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Background Paper

Effective Responses to Malaria Importation

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From evidence to action

Contents

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Acronyms

APMEN – Asia Pacific Malaria Elimination Network

APLMA – Asia Pacific Leaders Malaria Alliance

GCC – Gulf Cooperation Council

HIV – Human Immunodeficiency Virus

IRS – Indoor Residual Spraying

ITN – Insecticide Treated Net

LAMP – Loop-mediated Isothermal Amplification

LSDI – Lubombo Spatial Development Initiative

PCR – Polymerase Chain Reaction

PPP – Public Private Partnership

RACD – Reactive Case Detection

RDS – Respondent Driven Sampling

RDT – Rapid Diagnostic Test

WHO – World Health Organization

Introduction

Imported malaria infections must be addressed to achieve malaria elimination. The Global Malaria Eradication Program's failure to eliminate malaria in the 1950s and 1960s underlines the critical nature of this objective, as importation was partially blamed for its downfall by reintroducing transmission and spreading chloroquine resistance.[1,2] Currently, imported cases tend to make up the majority of recorded cases in elimination settings.[3] In Greece, Sri Lanka, Turkmenistan, Zanzibar and other countries, importation has contributed to resurgences of malaria.[4–7] In Swaziland, research suggests that imported cases help sustain local transmission.[8] With global human movement increasing, better methods to tackle the risk of imported malaria are essential.[9] While many malaria elimination programs attempt to address importation, little is known about the variety and effectiveness of current interventions. This paper reviews how imported malaria is defined and classified, relevant types of human movement and the strategies applied to address importation in the context of malaria and other diseases. This background paper identifies gaps in knowledge and research and recommends future strategies. While experiences from malaria-free countries are explored, this paper focuses on importation in elimination settings. Our findings were informed by published and grey literature and key informant interviews with members of malaria control and elimination programs and technical experts (see Appendix A for the Interview Guide).

Classifying cases as imported

Imported cases are defined and classified differently by country, limiting comparisons across countries (Box 1).

> **Box 1. Defining 'imported malaria'**
> The World Health Organization (WHO), the US Centers for Disease Control and Prevention and most countries define imported malaria as any malaria infection that can be traced to a malarious area outside the country.[9–11] Imported malaria is identified most often in patients who have traveled from endemic areas and are diagnosed in non-endemic areas.[9,12] Additionally, the WHO defines internal importation, as that which occurs when parasites are introduced from one area to another within a country.[13]

Malaria control programs most often use travel history to classify cases of malaria as imported (Table 1). The WHO recommends that case investigation include "administration of a standardized questionnaire…to allow classification of a malaria case by origin of infection," including travel during the past three years if screening for *P. vivax* and the past year for *P. falciparum*.[10] Classifying cases as internally imported is equally complicated because no formal border is crossed.

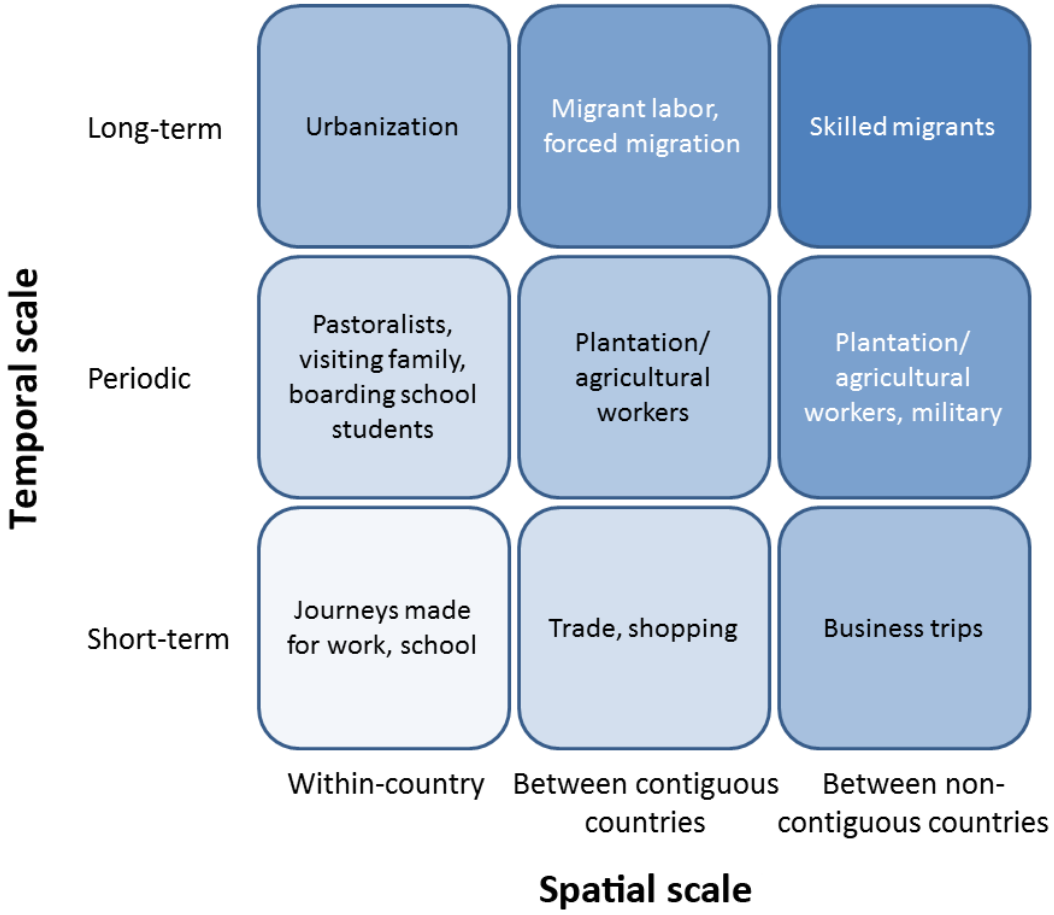
Table 1: Criteria to Classify Cases as Imported

Country/Organization	Time from Visit to Endemic Country
World Health Organization	3 years – *P. vivax*, 1 year - *P. falciparum*[10]
Malaysia	2 months[11]
Sri Lanka	18 days[12]
South Africa, Philippines	1 month[11,13]
Swaziland	4 weeks[14]
Turkmenistan	No limit, all cases assumed imported unless proven otherwise[4]

Human population movement and malaria importation

How, when and why people travel must inform control strategies for imported malaria. While movement typologies vary slightly according to different authors, broadly speaking the temporal scales of human movement can be described as short-term (e.g. daily, weekly or monthly), periodic (e.g. during holidays or seasons) and long-term (e.g. annually).[15–17] The spatial scales of travel over these periods are equally varied, ranging from within-country to between non-contiguous countries (Figure 1).

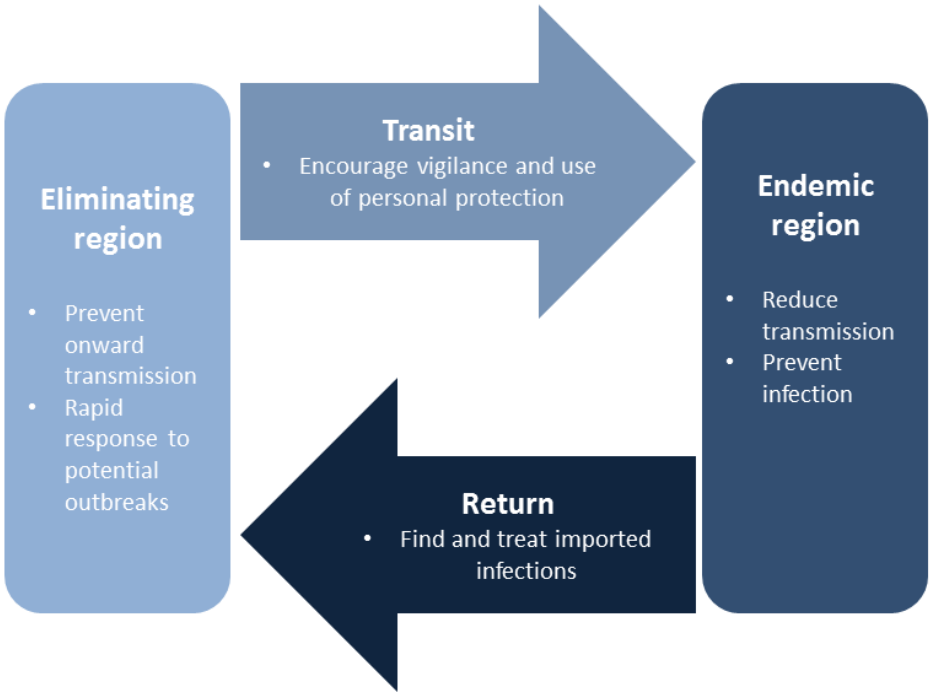
Figure 1. Types of human movement



Methods to identify and prevent imported malaria

There are four general stages of movement during which malaria importation can be addressed: in the eliminating region, during transit, in the endemic region and upon return to the eliminating country (Figure 2). Each stage presents an opportunity to confront imported parasites. In addition to these stage-specific approaches, overarching strategies can help inform and target interventions.

Figure 2. Key stages of human movement and corresponding objectives of intervention



When considering how to address malaria importation, programs may choose to employ multiple interventions at different stages of movement to ensure a comprehensive and holistic approach (Table 2). Some interventions, such as providing education about malaria prevention, symptoms and treatment, can have an impact at any stage of a journey, whereas others, like distributing chemoprophylaxis, are most effective during specific stages. Table 2 highlights key interventions to address imported malaria and when they should be implemented.

Table 2: Interventions to address importation at different stages of movement

Intervention	Eliminating Region	Transit	Endemic Region	Return
A. Improve healthcare access	o	o	o	o
B. Enhance active surveillance	o	o		o
C. Provide information, education and communication about prevention. Distribute personal protection	o	o	o	o
D. Reduce receptivity	o			
E. Facilitate cross-border partnerships and regional funding pools	o		o	
F. Introduce Public Private Partnerships	o			
G. Employ at-source testing and treatment			o	o
H. Explore screening incentives	o	o		o
I. Target networks	o			
J. Use mobile alerts and reminders	o	o	o	o

A. Improve healthcare access

In many elimination settings, both imported and local malaria cases occur predominantly in border areas. A number of countries currently address this clustering of cases by improving access to healthcare in border areas. Improving healthcare access is intended to increase the likelihood of screening, prompt diagnosis and treatment. Interventions to increase health access and improve passive surveillance include building health

facilities near borders, as in Saudi Arabia and Thailand, or extending free access to non-citizens at existing health facilities, such as access for Angolans in Namibia.[18–20] In addition to improving healthcare access in border regions, it is important to ensure that primary healthcare staff members are trained to suspect and correctly diagnose malaria as it becomes increasingly rare. Once malaria infections are identified, prompt treatment with radical cure ensures parasites are cleared before onward transmission to mosquitoes.[21]

B. Enhance active surveillance

Border screening, where individuals are tested and treated at border points such as airports, ferry terminals and border posts, is proposed frequently as an active surveillance strategy for detecting imported infections. This has been implemented in a number of settings including Bhutan, Mauritius and Oman.[22–24] However, border screening is resource and labor intensive and will overlook travelers using informal border crossings and asymptomatic carriers if only those with fever are screened. For example, of 11,000 travelers screened for fever on the Thai-Cambodia border in the first half of 2013, only nine fevers were identified, of which three were positive for malaria.[24] A recent pilot in Swaziland conducted by the National Malaria Control Program showed that, as implemented, border screening was prohibitively time and resource intensive and yielded few positive cases. The Zanzibar Malaria Control Program also deemed border screening unfeasible.[5] However, modeling of program data from Mauritius suggests that border screening successfully reduces the risk of reintroduction, despite costing US$0.70 per capita and missing around 74% of imported cases.[25] Lower income countries might not consider such an expensive program worthwhile.

[26,27] Groups at high risk for malaria are referred to as hot populations or hotpops.[3,27] Often hotpops are relatively easy to reach to allow delivery of interventions, but some groups, particularly undocumented migrants, are more difficult to reach, requiring more tailored approaches (see section “Target networks”). Workers migrating from Myanmar to Thailand were confirmed as a hotpop after a study showed that their prevalence of malaria infection (both *P. falciparum* and *P. vivax*) was 20 times higher than in the local Thai population.[28] Risk profiles may be based on place of origin, such as in Oman where travelers from Zanzibar and other regions in sub-Saharan Africa are screened selectively upon entry, due to the history of malaria importation from individuals arriving from sub-Saharan Africa.[29] A concern with targeting hotpops is that certain ethnic, socio-economic and otherwise vulnerable groups may be further marginalized if they are perceived to be responsible for carrying and spreading malaria. Therefore, any screening based on risk profiles needs to be grounded in rigorous evidence and be accompanied by monitoring to prevent and identify any unintended consequences.

In addition to focusing on hotpops, if importation is periodic and predictable, screening can be targeted during peak importation. For example, in Swaziland, imported cases peak in January following the Christmas holidays.[8] Such temporal targeting may have logistical implications as these could be periods with the highest movement of people into the country. To identify hotpops, peak importation periods and to track the efficacy of interventions such as border screening, a robust surveillance system is essential. (See UCSF Global Health Group Background Paper *Surveillance Systems to Facilitate Malaria Elimination, 2014*).

Another form of active surveillance is reactive case detection (RACD), whereby household members and neighbors of index cases are screened for parasites and treated where appropriate. This approach takes advantage of the fact that transmission clusters geographically, where some locations have higher transmission intensity than others, called hotspots.[30] Conducting RACD triggered by imported infections helps to ensure that onward transmission is identified quickly and interrupted before it has a chance to seed transmission elsewhere. This approach is used in a number of settings including Swaziland and several countries in the Asia Pacific.[11,27]

In theory, targeting active surveillance to hotpops and hotspots could be a cost-effective malaria screening strategy, however, the diagnostic tests typically used, rapid diagnostic tests (RDTs) and microscopy, commonly

miss the majority of infections due to high prevalence of low density infections.[31–33] For *P. vivax*, currently there is no point-of-care diagnostic to identify individuals harboring liver stage parasites. Use of more sensitive, rapid, molecular-based diagnostic tests, such as loop-mediated isothermal amplification (LAMP), could help overcome this, although no test yet exists for detecting the dormant *P. vivax* liver stage hypnozoites.[34] As yet, LAMP has not been adopted widely due to novelty, cost (around US$5 per sample) and difficult field application.[35,36]

C. Provide information, education, communication, distribution of protective measures

Media campaigns and community education programs that advocate use of personal protective measures, identification of malaria symptoms and health-seeking behaviors are important to prevent and address imported malaria. However, for the most part, current messaging is relevant to control rather than elimination settings, where behavior to identify sub-clinical infections or prevent importation is needed. For example, communication campaigns could ask people to seek testing after returning from malarious areas, even if they do not have symptoms, or encourage community members to provide insecticide treated nets (ITNs) for friends and family arriving from endemic regions.

In addition to information and education, other prevention options are available, such as providing travelers to high-risk areas with prophylactic drugs, ITNs and repellants.[37] Such options may be viable in better-resourced countries; however, studies show that use of and adherence to prophylaxis can be low irrespective of setting.[38–43] Providing ITNs to those traveling from endemic to eliminating countries, targeting indoor residual spraying (IRS) where they stay or providing presumptive treatment with radical cure or ivermectin, are potential options to prevent onward transmission of parasites carried into the country.[44] Such targeted interventions can reach individuals who may be carrying malaria, but might not visit a formal healthcare setting. Community and religious leaders can contribute to this outreach by sensitizing communities about malaria prevention, elimination and case detection. Community health workers or peer educators who have existing relationships with the population, particularly those that are hidden or hard-to-reach, can help facilitate community entry, conduct outreach and encourage buy-in and ownership of malaria elimination strategies.

D. Reduce receptivity

Altering receptivity may offer a more permanent solution to the threat of importation. Receptivity is defined as the relative abundance of anopheline vectors and the existence of other ecological and climatic factors favoring malaria transmission.[45] In recent times, ongoing IRS has been used to prevent reintroduction of malaria in newly eliminated settings. However, there is a long history, stretching back to the early 1900s, of using environmental engineering to reduce malaria receptivity, including draining marshes in Italy, improving drainage in Malaysia and varying flow in irrigation ditches in Cambodia.[46–48] Housing improvement, such as installing window screens and removing or covering areas where water collects, can also reduce receptivity. In the southern United States, house screening and other complementary programs were implemented to eliminate malaria in the 1950s. Although expensive to undertake on a large scale, these investments can provide long-term protection to a population. Reducing receptivity avoids recurrent costs, such as those involved in IRS programs, and insecticide resistance. House improvements could be supported through microfinance credits, incentivized conditional cash transfers or self-financed. House improvements may be particularly effective when targeted at geographically clustered hotpops, such as migrant workers. For example, through legislation and Public Private Partnerships (See section F), workers could be housed in low-cost air-conditioned housing as done in the UAE.

E. Facilitate cross-border partnerships and regional funding pools

Networks of countries can work together to support endemic nations or regions that tend to be the source of endemic infections, as it benefits both the endemic regions and their neighbors to reduce cases of malaria. One example of a cross-border partnership was the Lubombo Spatial Development Initiative (LSDI), a joint development program between the governments of Mozambique, South Africa and Swaziland, which is no

longer active due to lack of funding.[49,50] Malaria control was a core component of this economic development program. LSDI introduced IRS incrementally in southern Mozambique between November 2000 and February 2004. In addition to a marked reduction in infection prevalence in Mozambique, the initiative lead to a 78-96% decrease in cases in Swaziland and neighboring districts of South Africa.[51] The success of this program provides a strong argument for investment in regional malaria control interventions that target the sources of imported infections.[52]

Regional funding pools, where countries with mutual interest in malaria control efforts contribute to a joint fund, are an alternative collaborative approach. The Asia Pacific Leaders Malaria Alliance (APLMA) has committed to exploring opportunities for a regional funding pool, with funding currently led by Australia.[53] Regional funding pools have been suggested as a way to tackle imported malaria from Zanzibar to Oman.[5] Similarly, the Gulf Cooperation Council (GCC), a regional economic development initiative, gives financial support to malaria control efforts in local endemic countries such as Yemen.[54] In 2008 Haiti and the Dominican Republic initiated a joint malaria effort to address the importation of malaria from Haiti to the Dominican Republic, acknowledging that the reduction of malaria burden in Haiti would benefit both countries.[55,56] Additionally, the Global Fund is supporting the Regional Malaria Elimination Initiative in Mesoamerica and Hispaniola with $10 million to promote elimination in the region by 2020.[57] Other initiatives such as the Trans-Kunene and the Trans-Zambezi Malaria Initiatives are aimed at catalyzing multi-country control efforts, however moving from policy to practice is often slow.[20]

F. Introduce Public Private Partnerships

Public Private Partnerships (PPPs) offer an opportunity to target importation hotpops, such as migrant workers, who can be at high risk of importing parasites and often are employed by large-scale industries such as plantations and mines. Many private industries support or undertake malaria prevention, testing and treatment, often in collaboration with public health programs.[58] Sanders et al. recently described a successful partnership between palm oil, rubber and acacia plantations and the Malaria Control Program in the state of Sabah in Malaysia. These plantations devote resources to malaria elimination including financing, transportation, logistical support for IRS, ITNs and surveillance.[59] However achieving full coverage of interventions has been a challenge due to resource and logistics constraints. Alternatively, some private companies address malaria independently, such as ExxonMobil, which has its own “Malaria Visa” program, which documents employees’ participation in malaria education and prevention strategies. This program requires successful completion of an online education program for non-immune workers, which they must complete before arrival in an endemic country, participation in ongoing education after arrival, urinalysis to test compliance with chemoprophylaxis and home inspections of ITNs and screens. Potentially, this strategy could serve as an example for other multi-national corporations.[60,61]

PPPs can be effective on a much smaller scale as well. In such partnerships, national malaria programs work with community members to disseminate malaria information. For example, in Cambodia, many migrants’ first contact in the country is taxi drivers. In response, the Control and Prevention of Malaria Project is piloting a malaria education program with taxi drivers as malaria peer educators, with the provision of bed nets being a possible extension.[62] Similar strategies are used to provide healthcare on a small-scale basis on the Thai-Myanmar border, with malaria testing and treatment available through private clinics or NGOs along common migration routes.[63] These and similar strategies that reach migrants where they normally travel do not carry the threat of government interference, and therefore, they may be preferable to individuals who do not have required documentation.

In addition to the benefits of PPPs from a transmission perspective, improving the relationship between public and private healthcare sectors helps ensure that health authorities are aware of all malaria cases. For example, in Oman, private health centers may diagnose malaria, but patients must be treated by public authorities to

ensure appropriate drugs are used and complete surveillance data are collected.[29] This framework enables the surveillance system to capture all cases.

Relevant identification and prevention approaches used in other settings

While the control of importation of other infectious agents involves many of the same interventions as malaria, such as border screening for influenza and dengue, there are other novel approaches that may have relevance to malaria.

G. Employ at-source testing and treatment

Some countries require travelers to have proof of testing or vaccination for TB, HIV, yellow fever and other infectious diseases before an entry or residence visa is granted.[64,65] Malaria eliminating countries could require high-risk travelers, such as those arriving from endemic countries, to undergo testing, prophylaxis or treatment prior to being granted entry or visas. The United States refugee health policy includes presumptive pre-departure treatment of refugees from sub-Saharan Africa for *P. falciparum* with artemether-lumefantrine.[66,67] This treatment must be directly observed and documented on forms carried by refugees upon arrival. While such presumptive treatment on a broad scale may not be feasible or advisable, this approach could be useful for incoming travelers from particularly high-risk regions. However, this would miss important high-risk groups like individuals moving across unmanned borders or without documentation.

H. Explore screening incentives

Screening and treatment incentives are a successful approach for a number of diseases such as cancer and tuberculosis and might provide a cost-effective addition to active case detection for malaria.[65,68] For example, polio eradication campaigns in some countries offer treatment for worms in conjunction with vaccination campaigns to improve attendance and coverage. A cash incentive scheme in Pakistan, paid to community screeners who identified positive tuberculosis cases, more than doubled the number of reported cases.[68] Financial incentives are currently used to encourage patients in rural Thailand to return for follow-up malaria testing to identify potential drug resistance.[69] A similar scheme, using referrals within social or professional networks, whereby rewards are paid to imported cases for their referral of others with similar risk profiles, could facilitate screening of hard-to-reach populations (see following section 'Target networks'). An incentive scheme could bring patients to health facilities, potentially allowing the use of more sensitive molecular diagnostics and genotyping, rather than relying on field diagnostics. The ethics, sustainability and potential undue influence of incentive schemes require a cautious approach, as they could coerce participation or undermine current or future health promotion campaigns that do not offer incentives.

I. Target networks

Network targeting approaches can help identify and treat individuals with imported infections after they have entered the country. These methods have been used successfully to reach hidden and hard-to-reach populations such as sex workers and injection drug users.[70,71] In malaria research, respondent driven sampling (RDS) has been used in Thailand to identify the characteristics and migration patterns of migrants from Cambodia and Myanmar to better address artemisinin resistance.[19,72] RDS is ideal for hidden groups, where the population size is unknown and recognition of group membership could be harmful.[70] RDS uses chain-referral sampling often combined with financial or service-related incentives (e.g. free screening, counseling, education), the results of which allow researchers to robustly estimate population size and characteristics.[73] A recent study in Swaziland, using similar chain-referral and snowball sampling methodologies, showed that imported cases were able to lead researchers to fellow travelers, potentially at high risk of importing parasites.[74] Furthermore, individuals who traveled to high transmission regions in Mozambique appeared to congregate at events in Swaziland, such as weekly markets, offering an opportunity to target malaria screening and education. Such work could be expanded to develop typologies of individuals and groups likely to carry malaria and further target screening. An

important component will be identifying if certain incentives are required or whether being screened and treated is sufficient motivation to participate. If conducted appropriately, network sampling could provide an efficient method to access and better understand the demographics and movement patterns of easy and hard-to-reach importation hotpops, such as undocumented migrants, individuals using informal border crossings, frequent travelers to high-risk areas and other vulnerable groups. Furthermore, it may be possible to identify highly connected individuals who could act as community health workers or other roles related to treatment and prevention of malaria.

J. Use mobile alerts and reminders

Mobile phone technology offers an innovative approach to address malaria importation. With the advent of nearly ubiquitous mobile phone technology in most elimination settings, there are many opportunities for mobile disease surveillance and the delivery of education and prevention messaging in appropriate local languages. Short message service (SMS) alerts directed at individuals moving to and from endemic areas might increase use of preventive measures such as ITNs and prophylaxis.[75,76] Similarly, individuals could be alerted if they are in a zone where a malaria outbreak is occurring. The National Oceanographic and Atmospheric Administration is developing such 'wireless emergency alerts' to warn individuals near specific mobile phone towers of imminent local dangers such as tornadoes and floods.[77] Commercially available systems, such as the Commercial Mobile Alert System, provide governments with the ability to send location-based alerts to the general public about emergencies such as child abductions or natural disasters.[78] Malaria messaging currently includes Malaria No More's NightWatch campaigns in Cameroon, Chad, Senegal and Tanzania that provides nightly malaria control reminders via SMS, radio and television.[79] Their communications strategy includes messages and songs by national celebrities in an effort to change social norms and perceptions of malaria risk and response. An evaluation of NightWatch Cameroon concluded that approximately 500,000 more people sleep under ITNs because of this communications campaign.[80]

Evidence gaps

1. Standardized terms

To address imported malaria effectively, imported or locally acquired infections must be classified accurately. Current methods based on travel history vary between countries (see Table 1) and are likely to lead to misclassification. Untreated *P. falciparum* infections last an average of 200 days or more, therefore, asking about travel in the past 4-6 weeks can incorrectly identify an infection as imported or indigenous.[81,82] *P. vivax* infections last significantly longer and relapse if untreated, further complicating identification of imported cases.[81] Parasite genotyping provides an opportunity to differentiate local from imported infections to validate the use of travel history to classify cases and to generate standardized classifications. Genotyping has not been explored fully for this purpose in a malaria context, despite being recommended by WHO.[83] In addition, genotyping may reveal transmission connections between cases, allowing direct evaluation of the consequences of imported cases and the success or failure of measures aimed at reducing subsequent transmission.

2. Clear descriptions of characteristics and sources of imported infections

In many settings, the identities and travel patterns of hotpops responsible for importing malaria are unknown or unclear. Interviews with key informants from academic and programmatic realms of malaria control cited this lack of understanding as a primary hurdle to addressing imported malaria. A better understanding of importation hotpops and their associated risk factors would improve targeting of interventions such as screening and treatment. In addition, a better understanding of the behavior, knowledge and practices related to malaria prevention and treatment within those groups is needed to inform the development of appropriate and effective interventions.[40] Establishing the prevalence of self-treatment and use of private sector healthcare among different importation hotpops would also help identify cases that a surveillance system based in the public sector might miss.

Understanding how parasites and people move and are connected could inform targeted interventions at sources of infection and high-risk travel or trade routes. While reported travel history of people with malaria offers some insight, additional information can be gathered by combining human population movement data with malaria endemicity maps.[9,52,84] For example, Tatem and Smith estimated the degree of population connectivity between countries using human movement data.[9] This allowed them to better understand which countries would benefit from cross-border collaboration. On a smaller scale, by combining Zanzibari mobile phone records with endemicity maps, researchers were able to estimate the annual number of imported infections. The analysis showed that Zanzibari inhabitants making return trips to and from the mainland were likely responsible for the majority of imported infections.[37,84] A similar study in Kenya showed the existence of sources (receptive regions where infections are acquired) and sinks (non-receptive regions where infections acquired in sources have moved to) within the country.[52] Additional information on human movement to inform such analyses can be gleaned from case investigations, Malaria Indicator Surveys, Demographic Health Surveys and information from bus, rail and air travel companies.[16] While human movement information could help target interventions at sources and travel routes of imported infections, the value and validity of this approach has yet to be proven. In addition, the best platform to allow the integration, analysis and visualization of these data has not been established. Ideally, these data sources would be integrated into a strong national malaria surveillance system (see UCSF Background Paper *Surveillance Systems to Facilitate Malaria Elimination*, 2013).

3. Effective screening for infection

If screening is targeted at borders or with high-risk groups, then evidence of the sensitivity of field diagnostics, such as RDTs, microscopy or molecular methods is needed. Mathematical models can be used to assess the transmission implications of missed infections and the cost-effectiveness of implementing more costly and accurate diagnosis.[23] Research into the feasibility of using molecular testing, such as LAMP or polymerase chain reaction (PCR), mobile clinics or incentive schemes to encourage participation, is also needed.

4. Improved uptake of personal protection

Documentation of adherence to prophylaxis and personal protective measures is not conducted routinely. Such methods would help estimate adherence to prophylaxis in a population and could increase compliance among well-defined groups such as the military and organized labor. Rapid tests to monitor for adherence with mefloquine, atovaquone-proguanil and doxycycline in urine are being used and tested by the French military and ExxonMobil respectively.[85,86]

5. Impact assessment of strategies to reduce malaria importation

Currently, imported malaria is prevented and treated using many different approaches, yet it is unclear which combinations of methods are most cost-effective. Studies should establish the impact and relative cost-benefit ratios of different approaches in varying epidemiological and economic settings.[5,23] Mathematical modeling studies would help establish the optimal timing of interventions during different elimination stages. Field-based studies evaluating the impact and operational feasibility of different approaches are necessary. Standardization of impact assessment methodologies would allow comparisons of different strategies.

Conclusions and recommendations

Malaria importation undermines local control efforts and often is a final challenge for countries approaching elimination. Countries employ a variety of methods to address importation; however, interventions are inconsistent between settings and seldom evidenced-based. Based on this review the authors provide the following recommendations:

1. **Standardize classifications.** The development of standardized methods to classify infections as imported or local would allow accurate comparison between settings and support the evaluation of interventions.

Agreeing on standardized approaches based on travel history and exploring the use of genotyping would help address this.

2. **Improve methods for identifying and targeting groups most at risk for importing parasites (hotpops).** Risk profiling will make it possible to target high-risk groups at the times and places that interventions will have the most impact. Detailed understanding of the hotpops that contribute to importation should be possible with case-control studies, by exploring the social networks of proven cases, and by using routine surveillance data. For routine surveillance data to provide this understanding, a robust system that is capable of both the collection and analysis of epidemiological data is required. Studies of the movement and malaria-related risk behaviors of undocumented migrants, potentially using network-targeting approaches, are particularly important as little is known about these groups and they are likely at high risk of importing infections.

3. **Assess the performance of RDTs for identifying imported infections.** Screening for imported infections may be an inefficient use of resources due to their rarity and low density, unless screening is conducted in a very targeted manner with highly sensitive diagnostics. Researching the sensitivity of RDTs for imported infections is an important prerequisite to designing efficient screening programs. If RDTs are not sufficiently sensitive, alternative screening approaches using more sensitive existing molecular diagnostics may be required. Additionally, development of a rapid serological test that uses sensitive and specific antibodies and demonstrates recent exposure would be valuable.

4. **Improve uptake of self-protection.** The use of protective measures such as prophylaxis, ITNs or insecticide treated hammocks among individuals traveling to higher transmission settings can help prevent malaria transmission. However, this approach can be challenging when hotpops are not well characterized, are missed by outreach efforts and may not speak the local language. Personal protective measures to address importation are most suitable for well-defined populations, such as military or peacekeeping personnel during deployments or work in endemic areas. However, chemoprophylaxis uptake and adherence can be poor without definitive tests to confirm use. To address such noncompliance in well-organized groups, simple methods to document adherence can be used, such as double signature checklists and directly observed therapy by mobile devices. Proof of adherence could be required for reentry of these groups into malaria elimination zones. Guidelines and policies that govern how key stakeholders, such as industries employing migrant workers and NGOs working with displaced populations, address importation must be in place to ensure appropriate implementation.

5. **Support development and growth of regional and cross-border initiatives.** Taking a regional approach to elimination may be an extremely effective method to reduce the risk of imported malaria. However, this approach faces challenges including funding, political collaboration, management of cross-border activities and an understanding of the regional dynamics of parasite flow. Regional cash-on-delivery funding schemes, such as the Global Fund to Fight AIDS Tuberculosis and Malaria's Mesoamerica and Hispaniola regional collaboration, are a promising concept that may persuade countries to work together. It is also worth noting that the successful regional collaborations to date, such as LSDI and the GCC, were designed as initiatives to aid economic development, with malaria control being seen as integral to their success. Additionally, the success of PPPs in Malaysia show the ability of initiatives aimed at both development and malaria control to generate multi-sectorial investment. Embedding malaria control within regional development initiatives may therefore, be an effective and sustainable solution.

6. **Collate data on human movement to identify infectious sources and travel routes of hotpops.** While real-time information on human movement is not available, pairing projects that aim to quantify and map general human movement patterns, such as The Human Mobility Mapping Project and Flowminder, with freely available endemicity maps would help refine and better target interventions at infection sources and hotpop travel routes.[87,88] Similarly, genotyping parasites, potentially from samples collected through sentinel

surveillance sites, would allow further insight into the parasite population structure and movement to enable targeting, as done for H1N1 and HIV.[89,90] It is essential to ensure that the results of these analyses are up-to-date and easily interpretable by programs.

7. **Minimize transmission potential.** Programs should continue to minimize the receptivity of areas where individuals at high-risk of importing infections reside. In addition to traditional interventions, such as IRS and ITN distribution, altering receptivity via economic development, environmental engineering and housing improvements contributes to lasting effects and should be explored. Introducing PPPs to target interventions that reduce receptivity in high-risk groups should be encouraged. To minimize the transmission potential of imported infections, resources should be dedicated to RACD to rapidly identify and treat individuals who contract malaria due to an imported infection.
8. **Support measurement of impact of strategies.** There is a need for evidence of the impact and feasibility of interventions and combinations of interventions to address importation. To support evidence-based implementation researchers piloting these strategies should be encouraged to include standard measures of impact, including costs, acceptability and feasibility.

Imported malaria is a critical obstacle on the path to malaria elimination. Diverse opportunities exist to address importation and efforts should be tailored to the specific hotpop and country context. Collaboration is essential to build consensus on classification approaches, explore and implement interventions and build the knowledge base in order to continue shrinking the malaria map.

Appendix A

Effective Responses to Malaria Importation – Interview Guide

Thank you for agreeing to spend the time discussing malaria importation with us. We are currently working on a background paper about the issue, looking at what's been done in the past, what is happening now and where we should go from here. We're eager to hear about you experiences with imported malaria because we know that new knowledge and ongoing programming addressing this issue won't necessarily appear in published literature. I have a few questions for you, but we hope this will generally be more of a conversation than a strict question and answer session. Please keep in mind that this interview is confidential, and while we may cite some of the things you share in our upcoming background paper, we will refer to you as an expert, rather than by name. In addition, if there is anything you would like to tell us "off the record" please let us know.

1. To better understand how we're approaching this topic, how do you define imported malaria?

2. In your experience, how is malaria classified as imported on a case-by-case basis?

3. In addition to the background documents you've provided, what else can you tell us about the work you're doing, and how malaria importation fits in?

4. Thinking about imported malaria, what are the three biggest challenges to address the issue? Why? Are there particular populations or circumstances that contribute to malaria importation

5. Of the strategies that currently exist to address malaria importation, which do you believe are the most promising and why? Are there any strategies currently used that you think should be amended or improved? Are there any innovative/novel approaches?

6. What strategies would you research, test, or implement to address malaria importation if the decision was up to you and funding wasn't a concern?

7. Thinking about disease importation generally, do any diseases or surveillance systems come to mind that we should look into as models for malaria importation?

8. Who (or what organizations or groups) should we speak to about malaria importation, particularly about ongoing programming and research and evaluation? What documents or other resources that should we review?

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