Cross-Border malaria: A Major Obstacle for Malaria Elimination

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Abstract

Movement of malaria across international borders poses a major obstacle to achieving malaria elimination in the 34 countries that have committed to this goal. In border areas, malaria prevalence is often higher than in other areas due to lower access to health services, treatment-seeking behaviour of marginalised populations that typically inhabit border areas, difficulties in deploying prevention programs to hard-to-reach communities, often in difficult terrain, and constant movement of people across porous national boundaries. Malaria elimination in border areas will be challenging, and key to addressing the challenges is strengthening of surveillance activities for rapid identification of any importation or reintroduction of malaria. This could involve taking advantage of technological advances, such as spatial decision support systems, which can be deployed to assist program managers to carry out preventive and reactive measures, and mobile phone technology, which can be used to capture the movement of people in the border areas and likely sources of malaria importation. Additionally, joint collaboration in the prevention and control of cross-border malaria by neighbouring countries, and reinforcement of early diagnosis and prompt treatment are ways forward in addressing the problem of cross-border malaria.

1. Introduction

Globally, an estimated 3.4 billion people were at risk of malaria in 2012, with populations living in sub-Saharan Africa having the highest risk of acquiring malaria (World Health Orginization, 2013). Approximately 80% of cases and 90% of deaths are estimated to occur in the WHO African Region, with children under five years of age and pregnant women most severely affected (World Health Orginization, 2012; Casalino et al., 2002; Martens and Hall, 2000; World Health Orginization, 2013). WHO estimated 207 million cases of malaria occurred in 2012 (uncertainty range 135–287 million) and 627,000 deaths (uncertainty range 473,000–789,000) (World Health Orginization, 2013). Deaths attributed to malaria have declined by 32% between 2004 and 2010 (Murray et al., 2012). This reduction has most likely been a result of the combined effects of economic development in endemic countries, urbanization, and unprecedented financial support for malaria interventions from donors and the associated scaling up of malaria interventions. In sub-Saharan Africa, there was a 66-fold increase in the amount of official development assistance (ODA) disbursed for malaria control, from $9.8 million in 2002 to $651.7 million in 2008 (Akachi and Atun, 2011). Major funders include Roll Back Malaria (RBM), the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), the US President's Malaria Initiative and the World Bank's International Development Association (Feachem et al., 2010a) and funding from the Bill and Melinda Gates Foundation has been transformational in driving malaria elimination research. The increased funding has supported scaling up of preventive activities such as provision of long lasting insecticide-treated bed nets (LLINS) and indoor residual spraying (IRS) as the principal vector control measure, as well as improving timely diagnosis using rapid diagnostic tests (RDTs) and providing effective treatment with artemisinin-based combination therapy (ACT) (Gueye et al., 2012; Anderson et al., 2011). As a result of these gains, and renewed global interest, 32 of the 99 malaria-endemic countries are now pursuing

an elimination strategy, with the remaining 67 aiming to control malaria (Das and Horton, 2010; Feachem et al., 2010a; Feachem et al., 2010b).

The second generation Global Malaria Action Plan (GMAP2) for the period 2016–2025 has now commenced. The GMAP2 aims to accelerate progress in malaria elimination at global, regional and country levels and serve as a major advocacy instrument for the achievement of a malaria-free world. A three-part strategy to eliminate malaria has been developed and is now widely endorsed: (1) aggressive control in highly endemic countries, to lower transmission and mortality in countries that have the highest burden of disease and death; (2) progressive elimination of malaria from the endemic margins, to "shrink the malaria map" and (3) research into vaccines and improved drugs, diagnostics, insecticides, and other interventions, and into delivery methods that reach all at-risk populations (Feachem et al., 2010a; Roll Back Malaria, 2008; Breman and Brandling-Bennett, 2011; Feachem and Sabot, 2008; Mendis et al., 2009). The defining aspects of malaria elimination are outlined in Panel 1.

Although great gains have been made in reducing the overall burden of malaria, impact from elimination and control efforts proves more difficult in areas near international borders. The specific environmental (including physical, social and geopolitical), anthropological, administrative and geographic characteristics of border areas impact uniquely on the epidemiology and control of malaria, resulting in coinage of the terms "border malaria" and "cross-border malaria". Here, we apply the term cross-border malaria to encompass malaria transmission as a result of cross-border movement of people or vectors, in addition to the epidemiological situation that occurs in relation to malaria in areas adjacent or near to international borders (i.e. border malaria).

Cross-border malaria is difficult to manage due to political, economic and geographic constraints (Xu and Liu, 2012). Factors such as frequent movement of humans and vectors across-borders, lack of responsibility of individual countries in the border endemic areas, and relatively poor access to health care and preventative measures, particularly for mobile populations, leave space for reservoirs of infection that can lead to continued transmission of malaria and vulnerability to malaria outbreaks and epidemics (Gueye et al., 2012).

The aim of this review is to present a compilation of evidence in the available literature on the impact of cross-border malaria on elimination efforts. Drivers of cross-border malaria are described and measures to prevent or mitigate cross-border malaria are discussed. The review for this paper was carried out using the search engines PubMed, Medline and Google Scholar. The key search words were malaria, cross-border, migration, international borders and malaria elimination. We reviewed all relevant articles written in English.

2. Patterns of movement

Cross-border malaria encompasses malaria transmission along international borders as a result of interconnections between human settlements and population movement, including localised border crossings and population migration over larger distances (Guerra et al., 2006; Olson et al., 2010). Border crossings can be defined as movements of local people between countries that occur with or without passing border control checkpoints. Cross-border migration can be defined as movement of people from a country of origin to a destination country with or without passing border control checkpoints for either short-term or long-term immigration with different channels of migration (Panel 2) (Koyadun and Bhumiratana, 2005; Bhumiratana et al., 2010).

Population movements can be differentiated by their temporal and spatial dimensions. Temporal dimensions include circulation and migration. Circulation encompasses a variety of movement, usually short-term and cyclical and involving no longstanding change in residence. Migration movements involve a permanent change of residence (Prothero, 1977; Stoddard et al., 2009). Circulatory movement can be subdivided into daily, periodic, seasonal, and long term. Daily circulation involves leaving a place of residence for up to 24 hours. Periodic circulation may vary from one night to one year but is usually of a shorter duration than seasonal circulation. Seasonal circulation involves a period in which persons or groups are absent from their permanent homes during one or more seasons of the year. With regards to long-term circulation, there is absence from the home for longer than one year, but with maintenance of close social and economic ties with the home area (Wolpert, 1965; Martens and Hall, 2000; Roseman, 1971; Stoddard et al., 2009; Prothero, 1977; Pindolia et al., 2012).

People cross international borders for a number of reasons, including: migration for work opportunities, visiting friends and relatives (VFRs), tourism, travel for business purposes or cross-border trade, social relations, cultural exchanges (pilgrimages, festivities, fairs, etc.) and displacement as a result of natural and manmade calamities (such as wars) and major development projects, such as construction of dams. Some of these movements increase exposure to malaria parasites, particularly in forests or areas of deforestation, where occupational exposure may occur.

It is difficult to obtain basic data on key variables, such as the actual numbers of movements of people across borders, or for such data to be broken down by movement type (e.g. border crossings versus cross-border migrations) (Khamsiriwatchara et al., 2011). For example, migrations across the international borders of Yunnan Province, China, which shares >4000 km of border with Myanmar, Lao PDR (People's Democratic Republic) and Vietnam, take

place unchecked (Hu et al., 1998; Clements et al., 2009). Similarly unmonitored migration of people across the border from Myanmar into Bangladesh jeopardises the control efforts in Bangladesh (Reid et al., 2010a) and imported infections from Yemen into Saudi Arabia continue to challenge Saudi elimination efforts (Alkhalife, 2003).

Movement of people across international borders has contributed to maintaining high transmission at hotspots adjacent to border points (Clements et al., 2009; Carme, 2005b). A major challenge to sustaining elimination is addressing the potential reintroduction of cases, either via border areas or from migrant populations (Tatem and Smith, 2010). Nearly 20% of malaria cases treated in Iran in 2006 originated in Pakistan (Reza et al., 2009). Local transmission of malaria in the United Arab Emirates (UAE) came to an end in 1997 and no autochthonous cases were reported from 1998 to 2004. Therefore, UAE was certified as a malaria free country. However, there was importation of malaria into UAE from the neighbouring countries (Sultan et al., 2009).

2.1 Migration for work opportunity

The majority of migrants cross borders in search of better economic, work and social opportunities. Economic migrants are the world's fastest growing group of migrants. Economic motivations are the main reasons for people to migrate from countries with high levels of malaria to malaria-eliminating countries, impeding malaria elimination efforts in those countries (Carme, 2005a; Davin and Majidi, 2009; Kitvatanachai et al., 2003; Wangdi et al., 2011). Economic migration is exacerbated when there are substantial differences in the economic development and job opportunities in neighbouring countries. For instance, economic stagnation in Myanmar and rapid economic development in Thailand has stimulated migration from Myanmar to Thailand (Carrara et al., 2013; Delacollette et al., 2009; Huguet and Punpuing, 2005; Khamsiriwatchara et al., 2011; Wangroongsarb et al.,

2012), while temporary migration of seasonal workers from Cambodia to Thailand seems to be a key factor responsible for the malaria problem along the Cambodian-Thailand border (Hoyer et al., 2012; Kitvatanachai et al., 2003). It is estimated that 50–70% of all reported malaria cases in Argentina are linked to migration, in particular movement across the border from Bolivia; this migration is fuelled by economic growth on the Argentine side and is not well controlled due to a porous border between the two countries (Gueye et al., 2012). Malaria increased substantially in French Guiana due to the influx of Brazilians to work in gold mining (Carme, 2005b). Economic motivations are the main reasons for Afghans to migrate to Pakistan. As high as 64.6% of Afghan migrants crossing into Pakistan cited lack of work in Afghanistan as the main factor leading them to Pakistan (Davin and Majidi, 2009). Economic migration also happens beyond countries sharing common international borders. For instance, imported malaria in Jiangsu Province, China from 2001–2011 accounted for up to 12.4% of cases, mainly imported by Chinese nationals from African countries as a result of economic migration (Liu et al., 2014).

The resurgence of malaria in Swaziland in early 1970 occurred as a result of the migration of sugar cane workers from malaria-endemic Mozambique (Martens and Hall, 2000; Packard, 1986). More recently, the current migration of labourers into Swaziland from Mozambique is likely to be a challenge for Swaziland's stated plan of malaria elimination by 2015 (Koita et al., 2013). The rapid rise in malaria incidence in Brazil in the late 1970s and early 1980s was attributed to the influx of malaria-infected migrants from endemic Bolivia (Cruz Marques, 1987). The resurgence of malaria in Costa Rica resulted due to the development of the banana industry in which workers were moved from endemic areas into areas with increased suitability for vector breeding (Najera et al., 1998). The oil-exporting countries of the Middle East have attracted a large number of semi-skilled workers from malarious countries such as

India, Pakistan and Indonesia, who are a source of malaria introduction (Schultz, 1989). The importation of malaria to Kuwait occurs mostly from the Indian subcontinent (Hira et al., 1988; Hira et al., 1985; Iqbal et al., 2003). Saudi Arabia is an attractive employer of skilled workers from malaria-endemic countries such as Iran, Pakistan and India, as well as east Africa (Bruce et al., 2000; Babiker et al., 1998). The main source of malaria cases in UAE is from Pakistan and neighbouring Oman, including families of UAE nationals living across the border in Oman (Dar et al., 1993). These examples highlight the important role that economic migrations have in re-establishing malaria in areas where control efforts had previously been successful.

2.2 Visiting friends and relatives

Ethnic groups are often spread across borders, and people may cross the international border to meet relatives and friends (Pongvongsa et al., 2012; Noor et al., 2013). Immigrant VFRs frequently return to visit family members whom they had left behind or to introduce new additions to the family of origin. Last-minute travel to visit sick relatives or attend funerals is common, allowing little time for provision and receipt of pre-travel advice on malaria prevention. Other travel reasons include finding a spouse, locating missing family, or returning for traditional or cultural ceremonies (Xu and Liu, 1997). Many VFRs stay in family settings in which they may encounter suboptimal housing conditions and increased malaria risk (Bacaner et al., 2004; Scolari et al., 2002; Muentener et al., 1999; Fulford and Keystone, 2005; Di Perri et al., 1994; Barnett et al., 2010; Fenner et al., 2007; Froude et al., 1992; Wagner et al., 2013). VFRs may encounter barriers such as lack of information on services, language, trust of health systems, concerns on their legal status, and cost of malaria chemoprophylaxis, which may limit their access to travel clinics (Bacaner et al., 2004; Stager

et al., 2009). Migrants VFRs may be exposed to risk of malaria as they visit their families in rural areas with higher malaria transmission rates (Schlagenhauf et al., 2003).

2.3 Treatment seeking behaviour in border areas

The porous nature of many borders encourages people to migrate and seek treatment across borders. For example, malaria patients from the state of Assam, India, often travel to hospitals in neighbouring Bhutan to receive treatment because treatment is free on the Bhutanese side of the border (Yangzom et al., 2012). Due to poor health infrastructure in Nepal, a large number of people from the plains and hills in the south of the country travelled in the past to hospitals in India to access health care. However, in the last few decades, Nepal has been able to develop health facilities in the country, particularly in the plains, with the establishment of regional, zonal and district hospitals with modern medical facilities. This has resulted in the large-scale reverse flow of people from India seeking treatment in these hospitals (Kansakar, 2001).

Migrant workers are less likely than the general population to get blood tested for malaria parasites and get radical treatment (Hiwat et al., 2012). Migrant workers and border people have often demonstrate sub-optimal health-seeking behaviours and often self-medicate. Malaria treatment in the border areas is often inadequate. Inadequate public health facilities in border areas lead local populations to seek treatment from private health professionals, many of whom provide counterfeit or substandard antimalarial drugs, or mono-therapies, resulting in increased risk of antimalarial drug resistance (Pongvongsa et al., 2012; Wijeyaratne et al., 2005). Thus, these groups are among the principal contributors to the emergence of multi-drug resistant (MDR), which is a particular problem along the Thailand-Myanmar and Thailand-Cambodia borders (Satitvipawee et al., 2012; Thimasarn, 2003; WHO, 2010). Gold miners in French Guiana do not seek malaria treatment in their country

due to their illegal status and high local transportation costs; rather, they seek diagnosis and treatment in Suriname. Low accessibility to diagnosis and treatment for these gold miners have resulted in a flourishing black market for anti-malarial drugs, often with insufficient quality (Hiwat et al., 2012).

2.4 Displacement due to conflict and major development projects

The World Bank estimates more than 1.5 billion people live in violent, conflict-affected countries (The World Bank, 2012). Movement of displaced people, including refugees, and soldiers as a result of conflict or war has been implicated as a cause of malaria resurgence in Bangladesh, Vietnam, Sri Lanka, Sudan and Azerbaijan. Decades of internal conflict in Myanmar have resulted in massive population displacement and >150,000 refuges now live in camps in Thailand (Carrara et al., 2013). Similarly, the Islamic Republic of Iran hosts around 1.5 to 2 million Afghani refugees (Basseri et al., 2010). These displaced people play an important role in the transmission of malaria due to inadequate control and preventive measures. The displaced people face unreliable access to basic services including health care (Williams et al., 2013). People living in conflict zones, such as the Karen, have higher mortality rates irrespective of malaria incidence (Lee et al., 2006).

The construction of China's Three Gorges Dam resulted in relocation of 1.3 million people. There has been an epidemic of locally transmitted malaria among residents at the dam site in 1996, and this could recur and spread (Jackson and Sleigh, 2000). The construction of the Bargi dam in India saw a 2.4-fold increase in malaria cases and a more than four-fold increase in annual parasite incidence among children in the villages closer to the dam compared with more distant villages. In addition, there was a strong increase in prevalence in the partially submerged villages (Singh et al., 1999; Singh and Mishra, 2000). Dam construction, irrigation and other development projects, urbanization, and deforestation have

all resulted in changes in vector population densities and emergence of new diseases and re-emerge old diseases (Walsh et al., 1993; Patz et al., 2000; Gratz, 1999; Keiser et al., 2005).

3. Epidemiological drivers of malaria in border areas

Malaria control in border areas is often more difficult than in central and non-border areas due to heavily forested, mountainous and inaccessible terrain, and because of unregulated population movements across the border (Xu and Liu, 2012). In addition, many border areas are inhabited by ethnic minorities (Prothero, 1999; Erhart et al., 2005) with limited formal education (Erhart et al., 2007) and less access to health education efforts. The impact of different national policies for control and prevention in neighbouring countries is potentially causing a lack of political will to invest in border areas.

3.1 Misalignment of programmatic approaches

Differences in programmatic approaches between neighbouring countries commonly occur making the coordination of control and preventive measures in the border areas challenging. One such example is the Laos-Vietnam border where malaria control on the Laos side is based on distribution of long-lasting insecticidal nets (LLINs) but on the Vietnamese side relies mainly on indoor residual spraying (IRS) of insecticides (Anh et al., 2005; Hung le et al., 2002). There are also differences in malaria diagnosis and treatment between the two countries. Rapid diagnostic tests (RDT) are mostly used for diagnosis in Laos, while Vietnam uses microscopy as a rule.

Even where the approaches are similar between neighbouring countries, the specific drugs or chemicals used can influence their effectiveness due to parasite or vector resistance. For example, deltrametrin (a synthetic pyrethoid) is used for IRS in Bhutan, whereas dichlorodiphenyltrichloroethane (DDT) is still used in the neighbouring states of Assam,

India, even though there are reports of vector resistance to DDT (Dev et al., 2006; Wangdi et al., 2010; Mittal et al., 2004). Effective control or elimination requires both countries across the international boundary to be committed to malaria interventions. In addition, control and preventive activities including IRS need to be synchronized to achieve maximum benefit.

3.2 Forests and deforestation

Both the presence of forests and occurrence of deforestation impact on increasing malaria risks and transmission in border areas. Populations in border areas are at greater risk of malaria infections because they frequently visit forestlands, forest fringe areas, or forested plantations at or near the border (Chaveepojnkamjorn and Pichainarong, 2004). Forest-related activities and factors related to poverty are major drivers of malaria incidence in Viet Nam (Manh et al., 2011; Erhart et al., 2004). Many species of *Anopheles* mosquitoes that transmit malaria are common fauna of natural forests and forested plantations in border areas. Border populations are particularly at risk of occupational exposure to malaria through working in crop plantations, forestry, mining, development projects, and tourism (Pichainarong and Chaveepojnkamjorn, 2004). Occupational exposures affect the age profile of malaria infections – for example, in forest fringe villages, adult rather than childhood infections are more prevalent due to forest-related activities of workmen, such as logging, bamboo cutting, charcoaling, foraging and overnight stays in the forests (Dysoley et al., 2008). Migration of the population working in the forest and forest fringe, can result in spread via carriers to new areas previously not known for malaria transmission (Wisit Chaveepojnkamjorn, 2005). These result in an increase in human infection, not only within the mobile population, but also within the fixed population, to which the migrants return periodically.

Changes in land cover associated with economic activities can enhance contact with mosquitoes and thereby increase malaria transmission. Deforestation has occurred in many malaria-endemic areas as a result of colonisation and settlement programmes, logging, increased, large-scale agricultural activities, mining, the building of hydropower schemes and the collection of wood for fuel. Deforestation activities lead to a host of influences on the distribution and prevalence of vector borne diseases. New habitats for *Anopheles darlingi* mosquitoes are created through formation of large ponds and presence of leaf litter, algae and emergent grasses due to deforestation or activities associated with it. This has led to malaria epidemics in South America (Olson et al., 2010; Vittor et al., 2006; Vittor et al., 2009). Increased deforestation in Brazil lead to increased malaria cases in Mancio Lima County (Olson et al., 2010). Populations residing within or near the fragmented forests are at higher risk of malaria because of increased contact with the vectors at the forest edges and reduced biodiversity. Continued deforestation throughout the world will likely continue to result in increased vector-borne diseases (Guerra et al., 2006).

3.3 Socio-economic factors

Residual transmission in some malaria-eliminating countries is concentrated in a few hard-to-reach populations - so-called “hot pops”, of which mobile populations within border areas are included. These populations often have unofficial status and few economic resources, and can be difficult to locate for the purposes of control and effective treatment of malaria (Stern, 1998).

Ethnic minorities in border areas often have limited formal education, impeding health promotion efforts, resulting in prevalent risk behaviours such as improper use of insecticide-treated nets and other protective measures, and limiting access to healthcare (Prothero, 1999; Erhart et al., 2005). Such groups are typically impoverished and mobile, often driven to more

remote areas by marginalisation and safety concerns (Martens and Hall, 2000; Chuquiyauri et al., 2012; Prothero, 1995; Xu and Liu, 1997). They might avoid accessing the health systems because of fear of unwanted attention from government authorities, thus making monitoring and treatment of their malaria difficult (Hiwat et al., 2012). Distinctive ethnic minority groups can vary in terms of cultural practices, languages and life styles that are of relevance to malaria risk, including the practice of staying in the forest overnight.

Poverty serves as a motivating reason for people to seek income from occupational activities associated with forests and mining that might expose them to higher risks (Chaveepojnkamjorn and Pichainarong, 2004). Such activities may be illegal and as a result their members often face substantial barriers to healthcare access (Hiwat et al., 2012). For the poor, living conditions are associated with inadequate housing and overcrowding, which increase the risk of malaria. Houses are hastily constructed and are often made of locally available materials. Inadequate housing might allow mosquitoes to enter more easily than well-constructed housing with screened windows. The risk of getting malaria has been shown to be greater for inhabitants of the poorest type of house construction (incomplete, mud, or palm walls, and palm thatched roofs) compared to houses with complete brick and plaster walls and tiled roofs (Gamage-Mendis et al., 1991; Konradsen et al., 2003; Lindsay et al., 2002).

4. Way forward

4.1 International collaboration

Malaria control strategies and policies as well as the quality and management of the health care systems and conventions in data collection may differ across national borders, making cross-border collaboration difficult (Pongvongsa et al., 2012). However, the phenomenon of

cross-border malaria provides a strong rationale to develop harmonized cross-border programs in conjunction with national efforts (Delacollette et al., 2009). The philosophy of cross-border or regional collaboration has been well adopted in different regions and the results have been positive. One example is the Lubombo Spatial Development Initiative (LSDI) between South Africa, Swaziland, and Mozambique. The LSDI was made possible as a result of political commitment through the signing of a protocol of understanding by the head of three states, which created a platform for regional cooperation and delivery. The malaria control program of the LSDI aimed to achieve maximum effectiveness of malaria control in the highest-risk areas of South Africa and Swaziland bordering Mozambique. These efforts resulted in a drastic decrease in malaria cases in Swaziland and South Africa (Sharp et al., 2007; Maharaj et al., 2012).

Examples of cross-border collaborations for infectious disease surveillance and control, that in most cases are not malaria-specific, but which could provide models for malaria, include: the Connecting Organizations for Regional Disease Surveillance (CORDS), the Middle East Consortium on Infectious Disease Surveillance (MECIDS), the Mekong Basin Disease Surveillance (MBDS), the Asian Partnership on Emerging Infectious Diseases Research (APEIR), the East African Integrated Disease Surveillance Network (EAIDSNet), the South African Centre for Disease Surveillance (SACIDS), and the South Eastern European Health Network (SEE), which links the ministries of health of Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Macedonia, Moldova, Montenegro, Romania and Serbia (Gresham et al., 2011).

The Mekong Basin Disease Surveillance (MBDS) project, which commenced in 2006 established 16 sites at major border crossings between six countries with the aim to carry out joint, cross-border disease outbreak investigations and responses. The joint team carried out

outbreak investigation of malaria between provincial sites in Laos PDR (Savannkhet) and Vietnam (Quang Tri) in 2006 and contained the outbreak (Phommasack et al., 2013). Connecting Organizations for Regional Disease Surveillance (CORDS) was established in 2008 and provides a new tool for meeting this social networking challenge on a global scale by fostering the growth of trust-based partnerships among professionals that transcend not just organizational but also geopolitical boundaries (Gresham et al., 2011). MECIDS was established in 2003 and links public health experts and ministry of health officials from Israel, Jordan and Palestine (Gresham et al., 2011). MECIDS played a pivotal role in detecting salmonella and mumps outbreaks and containing the influenza viruses H5N1 and H1N1 (Gresham et al., 2009). The strength of such collaboration is prompt sharing of cross-border data. However, there are a number of impediments for such collaborations, including the time taken to build the trust required before cross-border data can be shared freely (Phommasack et al., 2013).

Other collaborations have moved beyond surveillance and disease containment. The Pacific Malaria Initiative was introduced in Vanuatu and Solomon Islands in 2007 to aid in their control efforts with the ultimate goal of malaria elimination. The Asia Pacific Malaria Elimination Network (APMEN) was established in 2009 and represents 15 countries in the Asian Pacific region. The Country Partners, together with regional partners from the academic, development, non-governmental and private sectors and global agencies, including the World Health Organization (WHO), collaboratively address the unique challenges of malaria elimination in the region through leadership, advocacy, capacity building, knowledge exchange, and building evidence to support more effective, sustained malaria elimination programmes across the region (APMEN, 2014). Similarly, the Elimination Eight Regional Initiative has been established in Southern Africa to support cross-border collaboration and

achievement of mutual goals for malaria elimination in that region. Such international initiatives naturally have a key role to play in developing and implementing strategies to mitigate the threat of cross-border malaria, which is inherently a shared problem between interconnected jurisdictions.

4.2 Surveillance-response and cross-border initiatives

The importance of a robust surveillance-response system at points of entry from areas with local malaria transmission, that facilitates swift treatment and follow-up of infected individuals and their environment, has been recognized (Cohen et al., 2009). Oman has been able to reduce imported cases through mass screening of individuals arriving at the airport from East African countries; those who test positive were treated for free and monitored for two weeks. Both Oman and the UAE have provided free treatment to everyone who tests positive, whether they are nationals or foreigners. Testing for malaria at entry points in Mauritius was shown to provide benefits for investment, by maintaining elimination despite large cyclones in 1994 and 2002 that caused costly damage and an increase in the number of travellers arriving from malaria-endemic countries (Tatarsky et al., 2011; Aboobakar et al., 2012). Screening arriving passengers for malaria at the border points and obtaining a detailed travel history has been deployed to assess the impact of human population movement on malaria in Djibouti (Noor et al., 2011). Proactive prevention programs to screen all prospective immigrants for malaria infection in their home countries, rather than point of entry, significantly reduced the numbers of imported infections in Kuwait (Iqbal et al., 2003). These approaches work well where border crossings are tightly controlled, but they may be of limited value in remote areas where people pass unchecked between countries.

Population-based surveys that measure cases of parasitaemia can be used to identify high-transmission areas, which often have a low clinical burden because of high rates of immunity

in the population. These surveys have the potential to assist malaria control programmes in active detection of transmission hotspots (Clements et al., 2013; Wangdi et al., 2014). However, such surveys become inefficient when malaria incidence is very low because few cases of parasitaemia are identified relative to the sampling effort. Once the interruption of transmission has been achieved in the context of malaria elimination programmes, intensified disease surveillance and swift intervention responses are the basic requirements to prevent the re-establishment of any introduced parasites. In the post-elimination period, the loss of immunity and the high reproductive rate of the malaria parasite in communities where competent vectors are still present could precipitate outbreaks if malaria infections are re-introduced into the population (Greenwood, 2008), emphasising the need for continued surveillance in areas receptive to resurgence.

In some cases, cross-border malaria control, i.e., expansion of malaria control programs from malaria-eliminating countries to neighbouring malaria-controlling countries, might be necessary to create buffering zones to thwart reintroduction of the parasite (Cui et al., 2012). For example, pilot trials of cross-border malaria control at the Thai–Myanmar and Chinese–Myanmar border areas suggest that organized control in these areas is feasible (Richards et al., 2009). Frequent population movements (every three months) across the Thai-Cambodia border and from the border area across Cambodia, indicate the need for heightened surveillance for artemisinin resistance outside what has been designated as the containment zone (Khamsiriwatchara et al., 2011b). Obviously, such cross-border activities demand coordination of governments between the neighbouring nations. Cross-border dialog in solving malaria related issues need to be initiated, and other control and preventive activities such as IRS need to be synchronized to achieve maximum benefits.

Fever surveillance of people who cross border area can be used to identify malaria associated fever. Offering free treatments would encourage people to avail this service. The GeoSentinel Surveillance in United States of America from March 1997 through March 2006, showed malaria was the most common specific etiologic diagnosis, found in 21% of ill returned travellers with fever (Wilson et al., 2007). Kuwait initiated proactive preventive program to screen all prospective immigrants for malaria infection in their home countries. As a result the malaria cases among the immigrants reduced by 52.6% per year (Iqbal et al., 2003). Fever surveillance was mostly used in tourists and travellers from Europe and North America (Wilson et al., 2007; Leder et al., 2004; Journal, 2004). However, it will not be possible to monitor fever, when border crossing takes place through informal border and forest areas. Additionally, fever surveillance would be of limited value in the people who have clinical immunity since these people will not develop fever even when they are infected with *Plasmodia* parasites.

4.3 Strengthening of preventive measures for cross-border malaria

Early diagnosis and prompt treatment of people infected with malaria in malaria-eliminated countries would serve a very important tool in preventing reintroduction. However, to deliver prompt diagnosis and treatment, the health systems in most border areas need to be strengthened. The need to take adequate chemoprophylaxis for people moving from non-endemic to malaria endemic countries and vice versa is often ignored due to deficient knowledge on the availability of chemoprophylaxis and for financial reasons. Drugs for chemoprophylaxis need to be made available in the border areas. The benefits of sleeping under LLINs needs to be highlighted through education, and LLINs being made available through social marketing, as has been done for refugees from Afghanistan in Pakistan (Rowland and Nosten, 2001). Alternative approaches such as the provision of insecticide-

treated hammocks for people frequenting forest areas in border areas (Magris et al., 2007; Thang et al., 2009), deltamethrin-sprayed tarpaulins or tents, and premethrin-treated blankets and top-sheets provide more promising options for people overnighting in the forest (Graham et al., 2002; Rowland and Nosten, 2001). These protective measures achieve the goal of reducing exposure to infected vectors for populations who do not live in traditional housing each night, a feature common of people in border areas.

4.4 Technological solutions to support operational decision making and surveillance-response

Spatial decision support system (SDSS) provide enhanced support for decision making, and management using data that has spatial or geographical components (Keenan, 2003). SDSS are generally based on a database housed within a geographic information system (GIS) with an interactive mapping interface. SDSS can contain modules for planning, monitoring and evaluating the delivery and coverage of interventions including IRS and LLIN within target populations, and for mapping malaria surveillance data (Kelly et al., 2013; Kelly et al., 2011; Reid et al., 2010; Srivastava et al., 2009; Zhang et al., 2008). One role of an SDSS in the context of malaria elimination can be to support high-resolution surveillance, by helping locate and classify active transmission foci (which is not limited to administrative boundaries). Such tools have been successfully used in a variety of countries. Creation of a regional (i.e. multi-country) SDSS framework could provide an opportunity to harmonise malaria data and provide a platform for stakeholders to disseminate and visualize malaria transmission across borders. This information could then be used by the relevant partners to target and coordinate cross-border malaria interventions. Additionally, modern geographical reconnaissance (GR) approaches and technologies can be used to develop rapid and accurate field-based procedures for the collection, spatial definition and mapping of malaria

elimination target populations in border areas (Bharati and Ganguly, 2013; Kelly et al., 2010).

The use of mobile phone data might provide a novel approach to tracking malaria in cross-border areas. Mobile technology, particularly the cellular phone, has not only penetrated the daily lives of people in metropolitan areas and large rural cities/towns; they have also become popular among those living in remote areas. Data on phone calls made and the location of the call can be captured by the nearest mast that each call was routed through. Such recordings can help to construct trajectories of the movements over time and space (2011; Gonzalez et al., 2008). The captured movement of the people across border areas, when coupled with information about the malaria endemicity of the area, could identify likely sources and rates of malaria importation (Tatem et al., 2009).

5. Conclusion

Cross-border malaria will continue to be a problem as long as there are differences in the malaria incidence between neighbouring countries. Cross-border malaria is difficult to control due to: (1) the huge number of people crossing international boundaries to engage in a wide variety of activities; (2) most crossings of international borders occurring informally through porous borders; (3) populations residing in the border areas comprising ethnic minority groups with limited formal education and few financial resources; (4) hard-to-reach populations who are typically impoverished and mobile, often being driven to more remote areas by marginalisation; (5) a paucity of information on cross-border movement of people; and (6) inadequate health systems in many border areas.

Cross-border malaria remains one of the main challenges to malaria elimination. In order to achieve successful malaria elimination, novel approaches for malaria control and prevention

need to be identified and implemented in border areas. These include joint collaboration in the prevention and of control measures targeting malaria by neighbouring countries, robust surveillance systems that can identify any importation or reintroduction of malaria for prompt treatment and containment, development of a regional (i.e. multi-country) data sharing framework (which could be based on a SDSS) that could be used by the relevant partners to target and coordinate cross-border malaria interventions and alternative personal protective measures focusing on the needs of border populations; and harnessing technological developments such as using mobile telecommunications data to assess likely sources and rates of malaria importation arising from the movement of people across borders.

Contributors

KW and ACAC conceived the idea for the report. KW did the literature review and wrote the review. ACAC provided substantial input in form of critical reviewing. MLG and GCK contributed by revision of the manuscript. All authors took part in the review, preparation, and final approval of the report.

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Glossary

Malaria Control: reducing the disease burden to a level at which it is no longer a significant public health problem.

Pre-elimination: monthly slide or RDT positivity rate among febrile patients with suspected malaria is < 5% throughout the year or malaria parasite rate of <5% among people of all age with current fever of history of fever in the past 24 hours in the peak transmission season in population-based survey.

Malaria Elimination: reducing to zero the incidence of locally acquired infection in a specific geographic area as a result of deliberate efforts, with continued measures in place to prevent establishment of transmission.

Malaria Eradication: permanent reduction to zero of the global incidence of infection caused by *Plasmodia* as a result of deliberate effort, so that intervention measures are no longer needed.

Vigilance: a function of the public health service during the programs for prevention of reintroduction of transmission, consisting of watchfulness for any occurrence of malaria in an area in which it did not exist or from which it had been eliminated and application of the necessary measures against it.

(Source: WHO Disease Surveillance for Malaria Control, 2012 and Disease Surveillance for Malaria Elimination, 2012)

Panel

Panel 1. Malaria elimination defining activities.

Malaria elimination requires:

- evidence-based data on the achievement of successful malaria control;
- sufficient evidence that transmission can be interrupted by scaling up planned interventions;

- clearly defined responsibilities for management, including decentralized authority and enforcement of regulatory and disciplinary measures;
- effective systems to ensure coordination between public, private and community based agencies and services, and to implement cross-border programmes;
- intensive joint inter-sectoral efforts;
- adequate pre- and in-service training of service providers and high-quality supervision/mentoring;
- sustained advocacy, social mobilization, health education and behaviour change communication to support the preparation and implementation of the elimination programme;
- the existence of a monitoring, evaluation and surveillance plan able to timely measure progress, including assessments by independent team(s);
- long-term predictable and sustainable funding available to support planned and unexpected expenses;
- eventually, systems in place for effective vigilance to prevent reintroduction.

(Source: WHO: A field manual for low and moderate endemics countries)

Panel 2. Different types of movement across borders.

- Circulation encompasses a variety of movements involving no longstanding change in residence.
- Migration involves a permanent change of residence.
- Daily circulation involves leaving a place of residence for up to 24 hours.
- Periodic circulation may vary from one night to one year, but is usually shorter than seasonal circulation.
- Seasonal circulation involves a period in which persons or groups are absent from their

permanent homes during a season or seasons of the year.

- Long-term circulation involves an absence from the home for longer than one year.
- Active transmitters 'source' harbour the parasite and transmit the disease when they move to new areas known as 'sinkers', which may have low-level or sporadic transmission.
- Passive acquirers are exposed to the disease through the movement from one environment to another; they may have a low level of immunity, which increases their risk of clinical malaria.

Panel 3. Different approaches in tackling cross-border malaria.

Joint colorations targeting malaria control and prevention between the countries that share the border.

Robust surveillance system for identifying the importation of malaria across borders and reintroduction of malaria after successful elimination.

Administration of anti-malarial drugs with use of protective measures.

Spatial decision support system (SDSS) could be used to target and coordinate cross-border malaria interventions.

Use of mobile technology in assessing the movement of people across borders.

Panel 4: Summary of different interventions to address cross-border malaria.

Approaches in tackling cross-border malaria	**Advantages**	**Limitations**
Joint Collaboration	Prompt sharing of cross-border data. Tackling any possibilities of out breaks.	Requires time to build trust among the health workers of the different countries.

Administration of anti-malarial drugs with use of protective measures for migrants	Avert the risk of spreading and introducing malaria into the naive population. Radical cure of malaria.	Ineffective in the mobile population, which involve in crossing border frequently-daily.
	Prevent development of drug-resistance malaria. The chemoprophylaxis can prevent malaria transmission from sources to sinks.	The cost of diagnosis and treatment will be main barrier if treatment is not provided free.
Surveillance systems	The robust surveillance at points of entry from areas of higher transmission will facilitate swift treatment and follow up of infected individuals.	The differences in the surveillance system among the countries need to be resolved so that neighbouring countries operate similar interface.
	Once the interruption of transmission has been achieved, surveillance systems will play important role in prevention of reintroduction.	Not easy to identify points of entry in remote border areas
Spatial decision support system (SDSS)	Conduct high-resolution surveillance and able to locate	The technical knowhow would be the main barrier

	and classify active transmission foci.	while implementing SDSS.
	A regional SDSS framework could provide malaria data and malaria transmission across borders. This information could be used by the relevant partners to target and coordinate cross-border malaria interventions.	SDSS may not be able to work well amongst transient/floating population.
Mobile telecommunication on tracking cross-border malaria	Quantify the volume of the people crossing the border areas.	Use of mobile technology in tracking cross-border malaria is new concept.
	Movement patterns derived from phone records can inform on the likely sources and rates of malaria importation.	Restricted to areas with mobile network coverage; Access to proprietary data will probably be difficult; data quality and completeness potentially low.

Panel 5: Search strategy and selection criteria.

The review for this paper was carried out using online search engines including PubMed,

Medline and Google Scholar. The key search words were “malaria”, “cross-border”, “migration of people across international borders” and “malaria elimination”. We reviewed all the articles written in English with preference for recent publications.