner in recent years has been Global Fund (GF). Until 2011 China had two GF grants:

- The GF National Strategy Application (NSA) grant was recently rescinded and is due

to close in June 2012 (Prof Xiao-Nong Zhou 2012, personal communication).

- GF R10 grant (recently truncated to cover Phase 1 only) - USD4.5M during 2012-2013 providing basic malaria control services for 586,000 Myanmar residents plus Chinese migrants (100,000 long-term and 1.5 million short-term) in five 'Special Regions' (autonomous regions) of Myanmar bordering Yunnan.

Implementing partners include:

- Simao Institute of Parasitic Disease Control (part of China CDC) which provides technical support to the national program and to activities supported by the GF grant.

- China Red Cross Society (CRCS) Under Global Fund (GF) support CRCS has managed mass distribution of free LLINs in collaboration with the People's Committee at local level. Its role following the withdrawal of GF support is uncertain.

- Health Poverty Action (HPA) (formerly Health Unlimited), which is involved in cross-border management support for malaria control activities in northern states of Myanmar (financed by GF R10).

4.2.3 Lao PDR. In **Lao PDR** the national malaria control effort is led by the Ministry of Health's Centre for Malaria, Parasitology, and Entomology (CMPE). Management of implementation is largely decentralized through Provincial Health Departments.

Lao PDR's main external funding partner in recent years has been Global Fund (GF). It currently has one expiring grant:

- GF R7 grant is implemented by the CMPE and partners and is expected to provide USD6.1 M during 2012-2013 but is due to expire in June 2013 (The Global Fund, 2007a).

- An application to GF's Transitional Funding Mechanism (TFM) for USD7M for essential malaria control activities between mid-2013 to mid-2015 has recently been approved but is now subject to further reductions in budgets from the TRP and further anticipated from the GF secretariat. This grant will be implemented by CMPE alone with a small component for the national FDA.

In 2012, PMI/USAID has supported the program with the procurement of bed nets and hammock nets for an outbreak in a southern province. Potential further assistance is in discussion.

Implementing partners include:

- Health Poverty Action – Providing management support for malaria control activities in Attapeu, Saravane and Sekong Provinces including support for outbreaks in the south through ECHO funding.

- Pasteur Institute – Primarily involved in research on arboviruses but well positioned for

research on malaria transmission and vector biology, support for routine entomological surveillance, and in depth assessment of insecticide resistance using biochemical and molecular tools as well as bioassays.

- The Wellcome Trust–Mahidol University–Oxford Tropical Medicine Research Programme –Drug resistance monitoring and clinical studies on ACTs and new antimalarial treatments in partnership with the Mahosot Hospital in Vientiane.

- Promotion Education Development Association (PEDA) – Communication for behavior change associated with malaria prevention and control (focusing on EMGs).

Collaborations planned between CMPE and its implementing partners under GF R11 have been shelved pending the announcement of the next funding opportunity.

4.2.4 Myanmar. In **Myanmar** the national malaria control effort is led by the Vector-Borne Disease Control (VBDC) Programme within the Department of Health located in the Ministry of Health (MoH). The VBDC is aided by the Malaria Technical Strategic Group (TSG), which includes representatives from VBDC, WHO, the Myanmar Medical Association, Department of Medical Research Lower Myanmar, FDA, United Nations Children's Fund (UNICEF), and the Japan International Cooperation Agency (JICA) and INGOs. Management of implementation is largely decentralized through State or Regional Health Departments and through Township Health Departments.

Numerous international as well as local partners are involved. Funding partners include:

- Global Fund (GF) Round 9 is expected to provide USD29.8M through to the end on Phase 1 in 2012 to scale-up prevention, early diagnosis and effective treatment in 14 of 17 States/Regions with a population of app 48 M (The Global Fund, 2009). Although Myanmar had planned to submit an application to GF under R11 it is not eligible for the Transitional Funding Mechanism and so is awaiting the development of the next GF funding opportunity.

- Three Diseases Fund (3DF) – 3DF is a consortium targeting HIV/AIDS, tuberculosis and malaria in Myanmar. Donors include the European Commission (EC) and the Governments of Australia, Denmark, the Netherlands, Norway, Sweden and the United Kingdom (UK). It has been supporting malaria control in Myanmar since the withdrawal of 3rd round GFATM in 2006 with the app amount of USD32 M including the rolling fund for containment. 3DF is currently providing a year's worth of start-up support to establish an artemisinin resistance containment effort in Myanmar. 3DF is expected to close by December 2012 and turned into its phase II - 3MDG Fund and will broaden its scope to cover maternal and child health, and health system. The 3MDG will continue to support 3 diseases (HIV/TB/Malaria) though funding expected to be smaller than that in the 3DF. However, this will help supplement the program being run by the Global Fund to Fight AIDS, Tuberculosis and Malaria, in areas which it is currently unable

to support. For malaria, the primary focus of the 3MDG will be containment of arteminisin resistance.

- Bill and Melinda Gates Foundation (BMGF) – In November 2011 BMGF awarded two 3-year grants, one of USD3M to the University of Oxford for research to identify molecular markers for artemisinin resistance and another of USD7.5M to PSI to implement artemisinin monotherapy replacement scheme, and contributing to artemisinin resistance containment (DFID also contribute to this activity).

- USAID/President's Malaria Initiative (PMI) – In 2012 USAID/PMI will launch its Greater Mekong Subregion-Malaria Control Program focusing on implementation of malaria control and containment of artemisinin resistance and related operational research in selected sites in Myanmar, Thailand and Cambodia (to be managed by a consortium led by University Research Co, LLC which recently implemented a similar project in Cambodia). Approximately USD3M of the USD23M fund will be spent in Myanmar annually until 2016. In addition PMI will provide USD0.4M annually through WHO for surveillance of artemisinin resistance.

Implementing partners include:

- United Nations Office for Project Services (UNOPS) – UNOPS is fund manager for 3DF and is the 'Principle Recipient' (PR) for the component of the GF R9 grant implemented by VBDC and the Ministry of Health (MoH), 3 National NGOs (MMA, MCC, MRCS) and for WHO for technical assistance to the NMCP.

- Save the Children-US (SCF-US) – SCF-US has been working in Myanmar since 1995 and is currently active in 9 states and regions. Its focus is on community-based programs, action research, monitoring and evaluation (M&E) and capacity building within communities. SCF-US is the PR of the non-governmental component of the GF R9 grant.

- Cooperazione e Sviluppo (CESVI) – An Italian NGO working in Myanmar since 2001. CESVI is currently operating a community-based malaria prevention and control project in four townships in Mandalay Division and Northern Shan State (funds from 3DF and CESVI).

- The International Organization for Migration (IOM) – An intergovernmental organization (UN) working in Myanmar since 2004 on a community-based migration health project in Mon State covering malaria prevention, diagnosis and treatment (funded by the Swiss Development Cooperation and the 3DF). It also plays role in mapping of migrants in the artemisinin resistance containment project

- Médecins Sans Frontières-Holland (MSF-H) – A Dutch NGO working in Myanmar since 1994 in Rakhine, Kachin and Shan states, providing diagnosis and treatment for malaria plus LLINs for pregnant women including behavior change communication (BCC) (funded by MSF-H and GF).

- MERLIN – A UK NGO working in Myanmar since 2007 providing malaria diagnosis and treatment, LLINs and BCC through mobile teams and community health workers in Chin State and Sagaing Region. Providing training and information for the private sector.

- Myanmar Council of Churches (MCC) – A national faith-based organization implementing community-based malaria prevention and control in Chin State, Kachin State and Sagaing Region since 2005 (funded by 3DF and GF).

- Myanmar Medical Association (MMA) – A national professional membership organization and registered NGO established in 1949 with 10,000 members (all medical professionals) in 76 branches nationwide. MMA has been working with WHO and the VBDC in malaria prevention and case management since 2000 and is currently providing diagnostic and treatment services through 163 trained doctors in 46 highly endemic townships across 12 States and Regions (funds from 3DF and GF).

- Myanmar Red Cross Society (MRCS) – Has an extensive nationwide network for community health activities and has been a key partner for the VBDC in mobilizing communities for bednet surveys, LLIN distribution and ITN re-treatment campaigns. MRCS has been implementing a malaria prevention project in 19 townships since 2008 (with funding from the International Federation of the Red Cross and GF).

- Population Services International (PSI) has been involved in malaria prevention activities in Myanmar since 2001 when it first introduced insecticide treated bednet (ITN) treatment tablets and is currently involved in targeted delivery of free LLINs, provision of rapid diagnostic tests (RDTs) and artemisinin based combination therapy (ACT) through the private sector and associated BCC (funding from PSI, UNICEF, PMI, BMGF and GF). It plays important role in replacing artemisinin monotherapy through social marketing effort of qualified ACTs.

- World Vision Myanmar (WVM) is another international NGO involved in community-based malaria prevention and associated behavior change communication and monitoring and evaluation (funding from 3DF and GF R9).

- United Nations Children's Fund (UNICEF) – UNICEF provided LLINs, and supports supply chain management to improve logistics of supply provisions including LLINs.

- Medical Action Myanmar (MAM) – Is a Dutch NGO based in Myanmar and established in 2009. MAM has a special interest in malaria and provides clinic-based diagnosis and treatment services and is involved in the distribution of LLINs in its project areas.

- Malaria Consortium (MC) is providing technical support for surveillance, monitoring and evaluation including large scale malaria household, facility and outlet surveys.

- Other partners involved in the GF R9 grant as 'sub-sub-recipients' include: the Myanmar Business Coalition on AIDS, Myanmar Health Assistant Association and the Myanmar

Union of Seventh-day Adventists. Each has prior experience in implementing health programs (especially in HIV prevention) and each will now be supported by the VBDC to implement a package of malaria prevention, diagnosis and treatment in its designated geographical area, targeting communities and groups most at risk including migrants and forestry workers.

- University Research Co, LLC will provide management support for malaria control and artemisinin resistance containment efforts and operational research under GMS-MCP in project sites (funded by PMI).

4.2.5 Thailand

In **Thailand** the national malaria control effort is led by the Ministry of Public Health's Bureau of Vector Borne Disease (BVBD). Management of implementation is largely decentralized through the Offices of Disease Prevention and Control and Provincial Public Health Offices.

Funding partners include (in addition to the national malaria budget which is mainly supporting malaria staff in BVBD, vector borne centers and Units):

- GF R7 and R10 consolidated into SSF worth approximately USD16M annually through to 2016 to contain artemisinin resistance and move towards malaria elimination. The grant is implemented by BVBD and the broader Department of Disease Control (under the Ministry of Public Health) with 9 partners.

- USAID/PMI has launched the Control and Prevention – Malaria (CAP-M) project starting in 2012 on implementation of malaria control and containment of artemisinin resistance and related operational research in selected cross border provinces in Myanmar, Thailand and Cambodia. The cross border project amounting to USD25M over 5-year is managed by a consortium of NGOs led by University Research Co, LLC which recently implemented a similar project in Cambodia. Approximately USD340,000 will be directly managed by BVBD in 2013 and 2014.

Implementing partners include:

- Raks Thai Foundation – Local NGO which evolved from CARE international. Involved in program management support with special focus on working with migrants.

- Institute of Migration – Working on improving public-health related knowledge, awareness and practices among uprooted people, particularly internationally displaced persons, indigenous persons and cross-border economic migrants, as well as the Thai host communities.

- The Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS) and the Geographic Information Unit of the Faculty of Tropical Medicine, Mahidol University – Leads the consortium developing the Public Health Informatics System in collaboration with MoPH/BVBD.

- Kenan Institute Asia (K.I.Asia) – Implementing the USD3M USAID 'Border Action Against Malaria Program' in collaboration with BVBD and provincial health offices. Its focus has been on slowing the emergence and spread of multi-drug resistant malaria in Thailand's border areas. K. I. Asia has placed emphasis on strengthening national capacity for surveillance of drug resistance, evidence-based policy development and supply management systems. It is a member of the consortium selected to implement the Greater Mekong Subregion-Malaria Control Program.

- American Refugee Committee – has been implementing health-related programs with refugee and migrant populations in Thailand for more than 20 years.

- Malaria Consortium (MC) has its regional office in Thailand and supports the national programme (*eg*, as sub PR of GFR10) in monitoring and evaluation, surveillance, operational research and IEC/BCC.

- Mahidol-Oxford Research Unit/Shoklo Malaria Research Unit – Based in Tak Province on the Thai-Myanmar border, established in 1986 and is supported by the Wellcome Trust (UK), this group undertakes large-scale clinical studies in refugee camps and migrant worker communities.

- University Research Company will provide management support for malaria control and artemisinin resistance containment efforts and operational research in Greater Mekong Subregion-Malaria Control Program project sites.

4.2.6 Viet Nam

In **Viet Nam** malaria remains an important public health issue and the NMCP receives strong political support with malaria recently reaffirmed by the MoH as one of the country's five priority communicable diseases. Viet Nam's national malaria control effort is led by the National Institute for Malariology, Parasitology and Entomology (NIMPE) in Hanoi and two regional level IMPEs. Implementation is managed by provincial centers for malaria control in more endemic provinces and by departments for malaria control within provincial centers for preventive medicine elsewhere. Endemic districts have a malaria focal point and commune health centers in endemic communes have specialized staff responsible for malaria control.

Funding partners include:

- Global Fund (GF) R7 which is implemented by the NIMPE (PR) and partners is expected to provide approximately USD4.5M annually during 2012-2013 to intensify community-based malaria control by targeting key risk groups and to enhance the functioning and sustainability of the country's control efforts (The Global Fund, 2007). The R7 grant is due to expire in December 2013. An application has been submitted under the GF's TFM for USD7.4M for essential malaria control activities during 2014 and 2015.

Table 8

Estimated countrywise funding situation for the period 2012-16 in the GMS[a].

	Source of funds	Cambodia (Yunnan)	China	Lao PDR	Myanmar	Thailand	Viet Nam	Total
Funds required		169,420,000	69,810,648	27,500,000	254,223,893	152,779,569	78,904,300	752,638,410
Funds available by source	Domestic	17,500,000	56,698,777	2,365,925	?	20,498,309	23,000,000	120,063,011
	GF	60,000,000	6,008,934	6,499,001	56,119,141	80,764,085	9,046,050	218,437,211
	GF pending			7,039,151			7,427,969	14,467,120
	3DF			-	12,000,000			12,000,000
	BMGF			-	7,500,000		192,000	7,692,000
	PMI	5,688,000		-	16,000,000	1,750,000		23,438,000
	WHO	1,750,000		250,000	2,200,000	525,000	880,000	5,605,000
Funding gap		84,482,000	7,102,937	11,345,923	160,404,752	49,242,175	38,358,281	350,936,068
Gap as % of requirement		50%	10%	41%	63%	32%	49%	47%
Flexibility of funding		Flexible	Flexible	Not flexible	Flexible	Not flexible	Not flexible	

[a]based on rapid analysis conducted by WHO in January 2012.

Implementing partners include a number of community based groups including the People's Committee, Women's Union and the Youth Union which are involved in communication for behavior change and in community mobilization associated with ITN treatment, LLIN distribution and IRS.

Two additional implementing partners were planning to collaborate with NIMPE under a GF R11 grant: the Population Council (focus on operational research on accessing mobile and migrant populations) and Medisch Comite Nederland-Viet Nam (MCNV) (focus on entomological and epidemiological research), but these plans have been shelved following the cancellation of R11 and are awaiting the next funding opportunity.

DISCUSSION

1. Remaining gaps in national and regional malaria control and elimination efforts and action required to address these gaps

Malaria elimination in the GMS will only be achieved if every country reaches and then sustains universal coverage of key interventions. Coverage is already falling and without urgent action a resurgence of malaria is likely to occur. Further work is needed to tailor existing tools and delivery mechanisms (taking advantage of potential synergies with other health programs) and to develop new interventions to address the needs of populations not adequately served by existing approaches. In addition continued efforts are needed to strengthen the management of NMCPs and the coordination of multiple partners. Continued political support is key to securing adequate funding and ensuring that malaria control and elimination targets are achieved.

1.1 Coverage of key services

The coverage of key interventions is critically low in some countries and sub-optimal in others threatening progress across the GMS as a whole. With the economic crisis now affecting financial support for malaria programs in many countries, major gaps already exist in the immediate funding requirements for essential commodities. Unless funding can be secured immediately, then current gaps in coverage will widen quickly and a resurgence of malaria is likely to occur.

1.2 Addressing the problem of declining financial support

The precarious nature of external financial support, which provides a large proportion of overall funding in all GMS countries except China, is now a major issue in the region. In several countries the situation is critical:

- In **Cambodia** funding for national malaria control and for the artemisinin resistance containment effort is adequate but mainly externally driven. Significant additional funds will be

required to achieve the target of elimination of all species of malaria by 2025.

- **China**'s main Global Fund (GF) grant has recently been rescinded as part of the GF's response to the current financial crisis. GF is however continuing with the first phase of its support for China's Round 10 grant, which focuses primarily on operations inside Myanmar.

- In **Lao PDR** funding for the national malaria control and elimination effort is inadequate and becoming critical. Lao PDR has received little attention from the international malaria control community despite its expressed needs.

- In **Myanmar** substantially more funding will be needed in order to first mount a comprehensive malaria control effort covering the whole country and then to address the artemisinin resistance problem.

- Even in **Thailand** the situation is serious, following drastic reductions in the domestic contribution to malaria control since 2007 (WHO, 2012d).

- Funding for the national malaria control effort in **Viet Nam** has been adequate in recent years (although it has fallen short of the requirements for elimination). However, with the existing Global Fund grant coming to an end in December 2013 the funding situation is now becoming critical. Funding for containment is totally inadequate.

1.3 Addressing the problem of artemisinin resistance

Experts agree that there is a limited window of opportunity for containing or eliminating artemisinin resistant parasites before they spread to areas of higher transmission, putting at risk recent progress in malaria control. The urgency is increased by the fact that no other antimalarial medicines are available that offer the same level of efficacy and tolerability as artemisinin-based combination therapies (ACTs), and few promising alternatives are available in the immediate research and development pipeline. While efforts to contain and prevent artemisinin resistance at global, regional, national and local levels have begun, they are not sufficient and must be expanded, intensified and better coordinated.

Affected countries need to make containment specific improvements to case management, management of antimalarial medicines and cross-border surveillance and response systems in-line with GPARC. These challenges will require intensive and sustained scientific, strategic and technical cooperation between affected countries and countries directly threatened by artemisinin resistance, and this will require the strong involvement of WHO and other technical partners.

Successful implementation of the GPARC will depend on the support and cooperation of many groups: Research and academic institutions will lead the execution of artemisinin resistance-related research and support surveillance and reporting; Funding agencies will have

a primary role in resource mobilization and funding support; Non-governmental organizations will play a key role as partners of national malaria control programs in implementing containment; and, WHO will play a critical role providing technical oversight and support and overall coordination of stakeholder contributions at global, regional and country level.

Experts agree that the way forward is to accelerate elimination (placing special emphasis on foci of resistance) before existing drugs fail further.

Plans have been drawn-up for artemisinin resistance containment operations in Myanmar and Viet Nam, but additional funds for these efforts still need to be identified.

1.4 Strengthening weak surveillance systems

Epidemiological, parasitological, entomological and drug quality surveillance is a central and critical component of any functional malaria control program. All six GMS countries have surveillance systems in place but their quality and coverage varies considerably from one to another. More effort is needed to encourage countries with weaker systems to learn from countries with stronger systems. Surveillance is discussed in detail in Chapter 2.

1.5 Strengthening weak health systems

NMCPs are implemented in the context of local health systems and weaknesses in these health systems impact negatively on the effectiveness of malaria control efforts.

Additional support is needed for the development of human resources (HR), especially for programs moving towards elimination. Adequate HR are crucial to achieving programmatic success. Staffing levels within most national malaria programs fell dramatically following the close of the Global Malaria Eradication Program in 1969 (Lepes, 1974) and although there has been some recovery during the last decade, a serious shortfall remains in most endemic countries. A lot of training takes place at present but in many countries it is not based on the needs of the programs or on the needs of the individual staff. There are now very few well-trained malariologists and the shortage has been exacerbated by the recent sharp increase in the number of organizations involved in malaria control and the resulting recruitment competition both at national and sub-national levels (Mendis *et al*, 2009). Countries need to conduct expert HR assessments and prepare comprehensive HR development plans, modifying program structure and updating job descriptions as necessary in-line with the changing skill requirements as programs evolve from control towards pre-elimination and elimination (WHO, 2007a). External technical assistance to support various aspects of project implementation remains crucial in many countries and this is likely to be so for the foreseeable future.

Inadequate pay is one of the key issues adversely affecting recruitment and performance

across the entire public sector in all GMS countries.

1.6 Continued innovation

1.6.1 Protecting people from early biting and outdoor resting vectors through habitat management and barrier systems. New rubber plantations provide particularly dense shade and therefore a potentially ideal habitat for major vectors. Restricting the positioning of rubber plantations (through planning controls) to ensure that they are a safe distance from settlements should help to minimize peri-domestic transmission.

Habitat modification may offer more promise than source reduction as a sustainable means of reducing malaria transmission in highly endemic hotspots. Anecdotal evidence suggests that malaria transmission in forest areas is highest in compact nuclear settlements where mature trees (usually mango and coconut trees) provide dense shade within the village itself. The high humidity and proximity of resting sites for vectors provided by the trees is likely to increase vectorial capacity. Convincing villagers to plant fruit trees in orchards outside their villages (rather than within the boundaries of their villages) may be difficult but could have a profound impact on transmission in these settings.

Barrier systems. Barriers or large outdoor treated nets may prove an effective means of vector control or personal protection in certain circumstances in places where groups gather outside in the evening (*eg*, bathing areas, restaurants and bars).

1.6.2 Standby treatment for those beyond the reach of facility-based and community-based case management services. ACT-based standby treatment for malaria offers great promise as a means of ensuring early access to treatment for hard to reach patients in the forest. Further research and development is needed to fine-tune the standby treatment approach used in Viet Nam and perhaps incorporate RDT-based diagnosis for the protection of mobile individuals in endemic areas.

1.6.3 Engaging with the private sector to strengthen service delivery. Greater engagement with the private sector is key to the success of the national malaria control effort in many countries, as universal coverage targets are not attainable without private sector involvement.

1.6.4 Appropriate treatment for vivax patients where 'G6PD' deficiency is prevalent. The widespread reluctance of clinicians to treat patients with primaquine for fear of causing a severe adverse reaction in patients who are G6PD deficient threatens to completely undermine the *P. vivax* elimination effort. As described in section IV above, this fear is largely unfounded as long as treatment guidelines are followed closely. More energy is needed from technical partners to promote the implementation of evidence-based guidelines for treatment with primaquine. The development of point of use tests for G6PD status should result in better adherence to

treatment guidelines in future.

1.6.5 Intermittent preventive treatment for malaria in pregnancy (IPTp). WHO (2009) recommends that women in high transmission settings are provided with at least two doses of IPTp during pregnancy. However the focal nature of malaria transmission in the GMS means that a district or commune wide approach to the provision of IPTp would be inappropriate as most pregnant women would be at very low risk of disease. Because, up until now, the village level incidence data needed to enable appropriate targeting of IPTp has not been widely available, programs have not generally implemented the intervention. However, increasingly, the necessary data is now becoming available, and so more emphasis needs to be placed on rolling-out IPTp based on village level stratifications of risk.

In addition, more emphasis needs to be placed on developing a broader locally appropriate policy for addressing the risks associated with '*malaria in pregnancy'.* In endemic areas, ITNs and associated BCC should be integrated into the standard antenatal-care package along with parasite-based screening and treatment with ACT as appropriate.

1.6.6 Maintaining political support. It is notoriously difficult to sustain political commitment and maintain funding levels as elimination efforts move from the 'pre-elimination' to the 'elimination' and 'prevention of reintroduction' phases. There are several well-documented cases in recent history where reduced malaria burden has led to political complacency, withdrawal of funding and ultimately major resurgence of disease (Kidson and Indaratna, 1998). In Viet Nam, 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 (Ettling, 2002). 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.

CONCLUSION

National Malaria Control Programs in the GMS have implemented a number of key strategies including: providing people at risk with free insecticide treated mosquito nets; spraying walls and ceilings of homes with insecticide; diagnosing suspected malaria cases with appropriate blood tests; providing positive cases with the correct antimalarial treatment; and communicating with the population at risk to maximise utilization of each of these services. They have overcome a number of local issues affecting the impact of these *standard* interventions by developing a range of innovative tools and delivery mechanisms, which they have implemented in collaboration with a broad range of stakeholders. These efforts have resulted in significant reductions in the number of malaria cases and deaths and as a result Cambodia, China, Thailand and Viet

Nam have all set targets for the elimination of the disease (Chapter 2 and Table 1).

Despite these impressive gains much remains to be done. The burden of disease in the region remains unacceptably high and malaria continues to be a public health priority. The coverage of key interventions is critically low in some countries and sub-optimal in most others, threatening progress across the region as a whole. The current precarious funding situation could undermine elimination plans and result in a resurgence of disease. The threat posed to regional and global malaria control and elimination efforts by artemisinin resistant *P. falciparum* parasites is imminent and potentially severe. There is a need to strengthen health systems and health information systems in support of malaria control and elimination efforts. Continued innovation is needed to address remaining gaps in the knowledge base and to maximise provision of services to sections of the population currently underserved. Maintaining political and financial support will be key to all of these efforts.

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