

Accelerating malaria elimination in northern Cambodia through early diagnosis and treatment

Malaria in Cambodia

Artemisinin-based combination therapies (ACTs) are the recommended treatment for *Plasmodium falciparum* malaria and are one of the most effective antimalarials at our disposal. However, delayed parasite clearance after treatment with artemisinin has been confirmed in countries of the Greater Mekong Subregion.^[1,2] This has rendered treatment of the disease increasingly challenging and threatens malaria control achievements made in the subregion thus far.

With nearly three-quarters (71 percent) of its population living in malaria-endemic areas, Cambodia has made great strides towards eliminating *P. falciparum* and *P. vivax* by 2020 and 2025 respectively; just 76,804 people were confirmed to be infected with malaria and with one death from the disease in 2017.^[3]

To take the final steps towards eliminating *P. falciparum* in the country altogether, and to avoid further emergence of artemisinin-resistant mutations, a specific focus on preventing malaria among vulnerable groups is required.

As the northeast region — the forested areas bordering Laos, Thailand and Vietnam in particular — accounts for the majority (over 70 percent) of Cambodia's malaria cases and the highest prevalence is reported among mobile and migrant populations,^[3,4] interventions that target these individuals are crucial.

Early diagnosis and treatment

To interrupt and prevent transmission of *P. falciparum*, symptomatic individuals need to be diagnosed and treated as early as possible in the course of their illness. This means that easy access to reliable diagnostic tools and effective treatment for at-risk populations is essential.^[5] This is usually provided via one of two approaches: **passive case detection**, which is triggered by symptomatic patients seeking consultation at static facilities; or **active case detection**, which sees health staff actively seek out and test individuals who are high-risk (proactive detection) or who are linked to a confirmed malaria case — the index case — (reactive detection).

In northern Cambodia, forest goers who work in remote and hard-to-reach settings are most at risk of being infected with malaria due to their itinerant lifestyle and limited access to health services.^[6] Prevalence of malaria in the region is highly heterogeneous and varies between villages and between households therein.^[7] This context requires community-based and flexible case detection and treatment.

Our approach

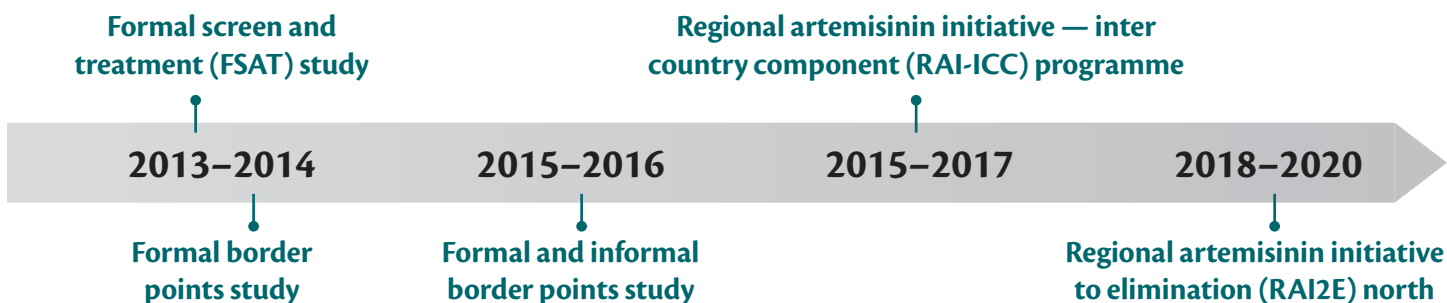
We use a flexible approach to delivering our early detection and treatment interventions. We continually review quantitative evidence, operational experience and local knowledge to ensure we are delivering the most appropriately designed and targeted interventions possible (see Figure 1). The approach revolves around systematically revisiting five key questions:

1. Who is our target population?
2. Where can we reach them?
3. When is the best time to reach them?
4. What diagnostic tools are the most appropriate?
5. How can we increase their access to services efficiently?

Figure 1: Our systematic approach to optimising interventions



Figure 2: Timeline of our early diagnosis and treatment studies and projects



Our contribution

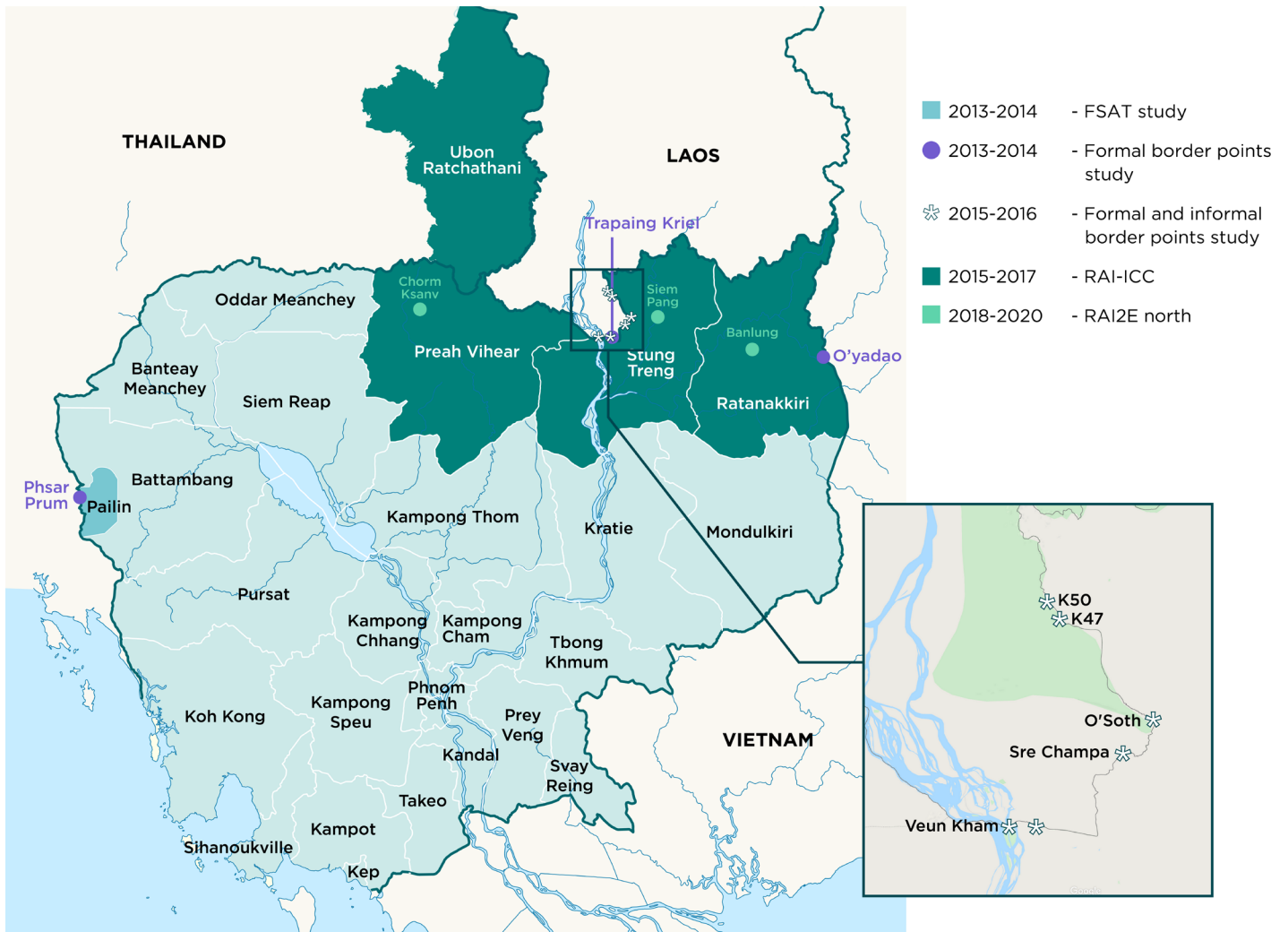
Malaria Consortium has been operating in border regions in northern Cambodia since 2008. We have been building the evidence base around the best approaches for reaching the most at-risk populations with early diagnosis and treatment since 2013 (see Figure 2).

In our [first study](#), we tested the feasibility and impact of using reactive case detection to identify asymptomatic malaria in households in Pailin — the province on the Thai border where artemisinin resistance first emerged (see Figure 3) — in which a malaria case had been confirmed through passive case detection at a health facility. We demonstrated that targeting household members and neighbours of an index case for screening was not an effective approach in a setting where exposure to malaria most likely occurs away from the community.^[8]

As such, our [second study](#) sought to quantify *P. falciparum* infection — including asymptomatic and artemisinin resistant cases — among people who regularly cross the Laotian, Thai and Vietnamese borders for work. This revealed that the highest *P. falciparum* caseload was among migrant populations in Stung Treng province near the Laotian border.^[9]

Given this, our [third study](#) aimed to understand better the impact of migrant populations on malaria transmission in this region. We screened people crossing seven border points — the formal Cambodia-Laos border in Stung Treng province and six informal border crossings. We also trained mobile malaria workers (MMWs) — respected and trusted members of the target population — to screen plantation and farm workers who had recently crossed the border. We found that most border-crossers came from work sites within the forests that hug the border and that malaria infection was significantly associated with construction workers/sites.^[10]

Figure 3: Map of our early diagnosis and treatment studies and projects in Cambodia



Based on these insights, under the [RAI-ICC programme](#) we trained village malaria workers in passive case detection and MMWs in active case detection. Both forms of detection were conducted in sites — villages and strategically placed screening points respectively — that were within five kilometres from forests, with further outreach activities (e.g. social and behaviour change interventions to promote the uptake of preventive behaviours) delivered inside the forests. These activities were more efficient at reaching the at-risk population than our previous projects implemented in villages far from forest areas.^[11] In total, we reached 24,036 people with our testing services, detecting and treating 2,172 *P. falciparum* and mixed cases, and 1,085 *P. vivax* cases.

In light of this success, we are currently working with partners to implement the [RAI2E north project](#) via

which we are providing free-of-charge early diagnosis and treatment services to hard-to-reach communities — particularly mobile and migrant workers — in border areas of three provinces in northeastern Cambodia: Preah Vihear, Ratanakkiri and Stung Treng. Core activities include:

1. **Mobile malaria posts:** continuing our RAI-ICC programme approach of delivering services as close to the forest as possible, we have strategically placed mobile malaria posts at border crossings, forest entry points and other meeting points where high caseloads of *P. falciparum* cases have been reported. Here, trained MMWs proactively provide forest goers with testing and treatment services including rapid diagnostic tests (RDTs), ACTs and low dose primaquine treatment.

2. **Outreach activities:** to ensure that forest goers who infrequently pass mobile malaria posts or reside in the forest permanently have access to early detection and treatment, we have recruited and trained MMWs to proactively screen and treat forest goers at their workplaces (i.e. inside the forests). Hired directly from target communities, MMWs have insights into the seasonality of forest activities and location of work sites, and are trusted community members.
3. **Reactive case detection:** having learnt from our FSAT study that screening in index and neighbouring households of a confirmed positive was inefficient,^[8] we now seek to ascertain whether the infected

individual has recently spent time in a forest and, if so, endeavour to identify, test and treat any co-travellers or co-workers who might have been co-exposed.

These activities are all embedded into the government's overall health education programme and vector control strategy; MMWs, recruited and trained by Malaria Consortium, support government staff in delivering community-based health promotion and education activities and target forest goers with long lasting insecticidal nets and impregnated hammock nets.^[4]



An MMW visits an at-risk family of cashew nut farmers near Lom Kob village on the Vietnamese border

Achievements

Our results from the RAI2E north project thus far show that tailored early diagnosis and treatment interventions have contributed to:

- an increase in access to much needed services among at-risk populations
- decreasing RDT-detectable *P. falciparum* malaria to almost zero
- efficiently inverting the *P. falciparum* and mixed/*P. vivax* case ratio.

Between January 2018 and June 2019, 55 MMWs provided early testing and treatment services to 26,274 people (see Table 1) and were able to treat 83 percent of confirmed positive cases directly. The remaining positive cases had to be referred to the nearest health facility for treatment due to initial treatment supply challenges, which have since been resolved.

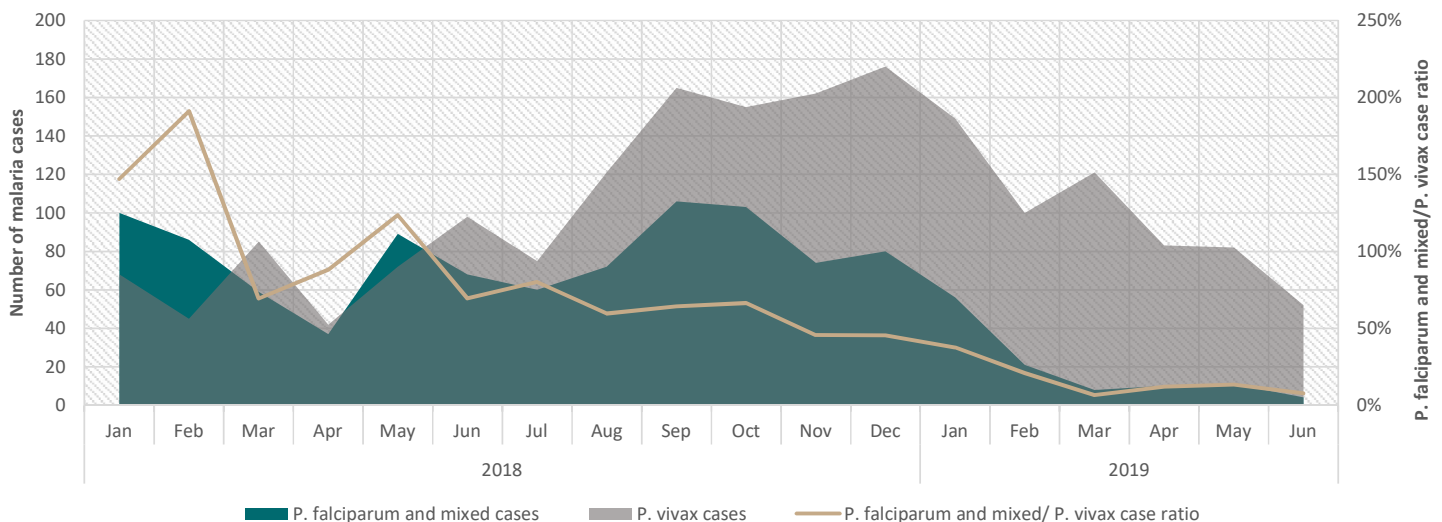
As Figure 4 shows, RDT-detectable *P. falciparum* malaria decreased by 75 percent in 2019 compared to the same period in 2018 (January to June). The *P. falciparum* and mixed/*P. vivax* case ratio decreased by 82 percent over the same period, which is a significant achievement on the path to *P. falciparum* elimination. Meanwhile, the *P. vivax* malaria caseload remained approximately constant. This indicates that distinct approaches for targeting *P. vivax* malaria need to be developed alongside the continued delivery of tailored *P. falciparum* interventions. These should take into consideration the unique challenges *P. vivax* malaria poses; for example, difficulties preventing relapses in patients who are pregnant or G6PD-deficient and are, therefore, unable to be treated with primaquine radical cure, the only treatment currently available.

Table 1: Number of people screened and cases detected, by case detection approach

Case detection approach	Number of people screened via RDTs	Number of positive cases (all species)	Number of <i>P. falciparum</i> and mixed cases
Reactive case detection	730	67	49
Mobile malaria posts	10,902	1,559	594
Outreach activities	14,642	1,269	401
Total	26,274	2,895	1,044

Source: RAI2E north project data, January 2018 to June 2019 (n=26,274).

Figure 4: Number of malaria cases by species and *P. falciparum* and mixed/*P. vivax* case ratio



Source: RAI2E north project data, January 2018 to June 2019 (n=26,274).

Outlook

We believe that the following must be prioritised if *P. falciparum* is to be eliminated in the region:

1. **Expansion of surveillance-related capacity building:** achieving elimination in a very low transmission setting requires in-depth data on each malaria case and comprehensive analysis of the local malaria situation. To achieve this, community and health facility-level data from active and passive case detection activities need to be integrated and health workers' capacity must be built to use this data for decision-making at the local level.
2. **Targeting of the *P. falciparum* asymptomatic reservoir:** as RDT-detectable *P. falciparum* malaria decreases, the importance of specifically targeting asymptomatic carriers — crucial players in pre-elimination settings^[12] — increases. New, tailored approaches must be urgently developed as current early diagnosis and treatment approaches are only partially sufficient for targeting this reservoir: RDTs' poor sensitivity limits the use of active case detection approaches among asymptomatic cases.

To this end, in addition to continuing to deliver free access to early diagnosis and treatment services as close to forests as possible through our established MMW network, we will expand our reach in northeastern Cambodia via two new projects:

1. **Accelerated malaria elimination project:** building on an earlier Médecins Sans Frontières operational research project (2015–2019), we will implement a combination of established interventions in areas surrounding the Prey Lang forest in Preah Vihear and Stung Treng provinces. We will provide early diagnosis and treatment through strengthened passive case detection that targets symptomatic cases. We will also undertake proactive and reactive case detection in selected high-risk villages to target the asymptomatic *P. falciparum* reservoir and to reach pauci-symptomaticⁱ forest goers who might not be reached by passive case detection services.
2. **Prey Lang forest project (2019–2020):** under this Institut Pasteur du Cambodge-funded operational research project, we will provide free access to early diagnosis and treatment exclusively within forest areas in Preah Vihear province through designated

forest malaria workers. Each forest malaria worker will cover a specific section of the forest and will collect dry blood spots (including follow-ups 28 and 42 days post-diagnosis). These will undergo polymerase chain reaction analysis to quantify the *P. falciparum* asymptomatic reservoir and identify possible treatment failures. The project also aims to investigate the feasibility and efficacy of targeting forest goers in remote areas with mass screening and treatment (MSAT). When implemented in addition to other interventions, targeted mass drug administration delivered through MSAT activities is a feasible approach for reducing *P. falciparum* malaria in the symptomatic and asymptomatic reservoirs.^[12]

Lessons learnt from implementation of these two projects will inform future project design to ensure that we are implementing feasible and tailored interventions that continue to contribute to malaria elimination in northeastern Cambodia.

ⁱ Malaria cases who present with fewer symptoms than usual symptomatic patients.



A Malaria Consortium staff member at work at the local health centre near Srae Sambor village

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