Understanding the feasibility and potential impact of screening for asymptomatic malaria in households where a febrile case of malaria has been reported in a malaria elimination setting in Pailin province, Western Cambodia

Sara E. Canavati de la Torre[1,5], John Hustedt[1], Sophal Uth[1], Chandary Rang[1], Po Ly[2], Siv Sovannaroths[2], Sylvia Meek[3], and Arantxa Roca-Feltrer[4]

[1]Malaria Consortium, Phnom Penh, Cambodia [2]National Center for Parasitology, Entomology and Malaria, Cambodia
[3]Malaria Consortium [4]Malaria Consortium Asia [5]Faculty of Tropical Medicine, Mahidol University, Thailand

Introduction

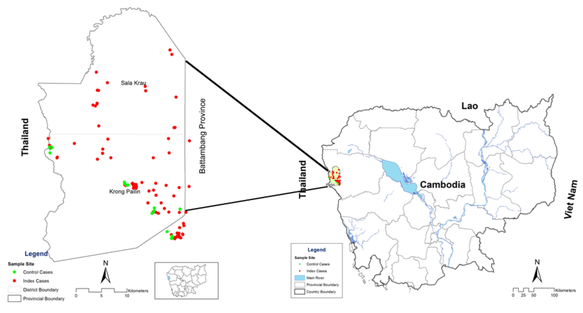
- Cambodia is moving towards malaria elimination.
- There is a need to strengthen active detection and response systems to all malaria cases in elimination settings.
- Although several pilot focused screening and treatment attempts were conducted during the World Health Organization 's containment project[1], there is still a need to better understand the mechanisms by which reactive case detection strategies contribute to reducing and sustaining transmission below the critical level in these settings.
- Based on series data from Cambodia Malaria Surveys conducted in 2004, 2007 and 2010[2], out of the total number of households found with at least one case of asymptomatic parasitaemia (not with fever), 16% had other individuals infected in the same household.
- This suggests that screening households for asymptomatic parasitaemia where a case of febrile malaria is reported may help avert episodes of malaria and reduce transmission.
- In Pailin (Cambodia), a fully functional malaria alert system (Day 0 SMS system) is currently in place where village malaria workers (VMWs) test, treat, and track malaria cases at the village level[3].

Aim
The long-term overarching goal of the project is to generate the necessary information to develop an interventional tool consisting of screening households with a malaria case and eliminating the asymptomatic reservoir.

Objective
To understand the feasibility and potential impact of screening for asymptomatic malaria in households where a febrile case of malaria has been reported (index household).

Methods

Study Site
The study site includes all 114 malaria endemic villages within Pailin Province in Cambodia (see map), and is being conducted from July 2013-June 2014. Green dots indicate geographical coordinates where a case investigation has taken place.



Sample Size
Due to low and sub-microscopic parasitemic levels in this setting, all members of index households are being screened for malaria parasites using microscopy, Rapid Diagnostic Tests (RDT) and molecular Polymerase Chain Reaction (PCR) technology (using dry blood spots). It is anticipated that 270 index households and 190 control households will be followed up during the study period.

Sampling
All households with malaria infected patients identified through VMWs and at Pailin health facilities throughout the study period are eligible for the study. Control households will be sampled by taking the five nearest houses every 15th index case and the 10 nearest houses every 30th index case. In addition, every month five additional households within the study site will be chosen at random and used as control households.

Data Collection
VMWs residing in intervention villages are screening all household members of the index cases. Screening of malaria parasitaemia by VMWs is being done by RDT and patients testing positive are treated according to the national guidelines. In addition, each participant tested is interviewed using a structured case investigation form. This includes basic demographic characteristics, history of travel/residence outside of the area (to identify possible origin of infection), type of work, etc. Each household is also being geo-referenced to identify potential geographical clustering of cases.

Data Analysis
Data is being entered and verified using EpiDATA® software, and is being analysed using Stata® version 12. *P*-values < 0.05 are being used to indicate statistically significant differences.

Ethical Review
Ethical clearance was received from the Cambodian National Ethics Committee for Health Research.

Results

From July 2013 to January 2014, a total of 1416 individuals within 250 index households and 560 individuals within 110 control households have been screened for malaria parasites. We have received RDT results for all 1976 individuals and microscopy results for 1089 individuals, however PCR results are still outstanding (See Table 1).

Preliminary RDT results show 90.8% of index cases were positive for Pv, 7.2% for Pf, and 2% Mixed. Preliminary microscopy results show the risk of being positive is 2.6 times greater in Households (HHs) with an index case as compared to those HHs without an index case.

Table 1: *Preliminary results based on RDT and microscopy samples analysed*

Lab Technique	Index/Control	*Pv*		*Pf*		Mixed	
		n	%	n	%	n	%
RDT	Index Cases (N=250)	227	90.8	18	7.2	5	2.0
	Index HH Members (N=1163)	3	0.2	1	0.1	0	0
	Control HH Members (N=563)	4	0.7	1	0.2	0	0
Microscopy	Index HH Members (N= 732)	16	2.2	0	0	0	0
	Control HH Members (N=357)	3	0.8	0	0	0	0

We are able to reach 95.5% of individuals within 3 days of a VMW report, and an additional 0.4% on a follow up visit within 14 days. The time it took to reach individuals on follow up visits averaged 7 days with a range of 1-14 days. After 14 days they were considered lost to follow up. The average family household size was 6 people.

Challenges

- Cases are usually detected in very remote areas which makes it very difficult for the investigation team to access, especially in the rainy season. Our team routinely has to walk several kilometers to reach study HHs.
- Re-active screening consumes significant time and human resources. We found that a team of 5-6 people can complete approximately 2 HHs per day (with an average of 6 members in each HH).
- Need for a sensitive molecular tool for field use that would allow for a more accurate diagnosis and prompt treatment. Potential use of other diagnostic techniques such as LAMP are being explore in this project.

Discussion and conclusions

This study will serve as the basis to evaluate a novel strategy to reduce the malaria reservoir and prevent malaria episodes amongst individuals harboring malaria parasites. Results will provide evidence on whether Active Case Detection and Treatment (ADAT) activities are operationally feasible and effective in an area where pre-elimination conditions already exist and a malaria alert system is fully functional.

This information can be a valuable addition to the strategy to eliminate *P. falciparum & P. vivax* infections by 2015 and 2020, respectively.

Keywords: malaria elimination, re-active surveillance, Western Cambodia

References
[1] World Health Organization. Containment Project. Accessed Jan 31 2014. http://www.searo.who.int/thailand/areas/malaria/containment/en/index.html
[2] National Malaria Control Programme (NMCP) [Cambodia]. *Cambodia Malaria Survey 2012*; Final Report 2012
[3] Malaria Consortium *Moving Towards Malaria Elimination: Tools for Strengthening Malaria Surveillance in Cambodia* 2011

Acknowledgements
This study was funded by the Malaria Eradication Scientific Alliance (MESA). The authors thank all organisations and individuals that supported this project in field implementation, discussion, and comments. A special thanks to all volunteers that agreed to participate in this study and to our collaborators Ménard Didier (IPC) and Jonathan Cox (LSHTM).