# Applied Epidemiology in Cambodia

A thesis submitted for the degree of Master of Philosophy (Applied Epidemiology) of the Australian National University


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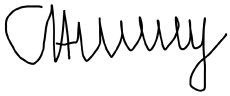
# Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university. To the best of the author's knowledge, it contains no material previously published or written by another person, except where due reference is made in the text.

Srean Chhim



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# Acknowledgments

I am enormously grateful to my academic supervisors, Dr. Tambri Housen and Amy Parry, and field supervisors, Dr. Patrice Piola, and Dr. Vincent Herbreteau, for their continuous support and patient guidance, encouragement, constructive and helpful comments to help me fulfill my MAE competencies during the past two years.

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I have learned from the past MAE students through their teaching in MAE, guest lectures, and thesis. I thank them for sharing their experience.

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# Thesis abstract

In meeting the Master of Philosophy in Applied Epidemiology (MAE)'s, I completed two of my core projects at the Institute Pasteur of Cambodia (IPC), a non-governmental organization. The other two core projects I completed at the Ministry of Health's Cambodian Communicable Disease Control Department (CCDC), where I was later deployed to support Coronavirus Disease 2019 (COVID-19) contact tracing and surveillance. In this thesis, I demonstrate how I met the core competencies of the MAE program.

In late November and early December 2019, a provincial health department notified CCDC about what they called a food poisoning event that had affected more than 200 people, and resulted in two deaths in a residential facility in a province of Cambodia. We conducted a case-control study. We found a strong association between eating cucumbers and illness. However, laboratory analysis failed to detect a causative agent. Toxicology testing was not conducted, and therefore we were unable to rule out contamination of the cucumbers. This project is described in chapter two, "An outbreak of unknown etiology associated with fresh cucumbers in a residential facility in Cambodia, 2019".

We aimed at describing how malaria has evolved spatially from 2006 to 2019. We undertook a secondary analysis of existing malaria data from all public health facilities in Cambodia between 2006 and 2019 in combination with metadata. Overall, incidence fluctuated between 1.5 and 7.4 cases/1000 inhabitants per year. Malaria clusters were detected in seven northern provinces, along borders. We recommended that interventions aimed at preventing new infections of Plasmodium vivax and relapses should be prioritized. All confirmed malaria cases should be reported to Health Management Information System to avoid misleading trends. This project is detailed in chapter three, "Malaria in Cambodia: retrospective analysis of a changing epidemiology 2006-2019."

I implemented and evaluated the RAI2 surveillance system as part of activities associated with a funded malaria project. Nine attributes, adapted from the US CDC guideline 2001, were used to assess the performance of the system. Usefulness was described based on the outcome of the evaluation of the other eight attributes. Simplicity, flexibility, acceptability, and stability were assessed using a short online survey with health center staff. Sensitivity, positive predictive value, data quality, and timeliness were assessed using document review and data from the RAI2 surveillance system. Findings suggested

that the RAI2 surveillance system was simple, flexible, stable, timely but did not meet its primary objective. We recommended that the RAI2 surveillance system should be integrated into the national malaria information system and moved to be a real-time data collection. Additional exposure variables should be captured. I placed this project in chapter four, “Using Kobo Toolbox as a malaria project-based surveillance system in Cambodia: surveillance evaluation.”

My final project was to estimate the proportion of COVID-19 cases that were asymptomatic and understand how the asymptomatic transmission may occur. I analyzed data from 22 cases as part of a cluster of returned travelers, with what was believed to be a common exposure site. Their 491 uninfected contacts and ten infected contacts were also included in the analysis. The findings suggested asymptomatic cases made up a larger proportion of total cases within the cluster. This project is described in chapter five, “Coronavirus Disease 2019 asymptomatic transmission: A cluster review in Cambodia, 2020.”

Finally, other required activities presented in this thesis include an oral presentation, a scientific manuscript submitted to a peer-reviewed journal, a literature review, a summary for a layperson, lessons learned from the field, and teaching.

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# Chapter 1 Introduction

“My journey during the Master of Philosophy in Applied Epidemiology”

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## Field placement

During my time on the Master of Philosophy in Applied Epidemiology (MAE), I was so fortunate that I could get field epidemiology experience and learned from a large field epidemiologist network including epidemiologists and staff at the Australian National University (ANU), Institut Pasteur du Cambodge (IPC), Cambodian Communicable Disease Control (CCDC), US Center for Disease Control (US CDC), and World Health Organization (WHO).

In meeting the MAE's competencies, I completed two core projects at IPC and the other two core projects at CCDC.

The agreement between ANU and IPC at the beginning of MAE stated my primary field placement was at IPC in Phnom Penh, Cambodia, between 18 March 2019 and 18 November 2020. It was the first time that IPC supervised a field epidemiology scholar with ANU, and the first time, ANU had an MAE scholar from Southeast Asian countries. We could say that a lot of things were in the experiment.

Although it was the IPC's first experience with MAE, the IPC team is strong in epidemiology and laboratory capacity related to infectious disease. Having a long history since the 1950s, IPC is a not-for-profit institute that has strong support from Cambodia's Ministry of Health (1). The IPC's scope focuses on laboratory-based research and surveillance of infectious diseases, promoting knowledge on infectious diseases through training to its partners, laboratory service, and international vaccination services. IPC has the highest medical laboratory qualification with its biosafety facilities (BSL2+ and BSL3). It is also the first Cambodian medical laboratory which obtained accreditation under the recognized international standard NF EN ISO 15189 by COFRAC in 2018. IPC provides a variety of vaccinations such as Haemophilus influenza type-b infection, bacterium Bordetella pertussis infection, Mycobacterium tuberculosis (MTB) bacterial infection, tetanus bacterial infection, Japanese encephalitis virus infection, hepatitis B virus infection, human papillomavirus infection, poliovirus infection, bacterium Neisseria meningitides infection, rotavirus infection, yellow fever viral infection, typhoid fever, varicella virus infection, influenza virus infection, and rabies virus infection rabies. On infectious disease research, IPC conducts infectious disease-related research on pathogens including respiratory virus': seasonal influenza, and influenza, arbovirus disease: dengue, chikungunya, and Zika, zoonosis: rabies, Japanese encephalitis, other zoonotic viruses, and novel pathogens, neurotropic infection: meninges encephalitis, and enteroviruses.

While placed at the IPC's Epidemiology and Public Health Unit, my field supervisor was Dr. Patrice Piola, a medical epidemiologist. Dr Piola is French and obtained his medical degree and PhD in Epidemiology from a University in France. Patrice has worked in several counties in Asia, Africa, and Europe with the Pasteur Institute, Oxford University and Médecins Sans Frontières (Doctors without Borders).

When I arrived at IPC, my field supervisor had two research projects on malaria under his direct supervision and several others under his senior staff's supervision. At this point, I learned that he had a strong interest in malaria. This drove me to choose malaria-related projects.

My first project at IPC was the analysis of national malaria data. This project was selected because I intended to learn new skills in spatial analysis and understand more about malaria through national surveillance data analysis. However, at that time, the data I needed was owned by the National Center for Parasitology, Entomology, and Malaria Control. I was able to negotiate access to the data from the National Center for Parasitology Entomology and Malaria Control. I learned skills in the geographic information system (GIS), spatial Poisson scan statistic by Kulldorff M. (2), and R programming software to complete this project. It was at this time that I got my secondary supervisor, Dr. Vincent Herbreteau. My primary field supervisor invited Dr. Herbreteau to be my secondary supervisor. Dr. Herbreteau was a researcher at the French National Research Institute for Sustainable Development (IRD), based at Institut Pasteur du Cambodge. He graduated with his PhD in Health Geography at Paris-X University and Master of Engineering Geographic Information System and remote sensing at STAR program (Space Technology Applications and Research), Asian Institute of Technology (AIT) in Thailand. Dr. Herbreteau has expertise in spatial analysis (GIS, remote sensing, geostatistics), spatial epidemiology, habitat modeling.

The second project was the evaluation of a surveillance system. When I started my placement, I was part of one project called the "RIA2" project. Its objective was to eliminate malaria transmissions in forested areas (and subsequently in surrounding villages) within a year. The projects planned to do active screenings (Mass Screening and Treatments with rapid diagnostic tests (RDTs)) and continuous passive detection to efficiently treat all malaria infections and provide patients with a vector control kit. The study compared malaria incidence trends from six health centers neighboring intervention forests and compared these trends to the other 41 health centers neighboring non-intervention forests

in Cambodia (control forests). A significant drop in malaria notifications among health centers surrounding intervention forests compared to control forests would strongly suggest the effectiveness of the interventions inside forests.

I was asked to set up a project-based surveillance system, I was responsible for selecting the intervention and control health centers, defining inclusion criteria, designing the surveillance system, and was responsible for overall project management, including training staff and monitoring data quality. I met with people I knew to explore the existing system, and later I established a surveillance system, the so-called “RAI2 surveillance system”. It started running in late August 2019. After a five-month implementation, I evaluated this surveillance system and used this as one of my four competencies.

I completed my outbreak investigation and epidemiology projects with CCDC. CCDC is under the umbrella of the Ministry of Health (3). Its scope is broadly defined to prevent and control infectious diseases in the country. CCDC actively works to prevent, detect and control outbreaks of Avian Influenza, severe acute respiratory syndrome (SARS), Severe Watery Diarrhea, Swine Influenza, Middle-East respiratory syndrome (MERS), other diseases (e.g., mass fainting and food poisoning) (4), through its Cambodia Early Warning System (CamEWARN). During the Coronavirus disease 2019 (COVID-19) pandemic, CCDC worked closely with national and international agencies to respond to the COVID-19 spread (5).

In terms of outbreak investigation, CCDC has a mandate to conduct outbreak investigations. IPC provides technical support when it is invited. This means IPC had a low chance of being able to provide an opportunity for me to conduct an outbreak investigation. My supervisors at IPC agreed that I could join an outbreak investigation with a third-party institution, either with the National Institute of Public Health (NIPH), my previous workplace, or CCDC, the lead state institution in doing an outbreak investigation in Cambodia. I communicated and kept in touch with people at CCDC, letting them know that I was enthusiastic about an opportunity to participate in an outbreak investigation.

In late November 2019, there was an outbreak of an unknown illness in a residential facility. The outbreak caused 237 people to fall ill, including two deaths, in two days. A multi-sectoral investigation team was established on Monday, 2 December 2019, to investigate the outbreak’s source. I was informed about the outbreak. After discussing with my supervisors, I received permission from the CCDC director and joined the outbreak investigation. I was not sure at the beginning whether I could use this for my outbreak

investigation project. It depended on how much I could be involved and whether my involvement met the outbreak investigation competency defined by ANU. I was fortunate that my role ended up encompassing data collection and management, data analysis, the presentation of findings to the local authorities, and construction of the outbreak report. My academic supervisor advised that I could use this project for my outbreak investigation project if CCDC allowed. My academic supervisor at ANU sent an official letter to the CCDC's director to request his approval to let me use the report written by me for my project. I later received authorization to include the report in this thesis.

For the second project with CCDC, I reviewed a Coronavirus Disease 2019 (COVID-19) cluster of returned travelers from abroad. This project aimed to estimate the proportion of asymptomatic cases and compare the attack rate and basic reproduction number generated by symptomatic primary cases and asymptomatic primary cases. This project was initiated three months after I was deployed to support contact tracing at CCDC. I started my involvement with contact tracing activities on 6 March 2020 when Cambodia detected its second COVID-19 case. When the number of COVID-19 cases increased, I travelled to different provinces to train contact tracers and participate in field investigations from case notifications. When more and more provinces detected new cases, I was part of the national team based in Phnom Penh and remotely supported the provincial teams. After the 123rd case of COVID-19 was detected on 10 April, Cambodia had zero cases for more than a month, until 29 May 2020. At the time I was less involved with contact tracing activities since there were not many contact tracing activities, and I had to speed up my projects for MAE. At that time, I have not yet identified my epidemiology project. With consultation with my supervisors and other epidemiologists, I chose to review a COVID-19 cluster with the purpose stated above. This project was special because it was like a nature experiment. People went abroad to join a super-spreading event where we believed all 22 cases were infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). They travelled back home and stayed with their family for more than ten days without preventing their family members from SARS-CoV-2 infection. Some of the 22 index cases developed symptoms, and some did not. These features possibly allowed us to compare the attack rate and basic reproduction numbers of asymptomatic and symptomatic cases even though we expected there would be limitation from a small sample size.

CCDC had a strong collaboration with the WHO's country office, US CDC in Cambodia, and other government institutions. My involvement with both projects at CCDC allowed

me to learn from experts and staff of CCDC's partners, which experienced dealing with outbreak and pandemic.

## Requirements for MAE

Students must do four core competency projects in meeting the MAE's competencies, including an outbreak investigation, public health data analysis, surveillance data evaluation, and epidemiology research study. Students are also required to do an oral presentation in a national or international conference, demonstrate competency in conducting a literature review, have written a late draft of a scientific manuscript for a peer-review journal, a summary for a layperson, shared lessons learned from the field and demonstrated competency in transferring knowledge and skills through teaching. This thesis describes how I met these competencies and the additional required activities. The projects and activities have been divided into six chapters, as summarized in Table 1.1 below.

Table 1.1: Summary of MAE projects and experiences fulfilling core degree requirements

| Requirement | Chapter | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Introduction | √ | | | | | |
| Outbreak investigation | | √ | | | | |
| Public health data analysis | | | √ | | | |
| Surveillance data evaluation | | | | √ | | |
| Epidemiology study | | | | | √ | |
| Oral presentations | | | √ | | | |
| Literature review | | | | √ | | |
| Scientific manuscript for the peer-review journal | | | √ | | | |
| Summary for a layperson | | | | | √ | |
| Sharing lessons learned from the field and teaching | | | | | | √ |

To enable students to do their projects, MAE provided extensive training. Of those topics, some were compulsory and must be passed. Those compulsory courses were summarized in Table 1.2 below.

Table 1.2: List of compulsory courses for MAE

| Compulsory courses for MAE Title | Time | Credit in unit |
|---|---|---|
| **POPH8917 - Public Health Surveillance** | First Semester, 2019 | 6 |
| **POPH8916 - Outbreak Investigation** | First Semester, 2019 | 6 |
| **POPH8920F - Applied Epidemiology Thesis** | First Semester, 2019 | 0 |
| **POPH8915 - Research Design and Methods** | First Semester, 2019 | 6 |
| **POPH8913 - Analysis of Public Health Data** | First Semester, 2019 | 6 |
| **POPH8920F - Applied Epidemiology Thesis** | Second Semester, 2019 | 17 |
| **POPH8920F - Applied Epidemiology Thesis** | First Semester, 2020 | 24 |

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4. Cambodia Communicable Diseas Control (CCDC). CamEWARN Phnom Penh: CCDC; 2020 [Available from: http://www.cdcmoh.gov.kh/surveillance/camewarn.

5. Cambodia Communicable Diseas Control (CCDC). COVID-19 Documentation Phnom Penh: CCDC; 2020 [Available from: http://www.cdcmoh.gov.kh/resource-documents/covid-19-documents.

# Chapter 2 : An outbreak of unknown etiology associated with fresh cucumbers in a residential facility in Cambodia, 2019

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# Prologue

## Rationale

This chapter presents an internal report of an outbreak of unknown etiology associated with fresh cucumbers in a residential facility in Cambodia, in 2019. This outbreak investigation is my first out of four projects to fulfill the competencies of the MAE program.

The investigation was led by Cambodia Communicable Disease Control Department (CCDC) in collaboration with the Department of Drugs, Food Safety, Medical Equipment, and Cosmetics, Ministry of Health; Department of Agro-Industry, Ministry of Agriculture, Forestry and Fisheries; Banteay Mean Chey Provincial Health Department; Pursat Provincial Health Deportment; US Centre for Disease Control, Cambodia; and World Health Organization, Cambodia.

I received permission from Dr. Sovann Ly, Director of Cambodia's CDC, to join the investigation team for my learning purposes.

## Roles

Dr. Chan Vuthy, principal investigator, allowed me to do the following tasks.

1. Interviewing the cases and controls
2. Creating a data entry frame using Epi-Data software
3. Performing data analysis
4. Present findings to the local authorities, and
5. Writing the outbreak report

## Lessons Learnt

From my role in the outbreak investigation, I have gained significant knowledge, which will help me to provide a better contribution to a similar outbreak in the future.

1. Coordination was key. An outbreak usually requires a rapid response. The principal investigator needs to manage people from different institutes, which might have limited or no previous experience in outbreak investigations. Giving the team

members explicit instruction can reduce the risk of missing information, which is helpful for data interpretation and conclusion.

2. Without human specimen collection, the investigation was incomplete. Epidemiological investigation can help us to identify the risk factors but does not necessarily help us to draw definitive conclusions about the source of acquisition. Sample collection and pathogen isolation are essential to help us conclude our investigation. In our case, we failed to collect human specimens. We relied on our original hypothesis that the cause of illness would be associated with pesticide detection from cucumbers, which were found to be a risk factor of the illness. However, pesticides were not detected from the implicated cucumbers. Blood and stool samples from ill individuals may have assisted in identifying an alternative hypothesis for the cause of the outbreak.

3. The retrospective cohort design may only need similar resources compared to case-control. However, it would give a better measurement than the case-control design. In our case, we wanted to test whether the illness was associated with eating fresh cucumbers. The population was in a residential facility where a list of names of all people in the facility could be obtained. We knew through the notification from the Provincial Health Department to CCDC that 29.3% (n=237/810) of the residents in the facility were ill, suggesting a high attack rate among residents. The well-defined population and high proportion of illness of the population meant a cohort study design was possible. I re-calculated the sample size if the cohort study design would have been chosen. We would have needed a very similar sample size to the sample size of the case-control study. However, we could have calculated absolute risk after exposure and the risk ratio from a cohort study design. This is better than an odd ratio in estimating the strength of association between exposure and outcome of interest.

4. The way that we asked cases to nominate controls led to a change in our design unintentionally. This happened because cases nominated controls who were their roommates. This means that they were in the same building and slept in the same room. In this facility, men stayed in separate buildings to women. This led to men inviting men and women inviting women to participate. On top of that, roommates were of a similar age. This sampling methodology prevented us from controlling for

these three variables—building, sex, and age—in our analysis, all of which were potential risk factors.

5. During a field investigation, the risk of recall bias cannot be ignored. During the interviews, I observed that the majority of my interviewees could not remember what they ate in the past three days. The other interviewers reported similar issues. We addressed this by reviewing the vegetable and meat invoice and notebook of the facility's cook who prepared the food for all residents. All respondents had no alternative for food in the residential facility, they all at the same food from the facility's cook. We then only asked if they ate the food prepared by the facility's cook if they were not able to remember details. If the answer was "Yes," we used the cooks record to identify specific details on what they have eaten.

## Public Health Impact

The immediate impact of this investigation was that we were rapidly able to stop the outbreak in the facility. However, the further impact on the community was not assessable.

## Acknowledgments

My involvement in the project could not have happened without kindness from the CCDC management team. I sincerely thank Dr. Ly Sovann, Director of CCDC, for this approval to let me join the investigation team and Dr. Chan Vuthy, Deputy Director of CCDC, and the principal investigator of the investigation, for allowing to do data analysis, present the findings and write the report. These tasks were critical for me to meet the MAE competencies for the outbreak project.

Profound thanks to the inputs from staff and experts of the Department of Drugs, Food Safety, Medical Equipment, and Cosmetics, Ministry of Health; Department of Agro-Industry, Ministry of Agriculture, Forestry and Fisheries; Banteay Mean Chey Provincial Health Department; Pursat Provincial Health Deportment; US Centre for Disease Control, Cambodia; and World Health Organization, Cambodia.

My sincere thanks to all study participants who kindly shared their personal information, which is valuable to make the analysis more meaningful.

Finally, profound thanks to all my supervisors—Patrice Piola, Tambri Housen, and Vincent Herbreteau – for their constructive comments during the report writing. It was a great learning opportunity to write an outbreak report.

## Abstract

*Background*: Between 30 November and 2 December 2019, an outbreak of unknown etiology affected more than 200 people, including two deaths in a residential facility in Banteay Mean Chey province in Cambodia. We investigated the outbreak to identify the cause, mode of transmission, and recommend appropriate control measures.

*Method:* A case-control study with 28 cases and 60 controls was conducted between 3-5 December 2019. The cucumbers, spinach, and water were transported for microbiological testing *of E. Coli, Salmonella, Clostridium perfringens,* and *Staphylococcus aureus* at the National Reference Medical Laboratory. In addition, pesticide residues testing by Gas chromatography-mass spectrometry (GC-MS) machine against 999 pesticide types provided by pesticide library software was done at the Industrial Laboratory Centre of Cambodia.

*Result*: 810 residents lived in the affected facility at the time of the event. Two-hundred-thirty-seven residents (n=237, 29.3%) became ill between 30 November and 2 December 2019. Of the 28 cases interviewed, symptoms included headache (n=24, 85.7%), stomach-aches (n=19, 67.9%), dizziness (n=19, 67.9%), vomiting (n=17, 60.7%), fever (n=17, 60.7%), nausea (n=16, 57.1%), chest oppression (n=16, 57.1%), diarrhea (n=13, 46.4%), neck pain (n=9, 32.1%), blurred vision (n=9, 32.1%), and seizure (n=1, 3.6%). Of the meals and snacks consumed between 30 November and 1 December 2019, eating cucumber was the only risk factor associated with illness. Of the cases, 85.7% (n=24/28) had eaten cucumbers compared to 30.5% (n=18/60) of controls, OR = 13.7 (95% CI; 4.1, 45.1, *P*-value <0.001). Cases were 10.3 times (95% CI; 2.5, 42.4) and 16.4 times (95% CI; 4.5, 59.9), more likely to have eaten cleaned and uncleaned cucumbers than controls. However, laboratory analysis failed to detect *pathogens* and any pesticide residue from cucumber samples.

*Conclusion:* Our epidemiological study suggests a strong association between eating cucumbers and illness. However, laboratory analysis failed to detect a causative agent. Toxicology testing was not conducted, and therefore we were unable to rule out contamination of the cucumbers.

## Abbreviation

| | |
|---|---|
| CamEWARN | Cambodia Early Warning System |
| CDC | Communicable Disease Control Department |
| DAI | Investigation team members from the Department of Agro-Industry |
| GC-MS | Gas chromatography-mass spectrometry |
| MAFF | Ministry of Agriculture Forestry and Fisheries |
| MERS | Middle East Respiratory Syndrome |
| MoH | Ministry of Health |
| RRT | Rapid Response Team |
| SARS | Severe Acute Respiratory Syndrome |
| STEC | Shiga toxin-producing Escherichia |
| US CDC | US Centers for Disease Control and Prevention |

## Introduction

On the morning of 1 December 2019, the Communicable Disease Control Department (CDC) of the Ministry of Health (MoH) of Cambodia declared an outbreak of unknown etiology and source. The outbreak resulted in 237 cases, including two deaths, in a two-day period, over Saturday 30 November and Sunday 1 December 2019. A multi-sectoral investigation team was established on Monday, 2 December 2019, to investigate the source of the outbreak.

The outbreak of unknown etiology occurred in a residential facility in Banteay Mean Chey province of Cambodia. At the time of the outbreak of unknown etiology, the residential facility had 810 residents. The majority (762 out of 810) of the residents were males. On the premises, 48 female residents stayed in one building while the 762 male residents lived in three buildings (over 200 people per building). As part of the residential facility's policy, residents were not allowed to go outside the premises. The residential facility's cook prepared the food. Without any alternative, all residents ate the same food, which was a single type of food at every meal.

On Saturday, 30 November, in the evening (between 7-9 PM), three residents complained they were ill with symptoms such as vomiting, diarrhea, abdominal pain, and dizziness. In the meantime, other residents became ill with similar symptoms. Some 72 residents were hospitalized on that day, 160 residents on Sunday 1 December, and five others on Monday 2 December. Two of the affected residents died on Sunday, 1 December 2019. One died in a private clinic at around 2 PM or around 20 hours after symptom onset, and another one died at the provincial referral hospital, at 7 PM or around 24 hours after symptom onset.

Illness due to contaminated food is life-threatening and a public health concern around the globe. According to the World Health Organization (WHO), globally, 1 in 10 people fell ill after eating unsafe, contaminated food in 2015 (1). The same source suggested that 31 agents – bacteria, viruses, parasites, toxins, and chemicals—were identified as the source of food poisoning or gastro-intestinal disease (1). Southeast Asian countries have the highest prevalence of food poisoning events (1). According to Dewanti-Hariyadi, and Gitapratiwi, *Shigella flexneri*, *Salmonella,* and *Vibrio cholerae O1* are the most common agents in the region (2). Pesticide-contaminated food outbreaks are also commonly reported in the region (3).

In Cambodia, food safety is a priority agenda for the Ministry of Health. However, illness due to contaminated food remains common. Under the leadership of MoH's CDC, with technical and financial support from its partners, Cambodia has a weekly outbreak tracking system, known as CamEWARN or Cambodia Early Warning System (4). CamEWARN notifies seven epidemic diseases-- Avian Influenza, Severe Acute Respiratory Syndrome (SARS), Severe Watery Diarrhea, Swine Influenza, Middle East Respiratory Syndrome (MERS), and other Diseases (e.g., food poisoning, mass fainting) (4). This system enables an early response by the Rapid Response Team (RRT) in each province and all relevant institutions.

This chapter describes the process of investigation related to this outbreak and the attempt to identify the cause, mode of transmission, and recommended appropriate control measures.

## Methods

As mentioned above, the outbreak occurred from 30 November to 2 December 2019. The investigation started on 3 December and finished on 5 December 2019 after no more cases were reported.

### Case definition

We defined a person as a case if he/she was a resident in the affected facility, and had ANY TWO of the following symptoms -- *Diarrhea (including bloody diarrhea), vomiting, dizziness, headache, seizure, difficulty breathing, chest oppression (tightness), mouth numbness, and blurred vision*-- between 30 November and 2 December 2019. The definition was formulated based on the medical records of ill residents.

All ill residents were sent for treatment in two nearby referral hospitals and returned to the residential facility when they felt better (some symptoms remained).

### Epidemiologic Investigation

The local Rapid Response Team (RRT) team was informed by the residential facility management that the residents fell hours after eating cucumbers. RRT team conducted a short interview with the 207 residents who fell ill, using an unstructured questionnaire. RRT team noted whether the affected residents ate fresh cucumbers, the number of cucumbers they ate, when they ate cucumbers, and what else they ate. We did a

descriptive analysis from this unstructured RRT's notes and found that 204 of them reported they ate fresh cucumbers ranging from 0.5 to 10 fresh cucumbers per person. We assumed the residents ate the same breakfast, lunch, and dinner because they had no alternative food except skipping meals.

The investigation team hypothesized that illness was associated with eating fresh cucumbers.

This hypothesis was generated from the first day of activities (3 December 2019) including:

- Meeting with provincial Rapid Response Team who learned about the outbreak and formed the initial response,

- Visiting the residential facility,

- Conducting unstructured interviews with the staff of the residential facility, medical staff at the hospital, mobile doctors and nurses who treated ill residents at the facility, and ill residents, and

- Reviewing the medical records. During the treatment period, the provincial Rapid Response Team (RRT) recorded patients' profile—age, gender, symptoms, time of symptom onset, and the consumption of cucumbers and/or spinach before getting sick. The information recorded was unstructured.

A case-control study with one case to two-control ratio was conducted to confirm this hypothesis. The case-control study design was selected due to time constraints and limited resources.

We defined a person as a control if he/she was a resident in the affected facility during the event, but did not meet the above case definition.

In our case-control study, we interviewed a sample of 30 cases and 60 controls. This sample size was calculated using OpenEpi Software with the following inputs: (1) two-sided confident level at 95%, (2) power or chance of detecting at 80%, (3) expected proportion of case with exposure at 83.3% (based on medical records), (4) proportion of control with exposure at 50% (based on brief interviews with residential facility staff), (5) ratio of control to the case of two to increase the power of the result (the ratio of two controls to one case is recognized as enough to draw robust statistical inferences with little

gained from increasing the number of controls per case)(6), and (6) Fleiss' continuity correction model was chosen due to its ability to generate the largest sample size compared to other models (7). With these assumptions, we needed 28 cases and 55 controls to detect the difference in exposure. We then rounded up to 30 cases and 60 control.

A three-page questionnaire was created to collect demographics (age, sex), main exposure (eating cucumber, cleaning cucumber, number of cucumbers eaten), other potential exposures (breakfast, lunch, dinner, snack), and drinking water.

The cases were randomly selected from medical records. Thirty unique integers without replacement were randomly selected from a list of 1-237 using a Web-based application, namely "Randomizer.org." During case interviews, every case was asked for names of two peers who slept next to them but did not become ill.

The data collection was conducted on Thursday, 5 December 2019, at a residential facility. After the cases were randomly selected, their names were listed. The staff of the residential facility was asked to refer the selected cases with a name list. The cases were briefly explained the process of data collection before the interview. Each interview lasted about 15 to 20 minutes. A body soap was given to the interviewee after interviewing. Before they left, they were asked to refer two of their peers who shared the sleeping room with them. The same questionnaire and process were used for controls as was used for cases.

Descriptive data analysis was conducted to determine the attack rate, common symptoms, date and time of symptom onset, and incubation period. Bivariate analysis was conducted to understand whether the characteristics of the cases and control were comparable. Chi-square or Fisher Exact test was used to determine the association between being a case and exposure to cucumbers; a *P*-value of less than 0.05 was considered indicative of a significant association (8). Additional variables such as cleaning the cucumber prior to eating, the number of cucumbers eaten, having a meal at the facility, and drinking water at the facility were also analyzed to support the interpretation. We aimed to include variables with a *P*-value > 0.25 in a multivariable analysis. However, no variable besides cucumber was significantly associated with the illness during the bivariate analysis (*P*-value > 0.25). Therefore, multivariate analysis was not performed in this study.

## Medical and chemical laboratory testing

Three cucumbers, a bunch of spinach, and a bottle of water were transported for testing for common pathogens including *E. Coli, Salmonella, Clostridium perfringens, Staphylococcus aureus* at National Reference Medical Laboratory, MoH.

Another set of three cucumbers and a bunch of spinach were also sent for pesticide residues testing by Gas chromatography-mass spectrometry (GC-MS) machine at Industrial Laboratory Centre of Cambodia, Institute of Standard Cambodia, Ministry of Industry and Handicraft. The samples were tested against the 999 pesticide type provided by the Pesticide library software.

Human specimens such as blood or stool were not collected due to miscommunication among the local RRT team. The absence of a laboratory technician in the investigation team also contributed to this investigation neglecting to include human samples.

## Environmental investigation

The investigation team spent one day on the premises of the residential facility to review the cleanliness of the kitchen, toilet, bathroom, sleeping space and material, and how the food was handled. In addition, the investigation team conducted unstructured interviews with the staff of the residential facility and residents on the premises to understand potential sources of acquisition and modes of transmission. Environmental samples were not collected.

## Trackback investigation

Investigation team members from the Department of Agro-Industry (DAI) and the Ministry of Agriculture Forestry and Fisheries (MAFF) conducted a trackback investigation to identify the supplier and source of the implicated cucumbers. The aim of the trackback was to learn whether the cucumbers had been sold or distributed to others and identify the chemical compounds in the fertilizers and pesticides used by the farmer before harvesting.

## Ethical approval

Ethical approval was not required due to the need for immediate public health action. Outbreak investigations are conducted under National and Regional public health acts, and review by an Ethics Review Board is not required. However, for the purposes of

publication in this investigation is covered under the Australian National University Human Research Ethics Committee approval (2017/909).

# Result

## Descriptive epidemiology

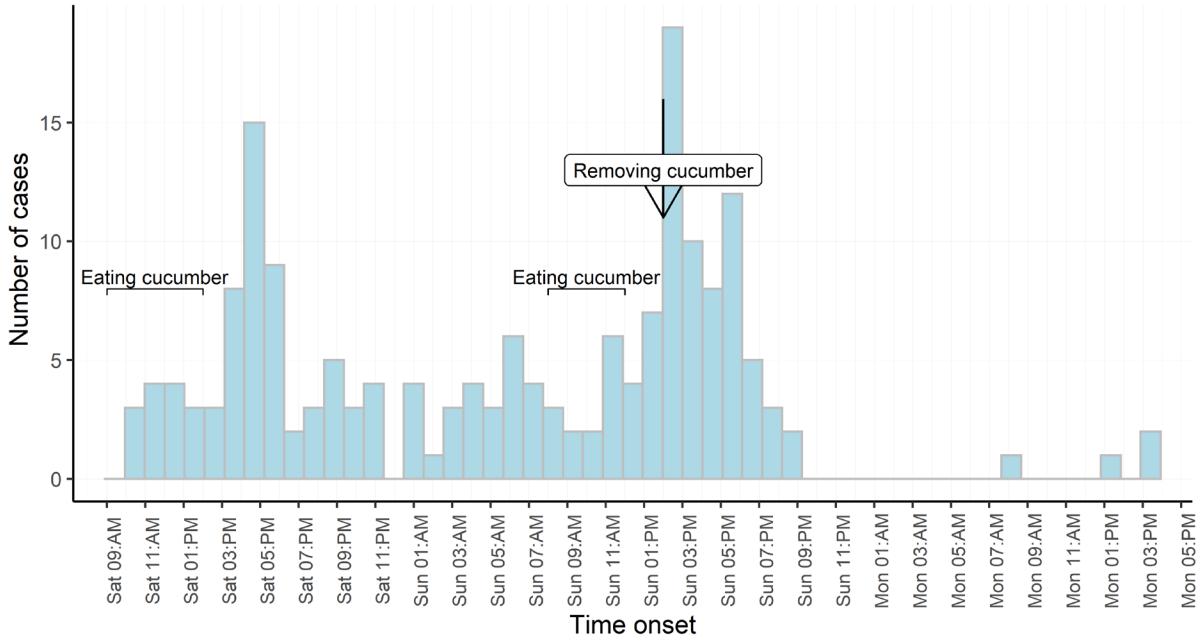
According to the medical records, 29.3% (n=237/810) of the residents in the residential facility met the case definition (Table 2.1). Stratified by residential building, three out of four buildings had similar attack rates at 42.8% (n=122/285) in building A, 43.8% (n=21/48) in building B, 6.8% (n=15/222) in building C, and 31.0% (n=79/255) in building D. The attack rate among males (n=216/761, 28.3%) appeared to be lower than the attack rate among females (n=21/48., 43.8%).

Table 2.1. Outbreak of unknown etiology at a residential facility in Cambodia, Attack rate, by building, and sex 30 Nov-2 Dec 2019

| | Total | Ill | Attack Rate (%) |
|---|---|---|---|
| Overall | 810 | 237 | 29.3 |
| Building | | | |
| A (for male only) | 285 | 122 | 42.8 |
| B (for female only) | 48 | 21 | 43.8 |
| C (for male only) | 222 | 15 | 6.8 |
| D (for male only) | 255 | 79 | 31.0 |
| Gender | | | |
| Male | 762 | 216 | 28.3 |
| Female | 48 | 21 | 43.8 |

Figure 2.1 is the epidemic curve, which was constructed from 197 out of 207 cases in which time of symptom onset data was available. The epidemic curve suggested that the outbreak was from a point source. The outbreak happened within 52 hours, with the first case reported at 10 AM on Saturday 30th November and the last case reported at 2 PM on the 2 December 2019. The onset of illness occurred predominantly in the afternoon of Saturday 30th November and the afternoon of Sunday 1st December. This coincided with residents eating fresh cucumbers as a snack after lunch on Saturday and after breakfast on Sunday.

Figure 2.1 Epidemic curve of the outbreak of unknown etiology at a residential facility in Cambodia between 30 Nov-2 Dec 2019




*Note: This epidemic curve was constructed from 178 cases out of 207 cases for which time of illness onset was available*

## Case-control

A total of 28 cases and 60 controls were interviewed. The sex and age distribution of study participants are presented in Table 2.2. As can be seen, sex and age distributions were comparable, with 85.7% (n=24/28) of cases and 86.7% (n=52/60) of the controls being male. Also, cases and controls had similar age median and interquartile ranges. For cases, the median age was 22 years old, with an interquartile range between 19.5 and 26 years old. In controls, the median age was 25 years old, with an interquartile range between 19.5 and 29.5 years.

Of the cases, the majority (85.7%, n=24/28) experienced a headache, followed by stomachaches (67.9%, n=19/28), dizziness (67.9%, n=19/28), vomiting (60.7%, n=17/28), fever (60.7%, n=17/28), nausea (57.1%, n=16/28)), chest oppression (57.1%, n=16/28), diarrhea (46.4%, n=13/28), neck pain (32.1%, n=9/28), blurred vision (32.1%, n=9/28), and seizure (3.6%, n=1/28).

Concerning hospitalization, six of the 28 spent less than one day in the hospital, 11 patients spent one day, seven patients spent two days, and one patient spent three days.

Table 2.2. Sex and age distribution of cases and controls in the investigation of an outbreak of unknown etiology in a residential facility in Cambodia between 30 Nov-2 Dec 2019

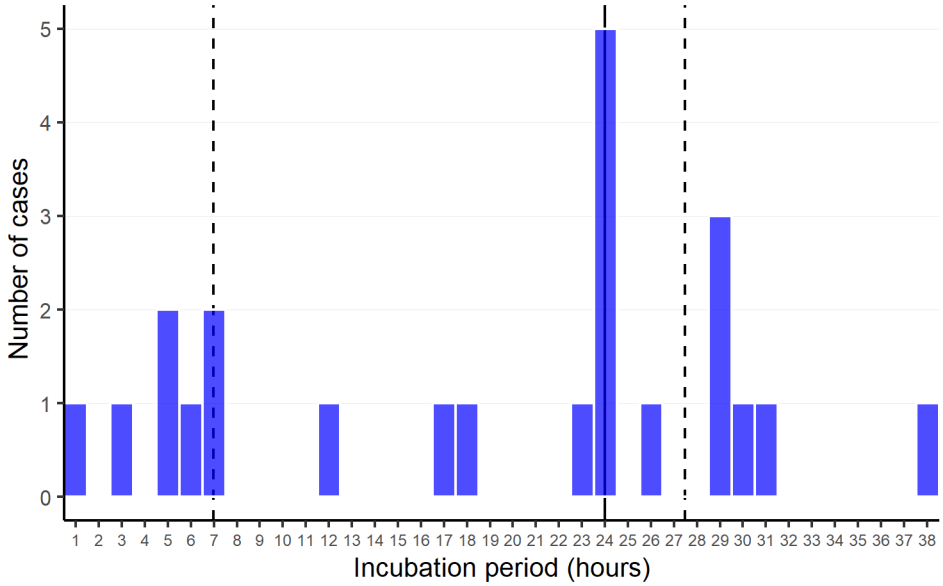
| Variable | Case (n=28) | Control (n=60) | *P*-value |
|---|---|---|---|
| | n (%) | n (%) | |
| Sex | | | |
| Male | 24 (85.7) | 52 (86.7) | 0.904 |
| Female | 4 (14.3) | 8 (13.3) | |
| Age in year | | | |
| Median (IQR) | 22 (19.5, 26) | 25 (19.5, 29.5) | |
| 15-19 | 7 (25.0) | 15 (25.0) | 0.55 |
| 20-24 | 10 (35.7) | 14 (23.3) | |
| 25-29 | 7 (25.0) | 16 (26.7) | |
| 30-34 | 4 (14.3) | 15 (25.0) | |
| Building of residents | | | |
| A | 14 (50.0) | 29 (48.3) | 1.00 |
| B | 4 (14.3) | 9 (15.0) | |
| C | 1 (3.6) | 2 (3.3) | |
| D | 9 (32.1) | 20 (33.3) | |
| Symptoms of the cases | | | |
| Headache | 24 (85.7) | — | |
| Stomachaches | 19 (67.9) | — | |
| Dizziness | 19 (67.9) | — | |
| Vomiting | 17 (60.7) | — | |
| Fever | 17 (60.7) | — | |
| Nausea | 16 (57.1) | — | |
| Chest Oppression | 16 (57.1) | — | |
| Diarrhea | 13 (46.4) | — | |
| Neck pain | 9 (32.1) | — | |
| Blurred vision | 9 (32.1) | — | |
| Seizure | 1 (3.6) | — | |
| Hospitalization period | | | |
| <1 day | 6 (24.0) | | |
| 1 day | 11 (44.0) | | |
| 2 days | 7 (28.0) | | |
| 3 days | 1 (4.0) | | |

*Abbreviation: IRQ, interquartile range*

## Incubation period

We visualized the period in hours between eating cucumbers and the first symptoms (Figure 2.2). The incubation period ranged from less than one hour to 38 hours with a median of 24 hours and interquartile range between 7 and 27.5 hours.

Figure 2.2. Time in hours between eating cucumbers and onset of first symptoms among cases in the case-control study at the residential facility between 30 Nov-2 Dec 2019 (N = 23)




*Abbreviation: Q1, first interquartile range; Q3, third interquartile range*
*Note: 23 cases out of 28 cases interviewed were included. The other five cases were not included due to missing data.*

## Bivariate analysis

Table 2.3 illustrates the main meal eaten by cases and controls one day before and during the outbreak. Prior to the outbreak, on Friday 30th November and Saturday 2nd December, almost 100% of cases and controls ate the same food provided by a residential facility for their main meal—breakfast, lunch, and dinner. The food served on those two days included:

- *On Friday, 29 November 2019*, porridge was served as breakfast, rice and radish with pork soup were served as lunch, and papaya fish soup was served as dinner.

- *On Saturday, 30 November 2019*, porridge was served as breakfast, rice and mixed fried vegetable were served as lunch, and Khmer mixed vegetables with fish soup was served as dinner.

There was a significantly lower proportion of cases eating a meal at the residential facility on 1st December 2019 due to the hospitalization of over 100 residents (exact number not known) on that day.

Table 2.3 Results of analysis of possible risk factors associated with an outbreak of unknown etiology in a residential facility in Cambodia between30 Nov-2 Dec 2019

| Variable | Case (N=28) n(%) | Control (N=60) n(%) | OR (95% CI) | *P*-value |
|---|---|---|---|---|
| **Friday meal** | | | | |
| Residential facility's breakfast (porridge) | | | | |
| No | 2 (7.1) | 3 (5.0) | Ref. | |
| Yes | 26 (92.9) | 57 (95.0) | 0.7 (0.1, 4.3) | 0.687 |
| Residential facility's lunch (radish with pork soup) | | | | |
| No | 0 (0.0) | 0 (0.0) | __ | __ |
| Yes | 28 (100.0) | 60 (100.0) | __ | __ |
| Residential facility's dinner (papaya fish soup) | | | | |
| No | 1 (3.6) | 0 (0.0) | __ | 0.318 |
| Yes | 27 (96.4) | 60 (100.0) | __ | |
| **Saturday meal** | | | | |
| Residential facility's breakfast (porridge) | | | | |
| No | 3 (10.7) | 1 (1.7) | __ | 0.093 |
| Yes | 25 (89.3) | 59 (98.3) | __ | |
| Residential facility's lunch (fried mixed vegetable ) | | | | |
| No | 0 (0.0) | 1 (1.7) | __ | 1.00 |
| Yes | 28 (100.0) | 59 (98.3) | __ | |
| Residential facility's dinner (Khmer mixed vegetable with fish soup (Korko)) | | | | |
| No | 1 (3.6) | 0 (0.0) | __ | 0.318 |
| Yes | 27 (96.4) | 60 (100.0) | __ | |
| **Sunday meal** | | | | |
| Residential facility's breakfast (porridge) | | | | |
| No | 5 (17.9) | 1 (1.8) | Ref. | |
| Yes | 23 (82.1) | 56 (98.3) | 0.1 (0.0, 0.7) | 0.026 |
| Residential facility's lunch (green spinach with pork soup) | | | | |
| No | 3 (11.1) | 0 (0.0) | __ | 0.028 |
| Yes | 24 (88.9) | 60 (100.0) | __ | |
| Residential facility's dinner (Vietnamese fish soup (Machu Youn) | | | | |
| No | 6 (22.2) | 0 (0.0) | __ | 0.001 |
| Yes | 22 (77.8) | 60 (100.0) | __ | |
| Pipped water (Fri-Sat) | | | | |
| No | 2 (7.1) | 8 (13.3) | Ref. | |
| Yes | 26 (92.9) | 52 (86.7) | 2.0 (0.4, 10.1) | 0.402 |

*Abbreviation: IRQ, interquartile range; OR, odds ratio; CI, confidence interval; Ref., reference*

Table 2.4 compares the proportions of cases and controls who ate cucumbers, which was our hypothesized exposure. In cases, 85.7% (n=24/28) ate cucumber on Saturday 30 November and/or Sunday 1 December 2019, compared to 30.5% (n=18/60) of the controls. Residents meeting the case definition were 13.7 times (95% CI; 4.1, 45.1, *P*-value <0.001), more likely to have eaten cucumbers than controls.

Regarding whether they cleaned cucumbers before eating or not, the risk was lower among those who cleaned cucumbers before eating and increased among those who did not clean before eating. The odds of eating cleaned and uncleaned cucumbers, among cases, were 10.3 (95% CI; 2.5, 42.4) and 16.4 (95% CI; 4.5, 59.9), respectively, times the odds of eating cleaned and uncleaned cucumbers among controls. Cases were 10.3 and 16.4 times more likely than controls to have eaten cleaned or uncleaned cucumbers, respectively.

Table 2.4 Cucumber consumption among cases and controls in a residential facility in Cambodia between 30 Nov-2 Dec 2019

| Variable | Case (n=28) N(%) | Control (n=60) N(%) | OR (95% CI) | *P*-value |
|---|---|---|---|---|
| Ate cucumber (clean and not clean) | | | | |
| No | 4 (14.3) | 41 (69.5) | Ref. | |
| Yes | 24 (85.7) | 18 (30.5) | 13.7 (4.1, 45.1) | <0.001 |
| Ate cucumber (cleaned) | | | | |
| Yes | 8 (28.6) | 8 (13.6) | 10.3 (2.5, 42.4) | <0.001 |
| No | 16 (57.1) | 10 (17.0) | 16.4 (4.5, 59.9) | <0.001 |
| Didn't eat | 4 (14.3) | 14 (69.5) | Ref. | |
| Number of cucumbers eaten (clean and not clean) | | | | |
| 0 | 2 (7.1) | 42 (70.0) | Ref. | |
| 0.5 | 14 (50.0) | 9 (15.0) | 32.7 (6.3, 169.6) | <0.001 |
| 1-2 | 5 (17.9) | 4 (6.7) | 26.3 (3.8, 181.6) | 0.001 |
| >=3 | 7 (25.0) | 5 (8.3) | 29.4 (4.7, 182.3) | <0.001 |
| Ate cucumber with salt and chilly | | | | |
| No | 13 (54.2) | 10 (55.6) | Ref. | |
| Yes | 11 (45.8) | 8 (44.4) | 1.1 (0.3, 3.6) | 0.929 |
| Ate cucumber with noodles (Fri-Sat) | | | | |
| No | 21 (75.0) | 51 (85.0) | Ref. | |
| Yes | 7 (25.0) | 9 (15.0) | 1.9 (0.6, 5.7) | 0.262 |

*Abbreviation: IRQ, interquartile range; OR, odds ratio; CI, confidence interval; Ref., reference*

## Medical and chemical laboratory testing

*E. Coli, Salmonella, Clostridium perfringens, Staphylococcus aureus,* and pesticide residue were not detected from the cucumber sample.

### Environmental investigation

The result from the environmental investigation suggested that residents were living with poor hygiene and sanitation, and the buildings were overcrowded. Poor sanitation and hygiene during cooking were also observed.

The cooking facilities, toilet facilities, drainage systems, water supply systems were not cleaned. The residents had no full access to safe drinking water. The residents did not have enough materials to wash their clothes, mats, mattresses, blankets, pillows, and bolsters.

### Trackback investigation

Findings from the trackback investigation suggested that the facility received 80 kilograms of cucumbers from a single source--a local vegetable whole seller-- as a donation. The whole seller bought these cucumbers from a single farmer in a neighboring province. Although the farmer and the whole seller claimed they had sold these cucumbers to others as well, the investigation was not extended to identify the other users. This was due to limited resources. We acknowledge this as a limitation.

In addition, our team members collected empty bags of insecticides and fertilizers from the farm to identify the chemical compounds. However, according to the farmer, these insecticides and fertilizers were used a long time before harvesting.

## Discussion

The outbreak of unknown etiology occurred between 30$^{th}$ November and 2$^{nd}$ December 2019 in a residential facility in Banteay Mean Chey province in Cambodia. A total of 29.3% (n=237/810) of residents who lived in the residential facility were hospitalized, and two died. These cases presented symptoms such as headache, stomachaches, dizziness, vomiting, fever, nausea, chest oppression, diarrhea, neck pain, blurred vision, and seizure. The outbreak lasted for a total of 52 hours from the first reported onset of symptoms until the last reported onset of symptoms.

From the epidemiological investigation, cucumbers were identified as the only risk factor of the outbreak. However, no causative pathogen or pesticide was isolated from the implicated cucumbers

From the epidemiological perspective, the association between consuming cucumbers and being ill was very strong. We discuss our findings against the Bradford Hill criteria of casual relationship (9). First, there was a strong association between eating cucumbers and getting ill. As presented in the result section, residents meeting the case definition were 13.7 times more likely to have eaten cucumbers than controls. Second, it was clear that people in the residential facility accessed to the same primary food – breakfast, lunch, and dinner-- and drinking water. There was no alternative food during the period of the investigation except cucumbers. In building C, cucumbers were distributed late, and only a small proportion of cucumbers was eaten. Building C had the lowest attack rate of 6.8%, compared to the attack rate between 31.0% and 43.8% in other buildings where all cucumbers were eaten. Third, symptom onset occurred after ingesting cucumbers. This implicates cucumbers as a possible source of the outbreak. Fourth, there was a biological explanation that those who reported cleaning cucumbers before eating had a lower risk of being ill. This provides evidence that cucumber was potentially contaminated with a poisoning substance or pathogen. According to some residents, those who died were people who ate the cucumbers before others, and they could eat as many as they wanted.

To our best knowledge, this is the first time in Cambodia that an outbreak was linked to cucumbers. However, several documented outbreaks have been linked to cucumbers in other settings, including cucumbers contaminated by Salmonella in the United States (10), cucumbers contaminated with microsporidia in Sweden (11), and cucumbers contaminated with Shiga toxin-producing Escherichia coli (STEC) in Germany (12).

In our investigation, the lack of biological investigation from those who became ill limited the ability to identify a causative agent. Reported signs and symptoms, incubation period, duration of illness, and severity of different agents—bacteria, virus, parasite, or chemical intoxication, are often similar and cannot be distinguished by a physician without laboratory evidence. Regarding this, we propose two possible sources of the outbreak. One possible source, with an incubation period starting at 1 hour, is a toxin. Based on symptoms, incubation period, and severity, the toxin could be *Staphylococcus aureus (Staph) (13-15), Clostridium perfringens(13, 15), Salmonella (13, 15), and Clostridium botulinum (Botulism) (13), E. Coli (13, 15), Bacillus cereus (14, 15), Vibrio parahaemolyticus enteritis (15, 16), and Aeromonas hydrophila (17).* In our study, we tested for common bacteria such as *E. Coli, Salmonella, Clostridium perfringens, Staphylococcus aureus* from the cucumbers. Nonetheless, we did not collect samples from cases. Another possible source was pesticide residues. However, the result of cucumber testing against 999 pesticide types

provided by the pesticide library software using GC-MS machine could not detect any pesticide residues (18, 19). The GC-MS machines are highly recognized and can detect various main chemical compounds (18, 19). According to this result, cucumbers were very unlikely to have been contaminated with harmful pesticides. This was somewhat supported by the trackback investigation, which found that cucumbers had been sold to different users, yet no other cases of illness had been reported. We would have expected to see high numbers of presentations to health facilities by community members who bought the cucumbers if they were contaminated with pesticides.

Our investigation had several limitations. First, and possibly our biggest limitation, was that the human specimens were not collected due to miscommunication within Rapid Response Team. This limited our ability to identify the etiology. Second, active case finding to identify other possible cases in the community was not done due to time constraints and resource-limited. In the context that the majority of Cambodians use private health services, where no mandatory notification system is in place, it is possible that people became ill due to cucumbers, but our investigation team was not made aware. Third, the microbiological laboratory testing of cucumbers was not comprehensive enough. Other pathogens that fit the clinical picture and incubation period were not tested for. Forth, our unmatched case-control unintentionally became a matched case-control study. We asked cases to refer roommates to act as controls. This automatically matched the cases and controls based on the building. Due to males and females residing in separated buildings, this also automatically matched the cases and controls based on their sex. In addition, it was likely that roommates had similar ages that led to matching based on their age. With this inadvertent matching, we were not able to control for building, sex, and age. Finally, recall bias on food items and time of eating was also observed as a common issue. This led to the initial incorrect calculation of the incubation period, which was important to establishing the hypothesis on causation. Researcher bias was also a factor, with cucumbers being implicated by the team early in the outbreak resulting in a less than thorough hypothesis-generating questionnaire. Other possible exposures such as environmental or alternate toxins were not considered.

## Conclusion

Our epidemiological study suggests a strong association between eating cucumbers and illness, but it lacked supporting evidence from laboratory findings. A causative agent was not identified. However, by employing Bradford Hill’s criteria, we concluded it was plausible

that the contaminated cucumbers were the cause of this outbreak even without a pathogen/agent being identified.

## Recommendation

We came up with several recommendations to prevent a future outbreak and investigation in the setting.

To prevent future outbreaks:

1. The residential facility should contract with a new vegetable supplier who was licensed by the government.

2. Residents should be educated to practice better personal hygiene and sanitation and provided enough cleaning material (e.g., soap, shampoo).

3. Cooking facilities, toilet facilities, drainage systems, water supply systems should be cleaned regularly and with appropriate cleaning materials.

4. Accessing safe drinking water should be prioritized. Water filtering should be an affordable choice.

5. Residents should be provided enough material to wash their clothes, mats, mattresses, blankets, pillows, and bolsters.

To improve future investigation:

6. Specimens from cases should always be collected because it is a critical aspect of all outbreak investigations, except other reasons justify it.

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# Chapter 3 : Malaria in Cambodia: a retrospective analysis of a changing epidemiology 2006-2019

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# Prologue

## Rational

This chapter describes my data analysis project, which is one of the four core competencies. Also, it was used to fulfil two other requirements—a conference presentation and a manuscript submission. Three data sources were used for the analysis. First, 14-year nationwide data between 2006 and 2019 were provided through the Epidemiology Unit of the National Centre for Parasitology Entomology and Malaria Control (CNM). Second, the health facilities' geographical data were provided by Institute Pasteur du Cambodia. Third, the population data were obtained from an open-access dataset of the United Nations for Coordination of Humanitarian Affairs (OCHA).

The report presents in this chapter is a modified version of a manuscript entitled *"Malaria in Cambodia: a retrospective analysis of a changing epidemiology 2006-2019",* submitted to the International Journal of Environmental Research and Public Health on 10 December 2020, and accepted for publication on 12 February 2021.

The preliminary result of this analysis was presented in the 11th International Conference on Public Health among Greater Mekong Sub-Region Countries "*Improving Health Equity among greater Mekong Sub-Region Countries: A Public Health Challenge"* between 18 to 19 October 2019 in Laos PDR. The slide presentation is included in Appendix 1 in this chapter.

## Roles

My role was to coordinate the collection of the data, clean the data, perform data analysis, interpret findings and write the report for this thesis and peer-review publication.

## Lessons Learnt

This analysis provided me with important knowledge of surveillance interpretation and technical skills for surveillance data analysis.

I learned to use three software—QGIS, R programming, and SatScan-- to perform spatial and temporal analysis. All of the three software were open-source. I started by

joining one-week GIS training at IPC. I initiated learning R programming and SatScan by myself, using online resources. Learning this new software was daunting at the beginning, but I was very happy when I developed proficiency. Spatial analysis is an important skill for applied epidemiologists. I can now employ my new skills to conduct spatial epidemiological analysis.

The interpretation of surveillance data was more challenging than I expected. In my case, I had 14-years of data to analyze. The malaria program in Cambodia had gone through several main events that affected data collection on malaria during this time period. Some of these events were not well documented. I sought out experienced people with knowledge of the changes that had taken place in the malaria program over time to further understand the context in which the data had been collected throughout the 14-year time frame. I, however, was excited as I could understand the big picture of malaria in Cambodia from this data analysis. I also learned the benefit of starting a study with a review of surveillance data and surveillance reports to familiarize myself with the topic.

## Public Health Impact

This study provides a summary of malaria incidence in Cambodia over the past 14 years. Findings will help to inform the approach to the malaria program in the future, including the design of interventions, planning, and resource allocation. The spatial analysis provides an up-to-date overview of clusters of malaria that will help to inform the prioritisation of resource allocation to hot spot areas.

## Acknowledgments

I sincerely thank Dr. Bunkea Tol, head of the Epidemiology Unit, and his staff at the National Centre for Parasitology Entomology and Malaria Control (CNM) for providing me the 14-year malaria surveillance data. In addition, Dr. Tol spent the time helping me interpret the data. He also took part in writing manuscripts and provided critical inputs to the manuscript.

Great thanks to all my supervisors— Vincent Herbreteau, Patrice Piola, and Tambri Housen. Dr. Herbreteau trained me on how to use QGIS and introduced SatScan to me.

These skills were essential for this data analysis project. Dr. Piola, and Dr. Housen spent a lot of time and energy to read, provide feedback and inputs during report writing.

## Abstract

*Background:* Malaria remains a serious public health issue globally, even though it is preventable and curable. In 2018, there were an estimated 228 million cases of malaria, with 405,000 deaths worldwide. In Cambodia, malaria has been endemic since the 1950s, and improvements in control and access to care have reduced its burden. However, malaria persists with changing epidemiology and resistance to antimalarials. This study aimed to describe how malaria has evolved spatially from 2006 to 2019 in Cambodia.

*Methods:* We undertook a secondary analysis of existing malaria data from all government healthcare facilities in Cambodia. The epidemiology of malaria was described by sex, age, seasonality, and species. Spatial clusters at the district level were identified with a Poisson model.

*Results:* A total of 737,210 malaria cases were notified to the Health Management Information System between 2006 and 2019. Overall, notifications decreased from 7.4 cases/1000 population in 2006 to 1.9 in 2019. The decrease has been drastic for females, from 6.7 to 0.6/1000. Adults aged 15-49 years had the highest malaria incidence among all age groups. The proportion of *Plasmodium (P.) falciparum* + *Mixed* among confirmed cases declined from 87.9% (n= 67,489) in 2006 to 16.6% (n= 5,290) in 2019. Clusters of *P. falciparum* + *Mixed* and *P. vivax* + *Mixed* were detected in forested provinces along all national borders.

*Conclusion:* There has been a noted decrease in *P. falciparum* cases in 2019, suggesting that intensification plan should be maintained. A decline in *P. vivax* cases was also noted, although less pronounced. Interventions aimed at preventing new infections of *P. vivax* and relapses should be prioritized. All detected malaria cases should be captured by the national surveillance system to avoid misleading trends.

# Abbreviations

| | |
|---|---|
| AS-MQ | Artesunate-mefloquine |
| AS-PYR | Artesunate-pyronaridine |
| DHA-PIP | Dihydroartemisinin-piperaquine |
| HMIS | Health Management Information System |
| MMW | Mobile Malaria Worker |
| P. falciparum | Plasmodium falciparum |
| P. vivax | Plasmodium vivax |
| VMW | Village Malaria Worker |
| PPM | Private Public Mix |

## Introduction

Malaria, an *Anopheles* mosquito-borne disease, remains a serious public health issue globally, although it is preventable and curable (1). According to the World Health Organization (WHO), an estimated 228 million malaria cases occurred worldwide in 2018, compared with 251 million cases in 2010 and 231 million cases in 2017 (2). Malaria was responsible for the loss of 405,000 lives in 2018, 416,000 lives in 2017, and 585,000 lives in 2010 worldwide. Morbidity and mortality rates due to malaria vary from one global region to another. The overall malaria incidence rate was 57.4 per 1000 at-risk population, ranging from 2.6 per 1000 at-risk population in WHO Western Pacific Region covering 37 countries of Oceania, East Asia, and Southeast Asia to 229.3 per 1000 at-risk population in WHO African Region covering 47 countries in Africa in 2018 (2-4). The deaths due to malaria were lowest at 0.4 per 100,000 population in the WHO Region of the Americas and highest at 41.0 per 100,000 in the WHO Africa Region. The Global mortality rate was 10.2 per 100,000 population in 2018. (2, 3, 5).

Historically Cambodia has had a high disease burden due to malaria since the 1950s (6, 7). Cambodia benefits from a tropical climate and is home to a diversity of mosquito species, including the *Anopheles species* (8). Malaria vectors mainly live in forests close to the Vietnamese, Laotian, and Thai borders (9, 10). People living or working in or near forested areas are at higher risk of contracting malaria (11, 12).

Cambodia has been widely recognized as successful in the fight against malaria because of the dramatic drop in malaria cases from a peak of over 100,000 cases or 7.4 per 1000 population in 2006 to over 62,000 cases or 3.9 per 1000 population in 2018. Deaths due to malaria also dropped from around 400 reported deaths in 2006 to zero reported malaria deaths in 2017, and 2018 (13, 14). However, Cambodia still has the highest malaria burden compared to its neighboring countries—Vietnam, Thailand, and Laos—and the WHO Western Pacific Region overall (2). The decline of malaria morbidity and mortality leads the Ministry of Health to acknowledge the impact of malaria interventions combined with the prevention, economic growth, improved infrastructure, and strengthening of the health system (13). All of which have enabled universal access to timely malaria diagnosis and treatment (13).

Built on this successful experience, since the year 2011, the government has worked with local and international partners on an elimination strategy (6, 7). Implementations were guided by the *"National Strategic Plan for Elimination of Malaria in the Kingdom of Cambodia, 2011-2025"* and the revised *"Cambodia Malaria Elimination Action Framework, 2016-2020".* Cambodia has divided the country's malaria-endemic areas into four zones based on the annual parasite index and malarial multi-drug resistance status (6, 7). All zones rely on quality diagnosis and treatment at health facilities, village malaria workers (VMWs), and vector control by promoting malaria prevention education and distribution of long-lasting insecticide nets (6, 7). However, to be more efficient and cost-effective, specific interventions were added for each zone (6, 7). First, the *elimination zone* focused on 'transmission interruption' through household testing, vector control, and expansion of VMWs (6, 7). Second, the *pre-elimination zone* focused on universal access to diagnosis and treatment by expanding VMWs (6, 7). Third, the *reduction zone* focused on the intensification plan -- re-activating and scaling up VMWs, switching to new antimalarial drugs, dihydroartemisinin-piperaquine (DHA-PIP) to artesunate-mefloquine (AS-MQ), and creating mobile malaria workers (MMWs) dedicated to the diagnosis and treatment of malaria among forest goers (7). Finally, the *non-endemic zone*, defined as areas where no local transmission had been reported, use government run healthcare facilities' basic services for diagnosis and treatment (6, 7).

As part of the elimination plan, the Ministry of Health licensed the private sector to test and treat malaria patients between 2011 and 2018 to increase early diagnosis and treatment accessibility. This initiative was known as "Private Public Mix (PPM)" (7). PPM provided private point-of-care--health facilities, pharmacies, and other retailers with malaria test kits and antimalarial drugs free-of-charge or with a subsidy (7, 15, 16). Private points of care sites charged patients for their service provision (6, 7, 13). These were rapidly scaled up in all endemic areas (15). According to available data through malaria outlet surveys between 2011 and 2015, private points of care sites detected over 50% of malaria patients in the country (15). PPM was later banned from implementing malaria testing and treatment in April 2018 (7, 15). The reason for banning was due to malarial drug resistance concerns and the inflexibility experienced in changing testing and treatment policy in the private sector compared to government run healthcare facilities (7).

The road to success has been fraught with challenges. One main challenge has been antimalarial drug resistance (17-22). Like other countries in the Greater Mekong sub-

region—China, Myanmar, Thailand, Laos, and Vietnam—Cambodia is facing the continual threat of antimalarial drug resistance (17-23). Cambodia first detected parasite resistance to artemisinin in 2006, but retrospective analysis of molecular markers suggested the resistance may have occurred as early as 2001 (6, 7, 23-25). After nine years of usage, the first-line treatment-- AS-MQ— was replaced by DHA-PPQ in Pailin province, in 2008, and nationally in 2010 (6, 7, 26). However, the efficacy of DHA-PPQ dropped after a short period of usage (19, 27-29). In 2014, the cure rate of DHA-PPQ ranged from 37.5% in Siem Reap province to 89.9% in Pursat province (6, 7, 28). In consultation with its partners, the Ministry of Health decided to re-introduced AS-MQ as the first-line treatment nationally in 2016 (7). However, full coverage was delayed until 2018 due to procurement issues and funding gaps (7, 30). Cambodia relies heavily on external funding. About 70% of malaria control funding was from the Global Fund, while the remaining 30% were from a combination of government funds and other partners (6, 7). Core activities were severely affected during an external funding interruption between 2015-2016, with all activities supported by Global Fund being suspended for more than a year. This likely influenced the increase in malaria notifications that followed in 2017 and 2018 (2, 14).

In the global fight against malaria, the WHO, in the global technical strategy for malaria 2016–2030, has called for the use of surveillance systems as a core intervention in all malaria-endemic settings (31). Data from the malaria surveillance systems are crucial to guide interventions, planning, and resource allocation (32-41). In 2019, malaria cases in Cambodia were reported through two surveillance systems under the Ministry of Health's umbrella. Those two systems are the Health Management Information System (HMIS) (42) and the Malaria Information System (43). Created in 1993, with multiple enhancements, HMIS captures data from all health services, including out-patient and in-patient services at government run healthcare facilities (42). Specifically for malaria, a more reliable HMIS was developed in 2004. Based on this data, this study aimed to describe how malaria incidence has evolved spatially and how the sequence of untoward events and malaria control interventions may have affected geospatial trends.

## Methods

We undertook a secondary data analysis of malaria data from all government healthcare facilities in Cambodia between 2006 and 2019. Data from private providers are not captured in this data.

## Data sources

### Malaria data

The Epidemiology Unit of the National Centre for Parasitology Entomology and Malaria Control provided HMIS malaria data for the cases notified between January 1st 2006 and December 31st 2019. This aggregated data included monthly malaria cases categorized by age group, gender, type of diagnosis (rapid diagnostic test (RDT), microscope), species (*Plasmodium (P.) falciparum*, *P. vivax*, *Mixed* meaning having both *P. falciparum* and *P. vivax*), points of care for diagnosis (public hospitals, health centers and VMW), case classification (uncomplicated, severe, death (44)), and hospitalization (yes, no).

HMIS is under the supervision of the Ministry of Health's Department of Planning and Health Information. It is the largest health information system in Cambodia, collecting information from all government-run services, including out-patient, in-patient, and national program data. At the hospital level, where computers are available, data are collected and entered by hospital staff. However, at the health center or health post level, data are recorded in patients' logbooks. Health center data is merged with data from health posts and VMWs by health center staff and aggregated using a standardized line-listing form before monthly submission to the operational district. Operational districts are responsible for entering data in the HMIS system, which is automatically synchronized to the national database of the Department of Planning and Health Information. The operational districts were created by the Ministry of Health to provide a local level to Cambodia's health system administration (central/national level, provincial level, and operational district level) (42). One operational district manages health facilities in one or more administrative districts and covers populations between 100,000 and 200,000 (42). Of note, HMIS did not record malaria cases diagnosed by the private sector.

### Population data and maps

The population data, disaggregated by gender and age group at the district-level, were obtained from an open-access dataset provided by the United Nations for Coordination of Humanitarian Affairs (OCHA) (45). Population data was only available for 2016 (45). To obtain population data for other years, we projected backward and forward using the National Institute of Statistics' national population growth rate (46). We also used the district map of Cambodia from OCHA (45).

### Untoward events

We gathered untoward events to contextualize the malaria surveillance data. Information such as treatment failures, key interventions, and events that may have impacted the case detection were obtained from the grey literature review. We mostly relied on governmental documents, including strategic plans and strategic plan reviews for additional untoward events presented in this paper.

## Inclusion criteria and setting

All government-run healthcare facilities (hospitals and health centers) reporting to the HMIS were included in this study. The number of healthcare facilities increased from 1,183 in 2006 to 1,350 in 2019 (Table 3.1). During this period, some health centers were upgraded to referral hospitals.

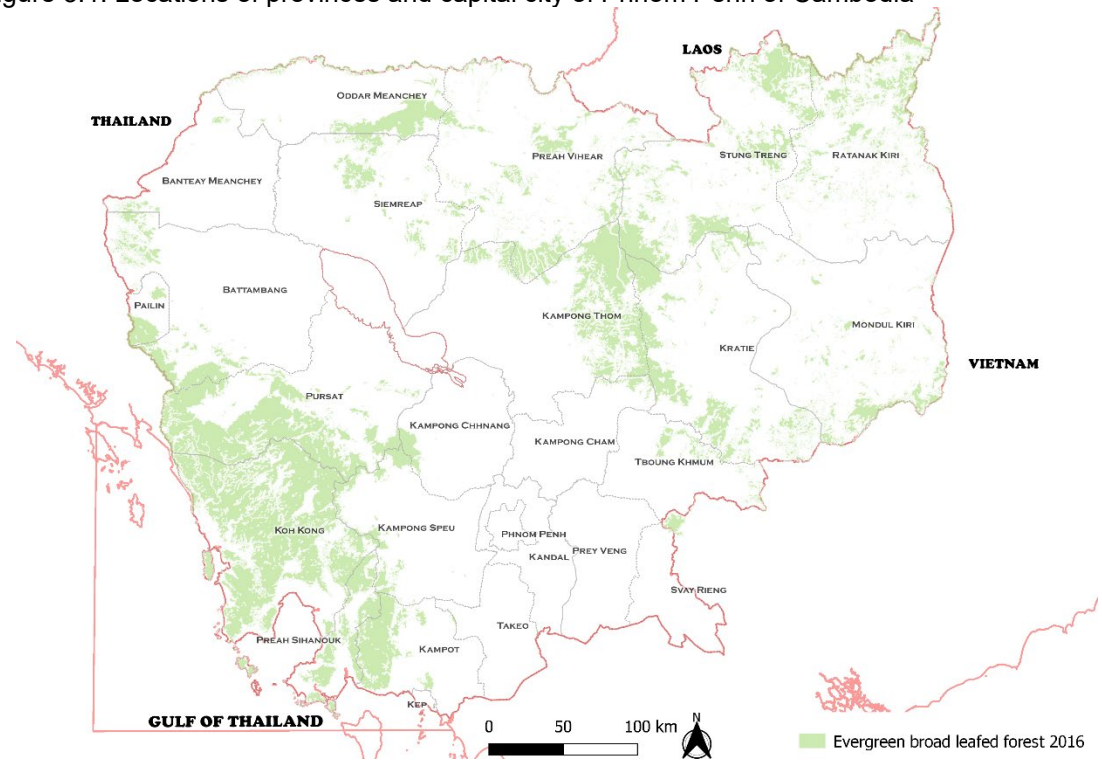
Table 3.1. Number of health centers and hospitals by year, reporting to the Health Management Information System (HMIS), Cambodia, 2016 and 2019

| Year | Number of health centers | Number of hospitals | Total number of facilities | Population(a) |
|---|---|---|---|---|
| 2006 | 1,087 | 96 | 1,183 | 13,474,489 |
| 2007 | 1,087 | 96 | 1,183 | 13,676,693 |
| 2008 | 1,087 | 96 | 1,183 | 13,880,509 |
| 2009 | 1,087 | 96 | 1,183 | 14,090,208 |
| 2010 | 1,087 | 96 | 1,183 | 14,308,740 |
| 2011 | 1,087 | 96 | 1,183 | 14,537,886 |
| 2012 | 1,087 | 96 | 1,183 | 14,776,866 |
| 2013 | 1,087 | 96 | 1,183 | 15,022,692 |
| 2014 | 1,138 | 104 | 1,242 | 15,270,790 |
| 2015 | 1,148 | 107 | 1,255 | 15,517,635 |
| 2016 | 1,168 | 111 | 1,279 | 15,762,370 |
| 2017 | 1,195 | 116 | 1,311 | 16,005,373 |
| 2018 | 1,213 | 121 | 1,334 | 16,245,454 |
| 2019 | 1,225 | 125 | 1350 | 16,489,135 |

Population data was only available for 2016 (45). To obtain population data for other years, we projected backward and forward using the National Institute of Statistics' national population growth rate (46).

These health facilities are located in 24 provinces and the capital city of Phnom Penh (Figure 3.1). This includes 197 administrative districts and a total of 94 operational districts. A health center covers a catchment area of between 10,000 to 20,000 people (42).

Figure 3.1. Locations of provinces and capital city of Phnom Penh of Cambodia




## Case definition

According to the National Treatment Guideline in Cambodia, confirmed malaria cases were persons who tested positive for *P. falciparum, P. vivax,* or both ("*Mixed*") by RDT or microscopy (47).

Before 2014, unconfirmed malaria cases were also counted in the HMIS system. The definition of an unconfirmed case was a person who had not been tested for malaria with a diagnosis based only on signs and symptoms. Unconfirmed cases were counted if they :

- had *(fever, chills, or sweats)* or *(two of the following: headache, nausea, vomiting, diarrhoea),*

**AND**

- any of the following: Travelled to the forest in the previous month, had confirmed malaria in the past 28 days, travelled to a malaria-endemic area from a non-endemic area, or lived or worked around others with a recently confirmed malaria diagnosis (47).

Our analysis included all cases (confirmed and unconfirmed) for overall incidence rates and rates by sex, age, district, and seasonality. We, however, used only confirmed cases to disaggregate by *Plasmodium* species as it was not possible to identify the species among unconfirmed cases.

## Data analysis

We calculated the annual malaria incidence (disaggregated by species) at the national and district levels by dividing each year's confirmed cases by their respective populations and obtaining incidences by gender and age group.

We investigated the existence of clusters (48, 49) by testing two hypotheses: 1) $H_0$= *malaria cases in each district throughout the country are proportional to the population*, and 2) $H_A$= *malaria cases in one or more districts are statistically higher than expected proportional to the population*. We ran the cluster analysis using a spatial Poisson model with SaTScan™ version 9.6 (Information Management Services Inc., Calverton, MD, USA) at the administrative district scale, using annual malaria cases and population data (48, 49). We introduced the assumption that the cluster's radius had to be smaller than 100 kilometers or cover less than 50% of the total country malaria cases to mitigate the effect of large cluster sizes on the analysis. Such clusters were split into smaller clusters. Another assumption we introduced was that the relative risk (RR) had to be greater than three. This restriction allowed us to focus the analysis on high burden clusters. RR was calculated as A/B where “A” was the ratio of the observed malaria rate per 1000 populations to the expected rate within the circle, and “B” was the ratio of the observed malaria rate per 1000 populations to the expected rate outside the circle. The expected rate was from dividing annual total notifications by the total population multiplied by 1000 in the same calendar year (48, 49). In our case, in identifying clusters, SatScan used a circle shape to scan districts with high malaria notifications. It starts from one district point. Suppose the rate within the circle is statistically significantly higher than the rate outside the circle. In that case, SatScan repeats scanning the same district, but it increases the size of the circle to cover more nearby district points. It repeats the process until it reaches the point where the rate inside and outside the circle is not statistically significant. When it reaches this point, SatScan records the circle of the last scanning remained statistically significant as a cluster. This is where the RR was obtained. The default Monte Carlo replication of 999 was used with a cut-off *P*-value <0.001 (48, 49). In this publication, we

used the term "cluster" in reference to SaTScan's "most likely cluster," which are clusters detected during the first run. In the Poisson model, after the first run, SaTScan removes all data inside the detected clusters and treats them as "no location," "no case," "no population." It then runs again to detect clusters with the remaining data. These newly detected clusters are called "secondary clusters." Since we are only interested in high burden areas or "most likely clusters," we did not allow the option to display "secondary clusters" in our analysis result.

We used Stata version 15.1 (StataCorp, College Station, Texas, USA) for descriptive data analysis and R version 4.0 (R Foundation for Statistical Computing, Vienna, Austria) to produce graphics and maps.

# Results

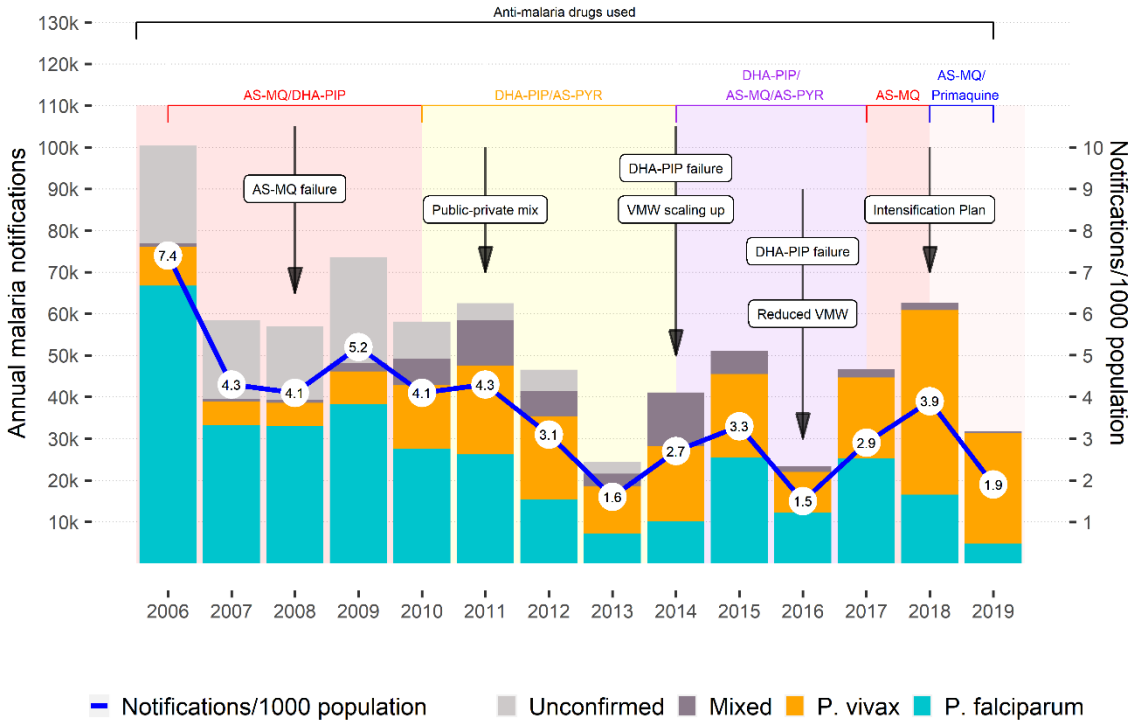
## Overall malaria cases and notification rate

A total of 737,210 malaria cases (confirmed or unconfirmed) was reported to HMIS between 2006 and 2019 (3.6/1,000 population) (Figure 3.2). The highest notification was reported in 2006, with 7.4 cases/1000 population (100,322 cases), and the lowest notification was reported in 2016, with 1.5 cases/1000 (23,367 cases). However, the notification did not decrease regularly over the time period, with a sharp increase to 3.9 cases/1000 in 2018 (62,582 cases) followed by a drop to 1.9 in 2019 (32,597 cases). Between 2006 and 2013, unconfirmed malaria cases were included in the HMIS. Unconfirmed cases made up a large proportion of all reported cases between 2006 and 2010, and subsequently dropped between 2011 and 2013. Nevertheless, the number of confirmed cases was particularly high in 2006, and stable between 2007 and 2011. Between 2007 and 2011, the total number of malaria cases was quite stable, with a drop in unconfirmed cases been compensated by an increase of the confirmed cases. Since 2014, all reported malaria cases met the confirmed case definition.

After the public-private mix (PPM) program was initiated in 2011, the malaria notification trends (in which data from the private sector was not included), dropped dramatically from 4.3 cases/1000 in 2011 to 1.6 cases/1000 in 2013. As a significant proportion of malaria cases were detected by private sector during this period, the decreasing trend in notification is unlikely to represent the actual notification of malaria in Cambodia for this period of time.

Therefore, data represented in this study must be considered in light of the changes in the surveillance case definition over time and changes in reporting sources.

Figure 3.2. Malaria confirmed notifications (by species) per 1000 population and untoward event, 2006-2019, Cambodia




Abbreviation: AS-MQ, Artesunate-mefloquine; DHA-PIP, Dihydroartemisinin Piperaquine; AS-PYR, Artesunate-pyronaridine; VMW, Village Malaria Worker
Note: unconfirmed cases were calculated by subtracting total cases with confirmed cases

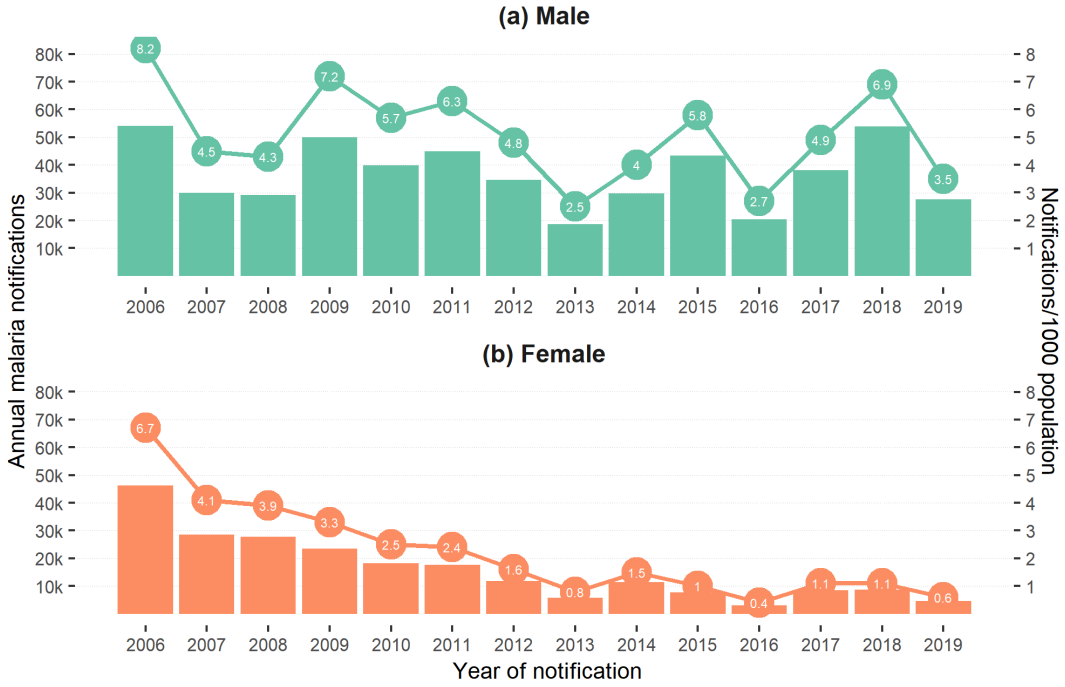
The proportion of *P. falciparum* + *Mixed* peaked at 87.9% (n= 67,489) of all confirmed malaria cases notified in 2006 to reach a lowest 16.6% (n= 5,290) of all notified cases in 2019. The proportion of *P. falciparum* + *Mixed* was highest between 2006 and 2009, when the country was using *P. falciparum-only* RDTs. The proportion of *P. vivax* + *Mixed* exceeded the proportion of *P. falciparum* + *Mixed* between 2011 and 2014, and then again from 2017 onwards. The change occurred a year after Cambodia started using dual RDT in late 2009, which detected both *P. falciparum* and *P. vivax*. More detailed information can be found in supplementary (Annex 1).

## Notification by sex

As presented in the previous section, the reporting changed from confirmed and unconfirmed cases to just confirmed cases after 2013. The notification of malaria

(confirmed + unconfirmed cases per 1000 population) among women decreased steadily from 6.7/1000 in 2006 to 0.5/1000 in 2019 (average decrease of 4.6% per year since 2006). This was not observed for men, whose notification fluctuated widely between a maximum of 8.2/1000 in 2006 and a minimum of 2.5/1000 in 2013 (Figure 3.3). Malaria notification among males has consistently been higher throughout the analysis period.

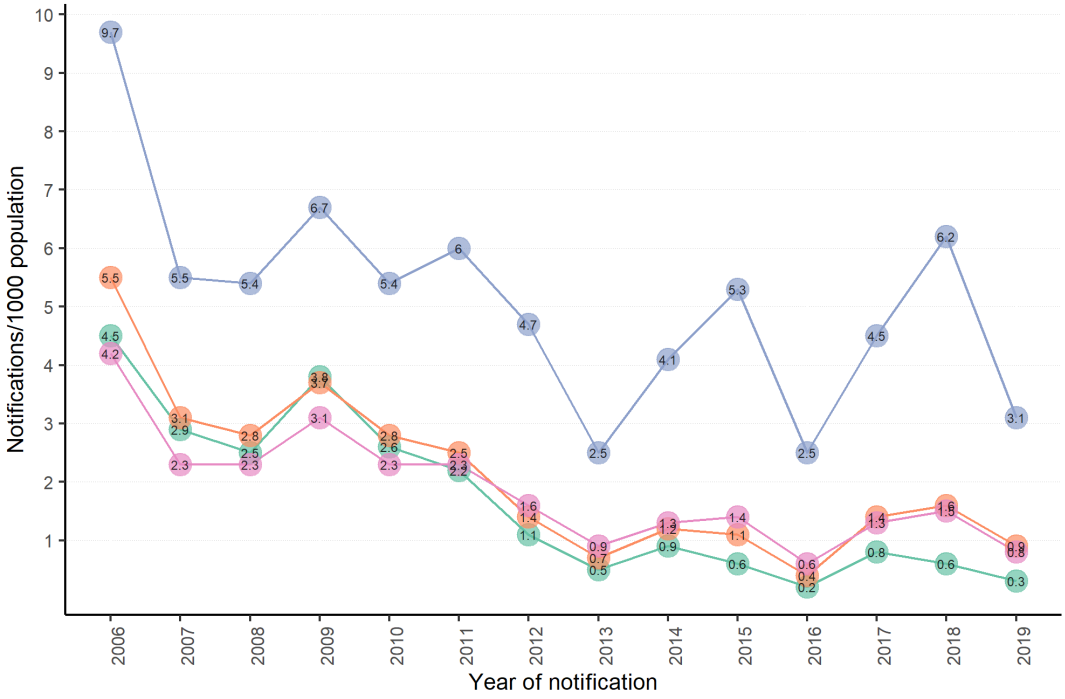
Figure 3.3. Malaria notifications (confirmed + unconfirmed cases) per 1000 males and females, between 2006-2019, Cambodia




## Notification by age group

Adults aged between 15-49 years had the highest malaria notification (confirmed + unconfirmed) among all age groups. The notification in this age group decreased from 9.7 cases /1000 in 2006 to 3.1/1000 in 2019 and was lowest at 2.5 in 2013 and 2016 (Figure 3.4). In other age groups (under five years, 5-14 years, 49 years and above), malaria notification rates presented similar trends, albeit much lower rates. Figure 3.4. Rate of malaria notifications (confirmed + unconfirmed

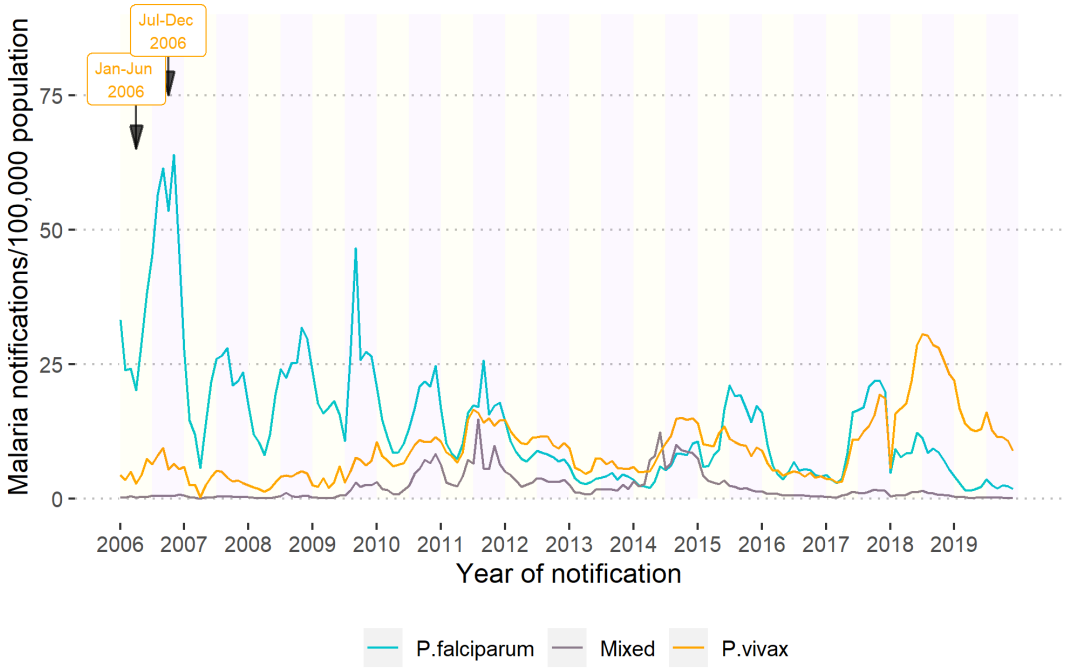
cases) per 1000 by age groups, 2006-2019, Cambodia




## Seasonality of malaria notifications

Both *P. falciparum + Mixed* and *P. vivax + Mixed* presented a similar seasonal pattern over time, except in 2016 and 2019 (Figure 3.5). Low *P. falciparum + Mixed* and *P. vivax + Mixed* cases were notified between February and May, while the high malaria season was observed between June and January. More detailed visualization of notifications by month are available in supplementary (Annex 2).

Figure 3.5. Number of malaria notifications (confirmed + unconfirmed) per 100,000 populations per month, 2006-2019, Cambodia

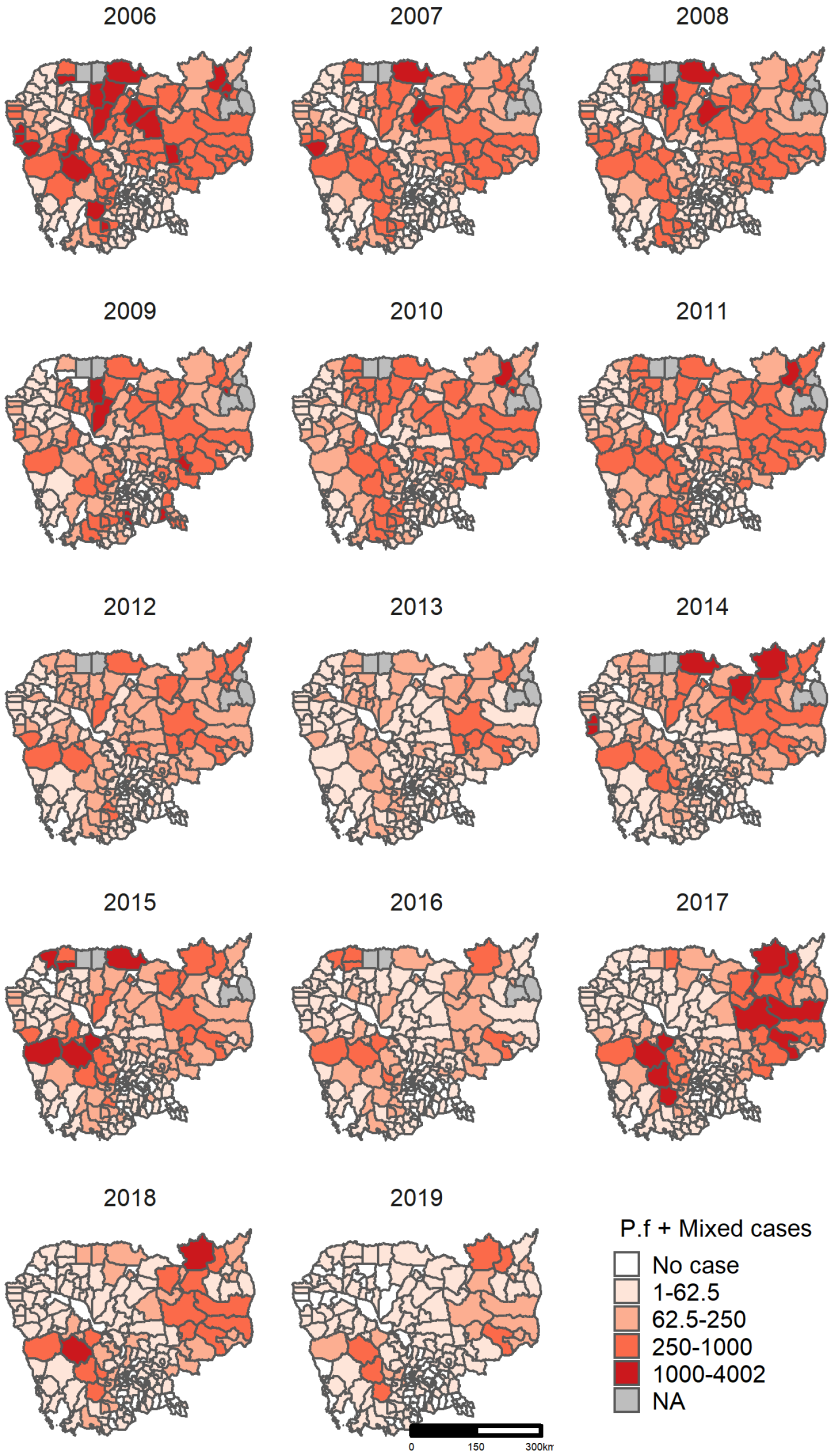


## Clusters of P. falciparum + Mixed

The number of confirmed *P. falciparum* + *Mixed* cases ranged from zero to 4,002 by district per year (Figure 3.6). The districts with a high burden of malaria, over 1,000 cases per year, were seen along the national borders, in the western provinces (Pursat, Kampong Speu, Koh Kong, and Pailin), northern provinces (Preah Vihear and Udor Mean Chey), northeast provinces (Kratie, Stung Treng), and eastern provinces (Mondul Kiri and Ratanakiri) (Figure 3.6). The majority of districts with a low malaria burden, lower than 250 cases per year, were observed in central and southern provinces (Figure 3.6).

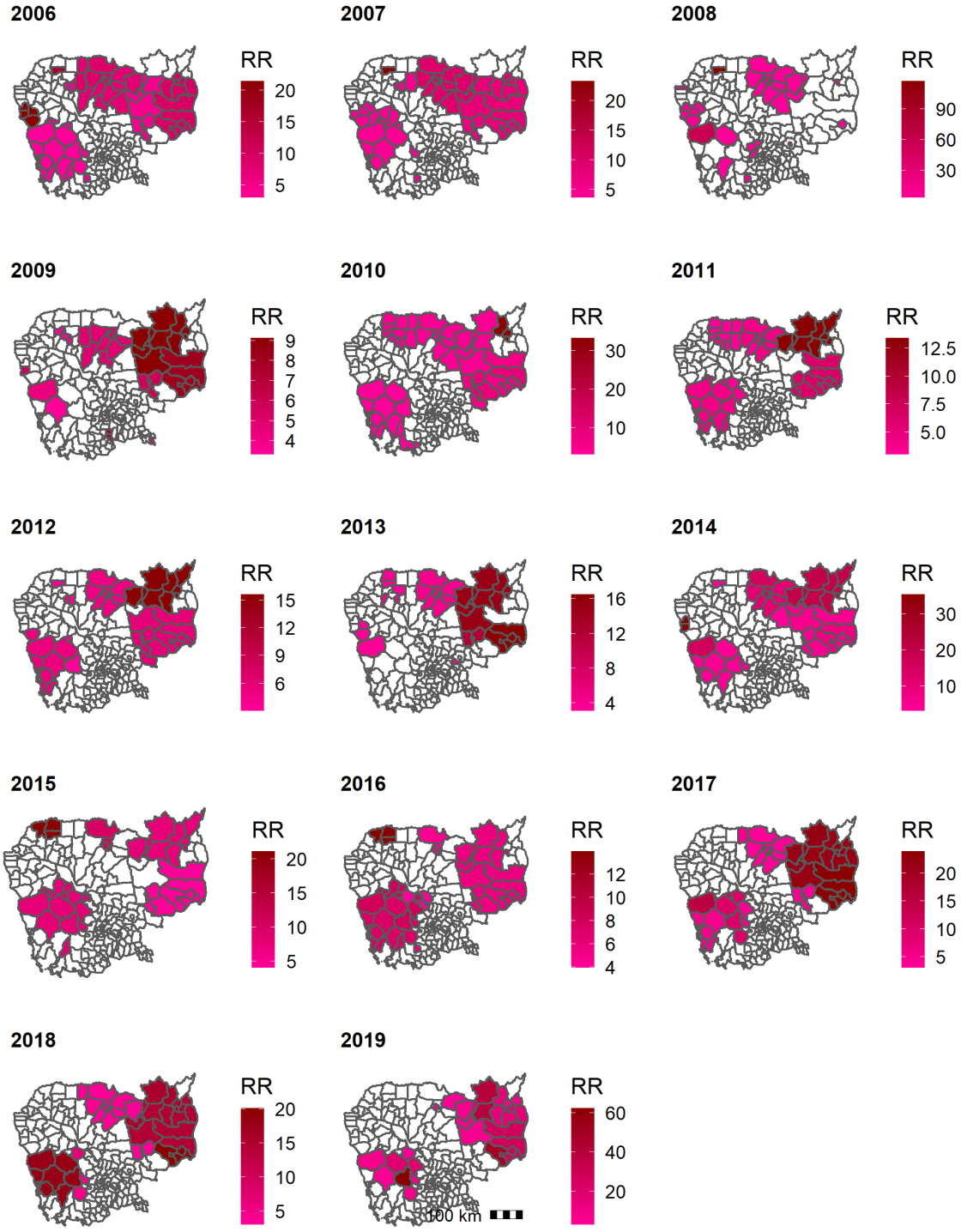
The cluster analysis revealed a decrease in size and number of the clusters of *P. falciparum* + *Mixed* cases during the last three years, 2017, 2018, and 2019 (Figure 3.7). Between 2017 and 2019, these clusters were detected in districts within the north-eastern and eastern provinces (Kratie, Stung Treng, Mondul Kiri, and Ratanak Kiri) and districts within the western provinces (Kampong Speu and Pursat). The malaria notifications were even more concentrated in the two regions in the last analysis year (2019), increasing relative risks from between 5 and 25 to between 20 and 60 times higher than the rest of the country (Figure 3.7).

Figure 3.6. Number of confirmed *P. falciparum* + *Mixed* notification distribution by district, 2006-2019, Cambodia




Abbreviation: NA = no data

Figure 3.7. Clusters of confirmed *P. falciparum* + *Mixed* ,measuring by relative risk, between 2006 and 2019 in Cambodia



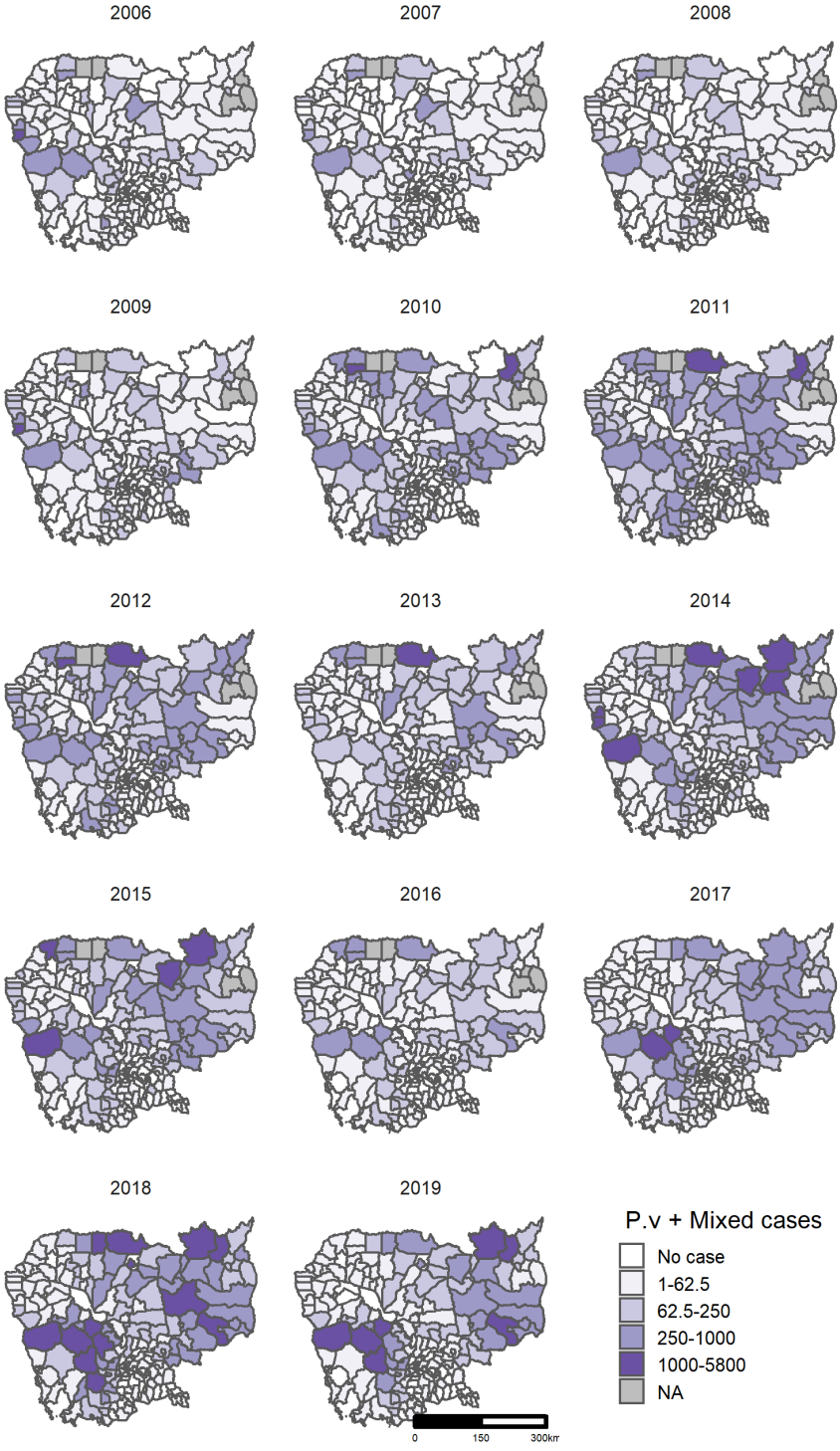

Abbreviation: RR, relative risk

### *Clusters of P. vivax + Mixed*

The number of confirmed *P. vivax + Mixed* cases ranged from zero to 5,800 cases by district per year. As for *P. falciparum + Mixed*, the districts with a high burden of malaria, over 1,000 cases per year, were seen along the national borders, in the western provinces (Pursat, Kampong Speu, Koh Kong, and Pailin), the northern provinces (Preah Vihear and Udor Mean Chey), northeast provinces (Kratie, and Stung Treng), and the eastern provinces (Mondul Kiri and Ratanak Kiri) (Figure 3.7).

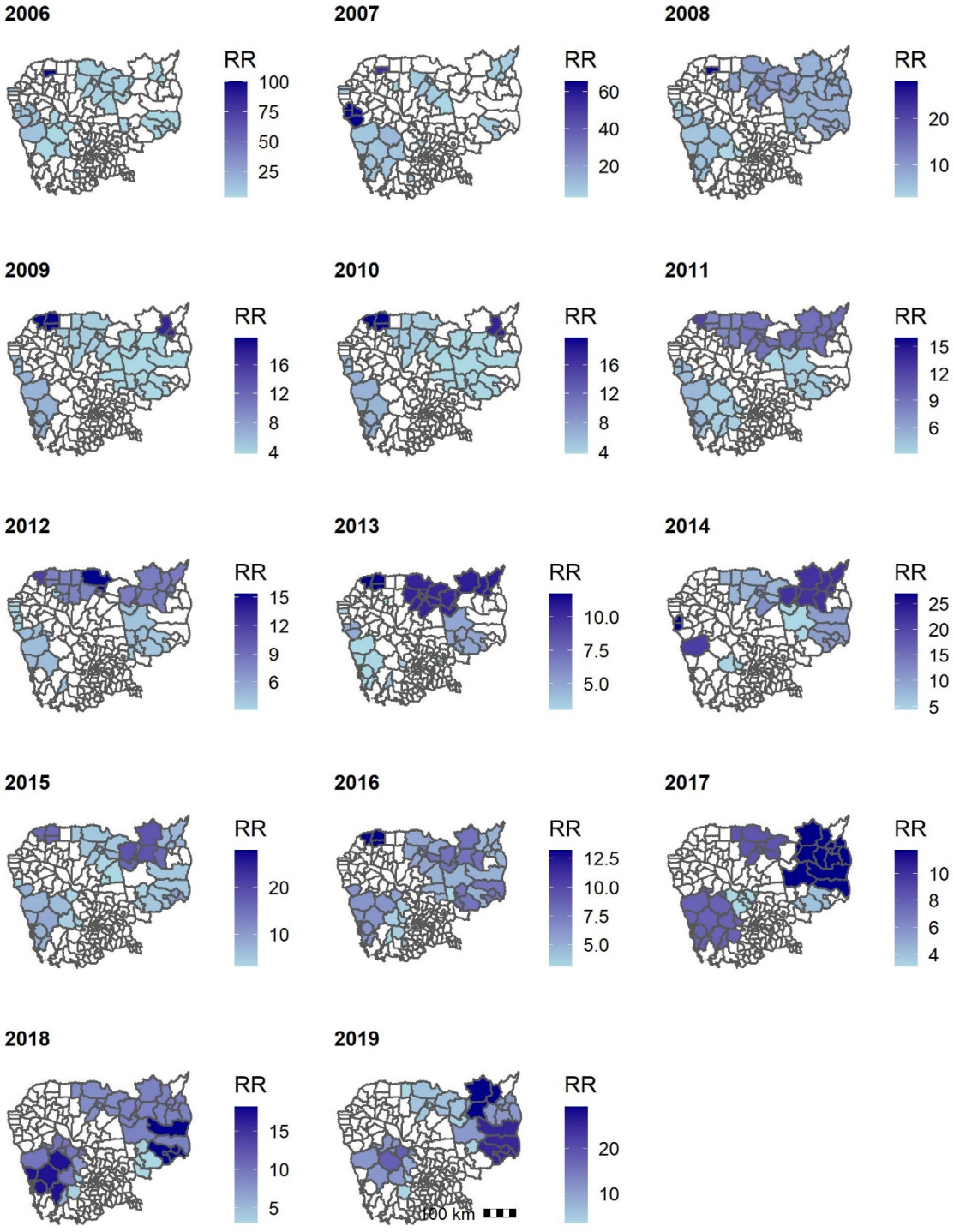
As for *P. falciparum,* fewer and smaller clusters of *P. vivax + Mixed* cases were detected in the last three years (2017-2019) (Figure 3.8). Between 2017 and 2019, the clusters were also seen along the national borders, in the northern provinces (Preah Vihear and Udor Mean Chey), north-eastern provinces (Kratie, and Stung Treng), eastern provinces (Mondul Kiri and Ratanak Kiri), and the western provinces (Pursat, Kampong Speu, and Koh Kong).

Figure 3.8. Number of confirmed P. vivax + Mixed cases by district between 2006 and 2019 in Cambodia




Abbreviation: NA = no data

Figure 3.9. Clusters of confirmed *P. vivax* + *Mixed*, measuring by relative, riskbetween 2006 and 2019 in Cambodia




Abbreviation: RR, relative risk

## Discussion

This study describes how malaria has evolved spatially from 2006 to 2019 in Cambodia. The peak malaria seasons were found to be between June and January. A similar finding was described by Maude *et al.* in 2014, based on Cambodia's national malaria data between 2004 and 2013 (50). The rainy season starts one month before the malaria season commences (May vs. June), while it ends two months before the malaria season ends (November vs. January). Previous studies in China, Tibet, Niger found that rainfall contributed to increased *Anopheles* and malaria notification (51-54).

Our analysis detected *P. falciparum* + *Mixed* and *P. vivax* + *Mixed* clusters in seven provinces along national borders with Vietnam, Laos, and Thailand. These areas are covered by evergreen broadleaf forests (55) where *P. falciparum* and *P. vivax* infected *Anopheles* are prevalent (8). This geographical distribution of malaria in Cambodia was previously known (50). However, this analysis provides updated information confirming that these areas, in the elimination phase, are the top priority. The population's livelihood in the greater notification regions remains dependent on the forests, including logging precious woods, agriculture activities, and residency in the fringe of the forests (11). To reduce *P. falciparum* and *P. vivax*, the intensification plan, which was effective in 2019 should be maintained, and innovative approaches aimed at blocking transmission from forests to communities, should be considered. The main limitation of this cluster analysis is that we can only locate cases at the place of diagnosis, *i.e.* the location of health facilities, and it is not possible to know where the case contracted malaria. This is a common limitation when using surveillance data.

The overall decrease in malaria has been observed mainly in women, while the annual notification has fluctuated in men, with the highest rate observed among men aged between 15-49 years old. Although the number of cases was similar in men and women in 2006 (8.2 vs. 6.7/1,000 population), the gap increased considerably in 2019 (3.5 vs. 0.6/1,000 population). The number of cases in women represented only 14% of the total cases. This notable difference in malaria notification in males and females is likely related to a change in exposure. The evolution of women's daily activities may have become less related to forests, with adult males being the most exposed to forest activities, and therefore, most at risk of malaria infections (11, 12, 56). According to malaria surveys of forest goers, 72.2% in 2004, 70.7% in 2007, 69.9% in 2010, 78.8% in 2013, 85.3% in 2017

were male aged 15 years old or older while 17.1% in 2004, 20.7% in 2007, 20.6% in 2010, 15.6% in 2013, and 9.7% in 2017 were female aged 15 years old or older (57-60). From these figures, the proportions of females who went to forests has decreased by half since 2010. Another possible reason could be the increasing distance between villages and forests due to deforestation. In Cambodia, two primary vectors—*Anopheles dirus* and *Anopheles minimus*—plays an important role in spreading malaria [61]. *Anopheles dirus* is more efficient (higher percentage of mosquitoes tested positive with *P. falciparum* and *P. vivax*) than *Anopheles minimus* [61]. They also have different habitats, *Anopheles dirus* living in natural forests and forest fringes, and *Anopheles minimus* living around the rice fields and forest fringes [61-62]. With Cambodia undergoing rapid deforestation in recent years [62], the territory of *Anopheles dirus* could decrease, leading to a lower risk of malaria transmission. However, deforestation activities correspond to influx loggers into *Anopheles dirus* habitat which can lead to increases in malaria cases. This highlights the importance of interventions targeting forest goers to block malaria transmission inside forests.

Several key factors may have impacted the malaria trends, although our study design does not provide evidence to prove causality.

First, we observed that all the upward trends in malaria have coincided with periods of high treatment failure rates to *P. falciparum* while all of the observed declines in notification occurred one to two years after a change in first-line treatment. It is plausible that the delayed parasite clearance due to ineffective antimalarial drugs increased malaria transmission among high-risk populations. In 2009, the total malaria cases increased by 29% (n= 16,493) compared to 2008. This rebound occurred after the first-line antimalarial-AS-MQ - showed high treatment failure rates (7, 24, 25, 61-71). A new first-line antimalarial (DHA-PIP) was introduced nationally in 2010 to replace AS-MQ (7, 15, 72). This was followed by an observed reduction of *P. falciparum* cases in Cambodia until 2013. DHA-PIP treatment failures emerged after a three-year of usage (27, 73, 74). Total malaria cases increased again by 68% (n= 16,679) in 2014 compared to 2013. Malaria notifications continued to increase in Cambodia until 2018. Of note, the ineffective DHA-PIP was still used in several parts of Cambodia due to procurement challenges until 2018 (7, 30). This finding suggests that antimalarial drug efficacy is key to control *P. falciparum*. Timely surveillance of drug efficacy provides critical information to respond to a malaria epidemic promptly.

Another key factor was that the dramatic drop in malaria cases was likely associated with the changing use of the private sector and an important limitation of the HMIS that did not capture data from the private sector. The private sector played a significant role in changing the national malaria trends between 2011 and 2018. However, the most substantial impact would have occurred between 2011 and 2013, when malaria notification dropped from 4.1 to 1.6 /1,000 population with a sharper decrease of *P. falciparum* notifications compared to *P. vivax*. This drop was possibly due to a public-private mix (PPM) project piloted in 2011 and scaled up in 2012 (7, 15, 16). It may have favored larger access to early detection and treatment of infections since more than 50% of antimalarial drugs were delivered at private points of care between 2011 and 2013 (16, 74). This is consistent with the findings from national malaria surveys that showed 7.3% of malaria patients used the private sector in 2007, 41.1% in 2010, 56.4% in 2013, with a reduction to 30.3% in 2017 (57-60). Therefore, the decreasing trend of malaria cases notified in the HMIS between 2011 and 2013 could be related to the increasing use of the private sector, which was not included in HMIS before it was banned in April 2018. This highlights the importance of comprehensive surveillance with mandatory reporting requirements for public and private sectors to the HMIS to avoid undercounting or misleading trends.

The decreasing trends may have been overestimated due to the inclusion of unconfirmed cases between 2006 and 2013, when the malaria test was not available throughout the country. Unconfirmed cases may include non-malaria cases with similar clinical symptoms. The malaria cases were overestimated if the unconfirmed cases were included and underestimated if the unconfirmed cases were excluded. However, there is no data on the proportion of actual cases among the unconfirmed cases. Changing case definitions and diagnostics have a significant impact on surveillance data and therefore it is important to recognize such events when interpreting surveillance data.

The role of VMWs also played a key role in malaria trends in Cambodia. The malaria notification increased from 2.7/1000 population in 2014 to 3.3/1,000 population in 2015. This increase happened after the scaling up of VMWs in 2014 (7, 15, 75). VMWs provided free services in villages and reported to HMIS through health centers, leading to greater malaria notifications. VMWs administered 41% of all antimalarial drug delivery in 2015 (74). The scaling up of VMWs helped change health-seeking behaviors with a noted decrease in private sector services and improved HMIS sensitivity.

In contrast, malaria cases dropped to the lowest point in 2016 but increased again in 2017 and 2018. This occurred after many VMWs were laid-off, and all other activities supported by Global Fund funding were suspended between July 2015 and December 2016 (30, 76). The immediate drop in malaria cases in 2016 may be due to the absence of notifications from VMWs. This finding implied that early access to diagnosis and treatment through VMWs or care points is another critical feature to control and eliminate malaria. Funding to maintain VMWs, or other equivalent interventions, should be prioritized until elimination is confirmed.

One more key factor was the intensification plan initiated in 2018 to respond to increasing case notifications in 2017 and 2018. A significant drop in malaria cases from 3.9/1,000 in 2018 to 1.9/1,000 in 2019 was observed after the plan started. For the first time, both species – *P. falciparum* and *P. vivax*— had a dramatic decline. The success of the new intensification plan targeting forest goers provides sufficient evidence that this plan should be maintained.

The final key factor, nationwide crackdowns by police and forest rangers on illegal logging, may also have had an impact on malaria trends. The massive crackdown started in 2019. It prevented the highest risk groups (forest goers) from entering forests where most malaria transmission was occurring (77). It is of interest that the effectiveness of malaria control programs may be positively affected by external and independent factors such as anti-deforestation activities.

Concerning the *Plasmodium* species, an increase of *P. vivax* proportions was observed over time. Two reasons may have contributed to these changes. Firstly, the index of species was likely affected by the shift from *P. falciparum-only* RDT to dual RDT, which could have detected both *P. falciparum* and *P. vivax*. As previously shown, *P. falciparum* notifications were predominant before 2010. This was due to Cambodia using *P. falciparum*-only RDT before 2010 (75). In that period, *P. vivax* cases could only be detected using microscopy, which availability was limited (78). According to an outlet survey in 2015, microscopy was available in only 28% of government health facilities included in the study. The dual RDT was only supplied in late 2009 (75). One year after using the dual RDT, the proportion of *P. vivax* exceeded the proportion of *P. falciparum*. However, *P. vivax* possibly remains under-detected due to the RDT's low sensitivity (ability to detect true positive) to *P. vivax* (88). RDTs do not perform well among individuals with

low parasitemia (<100 parasites/parasites/μL) (88). According to a meta-analysis study, the sensitivity of RDT in detecting *P. vivax* ranges from 57% to 77% compared to a polymerase chain reaction (PCR) as a gold standard [90]. Secondly, the proportion of malaria patients with *P. vivax* has increased. Relapses may explain these trends. Relapses among *P. vivax* patients was described as early as 1893 (79). According to Taylor A. et al., *P. vivax* patients along Thai-Myanmar borders neighboring country with Cambodia, suggested that 75% of *P. vivax* patients receiving standard treatment (without Primaquine radical curative treatment) relapsed within 12-month follow-up (80). One *P. vivax* patient is thought to have multiple episodes of relapse, but the exact number of relapses per lifetime per person has not yet been confirmed (81). The accumulation of *P. vivax* relapses constitutes a large proportion of all *P. vivax* cases and maintains the source of *P. vivax* infections. Radical cure to *P. vivax,* piloted in four provinces of Cambodia (Kampong Speu, Kampong Chhnang, Battambang, and Pailin), should also be prioritized in all *P. vivax* clusters.

In contrast to *P. vivax,* the proportion of *P. falciparum* notifications have declined faster over time. The decline of *P. falciparum* notifications may result from multiple factors. Firstly, the enhanced *P. falciparum* elimination efforts by the Ministry of Health have likely had a key role to play. Interventions such as expanding testing and treating sites to facilitate early diagnosis and treatment of cases (6, 7, 13). In addition, a focus on the interruption of *P. falciparum* transmission, or 1-3-7 strategy (reporting a confirmed case within one day, investigating within three days, and taking measures to prevent further transmission within seven days), in elimination areas may have also contributed to this decline (7, 82, 83). Secondly, *P. falciparum* is curable. The impact from effective interventions in reducing *P. falciparum* cases should be rapidly seen. Thirdly, biologically, there is evidence that prior exposure to *P. vivax* suppresses the course of *P. falciparum* infection (84-87). It is possible that this factor contributed to the decline of *P. falciparum*. However, the proportion by which *P. falciparum* is reduced by prior exposure to *P. vivax* is not known.

The overall *P. falciparum* prevalence decreased was concurrent with the emergence of drug resistance in *P. falciparum*. The scaling up of improved access to early testing and treatment probably had a greater impact than the emergence of drug resistance. Ongoing surveillance of antimalarial drug resistance also ensured that first-line treatments were promptly changed to efficient regimens.

## Conclusions

In this study, we used the nationwide surveillance data collected in the last 14 years between 2006 and 2019. There was a noted decrease in notifications of *P. falciparum* in 2019, suggesting that intensification plan should be maintained. *P. vivax* showed a slower but promising declining trend. Interventions aimed at achieving *P. falciparum* elimination and preventing *P. vivax* new infections and relapses should be prioritized. In the context of malaria elimination, all cases detected outside national system should be reported to national system to avoid misleading trends.

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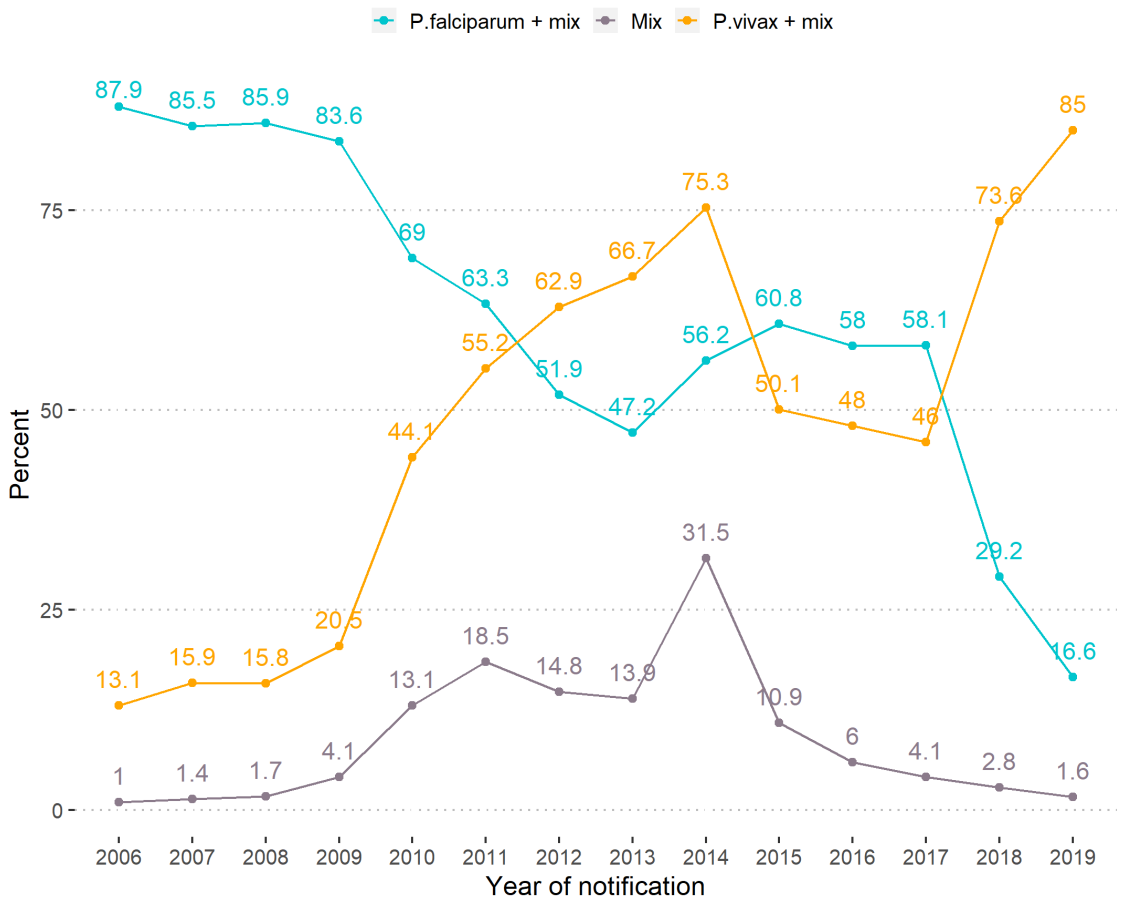
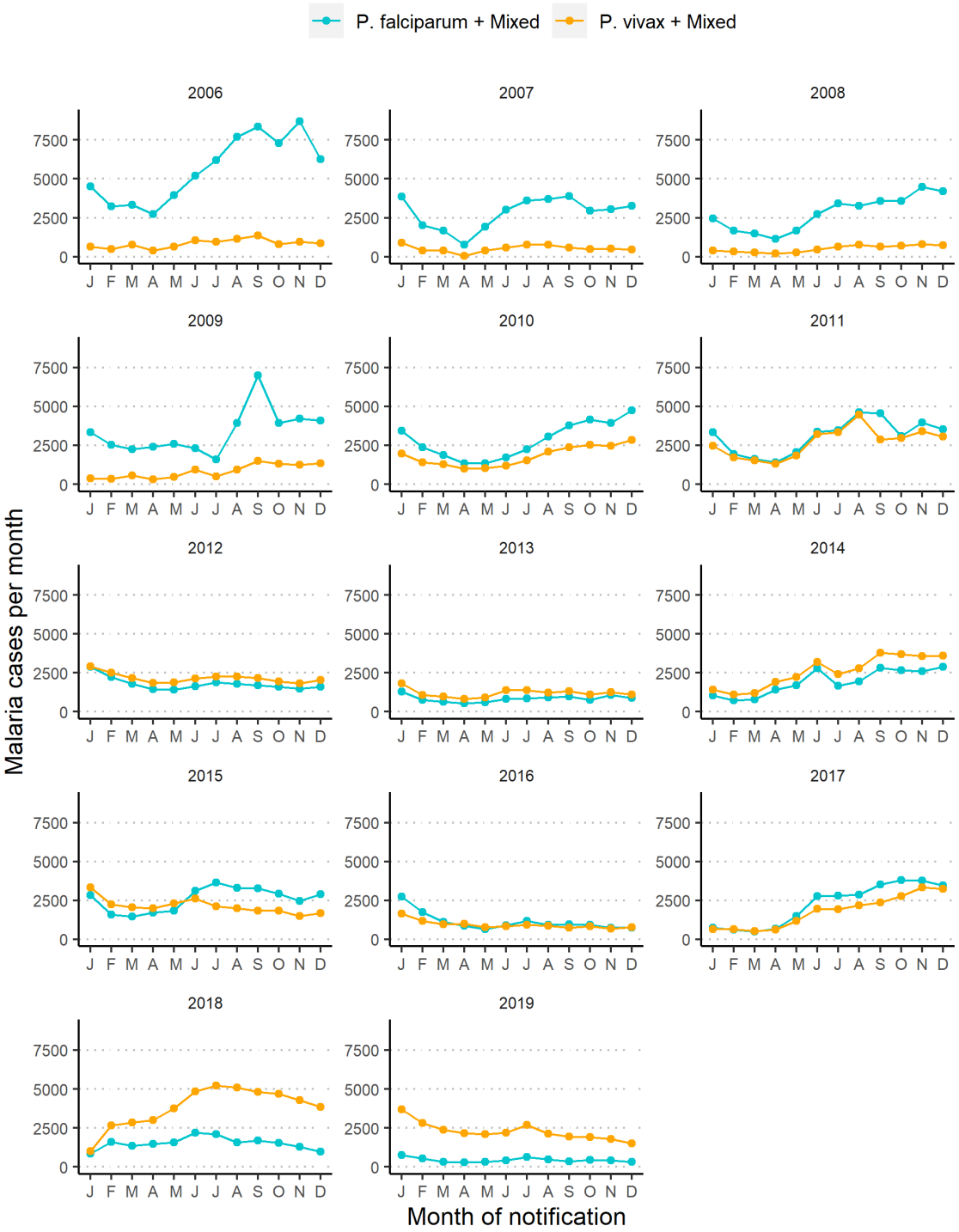
# Annex 1: Proportion of malaria notifications by Plasmodium specifies in Cambodia, 2006-2019



# Annex 2: Number of malaria notifications by month, 2006-2019 in Cambodia



# Chapter 4 : Using Kobo Toolbox as a malaria project-based surveillance system in Cambodia: surveillance evaluation

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# Prologue

## Rationale

This chapter is to fulfill the surveillance core competency of the MAE program and literature review requirement. The “Second-phase Regional Artemisinin-resistance Initiative (RAI2) surveillance system”, evaluated in this chapter, is a malaria project-based surveillance system launched in late August 2019. This surveillance system’s primary objective was to evaluate the effectiveness of in-forest interventions targeting malaria elimination in Cambodia.

## Roles

My role was to design the surveillance system, monitor, and evaluate it, to identify the system’s strengths and weaknesses. After returning from the first-course block in Australia in March 2020, my field supervisor planned to implement an operational research project related to malaria elimination. One part of the project was collecting data from health centers. I was asked to establish a project-based surveillance system, select intervention and control health centers, define inclusion criteria for intervention and control sites, train staff, and ensure the surveillance system met its objectives. I met with stakeholders to explore the existing system, and later established the “RAI2 surveillance system”. With administrative support from three other Institut Pasteur du Cambodge’s staff members, I provided training to 47 health center staff in late August 2019 to roll out the RAI2 surveillance system. After a five-month implementation, I evaluated this surveillance system and used it as one of my four competencies.

## Lessons Learnt

This was my first time managing a surveillance system for malaria and managing a surveillance system integrated into the government system. I learned several things from this work, which may help me build a better surveillance system next time.

- Maintaining a surveillance system nested in a government system is challenging. Health centers have competing priorities, of which some are mandatory. There is often no time for adequate and clean data collection and reporting, which affects the surveillance system’s data quality and sensitivity.

- A more comprehensive, informative assessment should be conducted prior to the surveillance design. During the setting up, I thought about choosing staff from each health center to join the data collection training to kick off the system running. I could not invite more than one person because of the limited budget. With consultation with stakeholders, I chose a staff responsible for entering data into the Malaria Information System (MIS) because these staff are the focal points for malaria. In retrospect, the laboratory staff who meet every malaria patient would have been a more appropriate choice. The staff who enter data into MIS do not meet every malaria patient; they use the laboratory registration book, noted by laboratory staff and enter data into the MIS when they have time. These staffs have other priorities, so they sometimes missed interviewing malaria patients for the RAI2 surveillance system.

- A phone-based application is a practical, cheaper, and faster tool to collect data than a paper-based form in Cambodia. Health center staff prefer phone-based forms over paper-based forms.

- Performance-based financial incentives for surveillance staff are practical and cheaper than the fixed incentive only if a health center has more malaria cases, generating a meaningful incentive for them.

- Regular supervision of staff through phone or in-person is essential. When health center staff are busy, they are likely to drop lower priority tasks. Therefore, it is crucial to have staff dedicated to regular monitoring.

## Public Health Impact

The ability to provide high sensitivity and quality data to evaluate a public health intervention's effectiveness is crucial. This evaluation will strengthen the malaria surveillance system in the areas where it has been implemented. The collection and reporting of timely and reliable data will allow the intervention team to confidently conclude their findings at the end of the project. This evaluation's results will also be used to inform the development of future project-based surveillance systems.

## Acknowledgments

I deeply thank the staff and management teams of the National Centre for Parasitology, Entomology and Malaria Control, Global Fund, Provincial Health Departments, and all participated health centers for their kind collaboration.

Thanks to all malaria patients who participated in the interviews.

Finally, I profoundly thank all my supervisors—Tambri Housen, Patrice Piola, Vincent Herbreteau, and Amy Parry—for constructive feedback. Special thanks to Tambri Housen for sharing her expertise on surveillance evaluation. Although the task is technically simple, it is hard to find the right way to do the job without clear guidance.

## Abstract

*Background*: The Second-phase Regional Artemisinin-resistance Initiative (RAI2) intervention was the first intervention targeted at reducing malaria transmission among forest goers inside forests in Cambodia. The RAI2 surveillance system was designed to be nested in the national Malaria Information System (MIS). Its primary objective was to evaluate the effectiveness of the RAI2 intervention. We evaluated whether the RAI2 surveillance system fulfilled its primary objective.

*Methods:* Nine attributes adapted from the US Centers for Disease Control and Prevention guidelines 2001 were used to evaluate the system's performance. Usefulness was described based on the outcome of the evaluation of the other eight attributes. Simplicity, flexibility, acceptability, and stability were assessed using a short online survey with health center staff. Sensitivity, positive predictive value (PPV), data quality, and timeliness were assessed using document review and data from the RAI2 surveillance system.

*Results:* Between September 2019 and January 2020, 765 malaria patients were interviewed under the RAI2 surveillance system. An online form was completed by the focal health center staff, 100% (n=6/6) in the intervention site, and 65.8% (n=27/41) in the control site. All users rated the system as simple, flexible, stable, and timely. 100% completeness for all variables was achieved. An area that needed greater attention was the low acceptability and low sensitivity. PPV was measured at the intervention sites only, by confirming the Rapid Diagnostic Test (RDT) result with PCR, and was found to be 100% for both *Plasmodium (P.) falciparum* and *P. vivax*, although case numbers were low.

*Conclusion:* Due to unstable sensitivity in the intervention site, we could not solely rely on the RAI2 surveillance system's data to evaluate the intervention's effectiveness. RAI2 surveillance data were found to be partially useful in describing the characteristics of patients testing positive for malaria and reporting risk factors such as exposure to forest. The RAI2 surveillance system should be integrated into the national MIS. MIS has already been a case-based system but is not timely due to a delay for at least one month for data to be made available at the central level, while missing a few key exposure variables. MIS should be moved to be a real-time data collection, adding few more exposure variables, and setting up an alert system to the district and provincial level to increase its usefulness.

# Abbreviation

ACT Artemisinin-based Combination Therapy,

CMS Central Medical Store

CNM National Centre for Parasitology, Entomology and Malaria control

DP Dihydroartemisinin plus Piperaquine;

HC Health Center

IPC Institute Pasteur du Cambodia

IRS Indoor Residual Spraying;

ITN Increasing Insecticide-Treated Nets;

LLIN Long-Lasting Insecticidal Nets;

MIS Malaria Information System

MMW Mobile Malaria Worker

MSAT Mass Screenings and Treatment

NGO Non-governmental Organization

OD Operational District

PHD Provincial Health Department

RAI2 Second-phase Regional Artemisinin-resistance Initiative

RDT Rapid Diagnostic Tests;

SMC Seasonal Malaria Chemoprevention

SP Sulphadoxine + Pyrimethamine;

US CDC United State Centers for Disease Control and Prevention

VMW Village Malaria Workers

WHO World Health Organization

# Introduction

## Malaria burden at the global level

Malaria, a mosquito-borne disease, disproportionally affects people in low-income countries (1, 2). Even though the disease is preventable and curable, it remains a critical public health concern and a leading cause of death (3). According to the 2018 World Health Organization (WHO) estimate 228 million malaria cases occurred worldwide, with 405,000 deaths (2). According to the latest comparison, malaria ranked 16th as the leading global cause of death among all-cause mortality in 2017 (4) and ranked 6$^{th}$ among low-income countries in 2016 (5). Globally, the highest malaria burden is found in Africa. Africa's population made up 17.2% of the world population in 2020; however, malaria cases in this continent shared 93% of global malaria cases (2, 6). The incidence rate due to malaria per 1000 populations at risk was high at 229.3 in Africa compared to 57.4 globally (2). WHO Western Pacific Region and the WHO Southeast Asia Region had the lowest reported incidence rate at 2.6 and 4.9 per 1000 population at risk of malaria (2).

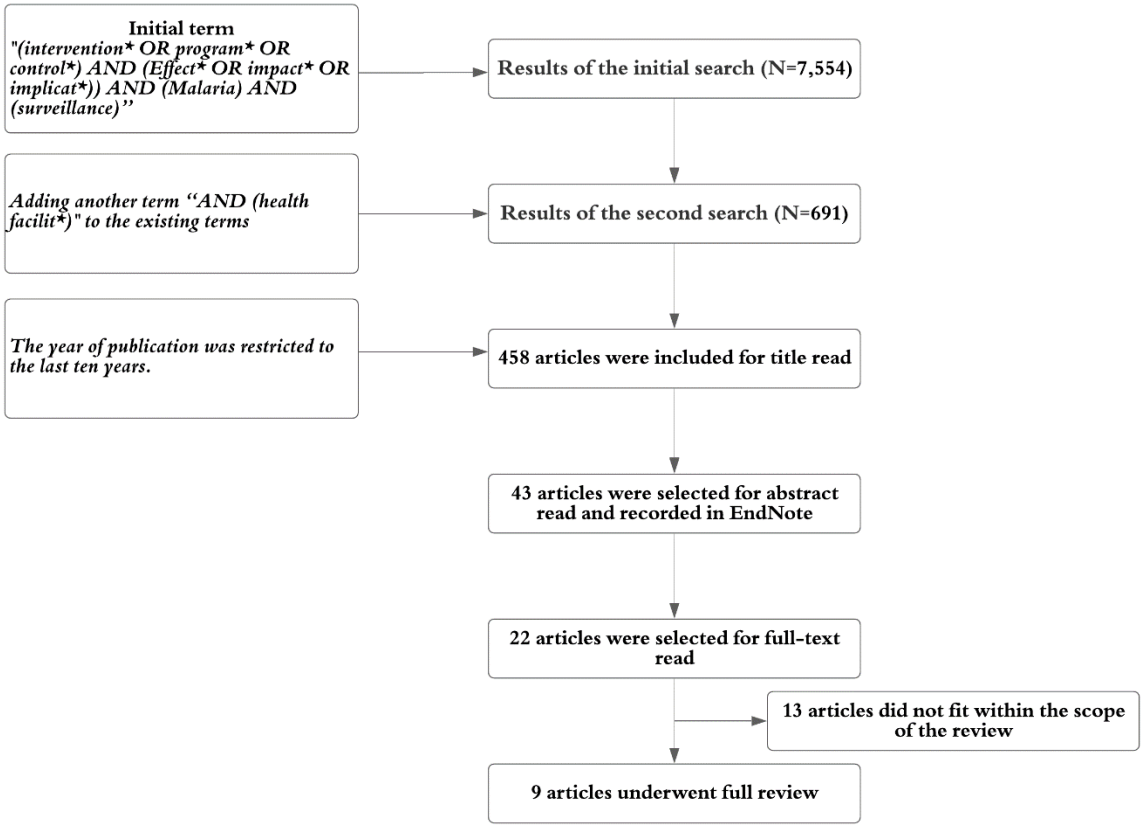
## Literature Review on the role of malaria surveillance system

The global technical strategy for malaria 2016–2030, developed by WHO, highlighted the malaria surveillance system as a core intervention in all malaria-endemic settings (7). An effective malaria surveillance system can be used to identify the most affected population, target interventions, evaluate the effectiveness of interventions, and advocate for resources (8).

To inform our evaluation, I conducted a scoping review of malaria literature related to health center surveillance systems with a focus on malaria. I searched for peer-reviewed articles on how malaria surveillance data had previously been used to evaluate malaria intervention impacts on malaria trends. As shown in Figure 4.1, in the initial search, I followed the PICO (population, intervention, comparison, outcome) framework (9). I searched the PubMed database using the terms "(intervention* OR program* OR control*) AND (Effect* OR impact* OR implicat*)) AND (Malaria) AND (surveillance)." With these terms, 7,554 articles were shown. I reduced the number of articles by adding another term "AND (health facilit*)" to the existing terms. In this second attempt, 691 articles were presented. In the next phase, the year of publication was restricted to the last ten years, reducing total articles to 458. Titles of all 458 articles were then screened, and 43 articles were selected for abstract read and recorded in EndNote X8.2. During the abstract read, 21 more articles were excluded. Of the 22 articles remaining, 13 additional articles were

dropped after a full-text read because they did not fit within the focus of the literature review. Finally, nine articles were selected for full review.

Figure 4.1. Schematic diagram of the malaria surveillance scoping review




As presented in Table 4.1, our final nine studies were conducted in seven countries (10-18). Of seven countries, six were in Africa, including Uganda (13, 15, 18), Democratic Republic of Congo (17), Zambia (11), Ethiopia (14), Ghana (10), and Senegal (12), and another country was Indonesia in Southeast Asia (16).

Indicators evaluated were predominantly malaria incidence, morbidity, and mortality. These indicators were assessed against the following interventions; increase in Insecticide-treated net (ITN) coverage (15), increasing in artemisinin-based combination therapy (ACT) coverage (15), introduction of rapid diagnostic tests (RDTs) (17), introduction of indoor residual spraying (18), combining long-lasting insecticidal nets (LLINs) with indoor residual spraying (10), replacing ITN by LLIN (14), administering Seasonal Malaria Chemoprevention (SMC) with sulfadoxine-pyrimethamine (SP) plus amodiaquine (AQ) among six- to 12-year children (12), and the replacement of existing antimalarial drugs with more efficacious antimalarial drugs (11, 16).

In drawing comparisons between intervention and control sites, one of the nine studies, by *Comfort et al*. 2014, solely relied on the surveillance data between pre- and post-intervention (11). Eight studies controlled for one or more of the following factors in their evaluation; socioeconomic status from national malaria survey, nightlight intensity as proximity of economic progress, entomological data to calculate human biting index over time, rainfall, and temperature (10, 12-18).

In terms of the studies' outcome, eight out of nine studies suggested the interventions reduced the malaria incidence, morbidity, and mortality, although the levels of reduction varied (10-16, 18). One intervention, which involved the introduction of RDT, showed a reversed outcome in which an increase in malaria incidence was observed (17). However, the reported increase was likely not due to an actual increase in malaria incidence in the population but due to improved detection (17).

Almost all the studies showed a positive outcome; this might be due to publication bias. Successful interventions were more likely to be published than the studies that did not show a positive impact.

We concluded that surveillance data from health facilities could be used to evaluate the effectiveness of an intervention. However, surveillance data alone is not enough; the data from other sources should also be collected to adjust in the analysis phase or to support the interpretation. Learning from this scoping review, we collected information on other interventions or events that might impact the malaria incidence or notification trends in their areas through informal discussions with our health center network. The information was used to support the interpretation of our surveillance evaluation findings and recommendations.

Table 4.1. Summary of research articles using malaria surveillance data at health facilities to evaluate the impacts of malaria interventions, 2011-2020

| Author, Year | Objective | Study Design, *Country* | Sample size | Intervention, *Comparing* | Outcome |
|---|---|---|---|---|---|
| **Ssempiira et al., 2018** | To estimate the effects of malaria interventions on the spatio-temporal patterns of the disease incidence in Uganda in children less than five years and individuals of 5 years and above | Retrospective data analysis<br><br>*Uganda* | 41,797,579 | Increasing Insecticide-Treated Nets (ITN) Artemisinin-based Combination Therapy (ACT) coverage<br><br>*Intervention and control sites (2013-2016)* | Incidence among individuals ≥ 5 years in a district was reduced by 44% for every one out of six ITN indicators the district achieved<br><br>Incidence was reduced by 28% in children < 5 years, and by 25% in individuals ≥ 5 years in the district that classified having full coverage of ACT |
| **Lechthaler et al., 2019** | To estimate the effects of interventions on malaria cases at the health facility level, using a retrospective trend analysis of malaria cases between 2005 and 2014 | Retrospective data analysis<br><br>*Democratic Republic of Congo* | NA | Introduction of Rapid Diagnostic Tests (RDTs)<br><br>*Pre-intervention (2005–2010) and post-intervention (2011–2014)* | Overall, malaria incidence increased by 51% after the introduction of RDT |
| **Kenangalem et al., 2019** | To investigate temporal trends in malaria-related morbidity and mortality in Papua, Indonesia, before and after the introduction of a universal, artemisinin-based antimalarial treatment strategy for all Plasmodium species | Retrospective data analysis<br><br>*Indonesia* | 418,238 | Changing antimalarials from “chloroquine and sulphadoxine + pyrimethamine (SP)” to “dihydroartemisinin plus piperaquine (DP)”<br><br>*Pre-intervention (2004-2006) and post- intervention (2008-2009)* | Hospital visits due to malaria were reduced by 12.9%<br><br>Mortality among *P. falciparum* patients was reduced by 0.21% |
| **Comfort et al., 2014** | To compare hospital admissions and outpatient visits for malaria and estimate costs incurred for malaria admissions before and after malaria control scale-up | Retrospective data analysis<br><br>*Zambia* | 23,994 | Scaling up test-and-treat campaigns with changing antimalarials from SP to “artemether-lumefantrine”<br><br>*For study site one, pre-intervention (2003) and post-intervention 2004-2008). Study site two, pre-intervention (2005-2006) and* | Outpatient and inpatient visits due to malaria were dramatically reduced, and total hospital expenditure was reduced by 9%. |

| | | | | | |
|---|---|---|---|---|---|
| | | | | *post-intervention 2007-2008)* | |
| **Aregawi et al., 2014** | Time series analysis of trends in malaria cases and deaths at hospitals and the effect of antimalarial interventions, 2001-2011, Ethiopia | Retrospective data analysis<br><br>*Ethiopia* | | Distribution of Long-Lasting Insecticidal Nets (LLINs) through mass campaigns, Indoor Residual Spraying (IRS), and increased diagnostic testing through RDT and microscopy<br><br>*Pre-intervention (2001–2005) and post-intervention (2006–2011)* | Total confirmed malaria cases declined by 66% |
| **Aregawi et al., 2017** | To assess the impact of control interventions on malaria cases, admissions, and deaths using data from district hospitals. | Retrospective data analysis<br><br>*Ghana* | 1,217,067 | Replaced ITN by LLIN mass campaign<br><br>*Pre-intervention (2005–2010) and post-intervention (2011–2015)* | Malaria incidence was reduced by 57%<br><br>Change in malaria admissions was insignificant<br><br>Malaria deaths reduced by 65% |
| **Tugume et al., 2019** | To assessed malaria morbidity trends before and after IRS with Actellic 300 CS in Lira District in Northern Uganda | Retrospective data analysis<br><br>*Uganda* | 171,250 | IRS with Actellic 300 CS<br><br>*Pre-intervention (Jan– July 2016) and post-intervention (Sep–2016 to March–2017)* | Outpatient visits due to malaria were reduced by 3.6% |
| **Katureebe et al., 2016** | To measure changes in key malaria indicators following universal LLIN distribution in three sites, with the addition of IRS at one of these sites | Retrospective data analysis<br><br>*Uganda* | 110,313 | LLIN only and LLIN with IRS<br><br>*Pre-LLIN (Oct1–2011 to Nov1–2013) and post-LLIN (Dec1–2013 to March 2016) Pre-LLIN with IRS (Dec1– 2013 to Jan1–2015) and post-LLIN with IRS (Feb–2015 to March –2016)* | Test positivity rates at health facilities were not changed between pre- and post-LLIN only. In the site of LLIN with IRS, the test positivity rate was reduced by 22.8% |
| **Cissé et al., 2016** | To determine the effectiveness of Seasonal Malaria Chemoprevention (SMC) in Senegalese children up to ten years of age | Stepped-Wedge Cluster-Randomised Trial<br><br>*Senegal* | 2,422 | SMC<br><br>*Intervention and control sites* | Incidence was reduced by 60%, but mortality was not different |

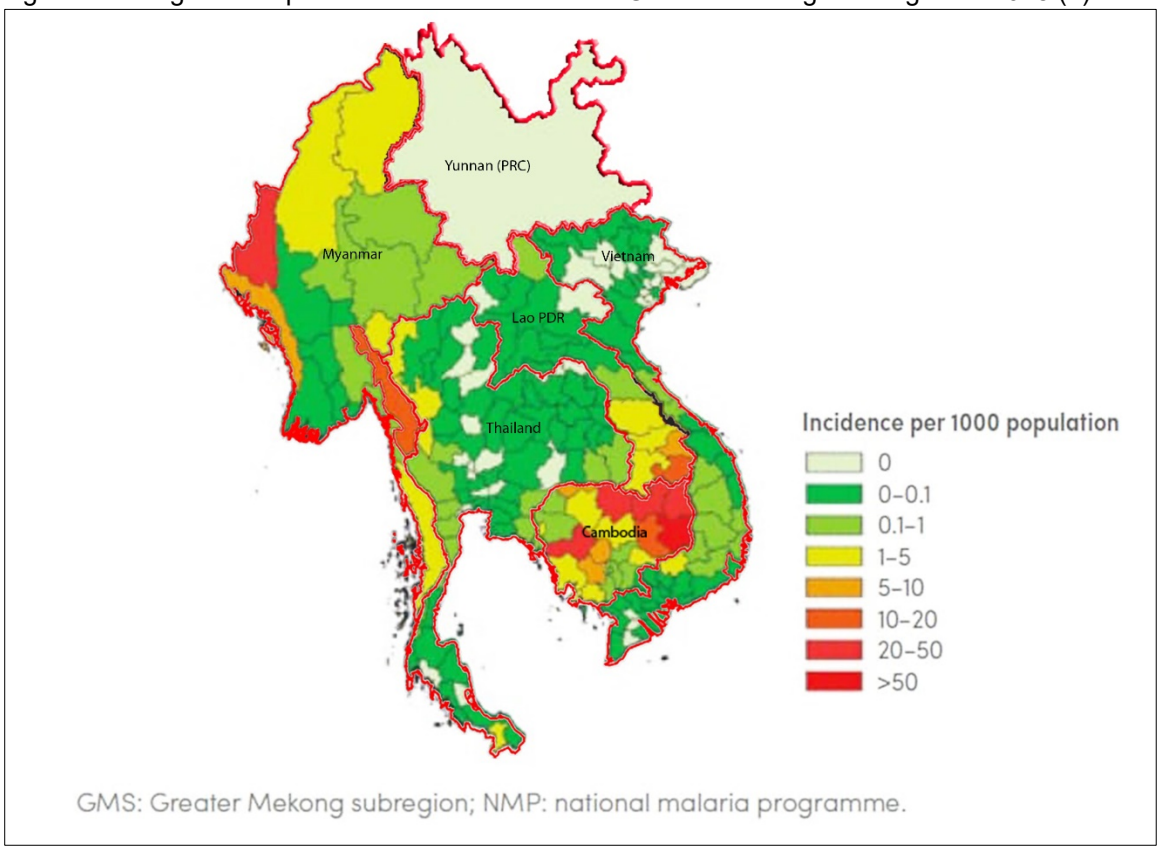
*Abbreviation: ITN, Increasing Insecticide-Treated Nets; ACT, Artemisinin-based Combination Therapy, RDT, Rapid Diagnostic Tests; SP, Sulphadoxine + Pyrimethamine; DP, Dihydroartemisinin plus Piperaquine; LLIN, Distribution of Long-Lasting Insecticidal Nets; IRS, Indoor Residual Spraying; SMC, Seasonal Malaria Chemoprevention*

## Malaria burden in Cambodia

Cambodia has been classified as an endemic malaria country since the first reported cases in the 1950s (19-21). A surveillance system to report malaria cases was not in place until 2004 (20, 21). The highest malaria incidence reported in Cambodia was more than 100,000 notifications, or 7.4 per 1000 population occurred in 2006 (22). Since 2006, malaria trends have fluctuated, with a dramatic reduction in 2019. In 2019, the malaria incidence rate was 1.9 cases per 1000 population, a reduction of 51% from 3.9 malaria cases per 1000 population in 2018 (22).

Although the incidence dropped significantly, Cambodia's malaria incidence of 3.9/1000 population in 2018 remained higher than the overall rate in its WHO Western Pacific Region of 2.6/1000 population in 2018 (2, 22). Cambodia's malaria incidence was also higher than the malaria incidence in its neighboring countries—Vietnam, Laos, and Thailand (Figure 4.2) (2).

Figure 4.2. Regional map of malaria incidence in the Greater Mekong Sub-region in 2018 (2)




*Note: the map is from the WHO's map in World Malaria Report 2019 (2)*

## RAI2 Intervention

In Cambodia, malaria vectors are predominantly located in forested areas along with the Thai, Vietnamese, and Laos borders (23-25). To date, there are no reported studies of interventions aimed at eliminating malaria transmission inside these forested areas.

The “Second-phase Regional Artemisinin-resistance Initiative (RAI2)” intervention aimed to block malaria transmission between forest goers; the initiative was launched in late August 2019. This project was funded by Global Fund and implemented by Institut Pasteur du Cambodge in collaboration with the National Centre for Parasitology Entomology and Malaria Control. The project was implemented in the Prey Lang forest, covering parts of two northeastern provinces, Kratie and Stung Treng. The RAI2 intervention hypothesized that the malaria incidence could be reduced through in-forest active mass screenings and treatment (MSAT) using a standard rapid diagnostic test (RDT) and RDT in combination with the distribution of a vector control kit— Long-lasting Insecticide Hammock-net and repellent. This was provided free-of-charge to all infected individuals inside the forest. Thirty-six forest malaria workers were employed by two partner organizations. These forest malaria workers spent five days and four nights per week in the forest to perform study activities. The project covered forest areas of about 1000 square kilometers, with an estimated 1800 forest-goers regularly entering the areas for their living.The RAI2 initiative aimed to compare malaria incidence trends in health centers located less than 30 kilometers from the intervention forest with malaria incidence in health centers neighboring forests in other provinces, where the RAI2 intervention was not implemented.

## RAI2 surveillance system

The “RAI2 surveillance system”, a malaria project-based surveillance system, was launched in late August 2019. This surveillance system’s primary objective was to contribute to evaluating the effectiveness of in-forest RAI2 interventions targeted at malaria elimination.

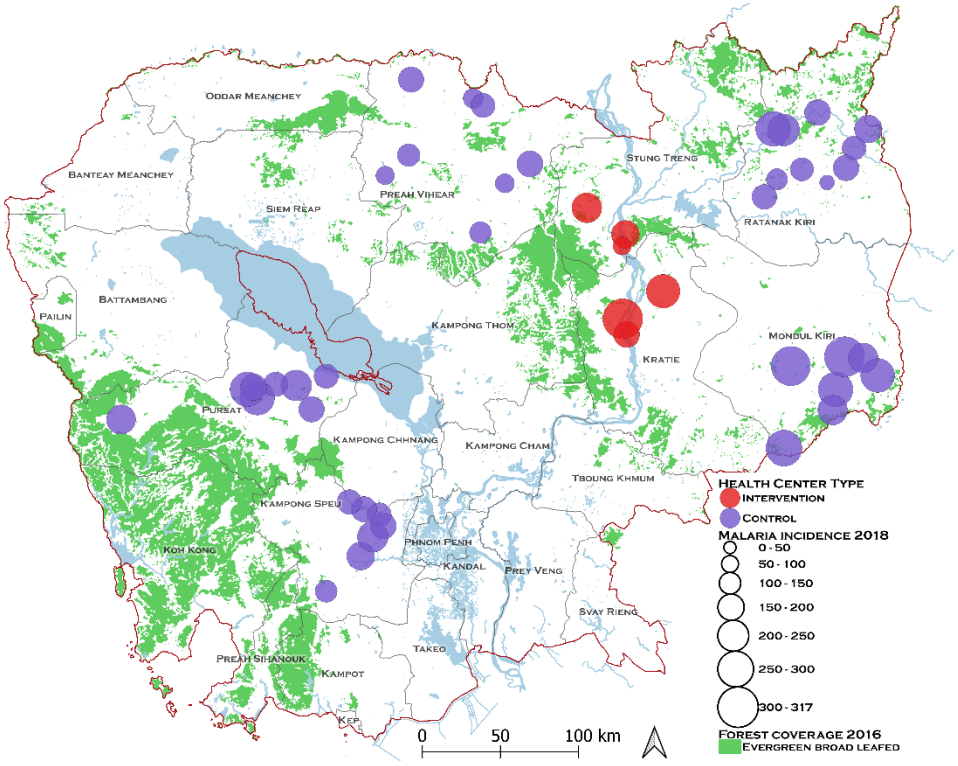
This surveillance system was designed to capture and notify all malaria cases testing positive (by RDT or microscopy), for *Plasmodium (p) falciparum*, *P*. *vivax*, or *Mixed* (having both *P. falciparum* and *P. vivax*). The period of data collection was 16 months, commencing September 2019 and concluding in December 2020. In collecting these data, malaria patients were interviewed when they met with health center staff to receive their malaria test results. A 27-item, tablet/smartphone-based questionnaire was used for

surveillance purposes. In addition to the test result, demographic data, history of prior malaria diagnosis, exposure to forested areas, knowledge and practice of malaria prevention, and exposure to malaria prevention intervention were also collected (annex 1). Some of our variables were the same as the variables collected by the routine Malaria Information System (MIS), including address, age, sex, type of diagnosis (RTD or Microscopy), and testing result (P. falciparum, P. vivax, or Mixed) (annex 2). However, MIS collected few variables that do not exist in our variables, such as severity (mild or severe), treatment (out-patient or in-patient), a drug used, referral status, recovery status, and pregnancy (annex 2). In contrast, we collected variables that do not exist in the MIS's form, including exposure to forested areas, knowledge, and practice of malaria prevention, and exposure to malaria prevention intervention.

The questionnaire was installed in the health centers' tablet provided by the National Centre for Parasitology Entomology and Malaria Control for its surveillance purpose. Some personal smartphones of health center staff were used in preference to the tablet, for greater flexibility. Kobo Toolbox, a free and open-source software, including an accessible server, was used to collect and submit data in the RAI2 surveillance system.

The system was implemented in 47 health centers - six intervention health centers and 41 control health centers (Figure 4.3). The six intervention health centers were all the eligible health centers in the two malaria-endemic provinces, Kratie and Stung Treng. The 41 control health centers were in the other five malaria-endemic provinces, Ratanak Kiri, Mondulkiri, Preah Vihear, Pursat, and Kampong Speu (Figure 4.3).

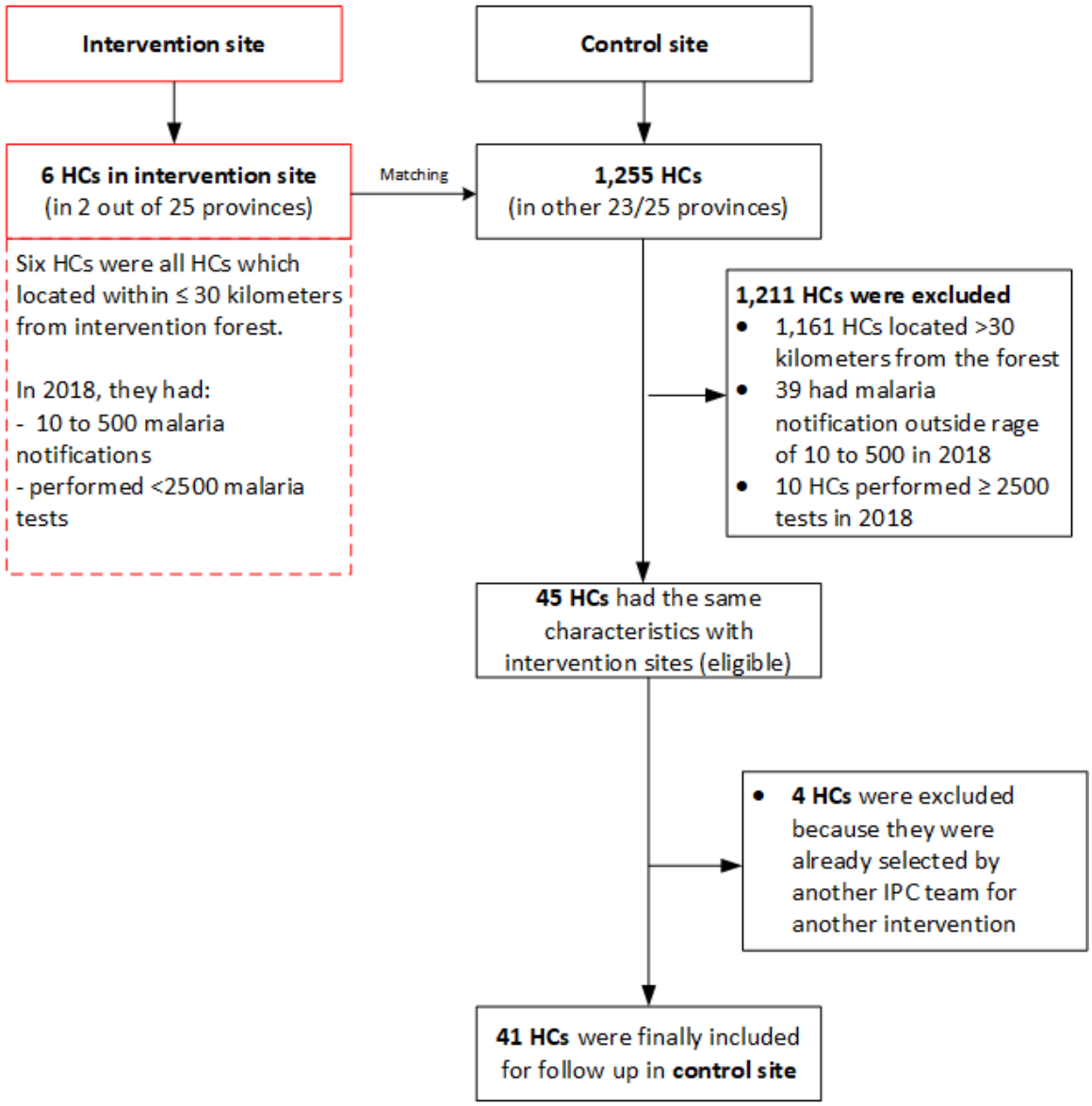
Figure 4.3. Map of intervention and control health centers in the RAI2 surveillance system, Cambodia 2019-2020




*Data source: Health Management Information System, Department of Planning Health Information (DPHI), Ministry of Health, 2018*

In the selection of intervention health centers, we established the following selection criteria: the health center (1) had between 10 and 500 *P. falciparum cases* in 2018, (2) where located less than 30 km from the forest, and (3) had less than 2500 malaria tests in 2018. We identified six health centers that met the selection criteria; all six health centers were selected as intervention sites The 41 control health centers were among 45 eligible health centers in the control site (Figure 4.4). The other four health centers out of 45 also met the above criteria, but they were not included because of administrative reasons. These four health centers were already selected for another intervention by another IPC team. Therefore, it could be burdened to the health centers if they were also chosen for RAI2. Between the two sites, all processes and questionnaires were the same, except there was a requirement to collect dried blood spots in all six intervention health centers and no such requirement in control health centers.

Figure 4.4 Diagram describing the selection of health centers for intervention and control sites in the early stage (2019), Cambodia

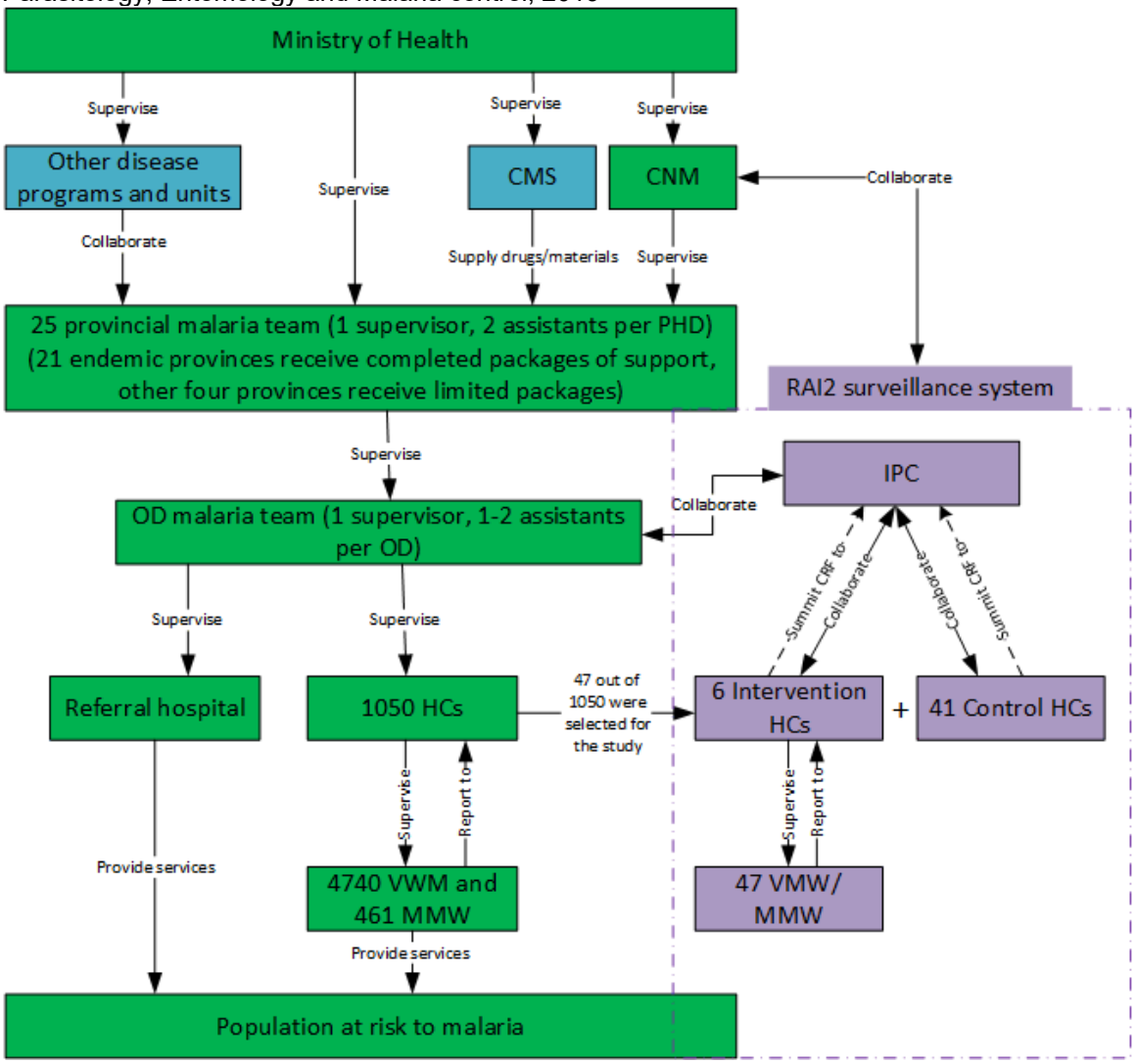



This system was nested into the national Malaria Information System (Figure 4.5). The RAI2 surveillance system was created and supervised by the Epidemiology and Public Health Unit at Institut Pasteur du Cambodge, with approval from the National Centre for Parasitology Entomology and Malaria Control. The research team at Institut Pasteur du Cambodge provided training to health center staff working for the Malaria Information System (MIS). We offered extra financial incentives to health center staff for their extra efforts in completing the surveillance form. In the intervention site, 3.5 USD was provided to health center staff for each interview and collection of blood samples using dried blood spots. In the control site, 2 USD was provided per interview only.

Although the RAI2 surveillance system was nested in MIS, enhanced data collection using the surveillance questionnaire was independent. The completed questionnaire was expected to be submitted to the Kobo Toolbox server on a monthly basis. However, staff could submit immediately after the interview, at the end of the day, at the end of the week, or at the end of the month, depending on access to the internet. At the end of the month, the staff at Institute Pasteur du Cambodia counted the number of cases (from completed questionnaires) and contacted the health center staff to pay them through money transfer agencies.

Staff of Institut Pasteur du Cambodge visited the health centers every two-to-three months to review the log-book and compare the number of malaria cases reported in health center registration books to the number notified to the Kobo Toolbox server. Remote communication with health workers responsible for surveillance activities was conducted through the Telegram™ App account group chat as needed. Individual phone calls were conducted to check if any issues had been identified and needed to be addressed.

Figure 4.5 Position of the RAI2 surveillance system within the structure of the National Centre for Parasitology, Entomology and Malaria control, 2019




Abbreviation: CMS, Central Medical Store; CNM, National Centre for Parasitology, Entomology and Malaria control; PHD, Provincial Health Department; OD, operational district; HC, health center; VMW, village malaria workers; MMW, mobile malaria worker; IPC, Institute Pasteur du Cambodia; CRF, case report form

## Resources

This was a funding dependent surveillance system for the life of the grant which discontinued in December 2020. The main cost associated with the RAI2 surveillance system was the case-based incentive, costs related to training, and ongoing supervision visits (Table 4.2).

Table 4.2. Expenditure for RAI2 project based surveillance system, Cambodia August 2019 - January 2021

| Items | Amount in USD |
|---|---|
| Training | 6,000 |

| | |
|---|---|
| Incentives for health center staff | 1,250 |
| Supervision (including staff's time, transportations, and per diem) | 10,700 |
| Total | 17,950 |

## Purpose of the evaluation

This project-based surveillance system was used to assess the effectiveness of the RAI2 interventions targeted at malaria elimination inside the forests. It was necessary to evaluate the system to ensure it was meeting its objective of capturing all malaria cases presenting to the health facilities in the RAI2 intervention and control areas. The sensitivity of the system was crucial to understanding the effectiveness of RAI2 interventions. We used the US Centers for Disease Control and Prevention (CDC) updated guidelines for evaluating public health surveillance systems (2001) (26) to guide our evaluation.

The specific objectives for the evaluation were:

1. To describe the usefulness of the RAI2 surveillance system.

2. To assess the simplicity, flexibility, acceptability, sensitivity, data quality, and timeliness, and stability of the RAI2 surveillance system.

3. To use findings to improve the implementation of the RAI2 surveillance system.

## Scope of evaluation

According to the US CDC guideline, a surveillance system should be assessed using ten attributes: simplicity, flexibility, acceptability, sensitivity, usefulness, data quality, timeliness, representativeness, positive projective value, and stability (26). These ten attributes are defined in Table 4.3 below.

Table 4.3. The standard definition of surveillance system attributes, according to the US CDC guide (26)

| Surveillance attribute | Definition |
|---|---|
| Simplicity | *Refers to both its structure and ease of operation. Surveillance systems should be as simple as possible while still meeting their objectives.* |
| Flexibility | *Ability to adapt to changing information needs or operating conditions with little additional time, personnel, or allocated funds* |
| Acceptability | *Reflects the willingness of persons and organizations to participate in the surveillance system* |
| Sensitivity | *Refers to the proportion of cases of a disease (or other health-related events) detected by the surveillance system* |
| Usefulness | *Does the system contribute to the prevention and control of adverse health-related events? The system can also be useful if it helps to identify other adverse health events.* |
| Data quality | *Reflects the completeness and validity of the data recorded in the public health surveillance system* |
| Timeliness | *The surveillance system ensures early detection of disease patterns above stipulated alert thresholds, facilitating a timely response and intervention. Examines the speed between steps in the surveillance system* |
| Representativeness [a] | *Accurately describes the occurrence of the event over time and its distribution in the population by person and place.* |
| Positive predictive value | *Proportion of reported cases that have the health-related event under surveillance* |
| Stability | *Refers to the reliability (i.e., the ability to collect, manage, and provide data properly without failure) and availability (the ability to be operational when it is needed) of the public health surveillance system* |

*[(a)] The attribute was not assessed in this evaluation*

There were some limitations in our evaluation that limited our scope. First, representativeness, defined as an accurate description of the event over time and its distribution in the population by person and place, was not assessed. To our best knowledge, there is no available data to evaluate representativeness. To evaluate the RAI2 surveillance system's representativeness, we would need to determine if the incidence of malaria captured by the RAI2 surveillance system reflects the actual malaria incidence in the catchment area. This was beyond the scope of this evaluation. Second, the definition of sensitivity in our evaluation was modified. The US CDC guide defines the sensitivity of a surveillance system as the proportion of all cases of a disease detected by the surveillance system (26). Due to the resource-constraints, we restricted the definition to the proportion of malaria cases that visited selected health centers and were notified through the RAI2 surveillance system. Third, the positive predicted value (PPV) is defined as the proportion of reported cases that actually have the health-related event under surveillance (26); due to logistical and resource constraints, this was assessed in the six intervention health centers only as they were collecting the additional blood specimens.

## Engaging stakeholders

The data collected was primarily used by the research team at Institute Pasteur du Cambodia to evaluate the RAI2 intervention. Key stakeholders at the Institute Pasteur du Cambodia team and the health center staff implementing the surveillance system were engaged in this evaluation. The principal investigator and relevant staff were consulted on the evaluation design and key indicators.

## Methodology

A quantitative method was used in this evaluation, including an online stakeholder survey and an analysis of the RAI2 surveillance system data. The data collection took place between 18 December 2019 and 24 January 2020.

Usefulness was described based on the outcome of evaluating the eight attributes of a surveillance system, as defined by the US CDC (26). Simplicity, flexibility, acceptability, and stability were assessed based on the health center head and health center staff's opinions through a short online survey. Sensitivity, PPV, data quality, and timeliness were assessed using document review and data of the RAI2 surveillance system extracted from the Kobo Toolbox server.

We sent the focal staff an online form through the Telegram™ App personal account. They were first approached through an initial phone call in which they were invited to participate prior to sending the link to the e-Survey. The Telegram™ App was chosen by Cambodia's government as a communication channel; therefore, the majority of government staff have a Telegram™ App account.

The questionnaire was created based on consultation with the RAI2 study team for the specific purpose of improving the implementation of the intervention. The questionnaire was provided in the Khmer language and consisted of questions about demographics data, simplicity, flexibility, acceptability, stability, and data quality. These questions had not been previously validated.

### Data analysis

Survey data were downloaded from the Kobo Toolbox server, and a descriptive analysis was performed to describe each indicator of interest under the relevant attribute.

Since our goal is to see whether data in each site is reliable enough to evaluate the effect of the intervention, we stratified the results into intervention and control sites. By so doing, we will be able to recommend whether the data is reliable enough to evaluate the effectiveness of RAI2 intervention.

### Ethics

The study protocol and tools were not submitted to the National Ethics Committee for Health Research (NECHR) for review and approval. This evaluation was for internal quality improvement only, and it is also covered under the Australian National University's blanket ethics waiver for surveillance evaluations (2017/909). Participation in the study was completely voluntary, and anticipated risk for participants was minimal. The study participants were informed that they were able to refuse or discontinue their participation at any time for any reason and without any consequences.

## Results

### Summary of RAI2 surveillance data

Characteristics of patients reported through the RAI2 surveillance system are described in Table 4.4. Between 1 September 2019 and 30 January 2020, 765 malaria cases were interviewed with 12.4% (n=95) *P. falciparum*, 86.3% (n=660) *P. vivax*, and 1.3% (n=10) *Mixed*.

Overall, the majority of the patients (82.1%, n=628/765) were male. The median age was 24 years (interquartile range – IQR, 17-33 years), 91.6% (n=701/765) were residents who had been living in their current village for more than a year at the time of interview (Table 4.4).

The three most frequent symptoms reported by patients were headache (94.9%, n=665/765), fever (83.7%, n=587/765), and body pain (61.1%, n=428/765) (Table 4.4).

The RDT was used to test most patients (93.3%, n=714/765), while the other 6.7% (n=51/765) were tested by microscopy (Table 4.4).

Table 4.4. Characteristics of patients reported through the RAI2 surveillance system, 1 September 2019 to 30 January 2020, Cambodia

| Variable | Total (N=765) | *P. falciparum* (N=95) | *P. vivax* (N=660) | *Mixed* (N=10) |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | n (%) |
| Sex | | | | |
| Female | 137 (17.9) | 16 (16.8) | 121 (18.3) | 0 (0.0) |
| Male | 628 (82.1) | 79 (83.2) | 539 (81.7) | 10 (100.0) |
| Age in year | | | | |
| Median (IQR) | 24 (17-33) | 30 (19-40) | 23 (16-32) | 23.5 (18-28) |
| <5 | 30 (3.9) | 2 (2.1) | 28 (4.2) | 0 (0.0) |
| 5-14 | 106 (13.9) | 12 (12.6) | 93 (14.1) | 1 (10.0) |
| 15-24 | 267 (34.9) | 25 (26.3) | 238 (36.1) | 4 (40.0) |
| 25-34 | 189 (24.7) | 18 (19.0) | 167 (25.3) | 4 (40.0) |
| 35-49 | 135 (17.7) | 30 (31.6) | 104 (15.8) | 1 (10.0) |
| >=50 | 38 (5.0) | 8 (8.4) | 30 (4.6) | 0 (0.0) |
| Resident status (period stayed in current village) | | | | |
| Mobile (<6 months) | 30 (3.9) | 2 (2.1) | 27 (4.1) | 1 (10.0) |
| Migrant (6-12 months) | 34 (4.4) | 4 (4.2) | 30 (4.6) | 0 (0.0) |
| Local (>12 months) | 701 (91.6) | 89 (93.7) | 603 (91.4) | 9 (90.0) |
| Symptoms[§] | | | | |
| Fever | 587 (83.7) | 65 (79.3) | 514 (84.3) | 8 (88.9) |
| Headache | 665 (94.9) | 79 (96.3) | 577 (94.6) | 9 (100.0) |
| Vomiting | 162 (23.1) | 26 (31.7) | 134 (22.0) | 2 (22.2) |
| Diarrhoea | 58 (8.3) | 9 (11.0) | 49 (8.0) | 0 (0.0) |
| Cough | 95 (13.6) | 15 (18.3) | 80 (13.1) | 0 (0.0) |
| Nausea | 137 (19.5) | 25 (30.5) | 111 (18.2) | 1 (11.1) |
| Body pain | 428 (61.1) | 50 (61.0) | 372 (61.0) | 6 (66.7) |
| Type of test kit used | | | | |
| Microscopy | 51 (6.7) | 12 (12.6) | 38 (5.8) | 1 (10.0) |
| RDT | 714 (93.3) | 83 (87.4) | 622 (94.2) | 9 (90.0) |
| The patient provided the phone number to the health center staff | | | | |
| Yes | 247 (32.4) | 37 (39.0) | 206 (31.3) | 4 (40.0) |
| Patients did not have a phone number | 347 (45.5) | 37 (39.0) | 308 (46.8) | 2 (20.0) |
| Staff did not ask for a phone number | 79 (10.4) | 7 (7.4) | 72 (10.9) | 0 (0.0) |
| Patients refused to give phone number | 90 (11.8) | 14 (14.7) | 72 (10.9) | 4 (40.0) |

Abbreviation: IQR, Interquartile Range; RDT, Rapid Diagnostic Test; ([§]) multiple symptoms were captured for each patient interviewed.

As shown in Table 4.5, almost two-third (60.4%, n=462/765) of patients interviewed had previously tested positive for malaria (either *P.faciparum or P. vivax*). The median time interval between the current positive status and previous positive status was three months, with an interquartile range between 2 and 8 months.

Approximately 64% (n=493/765) reported they had visited a forest in the past 12 months (Table 4.5). When we stratified by species, the proportion of patients that reported having visited the forests in the past 12 months and had tested positive for *P. falciparum* was 70.5% (n=67/95) compared to 63.3% (n=418/660) *P. vivax*. When we shortened the timeframe to the past three weeks, 88.1% (n=59/67) and 75.8% (n=317/418) of *P. falciparum* and *P. vivax* patients reported having visited the forest, respectively.

Table 4.5 : Reported risk factors and prior history of malaria infection in patients captured through the RAI2 surveillance system, 1 September 2019 to 30 January 2020, Cambodia

| Variable | Total (N=765) | *P. falciparum* (N=95) | *P. vivax* (N=660) | *Mixed* (N=10) |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | n (%) |
| Ever had malaria before | | | | |
| No | 303 (39.6) | (50.5) | 253 (38.3) | 2 (20.0) |
| Yes | 462 (60.4) | 47 (49.5) | 407 (61.7) | 8 (80.0) |
| Periods from the current positive test to the last malaria episode | | | | |
| Median in months (IQR) | 3 (2-8) | 6 (3-12) | 3 (2-8) | 2.5 (1.5-3) |
| Less than one year | 409 (88.5) | 37 (78.7) | 365 (89.7) | 7 (87.5) |
| More than one year | 53 (11.5) | 10 (21.3) | 42 (10.3) | 1 (12.5) |
| Place of last malaria treatment (before the current one) | | | | |
| Private clinic | 97 (21.0) | 10 (21.3) | 86 (21.1) | 1 (12.5) |
| Public clinic | 381 (82.5) | 36 (76.6) | 339 (83.3) | 6 (75.0) |
| Village Malaria Worker | 91 (19.7) | 8 (17.0) | 80 (19.7) | 3 (37.5) |
| Ever visited any forest in the past 12 months | | | | |
| No | 272 (35.6) | 28 (29.5) | 242 (36.7) | 2 (20.0) |
| Yes | 493 (64.4) | 67 (70.5) | 418 (63.3) | 8 (80.0) |
| (If yes to previous) ever visited the forest in the last three weeks (n=493) | | | | |
| No | 111 (22.5) | 8 (11.9) | 101 (24.2) | 2 (25.0) |
| Yes | 382 (77.5) | 59 (88.1) | 317 (75.8) | 6 (75.0) |
| Visited intervention forest or Prey Lung (from six health centers in intervention areas only) | | | | |
| No, but other forests | 46 (51.7) | 11 (57.9) | 35 (51.5) | 0 (0.0) |
| Yes | 43 (48.3) | 8 (42.1) | 33 (48.5) | 2 (100.0) |
| Number of nights spent in the forest (past three weeks) | | | | |
| Zero | 4 (1.1) | 0 (0.0) | 4 (1.3) | 0 (0.0) |
| 1 | 104 (27.2) | 19 (32.2) | 85 (26.8) | 0 (0.0) |
| 2-7 | 186 (48.7) | 22 (37.3) | 161 (50.8) | 3 (50.0) |
| >7 | 88 (23.0) | 18 (30.5) | 67 (21.1) | 3 (50.0) |
| Type of housing during the stay in the forest | | | | |
| Thatched grass | 50 (13.2) | 3 (5.1) | 47 (14.9) | 0 (0.0) |
| Sago palm leaves | 5 (1.3) | 0 (0.0) | 5 (1.6) | 0 (0.0) |
| Bamboo | 24 (6.3) | 5 (8.5) | 19 (6.0) | 0 (0.0) |
| Iron sheet | 66 (17.4) | 3 (5.1) | 62 (19.6) | 1 (20.0) |
| Wood | 36 (9.5) | 3 (5.1) | 33 (10.4) | 0 (0.0) |
| Tent | 158 (41.6) | 27 (45.8) | 128 (40.5) | 3 (60.0) |
| Hammock | 229 (60.3) | 39 (66.1) | 186 (58.9) | 4 (80.0) |
| No house | 38 (10.0) | 6 (10.2) | 32 (10.1) | 0 (0.0) |

Abbreviation: IQR, Interquartile Range

As presented in Table 4.6, of all patients who visited forests in the previous 12 months, 22.5% (n=111/493) reported they had met forest malaria workers inside forests. Forest malaria workers provided two common items to forest goers, including testing for malaria

(70.3%, n=78/111) and education on malaria prevention (55.9%, n=62/111). Forest goers used multiple methods to prevent themselves from malaria infection. The most commonly used method was insecticide-treated nets (80.9%, n=385/493), followed by insecticide-treated hammocks (64.3%, n=306/493) and wearing long-clothes (58.8%, n=280/493). Using repellent was the least commonly used method (12.2%, n=58/493).

Patients reported that they mainly learned about malaria prevention through their family/friends (67.5%, n=495/765), followed by radio (54.2%, n=397/765) and television (47.2%, n=346/765) (Table 4.6).

Table 4.6: Prior contact with malaria workers, knowledge on prevention strategies and source of information reported by patients captured through the RAI2 surveillance system, 1 September 2019 to 30 January 2020, Cambodia

| Variable | Total (N=765) | *P. falciparum* (N=95) | *P. vivax* (N=660) | *Mixed* (N=10) |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | n (%) |
| (If yes to forest visit) Ever met forest malaria worker inside the forest (past 12 months) (n=493) | | | | |
| No | 382 (77.5) | 47 (70.2) | 331 (79.2) | 4 (50.0) |
| Yes | 111 (22.5) | 20 (29.9) | 87 (20.8) | 4 (50.0) |
| Items provided by the forest malaria worker | | | | |
| Testing for malaria | 78 (70.3) | 13 (65.0) | 61 (70.1) | 4 (100.0) |
| Treatment for malaria | 32 (28.8) | 7 (35.0) | 25 (28.7) | 0 (0.0) |
| Malaria protection kits | 34 (30.6) | 3 (15.0) | 29 (33.3) | 2 (50.0) |
| Education on how to prevent malaria | 62 (55.9) | 8 (40.0) | 51 (58.6) | 3 (75.0) |
| None of the above | 16 (14.4) | 4 (20.0) | 12 (13.8) | 0 (0.0) |
| Measures heard of being used to prevent malaria (n=493) | | | | |
| Insecticide-treated nets | 385 (80.9) | 44 (66.7) | 337 (83.4) | 4 (66.7) |
| Insecticide-treated hammocks | 306 (64.3) | 50 (75.8) | 252 (62.4) | 4 (66.7) |
| Long clothes | 280 (58.8) | 33 (50.0) | 244 (60.4) | 3 (50.0) |
| Using repellent | 58 (12.2) | 7 (10.6) | 51 (12.6) | 0 (0.0) |
| Bonfire for smoke | 233 (49.0) | 35 (53.0) | 195 (48.3) | 3 (50.0) |
| Source of receiving malaria prevention information | | | | |
| Family/friends | 495 (67.5) | 56 (60.9) | 435 (68.7) | 4 (50.0) |
| Local NGO | 234 (31.9) | 31 (33.7) | 201 (31.8) | 2 (25.0) |
| Television | 346 (47.2) | 39 (42.4) | 305 (48.2) | 2 (25.0) |
| Radio | 397 (54.2) | 60 (65.2) | 333 (52.6) | 4 (50.0) |
| Campaign in my region | 308 (42.0) | 36 (39.1) | 266 (42.0) | 6 (75.0) |

*Abbreviation: NGO, Non-governmental Organization*

## Attributes of the RAI2 surveillance system

### *Characteristics of respondents*

A link to the online survey form was sent to 47 health center staff, and 70.0% (n=33/47) completed and submitted the form. One hundred percent (n=6/6) of focal health center staff in the intervention sites and 65.8% (n=27/41) in the control sites completed the form. Of 33 respondents, 54.6% (n=18/33) were the head of the health center, and 45.5% (n=15/33) were general health staff.

### *Simplicity*

According to the US CDC, simplicity refers to both the structure of the system and ease of operation. Surveillance systems should be as simple as possible while still meeting their objectives (26).

We assumed that the study team and implementers at the health center would benefit from using an electronic smartphone-based questionnaire (Kobo Toolbox). The proposed benefit was the ability to do direct data entry at the interview time, removing the need for health center staff to spend additional time entering data. The inclusion of skip logic made the interview process easier, removing irrelevant questions based on the previous answer. It was anticipated that using an electronic data collection system would reduce workload and additional time burdens on health center staff compared to using a paper-based questionnaire. It was anticipated that the study team would also reduce the time and expenses associated with traveling to the data collection sites to collect paper forms.

**Key finding:**

- The RAI2 surveillance system was simple for a large portion of users overall.

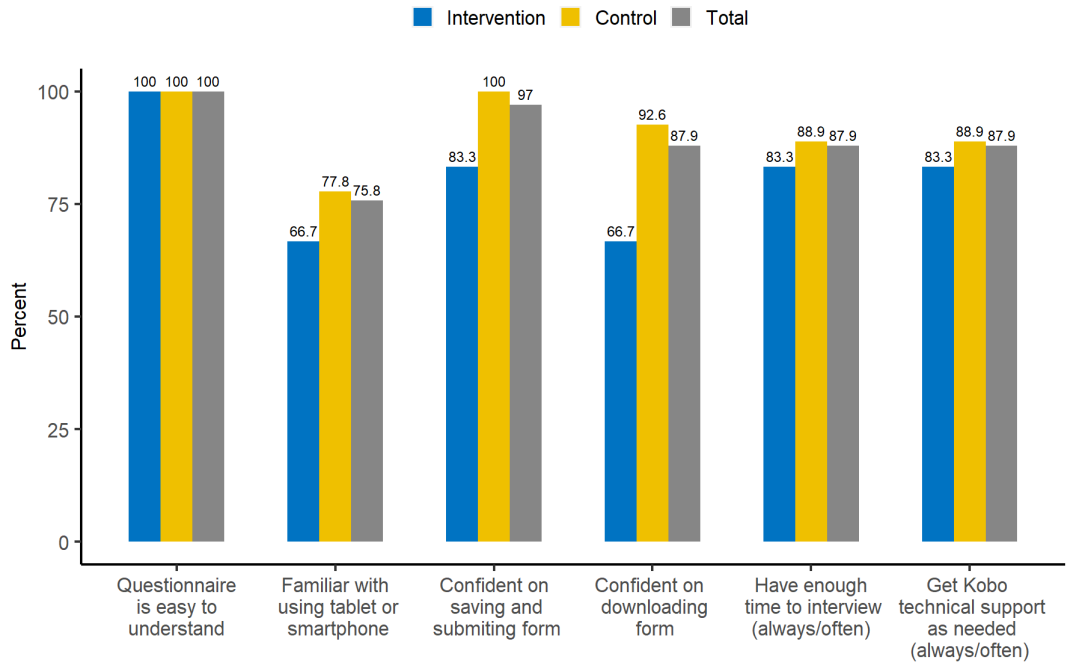
All users (n=33/33, 100%) rated the questionnaire simple/very simple from the evaluation survey results. Users were confident in saving and submitting completed forms, 97.0% (n=32/33) (Figure 4.6).

Of the total, 87.9% (n=29/33) rated they were confident with downloading the form, 87.9% (n=29/33) reported that they always had or often had enough time to interview patients,

and 87.9% (n=29/33) also agreed that they could always or often get technical support from Institute Pasteur du Cambodia team as needed.

The similarity in the proportion of users positively rating the simplicity variables was seen between intervention and control sites.

Figure 4.6. Indicators of the simplicity of the RAI2 surveillance system in Cambodia, Sep 2019 to Jan 2019



*Flexibility*

We assessed flexibility on whether users could choose to use a tablet/smartphone or a paper-based questionnaire. We also assessed users' preference for each method, whether they prefer any one of these or mixed. From the study team's perspective, using an electronic questionnaire made it very easy to add or remove variables from the questionnaire if required.

**Key findings:**

- Users had the ability to select the data entry tool, an electronic form using a tablet/smartphone or a paper-based questionnaire, reflecting the RAI2 surveillance system was flexible.
- There was a stronger preference for using the electronic-based questionnaire in intervention sites than in the control site.

Table 4.7 presents the indicators for assessing the flexibility of the RAI2 surveillance system. Approximately, 42.4% (n=14/33) reported using a tablet only, 42.4% (n=14/33) used smartphone only, and 15.4% (n=4) used both tablet and smartphone. Of the total respondents, 81.3% (n=26) reported having paper-based questionnaires in their health centers, which they used when necessary. These findings were similar between intervention and control sites.

However, 51.5% (n=17/33) said they preferred using tablet/smartphone-based over paper-based questionnaire while 45.5% (n=15/33) prefer having both electronic and paper-based questionnaires. A stronger preference for using tablet/smartphone-based questionnaire was seen in intervention site (83.3%, n=5/6) compared to 44.4% (n=12/27) in control site.

Table 4.7 Indicators of RAI2 surveillance system flexibility, Aug 2019-Jan 2020, in Cambodia

| Variable | Total (N=33) | Intervention (N=6) | Control (N=27) |
|---|---|---|---|
| | n (%) | n (%) | n (%) |
| Use a tablet or smartphone for interviewing | | | |
| Tablet | 14 (42.4) | 2 (33.3) | 12 (44.4) |
| Phone | 14 (42.4) | 3 (50.0) | 11 (40.7) |
| Both | 5 (15.2) | 1 (16.7) | 4 (14.8) |
| Number of devices which Kobo have been stalled in your health center | | | |
| One | 26 (78.8) | 4 (66.7) | 22 (81.5) |
| Two | 7 (21.2) | 2 (33.3) | 5 (18.5) |
| Paper-based questionnaire available in your health center | | | |
| Yes | 27 (81.8) | 5 (83.3) | 22 (81.5) |
| No | 6 (18.2) | 1 (16.7) | 5 (18.5) |
| Prefer using an electronic or paper-based questionnaire | | | |
| Paper-based | 1 (3.0) | 1 (16.7) | 0 (0.0) |
| Tablet/smartphone | 17 (51.5) | 5 (83.3) | 12 (44.4) |
| Both | 15 (45.5) | 0 (0.0) | 15 (55.6) |

### *Acceptability*

This evaluation focused on the acceptability of design and incentive from the perspective of health center staff responsible for data collection.

**Key findings:**

- Users favorably accepted a smartphone/tablet-based form designed.
- The financial incentive used as a means to motivate users to interview malaria patients for the RAI2 surveillance system was not well accepted.
- Health center staff were supported by the health center head to spend time on data collection for the RAI2 surveillance system.

As shown in Figure 4.7, Kobo was accepted as an appropriate platform to be used by health centers by 90.9% (n=30/33) of respondents. A high proportion of respondents (93.9%, n=31/33) reported they were supported by the health center head to spend time on data collection for the RAI2 surveillance system. In addition, 84.9% (n=28/33) reported that another staff was willing to help when they were on leave.

The financial incentive was not well accepted. The incentive provided was 2 USD per interview at a control site where dried blood collection was not required, and 3.5 USD per

interview at the intervention site where dried blood collection was required. Only 40.7% (n=11/27) of all respondents at the control site, and 50.0% (n=3/6) of all respondents at the intervention site, indicated that the incentive was appropriate. When asked to nominate an acceptable amount for the incentive, the average amount was 4.0 USD, with a standard deviation of 1.2 USD at the control site and an average of 5 USD with a standard deviation of 2.9 USD at the intervention sites.

Figure 4.7. Indicators of acceptability of RAI2 surveillance system in Cambodia, Sep 2019 to Jan 2020

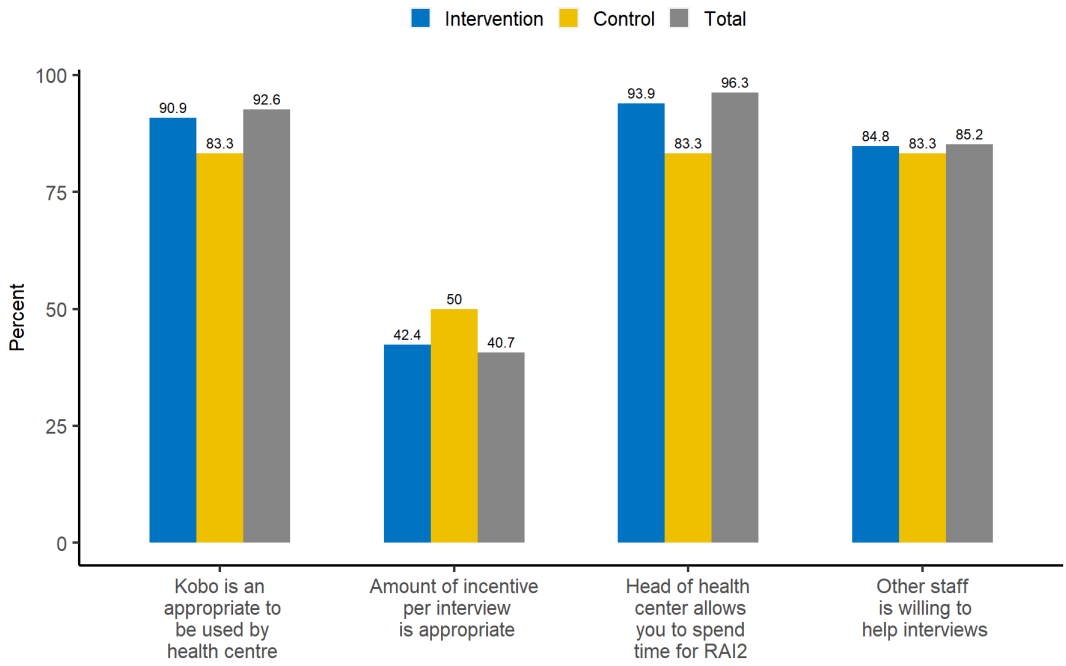
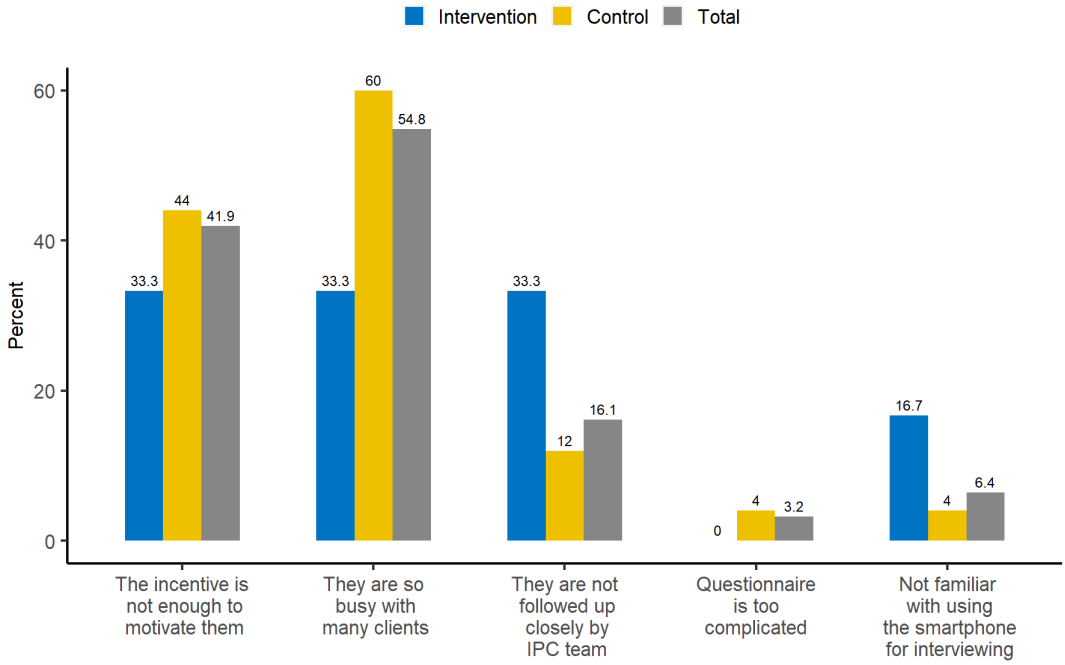



Figure 4.8 summarizes the common reasons why not all RAI2 surveillance questionnaires were completed, even when they had patients testing positive for malaria at the health center. The most common reason was they were busy with many clients (54.8%. n=17/31), and the incentive was not enough to motivate them (41.9%, n=13/31).

Figure 4.8. Perception of reasons for not interviewing the patients, Aug 2019 to Jan 2019




*Stability*

Stability refers to the reliability (i.e., the ability to collect, manage, and provide data properly without failure) and availability (the ability to be operational when needed) of the public health surveillance system (26). We assessed whether users could use the Kobo form every time needed, and users could always or almost always access the internet as needed.

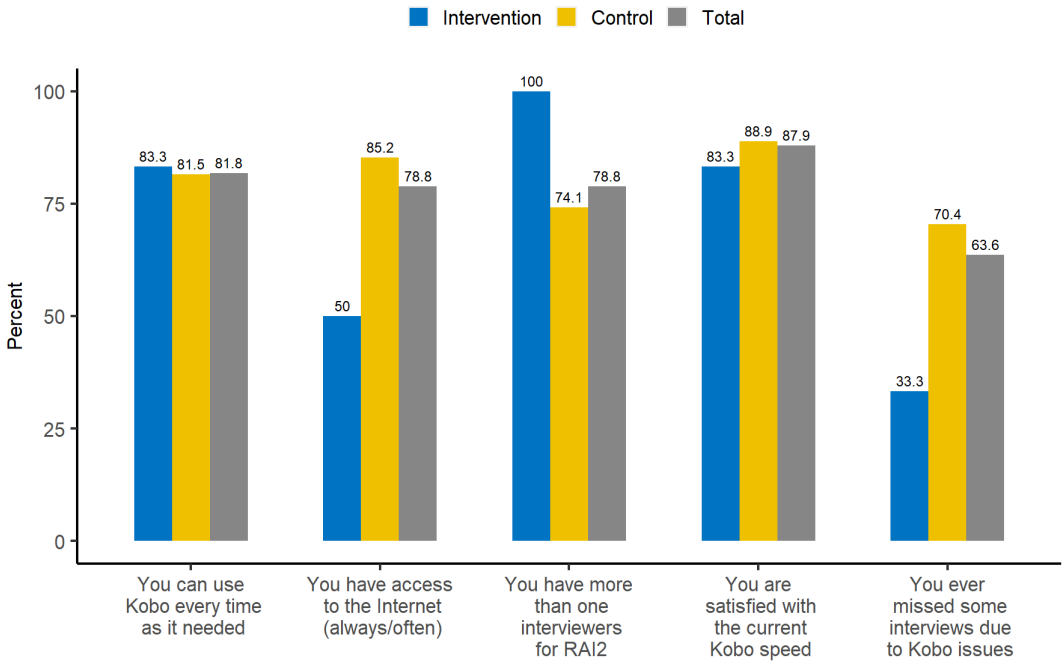
**Key findings:**

- The RAI2 surveillance system was reasonably stable despite reported issues, including tablet unavailability, and no staff replacement when the focal staff was absent.
- The RAI2 surveillance system's stability was more stable in the intervention site than in the control site.

Of all 33 users interviewed, 81.8% (n=27) reported they could use Kobo when needed, and 78.8% (n=26/33) always had access to the internet (Figure 4.9). Of the total, 78.8% (n=26/33) reported they had more than one staff who knew how to complete the RIA2

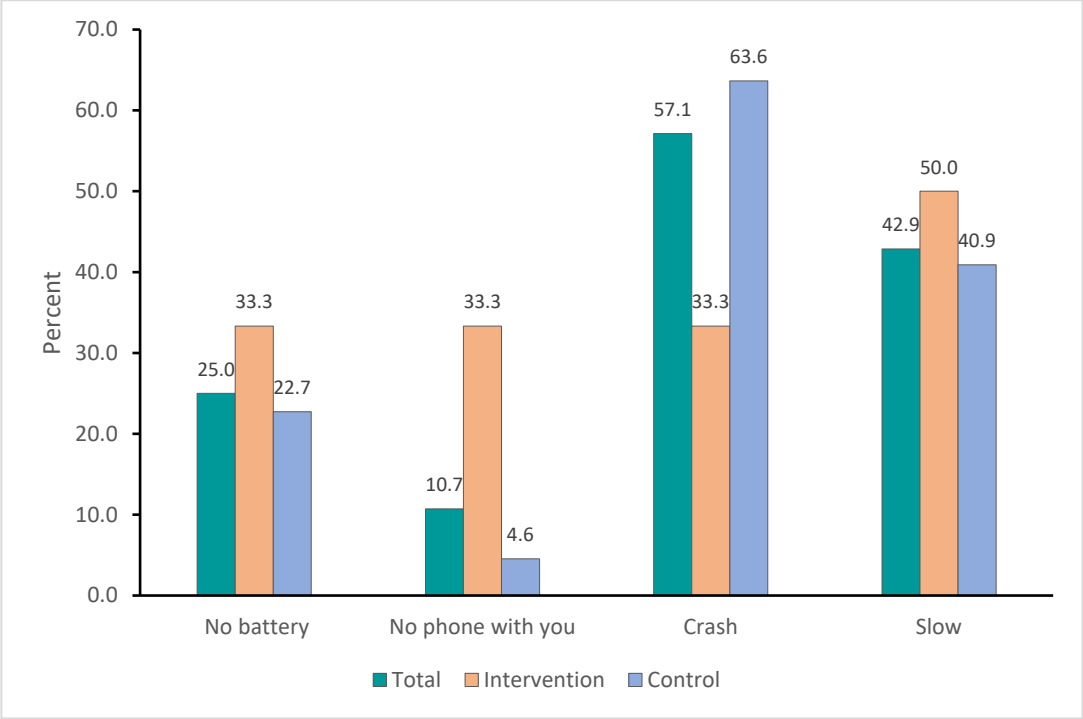
surveillance system's data collection. In the intervention sites, 100% (n=6/6) had at least one staff who knew how to complete the form compared to only 74.1% in the control site.

Figure 4.9. Indicators of stability of RAI2 Surveillance System in Cambodia, Aug 2019 to Jan 2020




In addition, we also accessed the reasons for missing interviews. Approximately 63.6% (n=21/33) reported they had ever missed some interviews due to issues associated with Kobo. The common Kobo related issues included system crashing (57.1%, n=16/33), and the system ran too slow (42.9%, n=12/33) (Figure 4.10).

Figure 4.10.Commonly identified issues with the use of Kobo Toolbox for data capture in a project-based surveillance system s, Aug 2019 to Jan 2020




*Sensitivity*

In this evaluation, sensitivity was defined as the proportion of malaria patients registered in the health center's log-book and notified in the RAI2 surveillance system. The sensitivity equals A/(A+B) where A was the malaria cases in the health center log-book notified to the RAI2 surveillance system, B was the malaria cases in the health center's log-book which were not notified to the RAI2 surveillance system.

**Key findings:**

- The sensitivity of the RAI2 surveillance system was low.

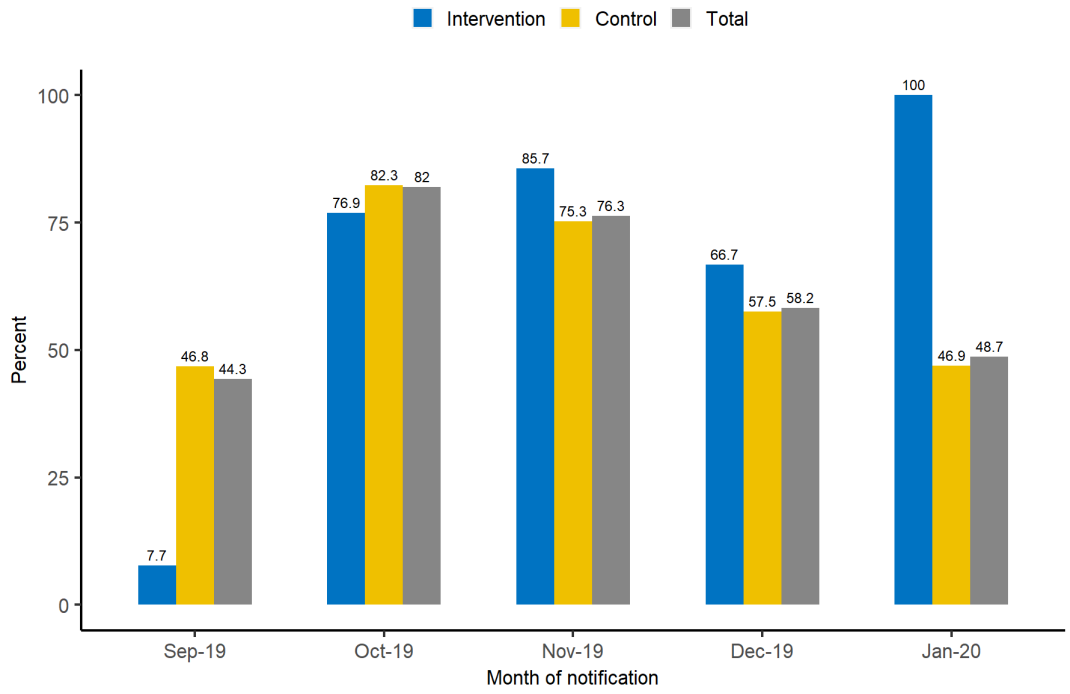
Overall, the sensitivity was 62.3% (n=599/961) between September 2019 and January 2020 (Table 4.8). The sensitivity was similar in the intervention and the control site (64.2% vs. 62.2%, respectively).

Table 4.8. The proportion of malaria patients entered into the RAI2 surveillance system among total cases reported at the health center, Sep 2019 – Jan 2020

| | Malaria cases in health centers' log-book | | |
|---|---|---|---|
| | Total | Intervention | Control |
| Number of cases notified to the RAI2 Surveillance System (A) | 599 | 43 | 556 |
| Number of cases not notified to the RAI2 Surveillance System (B) | 362 | 24 | 338 |
| Sensitivity (A/ (A+B)) | 62.3% | 64.2% | 62.2% |

Overall, the sensitivity improved over time from 44.3% in September 2019 to 82.0% in November 2019 but dropped to 58.2% in December 2019 and 48.7% in January 2020 (Figure 4.11).

Figure 4.11. The proportion of malaria patients entered into the RAI2 surveillance system among total cases reported at the health center by month, September 2019- January 2020




## *Positive predictive value*

Under the RAI2 surveillance system, six intervention health centers were asked to use dried blood spots to collect additional blood for Polymerase Chain Reaction (PCR) to identify Plasmodium strain and treatment failure. Taking this opportunity, we used data from these six health centers to estimate the Positive predictive value (PPV). The PPV equals A/A+B+C, where A is confirmed cases by PCR, B is the negative case by PCR, and C is positive for other species.

**Key findings:**

- The positive predictive value was noticeably 100% for *P. falciparum* and 100% for *P. vivax.* However, the finding was highly unreliable due to the small sample size.

As shown in Table 4.9, nine patients tested positive for *P. falciparum* by RDT at intervention health centers. Of these, 100.0% (n=9/9) were confirmed having *P. falciparum* by PCR. However, two of nine were also detected positive for both *P. falciparum* and *P.vivax*. From the same health centers, 25 patients tested positive for *P. vivax*, of which 100.0% (n=25/25) were confirmed to have *P. vivax* by PCR, and four of them (4/25) were also positive for both *P. falciparum* and *P.vivax.* RDT is likely to have limited ability to correctly capture the species when a patient has mixed Plasmodium. We recommend exercising caution in interpreting these findings due to the small sample size.

Table 4.9. Positive Predictive Value (PPV) of the RAI2 surveillance system, at the six intervention health centers, Cambodia, September 2019 to January 2020.

| | Total (A+B +C) | *P. falciparum* by PCR (A) | *P.vivax* by PCR (B) | *Mixed* by PCR (C) | PPV A/ (A+B+C) |
|---|---|---|---|---|---|
| *P. falciparum* notified to the RAI2 surveillance system | 9 | 7 | 0 | 2 | 100.0.0% |
| *P. vivax* notified to the RAI2 Surveillance System | 25 | 0 | 21 | 4 | 100.0% |

### *Timeliness*

In our context, we considered data collection and reporting timely if the month of the interview and month of form submission was the same. Of all forms uploaded through the RAI2 surveillance system, 87.7% (n=671/765) were submitted on time; 93.3% (n=111/119) in intervention site, and 86.7% (n= 560/646) in control site.

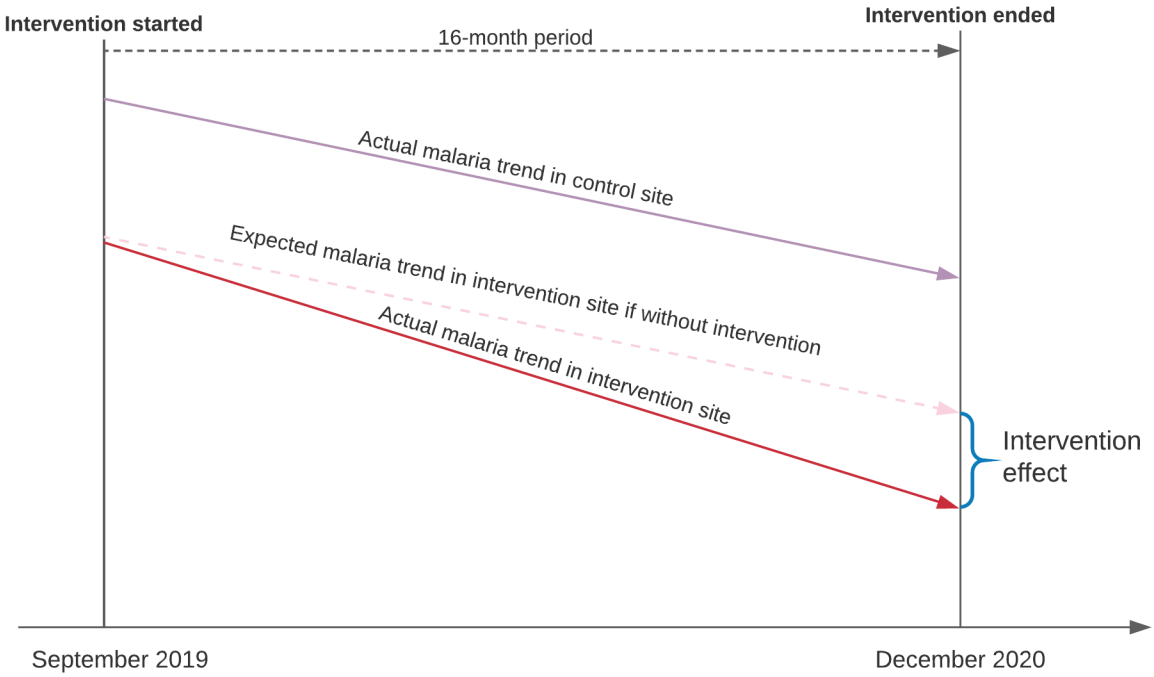
### *Data quality*

In this evaluation, we achieved 100% data completeness for all variables due to the force-to-answer option. All users (33/33) rated the quality of data they interviewed as very high; however, as this was self-reported, the rating may be affected by social desirability bias. To have a true data quality assessment, a validation of the interview data would be necessary. However, this was beyond the scope of this study.

*Usefulness*

In our evaluation, usefulness was referred to as whether or not the RAI2 surveillance system could be used to evaluate the effectiveness of the RAI2 intervention. As conceptualized in Figure 4.12, the trends of malaria cases detected by the RAI2 surveillance system in the intervention site were compared with the trends of malaria cases detected by the RAI2 surveillance system in the control site. This concept is known as difference-in-difference analysis (27).

Figure 4.12: Concept of evaluating intervention effectiveness using difference-in-difference analysis



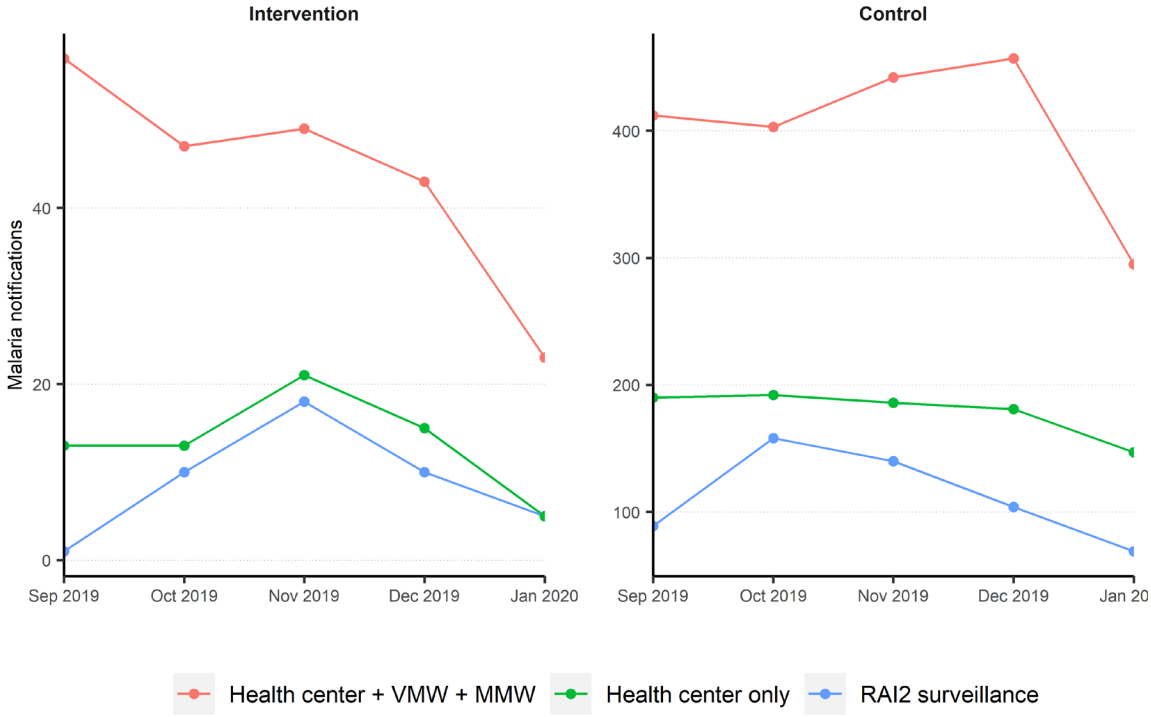

**Key findings:**

- The RAI2 surveillance system cannot be used to evaluate the intervention's effectiveness without assistance from data of the health center, village malaria workers, and mobile malaria workers.

A surveillance system's usefulness depends heavily on high and similar sensitivity between intervention and control site. During the surveillance evaluation period (September 2019 and January 2020), when comparing malaria incidence trends by month, the RAI2 surveillance system's sensitivity was not stable in the intervention site. The unstable sensitivity affected the ability to compare malaria incidence trends between the

intervention and control sites. It was unable to use RAI2 surveillance system data on its own. To investigate the validity of RAI2 surveillance data in evaluating RAI2 intervention's effectiveness, we compared the trends between three data sources: RAI2 only, health center only, and health center data combined with data collected by village malaria workers and mobile malaria workers (Figure 4.13). The data source combining health center data with data collected by village malaria workers and mobile malaria workers was the most comprehensive data, which we considered to be a gold standard for comparison. In the control site, we found trends were similar irrespective of the data source.

Figure 4.13: Comparing malaria incidence trends between three data sources, September 2019 and January 2020




Although the main objective of the RAI2 surveillance system was not met, its data can be partially useful to describe the characteristics of malaria patients. One of the most important additions in the RAI2 surveillance system was information about exposure to forests among malaria patients. We recommend that this information should be integrated into the national MIS. This evaluation has shown that the questions were simple and acceptable to the health center staff. This additional information could increase the national malaria system's ability to monitor or evaluate malaria interventions' impact on a large scale.

## Discussion

The literature review embedded in this RAI2 surveillance evaluation highlights that national surveillance data can be useful in evaluating an intervention's impact, however, the surveillance system alone does not collect all the information needed. Additional data sources are often needed in some contexts, such as socioeconomic status, entomological factor, rainfall, and temperature, to interpret their intervention impact (10, 12-18).

Our evaluation suggested that the RAI2 surveillance system was simple, flexible, stable, and timely; however, it did not meet its primary objective in evaluating the effectiveness of the RAI2 intervention. One attribute of the RAI2 surveillance system-- low sensitivity-- outweighs other positive attributes. During the evaluation period, only 43% of malaria cases reported by all selected health centers were detected by health centers, while VMWs and MMWs detected a larger proportion. Of those detected by selected health centers, only 62% were interviewed. The intervention site where six health centers were chosen reported few cases per month. The trends in the intervention site were affected when one or two interviews were missing. In addressing this issue, a possible solution is using the number of malaria cases from the health center log-books combined with data from village malaria workers and mobile malaria workers.

Attributes of surveillance systems affect each other. In our evaluation, the low acceptability of the RAI2 surveillance system amongst staff, may play a significant role in low sensitivity. The system's acceptability was low due to the overall consensus that the financial incentive provided was not considered sufficient for the additional work required. To increase the system's acceptability, health center staff could be motivated by both monetary and non-monetary incentives. On monetary incentives, increasing the incentive per interview is likely to increase participation and result in more reliable data. For short term participation, this may be appropriate, however, is not a sustainable way to run a surveillance system. On non-monetary incentives, for long-term surveillance, having a regular meeting (e.g., every three months) for discussion of implementation issues and support needed, refresher training, and providing additional skills needed (e.g., basic epidemiology, basic data cleaning, and analysis) may be helpful. Improving understanding about why the data is collected and how is it used, often helps participating staff to understand why the data needs to be clean and complete.

Another important aspect of surveillance is data quality. The RAI2 surveillance system performed well in terms of data completeness and PPV, however, the presence of

information bias could not be ruled out. On the data completeness, all variables were reported 100%. This achievement may be from a result of the force-to-answer logic using the electronic form. With respect to the PPV, all patients with *P. falciparum* or *P.vivax* were 100% confirmed by PCR. During our evaluation period, Cambodia used the RDT, namely "One Step Malaria HRP2/pLDH (P.f/P.v) Test," which was in the WHO recommendation list in 2018 (28). According to the latest WHO's annual RDT performance evaluation, the "One Step Malaria HRP2/pLDH (P.f/P.v) Test" had <5% false-positive rate at 200 parasites/μL, meaning the PPV is ≥95% (28). Our PPV rate may be overestimated due to the relatively small sample size. With respect to the risk associated with information bias, it was not in the scope of our evaluation to explore this further. There was a possibility that interviewees gave interviewers wrong information for social desirability (e.g., whether they visited forest for unapproved activities), to avoid risk of legal ramifications. Another possibility is that interviewers may incorrectly record the interviewees' information due to misunderstanding the answer or human error.

Besides the low sensitivity impacting the RAI2 surveillance system's ability to evaluate the RAI2 intervention, the system was not designed to capture other interventions affecting the malaria incidence trends. In assessing the effectiveness of the RAI2 intervention, the most significant assumption is that malaria incidence trends in control and intervention sites would be parallel if the intervention sites had been an absence of RAI2 intervention. Identifying other interventions that provide services in the forest or near the forest in the control site is critical, but it was out of RAI2 surveillance scope. From our informal interaction with all selected health centers, NGOs, and provincial health departments, we learned that intervention and control sites also have interventions providing services inside the forest or near the forest. MMWs target forest goers; MMWs, spend eight days per month inside forests or two days per week to seek as many forest goers as inside or near the forests for providing malaria testing and treatment. In addition, radical cure which prevents *P. vivax* patients from relapsing has been being implemented in two control provinces -- fully implemented in Kampong Speu and partially implemented (four health centers only) in Pursat since early 2019. Such information is useful to interpret the intervention impact evaluation. To increase the usefulness of a surveillance system aimed at evaluating an intervention impact, setting up a plan to collect information on potential factors impacting the disease trends should be a useful aspect.

Furthermore, the RAI2 surveillance system did not capture pre-intervention data requiring for the difference-in-difference (DID) technique used to evaluate RAI2 intervention's

effectiveness requires pre-intervention data (27). DID is a quasi-experimental design to estimate the causal effects of an intervention or treatment in an intervention site compared to a control site (27). It assumes that a disease's trends are not different in the absence of intervention or treatment (27). DID requires pre- and post-intervention data in the intervention and control group (27). DID's strengths are easy to interpret, can estimate the causal effects using observation data (surveillance data or cross-sectional survey data), the comparison group can start at a different level of outcome, and accounting for other non-intervention effects. The weakness is the pre-intervention data requirement in the intervention and control site, which is usually hard to obtain. It cannot be used if the trends are not stable or different, even without intervention.

## Conclusion

Due to unstable sensitivity in the intervention site, we could not solely rely on the RAI2 surveillance system's data to evaluate the intervention's effectiveness. RAI2 surveillance data were found to be partially useful in describing the characteristics of patients testing positive for malaria and reporting risk factors such as exposure to forest.

## Recommendation

We recommend that:

- The RAI2 surveillance system should be integrated into the national MIS. While there are overlapping variables between RAI2 form and MIS form, we can remove a large part of RAI2. Only several important variables related to forest exposure of RAI2 should be added to the MIS form.

- MIS should be moved to be a real-time data collection, add more exposure variables, and set up an alert system to the district and provincial level if the malaria trends are higher than the defined normal trends to increase its usefulness. MIS is already a case-based system, however is not timely due to the delay for at least one month to make data available at the central level, it is also missing key exposure variables. Building on current progress, moving MIS to real-time is possible and the benefits is significant.

- To motivate staff, staff should receive regular meetings (e.g., every three months) for discussion of implementation issues and support needed, refresher training, and providing additional skills needed (e.g., basic epidemiology, basic data cleaning, and analysis).

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# Annex 1: Quantitative questionnaire

| Code | Question | Answer | Skip |
|---|---|---|---|
| **Section 1: Simplicity** | | | |
| Q1 | How simple is the questionnaire in Kobo to understand? | 1. Very simple<br>2. simple<br>3. Not simple or difficult<br>4. Difficult<br>5. Very difficult | |
| Q2 | How familiar with using a tablet or smartphone are you? | 1. Very familiar<br>2. Familiar<br>3. Unfamiliar<br>5. Very unfamiliar | |
| Q3 | How confident are you on how to use, save, and submit the completed form in Kobo? | 1. Very confident<br>2. Confident<br>3. Not confident<br>5. Not confident at all | |
| Q4 | How confident are you on how to install Kobo and download the form for a new device? | 1. Very confident<br>2. Confident<br>3. Not confident<br>5. Not confident at all | |
| Q5 | Do you have enough time to do the interview when they have malaria patients? | 1. Yes, always<br>2. Often<br>3. Sometimes<br>4. Rarely<br>5. Never | |
| Q6 | Do you get Kobo-related technical support as needed? | 1. Yes, always<br>2. Often<br>3. Sometimes<br>4. Rarely<br>5. Never | |
| **Section 2: Flexibility** | | | |
| Q7 | Do you use a tablet or smartphone for interviewing? | Tablet<br>Phone<br>Both | |
| Q8 | How many devices which Kobo have been stalled in your health center? | Number of device_____ | |
| Q9 | Do you have a paper-based questionnaire available in your health center? | Yes<br>No | |
| Q10 | Do you think you can use the paper-based questionnaire or Kobo as you prefer? | Yes<br>No | |
| **Section 3: Acceptability** | | | |
| Q11 | Do you think Kobo is an appropriate platform to be used by health center staff? | 1. Yes<br>2. No<br>9. Don't know | |
| Q12 | Is the incentive of 2-USD per interview is appropriate? | 1. Yes<br>2. No<br>9. Don't know | For control site only |
| Q13 | Is the incentive of 3.5 USD appropriate? | 1. Yes<br>2. No<br>9. Don't know | For intervention site only |
| Q14 | If you can decide on an incentive, how much would you give per interview? | ……..USD | |

| | | | |
|---|---|---|---|
| Q15 | Does the head of the health center allow you to spend time interviewing the malaria patient for the RAI2 surveillance system? | 1. Yes<br>2. No<br>9. Don't know | Only staff |
| Q16 | Do you think other staff willing to help with interviews when you are on leave? | 1. Yes<br>2. No | |
| Q17 | Some staff at other health centers did not do an interview for us, may you think what might be the reasons? (multiple answers possible) | 1. The incentive is not enough to motivate them.<br>2. They are so busy with many clients.<br>3. Their boss does not allow<br>4. They are not followed up closely by the IPC team.<br>5. The questionnaire is too complicated.<br>6. It is a waste of time to do dried blood spots.<br>7. Not familiar with using the smartphone for interviewing<br>8. Other(specify)_____ | |
| **Section 4: Stability** | | | |
| Q18 | Can you use Kobo every time as needed? | 1. Yes<br>2. No | |
| 19 | Do you have access to the internet when you need it? | 1. Always<br>2. Often<br>3. Sometimes<br>4. Rarely<br>5. Never | |
| Q20 | Do you have more than one staff at your HC who can do an interview for RAI2 surveillance? | 1. Yes<br>2. No | |
| Q21 | Are you satisfied with the current Kobo speed when you open the form? | 1. Very satisfied<br>2. Satisfied<br>3. Not satisfied<br>4. Not satisfied at all | |
| Q22 | Have you ever missed some interviews due to Kobo does not work well? | 1. Yes<br>2. No | |
| Q23 | If yes, what was the main reason? | 1. No battery<br>2. No phone with you<br>3. Crash<br>4. Lost records<br>5. Slow<br>6. Other_____- | |
| Q24 | What is your opinion on the data quality collected by you? | 1. Very high quality<br>2. Ok quality<br>3. I don't know<br>4. Poor quality<br>5. Very poor quality | |

# Annex 2: Malaria Information System (MIS) data collection form

## Monthly Malaria Registry Book

**Province……..Operational District…… commune……. Health Center's Name……**

**1. For patients with positive result only**

| No | Address (Village, Commune, District, Province) | Age (0 if <1 year) | Sex (M/ F) | Pregna ncy (in month) | Diagnosis | | Treatment | | Type of diagnosis | | Result | | | Drugs | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Mild | Sever | Out-patient | In-patient | RTD | Microscopy | P.f | P.v | Mix | ASMQ | DHA-PIP | PQ | Other | Refe rred | Died |
| 1 | | | | | | | | | | | | | | | | | | | |
| 2 | | | | | | | | | | | | | | | | | | | |
| 3 | | | | | | | | | | | | | | | | | | | |
| 4 | | | | | | | | | | | | | | | | | | | |
| 5 | | | | | | | | | | | | | | | | | | | |
| 6 | | | | | | | | | | | | | | | | | | | |
| 7 | | | | | | | | | | | | | | | | | | | |
| 8 | | | | | | | | | | | | | | | | | | | |
| 9 | | | | | | | | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | | | | | | | | |

2. **Summarv**

# Chapter 5 : Coronavirus Disease 2019 asymptomatic transmission: A cluster review in Cambodia, 2020

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# Prologue

## Rationale

This chapter presents my fourth core competency of the MAE program—epidemiology project—and a summary for layperson included in annex 1.

In meeting this core competency, I reviewed a Coronavirus Disease 2019 (COVID-19) cluster of returned travelers to understand how asymptomatic transmission occurred. I used data provided by the Cambodian Communicable Disease Control Department (CCDC) collected during the contact tracing process and additional information, which I later collected through a phone interview with former COVID-19 patients. The study received ethical approval from the National Ethics Committee for Health Research (NECHR) in Cambodia and the Human Research Ethics Committee (HREC) of Australian National University, in Australia.

I chose to use COVID-19 data for my epidemiology project because of my four-month involvement with COVID-19 response in Cambodia. Roles

Specifically, for this study, I conducted the following roles.

1 Identified a research question

2 Facilitated discussions with the CCDC and its partners about using existing data

3 Designed the study, wrote the research protocol, and managed the approval process for the National Ethics Committee for Health Research (NECHR) in Cambodia and the Human Research Ethics Committee (HREC) of Australian National University in Australia.

4 Designed the questionnaire and interviewed the selected COVID-19 cases for additional information

5 Performed quantitative and qualitative data analysis and interpretation of findings

6 Wrote a report and a summary for lay audiences (the general public)

## Lessons Learnt

I learned several lessons from my role in the study.

1. A study with a small sample size of 22 can be enhanced with the collection of qualitative information. In an applied epidemiology career, we may need to present findings from a study with a small sample size making it difficult to generalize or make statistical inference. By including qualitative information, we can contextualize the findings. In my case, I used a combination of existing data collected during the contact tracing process, contact tracer's notes, and qualitative interviews.

2. Conducting phone-interviews months after COVID-19 patients were released from isolation is not ideal. I noticed some participants did not trust me even though I followed all the informed consent processes. Some individuals reported having had a bad experience as a result of their photos and personal information having been shared widely on social media. Some participants did not want to hear or talk about COVID-19. I only received short answers from some of them, they were still in pain with what happened, I could not get more details as it was not ethical to try to push for more information when they were hesitant. This highlighted the sensitivities that need to be considered in conducting interviews and the importance of ethical practice in research.

3. Study results should be produced as quickly as possible for better use. In my case, I delayed several months. In the beginning, I doubted whether or not I could use data from a COVID-19 cluster with just more than 20 primary cases for my epidemiology project. After clarification with supervisors, I submitted a protocol for expedited review to both Cambodia's and Australian National University's ethical committee. Both committees transferred my protocol to full-board review, which took two months to get approval. After approval, I was unable to commence the study immediately as I was distracted by other tasks. Finally, I produced results eight months after the event occurred. The findings are still useful, however, they may have been more useful if I could have released my findings a month or two months after the event occurred.

4. People may underestimate the severity of psychological impact of COVID-19 on patients and their family members. In responding to the spread of SARS-CoV-2, it is hard to balance between keeping privacy for a patient and the risk of SARS-CoV-2 in the community. The communities should be informed as quickly as possible so that they can implement or strengthen prevention measures. During the contact tracing in Cambodia, the contact tracers always disclose the personal information of a COVID-19 case to people in the community to assess the risk of SARS-CoV-2 infection if they have exposed to the identified cases. Due to the fear of COVID-19 transmission, the whole community socially disconnected themselves from the entire family of a COVID-

19 case despite the laboratory results suggesting that some family members were SARS-CoV-2 negative. At least two out of 12 families I interviewed relocated their whole family to another city. The main reason was the economic reason as they could not pursue their business in their community. It was also too painful when they saw their children were prevented from playing with other kids as they used to. Learning from this, I think both psychological and financial support should be included in the COVID-19 response. Education aimed at reducing stigma on former COVID-19 patients and family should be considered as well. This may reflect that a role of epidemiologists may not only advise on control measures focusing focused on social distancing, hygiene, stay at home messaging, but other aspects such as the psychological aspects and stigmatization should also be mentioned by epidemiologists.

## Public Health Impact

Although the information was not released as quickly as possible, it was still useful to understand how asymptomatic transmission may occur, contributing to local policy design. The local evidence that people without any symptoms can be a COVID-19 case and transmit the virus is useful information that can be used to communicate with the public. Such information may lead to better self-prevention in the community.

## Acknowledgments

I earnestly express gratitude toward Dr. Ly Sovann, Director of CCDC, for allowing me to join the response team and use CCDC to fulfil my MAE epidemiology competency.

Profound thanks to all contact tracers for collecting information and the former COVID-19 patients for providing information during the contact tracing process and response to my phone-interviews.

I gratefully thank all my supervisors—Patrice Piola, Tambri Housen, Vincent Herbreteau, and Amy Parry – for their kindness and helpful comments during since study design stage to the report writing. You spent your valuable time to support me since the beginning.

Chapter 5

# Abstract

*Background*: Since the global spread of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) was declared a pandemic, the role that asymptomatic transmission has played in fueling the pandemic not fully understood. Our study aimed to measure the proportion of asymptomatic cases and describe the transmission from asymptomatic primary cases to their contacts.

*Methods*: We undertook a secondary data analysis and qualitative exploratory study of a cluster of COVID-19 in returned travelers from a religious event (28 February to 2 March 2020) in a Southeast Asian country. We defined a COVID-19 case as a person who tested positive for SARS-CoV-2 by Real-time reverse transcription-polymerase chain reaction (rRT-PCR) and interviewed them with a standard questionnaire to identify their contacts. Identified contacts were categorized by risk and followed up for 14 days.

*Results:* The cluster of returned travelers had 22 primary cases (infected outside Cambodia), ten secondary cases (infected contacts in Cambodia), and 491 uninfected contacts. Of the 22 primary cases, 63.6% (n=14/22) were asymptomatic. Ten secondary cases out of the 501 contacts tested positive for SARS-CoV-2, giving the secondary attack rate (SAR) of 2.0%. The SAR in high-risk contacts was (5.9%, n=8/136), 1.2% (n=1/86) in medium-risk contacts and 0.4% (n=1/279) in low-risk contacts. A non-statistically higher SAR was observed in household contacts than in non-household contacts (3.4%, n=4/118 vs. 1.7%, n=1/60, *P*-value=0.256). In household, contacts the SAR in spouses was 18.8% (n=3/16), 1.7% (n=1/60) in children, and 0.0% (n=0/42) in other relatives (*P*-value=0.008). Of non-household contacts, a higher SAR of 4.0% (n=1/25) was observed in co-travelers with a primary case and 3.3% (n=5/153) in people praying in a mosque with a case. Overall SAR and stratified SAR among contacts exposed to asymptomatic and symptomatic primary cases were not statically different.

*Conclusion:* In this study, asymptomatic cases were shown to transmit SARS-CoV-2 to their contacts. Our study found no statistically different infectivity among contacts exposed to asymptomatic and symptomatic primary cases. A response to contain and mitigate COVID-19 spread must take into account asymptomatic transmission.

# Abbreviation

| | |
|---|---|
| CCDC | Cambodia Communicable Disease Control Department |
| COVID-19 | Coronavirus Disease 2019 |
| CRF | Case Report Forms |
| HREC | Human Research Ethics Committee |
| MoH | Ministry of Health |
| NECHR | National Ethics Committee for Health Research |
| rRT-PCR | Real-time reverse transcription-polymerase chain reaction |
| SAR | Secondary attack rate |
| SARS-Cov-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |

Chapter 5

# Introduction

A novel coronavirus was identified in Wuhan, Hubei Province, China, in December 2019. This virus was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2); the disease caused by this virus was named coronavirus disease 2019 (COVID-19). SARS-CoV-2 spreads from human-to-human through droplets, close contacts, and aerosol (1). The global spread of SARS-CoV-2 was declared as a pandemic by the World Health Organization (WHO) on 11 March 2020 (1). By 15 December 2020, 70 million people were reported to have tested positive for COVID-19 internationally, and 1.6 million people had died, giving a crude case fatality rate of 2.3% (2). These cases and deaths were reported by 222 countries territories. Three countries made up more than 46% of total cases, including the United States (23.0%), Brazil (13.4%), and India (9.5%) (2). The fatality rate was disproportionate across contexts, ranging from 1.5% in WHO Southeast Asia Region (SEARO) to 2.6% in the Pan American Health Organization (PAHO)(2). The high case fatality rate occurred mostly in high-income settings (3). The fatality rate in a country is directly affected by how quickly the number of cases exceeded the healthcare system's capacity, population's age distribution, and population's prevalence of chronic medical conditions such as diabetes, heart disease, obesity, cancer, and kidney disease (3-8). Studies suggest that the risk of dying is elevated among males, individuals aged 60 or older, and people with chronic medical conditions (3-8).

Without vaccine availability (at the time of the study), non-medical approaches known as containment and mitigation strategies have been used to reduce transmission. The containment strategy is to minimize the transmission from infected individuals to non-infected individuals to stop widespread transmission in the population (9). Containment strategies have included the isolation of the cases and the testing and quarantining of close contacts (9). The mitigation strategy is focused on slowing down the spread of the virus and reducing the demand on the healthcare system (9). Mitigation strategies have included social distancing, society lock-down, and improved personal and environmental hygiene (9). Mathematical modeling of the effectiveness of containment and mitigation strategies, suggested that containment and mitigation strategies' success may be associated with the timeliness of implementation of the containment measure, high temperatures, low population density, younger population, and the country's high health security index (10).

In Southeast Asia, as of 16 December 2020, 11 nations experienced a varied burden of COVID-19 incidence ranging from six cases per million population in Laos to 10,404 per

million population in Singapore, while the world rate was 9,632 per million population (11). After Singapore, the high incidence rate in our region was observed in the Philippines (4,352/million), followed by Malaysia (2,911/million), Indonesia (2,426/million), and Myanmar (2,140/million) (11). The lowest COVID-19 incidence rate in Southeast Asia was detected in four out of five countries in Greater Mekong Sub-region (11). While Laos had the lowest incidence rate (6/million) and Myanmar had the highest incidence rate (2,140/million) in this region, low incidence rates were observed in Vietnam (15/million), Cambodia (23/million), and Thailand (62/million) (11). The reasons these countries had a low incidence rate is not fully understood. Myanmar, which had the highest incidence rate share similar characteristics to its neighbors-- greeting culture, population density, transportation infrastructure, climate, and response strategy.

Cambodia, a lower-middle-income country, is ranked 89$^{th}$ out of 195 in the 2019 Global Health Security Index. The index reflects the rank of Cambodia's capacity to respond to health emergencies compared to other nations. Although the country's capacity was not high, the country did not experience COVID-19 community transmission until the 28$^{th}$ of November 2020. Cambodia reported 362 confirmed cases as of 15 December 2020 (12, 13). Of these cases, 88.7% were overseas acquired (12, 13). No deaths due to COVID-19 have been reported, and by 15 December 2020, 318 out of 362 (88.1%) of COVID-19 cases were classified as recovered (12).

Like many other countries, COVID-19 is having a negative impact on Cambodia's economy. Public fear and the government's actions, such as travel restriction, flight disconnection, closure of all schools, and closure of all gathering sites to reduce transmission, have had a detrimental impact on businesses and Cambodians' quality of life (14-18). In response, the government increased the health sector budget, while the country's income decreased (16).

The role asymptomatic transmission has had in fueling the pandemic is not fully understood. Early data in China suggested almost all COVID-19 cases (98.4%) were symptomatic (19). This may have misled initial control strategies and was further influenced by the WHO's early recommendation to screen only those who had symptoms. From February 2020, studies began to suggest asymptomatic carriage of the virus was possible and that asymptomatic carriers could transmit the disease to other people (20-29). A true proportion and basic reproduction number (number of secondary cases infected by a primary case) from asymptomatic cases are difficult to ascertain from the global or country-level data due to the application of different case definitions, variations in testing,

and control policies (29). Cluster investigations are a common study method for field epidemiological investigations, many of which have been carried out during the COVID-19 pandemic in order to further understand disease transmission. Of particular interest to the scientific community has been increasing knowledge and evidence around the asymptomatic transmission of the SARS-CoV-2. There is a need to add to the emerging evidence to inform the development of evidence-based policy and practice to contain the spread of COVID-19 (20-22).

Our study aimed to measure the proportion of asymptomatic cases and describe the transmission from asymptomatic primary cases to their contacts.

# Methods

## Study Design

We conducted secondary data analysis and a qualitative exploratory study of a cluster of COVID-19 cases in returned travelers.

## Case definition and primary and secondary case detection

### *Case definition*

A confirmed case was defined as an individual who tested positive for SARS-CoV-2 by Real-time reverse transcription-polymerase chain reaction (rRT-PCR) [29, 30]. We classified cases into two groups.

- Primary Case: A confirmed case who had traveled to a religious event in country x between 28 and 2 March and tested positive for SARS-Cov-2 by PCR within 14 days of returning home.

- Secondary Case: A close contact of a Primary Case who subsequently tested positive for the SARS-Cov-2 by PCR with no history of international travel one month prior to testing positive.

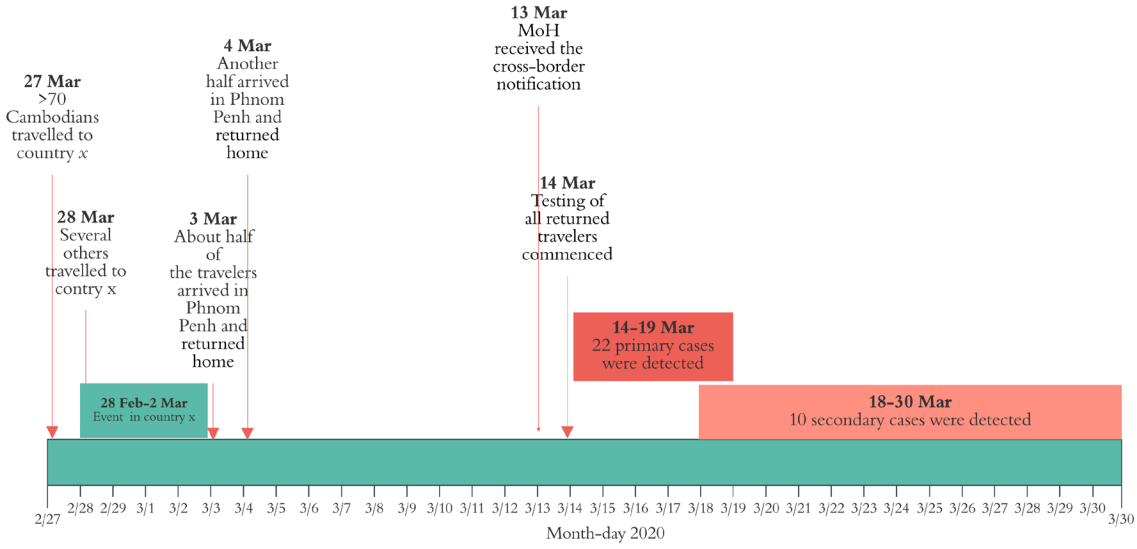
### *Primary cases detection*

The primary cases were detected using an event-based surveillance system 12-18 days after returning home from a country in Southeast Asia (country x).

A religious event was hosted between 28 February and 2 March 2020 in country x. According to the religious leader in Cambodia, 79 Cambodians joined the event. These 79 people were from 10 provinces in Cambodia.

The testing for SARS-CoV-2 among this group started on 14 March 2020 after country x reported a cluster of new COVID-19 cases linked to the religious event and similar reports from other Southeast Asian countries through the International Health Regulations (IHR) 's focal persons. Cambodia's response team decided to test all 79 returned travelers, 27.8% (n=22) of them were confirmed positive for SARS-CoV-2. Figure 5.1 provides a timeline of events related to this cluster. All individuals testing positive were required to undergo isolation in hospital until such time as they were classified as no longer infectious.

Figure 5.1. Summary of events, 27 February-30 March 2020, in Cambodia




Abbreviation: MoH, Ministry of Health

During isolation, at that time, the interval of sample collection from the cases was every three days if the result remained positive. If the result was negative, sample collection was done again after 48 hours. Within this 48-hour interval, if the result was negative, the patients were released from the isolation. However, if the result was positive again, the patient would be re-tested within the three-day interval. A detail time interval of testing was included in Figure 5.2 below.

## *Secondary case detection*

The secondary cases were detected during the contact tracing and quarantine process. Contact tracing commenced within 24 hours after the primary cases were notified. The contact tracing started by interviewing the confirmed primary cases to fill in the case report form and trace their movement, we asked questions to identify where they had been, at what time, and who they meet with in the past 14 days.

Our study included all contacts exposed to the primary cases since day one of arrival in Cambodia. We considered this period as the potential infectious period, which may not align with the available evidence (30).

The contacts were classified into three groups (Table 5.1). The first group, high-risk contacts, were defined as contacts who stayed closer than two meters to the primary case during their infectious period without protection for 30 minutes or with protection for one hour or longer. High-risk contacts were quarantined at hospitals and tested for SARS-CoV-2 within 24 hours after they were identified. All high-risk contacts were again tested for SARS-CoV-2, 13 days after the last date of exposure to the primary case, in order to receive the result on day 14 of their quarantine result was negative. All close contacts were called daily and asked, *"Do you have any symptoms such as fever, cough, sore throat, runny nose, or difficulty breathing today?"* for 14 days after the last date of exposure. If high-risk contacts developed any symptoms during the quarantine period, they were tested for SARS-CoV-2 on the day of follow up or the next day.

The second group, medium-risk contacts, were defined as contacts who stayed closer than two meters to the primary case without protection for a period of time between 15 and 30 minutes or with protection for a period between 15 and 60 minutes, at any time during the primary cases infectious period. All medium-risk contacts were quarantined at home and also tested 24 hours after they were identified. They were not required to undergo a repeat test on day 13 of quarantine, but they were called daily to check if they had developed any symptoms and were tested if they reported any symptoms.

The third group, low-risk contacts, were defined as those who did not meet the definition for a high-risk or medium-risk contact. Low-risk contacts were not tested, and their movements were not restricted. However, they were also followed up for symptoms for 14 days. Symptom-based testing was also applied.

Table 5.1. Criteria for testing for SARS-CoV-2, quarantine, and symptom follow up among contacts of confirmed cases in Cambodia, Mar-Sep 2020

| Activities | The risk level of contact | | |
|---|---|---|---|
| | High | Medium | Low |
| Quarantine for 14 days from the date of the last exposure to the case | Yes, at hospital or home | Yes, at home | No |
| Tested within 24hrs of being identified as a close contact of a primary case | Yes | Yes | No |
| Symptom follow-up daily for 14 days by phone-call | Yes | Yes | Yes |
| Testing for COVID-19 if contact had a symptom during symptom follow up | Yes | Yes | Yes |
| Testing for COVID-19 at day 13 of quarantine | Yes | No | No |

## Data source and data collection

The first part of the study analyzed existing data from the Ministry of Health in Cambodia. This data was collected as part of the national public health response to the COVID-19 pandemic under the Sub-Decree on Health Measures to Prevent and Respond to Public Health Emergency of International Concern at Points of Entry, 2015 (31). We used existing data from the case report forms (CRF) and contact tracing lists. Information from the case report form included name, age, gender, date of onset of symptoms, date of testing, date of known exposure, presence of symptoms (yes/no), and type of symptoms during testing. We obtained information about contacts from the contact tracing list. The information included contacts' names, age, gender, date of exposure, relationship to the primary cases, and risk level to SARS-CoV-2.

To better describe the cluster, the second part of the study collected additional data from primary cases. We conducted a follow-up telephone interview (in Khmer) with all primary cases listed as part of the cluster, where we administered an additional questionnaire. The questionnaire was semi-structured, where the first part was used to collect quantitative data, and the second part was used to collect qualitative data. All interviews were recorded with prior consent. The interview collected socio-demographic information: education, occupation, type of housing (concrete assuming closed setting or wooden house assuming open-air), interaction with high-risk contact: relationship with the contact (e.g., wife, son, friend, roommate), type of interaction (e.g., same household, traveling in the same car, chatting in the open air or closed setting). For asymptomatic cases, additional information such as symptoms during isolation (yes/no), if yes - type of symptoms, date of onset, when symptoms ceased were also collected.

## Study outcome

The outcome variables for this analysis are defined as follows.

The asymptomatic cases are referred to cases who did not have a history of fever, cough, sore throat, runny nose, or difficulty breathing when tested positive for the SARS-CoV-2 since the last date of exposure. Asymptomatic cases were asked only once following the positive result. Therefore, we were not able to follow whether cases have developed symptoms during isolation.

The attack rate refers to SARS-CoV-2 positivity among those exposed to the source of infection. In secondary cases, the attack rate was calculated as the number of contacts who tested positive for SARS-CoV-2 among all identified contacts.

In addition to the quantitative data, we described the interactions between asymptomatic primary cases and their contacts which subsequently tested positive for SARS-CoV-2.

## Sample size

For both retrospective data analysis and the qualitative component, we aimed to include all identified cases who participated in the religious event travelled back to Cambodia and their contacts in Cambodia.

## Data analysis

### *Secondary data analysis*

Descriptive analysis was conducted to describe the characteristics of primary and secondary cases in the cluster. The asymptomatic proportion was calculated among returned travelers by dividing asymptomatic primary cases by all primary cases. In producing the secondary attack rate (SAR), among non-travelers, we divided the number of secondary cases by the number of contacts. In determining the statistically significant difference in the SAR of contacts exposed to symptomatic and asymptomatic primary cases, we used the Chi-square test if all expected values were greater than five and used Fisher's exact test if one or more expected values were five or less (32). We also compared time taken to clear the virus where clearance was defined as having two consecutive negative PCR results within a 48-hour interval.

### *Interview analysis*

A rapid qualitative analysis was conducted on the qualitative data where interview recordings were listened to repeatedly through re-familiarisation with the content and pseudonymized. A summary table was developed in MS Word based on the semi-

structured interview guide. This table was used to summarize key themes from the interviews and to capture illustrative quotes. In the second phase of this rapid analysis, information from the summary tables was collated in a matrix in MS Excel. A matrix was created to capture the initial set of themes identified in the summary tables, a brief descriptor of each theme, key findings under each, and supporting quotations. Rapid qualitative data analysis is considered acceptable where resource and time constraints are barriers to interview transcription (33-35).

## Ethical Approvals

The protocol was reviewed and approved by the Human Research Ethics Committee (HREC) of Australian National University (No 2020/043, on 25 August 2020 for secondary data analysis and No 2020/506, on 01 October 2020 on the qualitative part) and the National Ethical Committee for Health Research (No 211 NECH R, on 28 August 2020) in Cambodia.

## Results

For the retrospective data analysis, we included all primary cases (n=22), all secondary cases (n=10), and all uninfected contacts (n=491)

For the qualitative component of the study, we analyzed data from 12 out of 22 primary cases. Ten were excluded because they either declined the invitation to participate (n=4) or could not be reached through a phone number in the database (n=6). Reasons of refusal was not recorded for ethical reasons.

### Description of the Returned Traveler Cluster

The religious event was hosted between 28 February and 2 March 2020 in country x. According to the religious leader in Cambodia, 79 Cambodians joined the event. These 79 people were from 10 provinces in Cambodia. The majority (>70 people) traveled together from Phnom Penh international airport to airport of country x on the evening of 27 February 2020. They were picked up by buses arranged by the religious event organizers and transported from the airport to the religious event. The bus journey was approximately 30 minutes from the airport to the religious facility. The buses used by the Cambodian travelers were for Cambodian nationals only.

All Cambodians stayed at the religious facility for the whole ceremony (four or five days from 27 February to 3 March 2020); they stayed in an open space in a building (~10x30 meters) prepared for Cambodians. Similar spaces were also prepared for other nationalities (e.g., Thai, Bruneian, Indonesian). Bathroom and toilets were shared by everyone who stayed in the facility.

> *"There was a block for Cambodia; they had a reserved place for Cambodia… Other countries had their block, but the toilets were shared for all countries "Case 1.*

Organizers prepared food, but all primary cases reported eating some meals at nearby local markets (5 to 10-minute walk). Many reported touring the local market, but not often and for a short period of time only, due to the event's busy schedule. The event was crowded, and every case interviewed reported hand-shaking with the preachers and with participants of other nationalities.

> *"We sometimes ate the food prepared by the organizer, but we walked down the hill to eat in a restaurant nearby…because there were many people waiting for the meals and the curry taste was a bit different from Khmer[Cambodian] food" Case 6.*

No COVID-19 prevention measures were implemented at a religious event. Temperature screening was conducted prior to boarding the airplane and prior to exiting the airport in Cambodia and country x.

> *"I saw several people from the Philippines wore a mask, but almost everyone did not wear a mask. We did not hear any advice from the organizers to prevent [SARS-Cov-2] transmission.", Case 6.*

The 79 Cambodians were split into two groups during their return trip to Cambodia. The first group traveled from the religious facility to the airport in country X on the evening of 2 March (the last day of the event) by the organizers' buses (about a 30-minute trip). They stayed in the airport to wait for boarding at approximately 4:30 AM on 3 March. The second group underwent the same process on the 3 March. They stayed at the airport to wait for boarding at approximately 4:30 AM on 4 March. The flight time from country x to Phnom Penh was approximately 3 hours. Cambodians shared flights with passengers who did not attend the religious event.

Temperature screening at Phnom Penh International Airport was in place. However, no other policies such as testing and quarantine at home/hotel/hospital for arrival passengers had been imposed at this time. Those who resided in the provinces took taxi vans as a

group (all in one taxi) to their home. The returned travelers in each province reported attending their local religious facilities in the days after returning home. Some reported traveling to other districts in their province or other provinces to share what they had learned at the religious event. Sometimes they were required to stay overnight.

> *"The taxi to my province was waiting for me in front of the airport. I traveled with all other people from province X ", Case 7.*

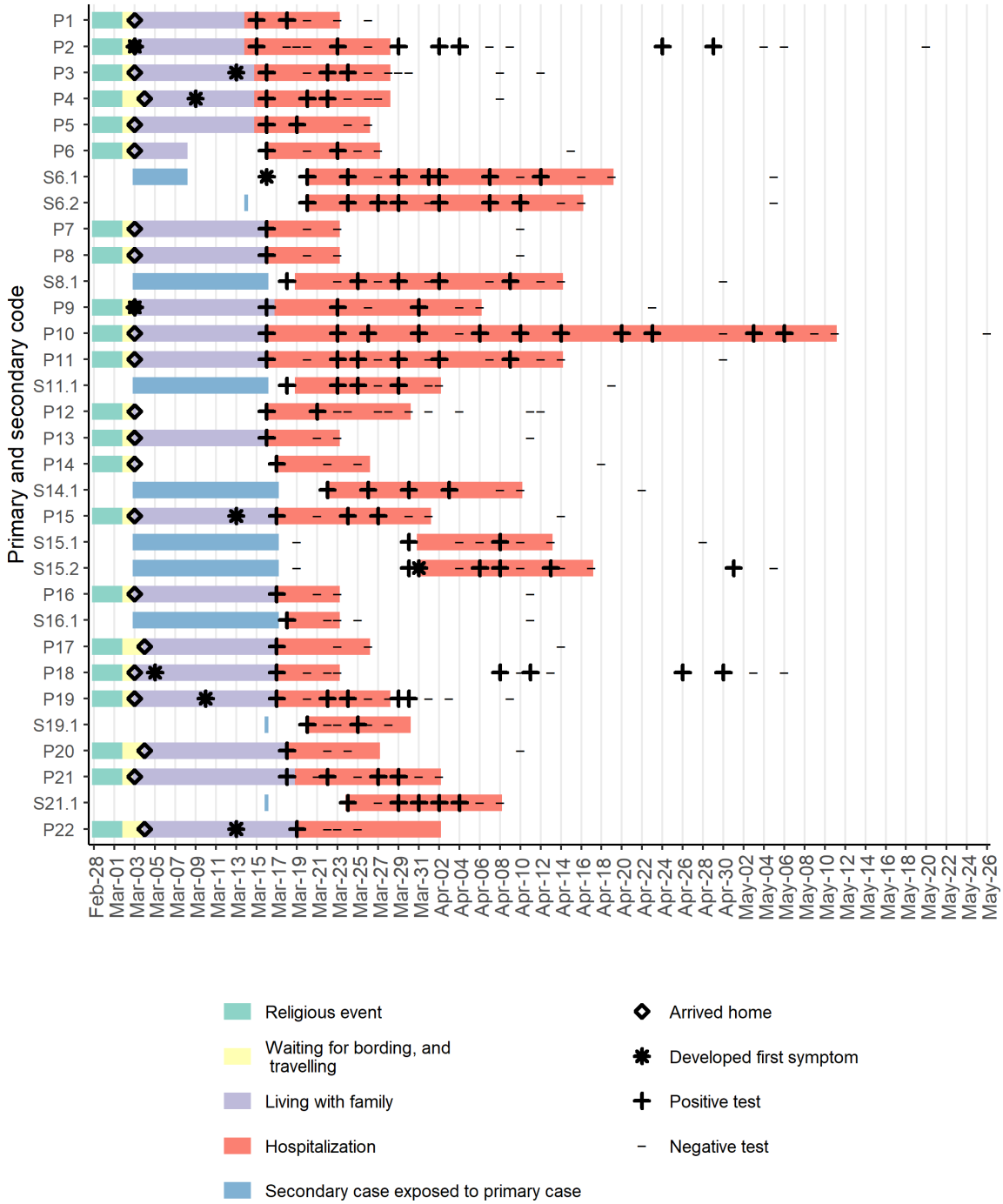
No precautionary prevention measures to protect family members from possible SARS-CoV-2 transmission were reported by interviewees. At least two respondents were misled by the fact they had temperature screening. They felt safe after they passed the screening process and did not think they posed a risk. Some said they had never heard about COVID-19 before, and some said they have heard about COVID-19 but never expected they could have had it because they were very healthy. Before the primary cases were tested, 19 out of 22 primary cases had exposed to their household members for a period ranging from 10 to 15 days with a median of 12 and interquartile ranging from 12 to 13 days (Figure 5.2). Two cases reported they had not stayed with their family until the day they were tested for SARS-CoV-2, while one case stayed with the family for the first five days before traveling away from home.

> *"I have never heard about COVID [19] until the day I was tested for it [SARS-CoV-2]", Case 4.*

> *"I did not want to transmit the virus to someone else. I thought I did not have it [SARS-CoV-2] because I was screened for the temperature at the airport, and they allowed me to leave the airport", Case 1*

Of secondary cases, two of them developed symptoms before they were tested for SARS-CoV-2. The first symptomatic secondary case had his/her symptom onset eight days after the last date of exposure with the primary cases. The second symptomatic secondary case had his/her symptom onset 14 days after the last date of exposure to the primary cases.

Figure 5.2. Exposure period of household members and secondary cases exposed to a primary case of COVID-19 in a Cambodian cluster of returned travelers, 3-19 Mar 2020



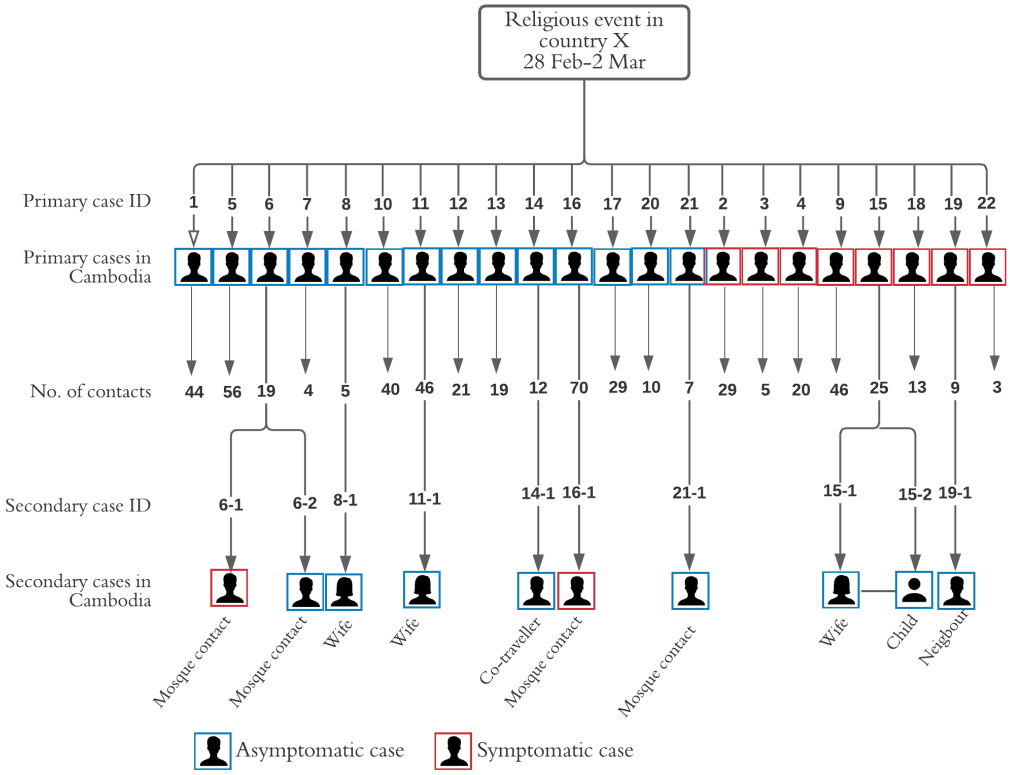

Note: On Y-axis, P denotes “primary case,” and S denotes “secondary case”, hospitalization was for isolation purposes not due to illness severity.

## Asymptomatic proportion, infection rate, and exposure

Over half of the total primary cases (63.6%, n=14/22) were asymptomatic at time of testing (Figure 5.3).

Overall, 22 primary cases generated ten secondary cases, giving the overall rate or so-called “basic reproduction number” of 0.5 secondary cases per primary case. The basic reproduction number generated by the asymptomatic primary case of 0.5 (n=7/14) was similar to the rate of 0.4 (n=3/8) generated by the symptomatic primary case (Figure 5.3).

Figure 5.3. A network between primary and secondary cases in a cluster of returned travelers in Cambodia, 27 Feb-19 Mar 2020, in Cambodia




From our qualitative data, we described how the secondary cases were exposed to their asymptomatic case.

**Primary case #6**: This asymptomatic case, a male in his 30s, generated two secondary cases. Case 6 tested positive 13 days after returning from country x, on 16 March. Case 6 spent the first five days living with his family (wife and three kids) in a wooden house (no air conditioner) and traveled away from home (stayed overnight) between day six and day 13. All of his family members were tested for SARS-CoV-2 and all tested negative by PCR. There was no reported further transmission in the communities he visited.

- Secondary case 6.1 was a male in his 30s, who was a close friend of case 6. After case 6 arrived home from country x, they met five times per day, every day, for five days in a nearby mosque for praying. They had physical and non-physical interactions, including praying and talking with less than one-meter distance many times, hand-shaking at least once a day for five days from day one to day five after case 6 had returned home. In addition, they had one meal together, including sharing water-drinking glass during that period. The secondary case was identified

during contact tracing. He was tested three days after Case 6 was confirmed positive for SARS-CoV-2.

- Secondary case 6.2 was a male in his 30s. He was not known to the primary case. The primary case met the secondary case on day 11 after the he arrived home from country x. It was one day before case 6 tested positive for SARS-CoV-2. Both of them claimed they shook hands and had a 5-10-minute talk. That was the only time they met. The secondary case was tested four days after they met by the contact tracing team.

**Case #8**: Case 8 was an asymptomatic male in his 40s, whom generated a secondary case. Case 8 tested positive 13 days after returning from country x, on 16 March. Case 8 lived with his family in a concrete house (no air conditioner) from the time he returned from country x until he tested positive for SARS-CoV-2. The couple had three children aged between 13-19 years living with them. No physical interaction with the children was reported, and all children tested negative for SARS-Cov-2.

- Secondary case 8.1 was the wife of case 8. She was in her 40s. She lived with her husband without any protections for 13 days after he arrived home from country x.

**Case #11**: This asymptomatic primary case, a male in his 40s, generated one secondary case. Case 11 tested positive 13 days after returning from country x, on 16 March. He lived in the family home, a wooden house (no air conditioner), from the time he returned from country x until he tested positive for SARS-CoV-2. He had four children aged between 5 and 12 years old. The family reported physical contact, sharing meals, and water-drinking glasses. Case 11 reported often spending time playing with his second and third child in the period between returning home and testing positive. However, all children tested negative for SARS-CoV-2 at the time of testing.

- Secondary case 11.1 was the wife of case 11. She was in her 30s. She lived with her husband without any protections for 13 days after he arrived home from country x.

**Case #14**: This asymptomatic primary case, a male in his 50s, generated one secondary case. Case 14 tested positive 14 days after returning from country x, on 17 March. Case 14 traveled with 13 people by van (with air conditioning) to three provinces—the day after

returning home from country x. Case 14 did not spend time with his family after returning to Cambodia from country x.

- Secondary case 14.1 was a male in his 30s. He travelled and prayed with case 14 for 14 days. He was the only contact that tested positive for SARS-CoV-2 out of 12 high-risk contacts. Besides sitting in the van together, they reported eating meals together, including using the same water-drinking glass.

**Case #16**: Case 16 tested positive 14 days after returning from country x, on 17 March. This asymptomatic primary case was a male in his 50s. Case 16 lived with his family in a wooden house from the day of his return from country x until the day he was tested for SARS-CoV-2. None of his family members tested positive for SARS-CoV-2.

- The secondary case, 16.1, was a male whom he prayed with in a mosque every day for more than ten days. They shook hands at least once a day and had multiple meals together during that period.

**Case #21**: This asymptomatic primary case, a male in his 60s, tested positive 16 days after returning from country x, on 19 March. Case 21 stayed with his family in a wooden house from the time of his arrival from country x until the day he was tested, and his family members were all tested negative for SARS-CoV-2.

- Case 21 met the secondary case 21.1, a male in his 50s, in a mosque. The meeting was 14 days after the religious event in country x had ended. They spent a day together in the mosque. The interaction reported was one-time hand-shaking and several conversations with less than 2-meter distance.

## Characteristics of primary and secondary case

All primary cases (100%, n=22) in our cluster were males with a median age of 41 years old (IQR 34-57 years) (Table 5.2). The age distribution between asymptomatic and symptomatic primary cases was similar. Of these primary cases, the period between their last exposed date and recovery dates ranges from 17 to 68 days. The asymptomatic primary cases took a non-statistically shorter time than the symptomatic primary cases to clear the virus (median of 26 days, IQR 22-19 compared to median 27, IQR 24-31, respectively). The individual was considered to have cleared the virus if they had two consecutive negative PCR results within a 48-hour interval.

Of all ten secondary cases, 60.0% (n=6/10) were female. The median age was 38 years old (IQR 35-48 years).

Table 5.2. Characteristics of primary and secondary cases in a cluster of returned travelers, Cambodia 14-19 March

| | Primary cases | | | | Secondary case | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | Total (N=22) column (%) | Asymp. (N=14) n (%) | Symp. (N=8) n (%) | *P* | Total (N=10) column (%) | Asymp. (N=8) n (%) | Symp. (N=2) n (%) | *P* |
| No. of primary cases (a) | 22 | 14 | 8 | | __ | __ | __ | |
| No. of secondary cases (b) | 10 | 7 | 3 | | __ | __ | __ | |
| Secondary cases per primary case (b/a) | 0.5 | 0.5 | 0.4 | | __ | __ | __ | |
| Sex | | | | | | | | |
| Male | 22 (100.0) | 14 (63.6) | 22 (36.4) | __ | 6 (60.0) | 5 (83.3) | 1 (16.7) | 0.7 |
| Female | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 4 (40.0) | 3 (75.0) | 1 (25.0) | |
| Age in years | | | | | | | | |
| Median [IQR] | 41[34-57] | 44 [39-57] | 37 [31-51] | | 38 [35-48] | 37 [34-40] | 59 [48-71] | |
| <27 | __ | __ | __ | 0.5 | 1 (10.0) | 1 (100.0) | 0 (0.0) | 0.2 |
| 27-39 | 8 (36.4) | 4 (50.0) | 4 (50.0) | | 5 (50.0) | 5 (100.0) | 0 (0.0) | |
| 40-59 | 9 (40.9) | 7 (77.8) | 2 (22.2) | | 3 (30.0) | 2 (66.7) | 1 (33.3) | |
| 60-75 | 5 (22.7) | 3 (60.0) | 2 (40.0) | | 1 (10.0) | 0 (0.0) | 1 (100.0) | |
| Type of symptoms among those who had symptoms | | | | | | | | |
| Fever | 7 (50.0) | __ | __ | _ | 1 | __ | __ | _ |
| Cough | 7 (50.0) | __ | __ | | 2 | __ | __ | |
| Sorethroat | 6 (42.9) | __ | __ | | 1 | __ | __ | |
| Runny nose | 6 (42.9) | __ | __ | | 1 | __ | __ | |
| Breathing difficulty | 5 (35.7) | __ | __ | | 1 | __ | __ | |
| Underlying condition (diabetes, hypertension, lung, and other) | | | | | | | | |
| No | 18 (81.8) | 11 (61.1) | 7 (38.9) | 0.5 | 10 (100.0) | 8 (80.0) | 2 (20.0) | __ |
| Yes | 4 (18.2) | 3 (75.0) | 1 (25.0) | | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| No. of days between last exposed date to recovery (two consecutive negative PCR) within 48-hour interval | | | | | | | | |
| Range | 17 to 68 | 22 to 44 | 17 to 68 | __ | __ | __ | _ | |
| Median [IQR] | 27 [22-31] | 26 [22-29] | 27 [24-31] | __ | __ | __ | _ | |
| Housing | | | | 0.01 | | | | |
| Wooden | 16 (72.7) | 13 (81.3) | 3 (18.7) | | | | | |
| Concrete | 6 (27.3) | 1 (16.7) | 5 (83.3) | | | | | |

Abbreviation: Asymp, Asymptomatic; Symp, Symptomatic; IQR, interquartile range

## Attack rate among contacts

Table 5.3 shows the attack rate among contacts. We detected ten secondary cases out of the 501 contacts, giving the crude attack rate of 2.0%. The highest attack rate was in high-risk contacts (5.9%, n=8/136), followed by 1.2% (n=1/86) in medium-risk contacts and 0.4% (n=1/279) in low-risk contacts with *P*-value=0.001. (Table 5.3).

A non-statistically higher attack rate was observed in household contacts than in non-household contacts (3.4%, n=118 vs. 1.7%, n=1/60, *P*-value=0.256). Of the household contacts, the highest attack rate was in spouse's (18.8%, n=3/16), followed by children (1.7%, n=1/60), while no other relatives (n=0/42) were reported to have tested positive (*P*-value=0.008).

Of non-household individuals, co-travelers who shared the car with a case had the highest attack rate of 4.0% (n=1/25), while the attack rate of people praying in a mosque with a case was 3.3% (n=5/153). We did not detect any cases among health care staff providing consultation to the cases (n=0/3), villagers talking with case (n=0/191), café staff and clients sharing a table with a case (n=0/5), or grocery sellers (n=0/5).

When stratifying between contacts exposed to asymptomatic and symptomatic primary cases, we observed that the attack rate was similar (2.0%, n=7/343 vs. 1.9%, n=3/158, respectively). Also, the attack rate among high-risk contacts exposed to the asymptomatic primary cases was similar (5.8%, n=5/86 vs. 6.0%, n=3/50).

Attack rate in wives whose husband was asymptomatic was 20.0% (n=2/10), similar to those whose husband was symptomatic 16.7% (n=1/6). One child was infected with SARS-CoV-2 in a family whose father was symptomatic.

Table 5.3. Characteristics of contacts of COVID-19 primary cases in a cluster of returned travelers, Cambodia 14-19 March

| Variable | Total (N=501) | Positive (N=10) | Tested Negative (N=294) | Not tested (N=197) |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | n (%) |
| Overall (all contacts) | | | | |
| Sex | | | | |
| Male | 369 (73.7) | 7 (1.9) | 211 (57.2) | 151 (40.9) |
| Female | 98 (19.6) | 3 (3.1) | 81 (82.7) | 14 (14.3) |
| Missing value | 34 (6.8) | 0 (0.0) | 2 (5.9) | 32 (94.1) |
| Classification of risk | | | | |
| High | 136 (27.2) | 8 (5.9) | 128 (94.1) | 0 (0.0) |
| Medium | 86 (17.2) | 1 (1.2) | 85 (98.8) | 0 (0.0) |
| Low | 279 (55.7) | 1 (0.4) | 81 (29.0) | 197 (70.6) |
| Household member of primary case | | | | |
| Yes | 118 (23.6) | 4 (3.4) | 95 (80.5) | 19 (16.1) |
| No | 383 (76.5) | 6 (1.6) | 199 (52.0) | 178 (46.5) |
| Type of household member | | | | |
| Spouse | 16 (13.6) | 3 (18.8) | 13 (81.3) | 0 (0.0) |
| Child | 60 (50.9) | 1 (1.7) | 51 (85.0) | 8 (13.3) |
| Other relatives | 42 (35.6) | 0 (0.0) | 31 (73.8) | 11 (26.2) |
| Type of non-household individual | | | | |
| Shared car/taxi with case | 25 (6.5) | 1 (4.0) | 23 (92.0) | 1 (4.0) |
| Praying in a mosque with case | 153 (40.0) | 4 (2.6) | 79 (52.0) | 69 (45.4) |
| Health care staff provided consultation to the case | 3 (0.8) | 0 (0.0) | 3 (100.0) | 0 (0.0) |
| Villager talked with case | 191 (49.9) | 1 (0.5) | 91 (47.4) | 100 (52.1) |
| Café staff and client shared table with case | 5 (1.3) | 0 (0.0) | 2 (40.0) | 3 (60.0) |
| Grocery seller | 5 (1.3) | 0 (0.0) | (100.0) | (0.0) |
| Co-worker (blue color) | 1 (0.3) | 0 (0.0) | 1 (20.0) | 4 (80.0) |
| Among contacts to asymptomatic primary cases | | | | |
| | N=343 | N=7 | N=218 | N=118 |
| Sex | | | | |
| Male | 53 (15.5) | 5 (1.8) | 168 (60.7) | 104 (37.6) |
| Female | 277 (80.8) | 2 (3.8) | 50 (94.3) | 1 (1.9) |
| Missing value | 13 (3.8) | 0 (0.0) | 0 (0.0) | 13 (100.0) |
| Classification of risk | | | | |
| High | 86 (25.1) | 5 (5.8) | 81 (94.2) | 0 (0.0) |
| Medium | 76 (22.2) | 1 (1.3) | 75 (98.7) | 0 (0.0) |
| Low | 181 (52.8) | 1 (0.6) | 62 (34.3) | 118 (65.2) |

| | | | | |
|---|---|---|---|---|
| Household member of primary case | | | | |
| Yes | 65 (19.0) | 2 (3.1) | 62 (95.4) | 1 (1.5) |
| No | 278 (81.1) | 5 (1.8) | 156 (56.1) | 117 (42.1) |
| Type of household member (n=65) | | | | |
| Spouse | 10 (15.4) | 2 (20.0) | 8 (80.0) | 0 (0.0) |
| Child | 37 (56.9) | 0 (0.0) | 36 (97.3) | 1 (2.7) |
| Other relatives | 18 (27.7) | 0 (0.0) | 18 (100.0) | 0 (0.0) |
| Type of non-household individual (n=278) | | | | |
| Shared car/taxi with case | 25 (9.0) | 1 (4.0) | 23 (92.0) | 1 (4.0) |
| Praying in a mosque with case | 118 (42.5) | 4 (3.4) | 78 (66.1) | 36 (30.5) |
| Health care staff provided consultation to the case | 1 (0.4) | 0 (0.0) | 1 (100.0) | 0 (0.0) |
| Villager talked with case | 128 (46.0) | 0 (0.0) | 52 (40.6) | 76 (59.4) |
| Café staff and client shared table with case | 2 (0.7) | 0 (0.0) | 2 (100.0) | 0 (0.0) |
| Grocery seller | 3 (1.1) | 0 (0.0) | 0 (0.0) | 3 (100.0) |
| Co-worker (blue color) | 1 (0.4) | 0 (0.0) | 0 (0.0) | 1 (100.0) |
| Among contacts to symptomatic primary cases | | | | |
| | N=158 | N=3 | N=76 | N=79 |
| Sex | | | | |
| Male | 92 (58.2) | 2 (2.2) | 43 (46.7) | 47 (51.1) |
| Female | 45 (28.5) | 1 (2.2) | 31 (68.9) | 13 (28.9) |
| Missing value | 21 (13.3) | 0 (0.0) | 2 (9.5) | 19 (90.5) |
| Classification of risk | | | | |
| High | 50 (31.7) | 3 (6.0) | 47 (94.0) | 0 (0.0) |
| Medium | 10 (6.3) | 0 (0.0) | 10 (100.0) | 0 (0.0) |
| Low | 98 (62.0) | 0 (0.0) | 19 (19.4) | 79 (80.6) |
| Household member of primary case | | | | |
| Yes | 53 (33.5) | 2 (3.8) | 33 (62.3) | 18 (34.0) |
| No | 105 (66.5) | 1 (1.0) | 43 (41.0) | 61 (58.1) |
| Type of household member | | | | |
| Spouse | 6 (11.3) | 1 (16.7) | 5 (83.3) | 0 (0.0) |
| Child | 23 (43.4) | 1 (4.4) | 15 (65.2) | 7 (30.4) |
| Other relatives | 24 (45.3) | 0 (0.0) | 13 (54.2) | 11 (45.8) |
| Type of non-household individual | | | | |
| Shared car/taxi with case | — | — | — | – |
| Praying in a mosque with case | 35 (33.3) | 1 (2.9) | 1 (2.9) | 33 (94.3) |
| Health care staff provided consultation to the case | 2 (1.9) | 0 (0.0) | 2 (100.0) | 0 (0.0) |
| Villager talked with case | 63 (60.0) | 0 (0.0) | 39 (61.9) | 24 (38.1) |

| | | | | |
|---|---|---|---|---|
| Café staff and client shared table with case | 3 (2.9) | 0 (0.0) | 0 (0.0) | 3 (100.0) |
| Grocery seller | 2 (1.9) | 0 (0.0) | 1 (50.0) | 1 (50.0) |
| Co-worker (blue color) | — | — | — | – |

## Discussion

This study provides evidence for asymptomatic transmission of the SARS-CoV-2 virus in Cambodia. Asymptomatic primary cases made up 63.6% of all primary cases within our cluster, and the asymptomatic cases generated seven out of 10 secondary cases. This provides additional evidence confirming that asymptomatic transmission is likely to play an important role in the transmission of SARS-CoV-2 (36-39).

Our study suggested the infectivity among contacts of an asymptomatic and symptomatic case was not statistically different. This finding was not consistent with findings of previous studies, suggesting that symptomatic cases are more infectious than asymptomatic (37). A meta-analysis study by *Buitrago-Garcia D et al*. suggested that contacts of symptomatic primary cases had an increased risk of SARS-CoV-2 infection by 65% compared to the risk of contacts of asymptomatic (37). The absence of evidence for differential infectivity in our study may have occurred due to the small sample size and mild symptom profile in primary cases, which may have led to inadequate power to detect the difference.

Another unexpected finding was the low infectivity. It was clear that we missed the opportunity to detect the 22 primary cases at the airport. The delay was dangerous as their family and community were exposed to those primary cases during their infectious period without any protection. We observed the overall reproduction number (secondary cases per a primary case) was low at 0.5. This basic reproduction number was much lower than that reported in the existing literature, between 1.9 and 6.5 in other settings [44]. Also, the household SAR of 3.4% in our study was much lower compared to that reported in the literature. A meta-analysis study by *Koh WC et al.* reported a pooled household SAR of 18.1% (95% CI: 15.7% and 20.6%), ranging from 3.9% to 54.9% (40). There are several factors that may influence the SAR. First, medium and low-risk contacts were only tested if symptomatic and not routinely at day 13. It is possible that asymptomatic infections were not detected, so attack rates are compromised. Second, it is possible that the primary cases in our study were not highly contagious because they were asymptomatic or mildly symptomatic, indicative of a low viral load (41). However, we have no data to support this argument. Third, housing and temperature could be another factor influencing infectivity.

The majority of our primary cases exposed to their household members (n=14/20) lived with them in a wooden house without an air conditioner in low population density areas. In March and April when the cluster was identified, Cambodia was in the middle of hot season. The combination between wooden housing where ventilation is usually adequate and hot temperatures could have reduced droplet and aerosolized transmission (41). In addition, although the contact tracing and quarantining of the contacts was delayed, it could have prevented further spread by the first wave of the infection chain.

The mode of transmission from the asymptomatic cases to their susceptible contacts remains a gap in our study. We were not able to distinguish whether the transmission was through physical contact or droplet. All asymptomatic primary cases with one or more secondary cases reported they had physical contacts and conversations with their SARS-CoV-2 positive contact. It was not possible to determine at what stage and which mode the virus was transmitted from the primary to the secondary case. This study's strength was that we analyzed a rare cluster in which time and place of exposure were known among primary and secondary cases, with no active preventative strategies in place. This provided an opportunity to calculate the basic reproduction number and attack rate.

We identified seven limitations within our study. First, we may have wrongly assumed the last date of exposure. We assumed the last date of exposure for primary cases was the last date of the event. They might have been infected on the return flight to Cambodia, therefore, the actual recovery period may be shorter than reported in our findings. Second, we assumed that all contacts were exposed to a single primary case based on our information. It was unlikely but possible that the secondary cases were exposed to other unknown or unidentified cases in their community. Third, our sample size was small which may not have enough power to detect statistical difference between groups. Fourth, we did not have information on viral load which would have strengthened our analysis. Despite this, our findings remain useful in understanding asymptomatic infection. Fifth, due to the frequency of testing was every three days (not every day), it has the potential to result in over-estimation of the time for viral clearance. Due to the frequency of testing was every three days (not every day), it has the potential to result in over-estimation of the time for viral clearance. Sixth, another limitation, leading to underestimating the attack rate among household members, is that children may be infected and naturally recovered before being tested for SARS-CoV-2. Finally, recall bias may have occurred during our interviews, which were conducted about six months after cases were discharged from isolation. However, by reminding interviewees what the information they provided contact tracers during the first interview, they were able to recall events. Also, the significance of the event

is likely to have enhanced the individual's ability to recall information associated with the event.

## Conclusions

In this study, asymptomatic COVID-19 cases were shown to transmit SARS-CoV-2 to their contacts. There was no statistically different infectivity among contacts exposed to asymptomatic and symptomatic primary cases. Future response to contain and mitigate COVID-19 spread must take into account asymptomatic transmission.

## Recommendations

- All people who travel back from abroad should be quarantined and tested regardless their symptomatic status.

- The SARS-CoV-2 testing should be done when passengers arrived at the airport or border gate and tested for a second time on day 13 of quarantine, regardless of their symptom status.The Cambodian Government should consider provide education about asymptomatic transmission to general public.

Chapter 5

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## Annex 1: Research summary for general public

# Can a Coronavirus Disease 2019 patient without any sign or symptom transmit the virus?

**Written by Mr. Chhim Srean, student of Master of Philosophy in Applied Epidemiology, Australian National University**

### Why was the study needed?

Coronavirus Disease 2019 (COVID-19) is caused by a virus called Severe Acute Respiratory Syndrome Coronavirus 2 – and commonly referred to as SARS-CoV-2. By 15 December 2020, according to the World Health Organization (WHO), 70 million people were reported to have tested positive for SARS-CoV-2 internationally, and about 1.6 million people had died globally.

SARS-CoV-2 positive people may or may not have any signs or symptoms such as fever, cough, sore throat, runny nose, or difficulty breathing. This is called asymptomatic. A SARS-CoV-2 positive person without any signs or symptoms may not know they have SARS-CoV-2 and can recover naturally without treatment. They can, however, still pass the virus to other people. This makes the disease hard to detect and difficult to prevent further people from getting the virus. Scientists need more evidence to understand how the virus is spread, especially from people who do not know they have the virus

In contributing to a new understanding, we reviewed a group of returned travelers who tested positive for SARS-CoV-2 to describe how the virus from asymptomatic people spread to others.

### Who did we include in our analysis?

We included three groups of people in our analysis as follows.

1 People who had traveled internationally to a religious event between 28 February and 2 March and tested positive for the SARS-Cov-2 within 14 days of returning home.

2 People who have been in contact with the positive cases then tested positive for the SARS-Cov-2 with no history of international travel one month prior to testing positive.

3 Uninfected contacts - people who have been in contact with positive cases (, but tested negative for the SARS-Cov-2 with no history of international travel one month prior to testing positive.

### How did we detect the primary cases?

Between 28 February and 2 March 2020, an international religious event was hosted in a Southeast Asian country. Seventy-nine Cambodians joined that 4-day religious event. They returned to Cambodia on 3 and 4 March 2020.

Eleven days later, on 13 March 2020, Cambodia's Ministry of Health got the information through international collaboration that hundreds of new COVID-19 cases were linked to a religious event. On 14 March, Cambodia's Ministry of Health tested some of the people who returned from that religious event. Two of them were tested positive for the virus. The Ministry of Health decided to test all 79 people who joined the event.

### How did we detect the secondary cases and uninfected contacts?

As part of the national response to stop the spread of SARS-CoV-2, when a person tested positive for SARS-CoV-2, he/she was interviewed within 24 hours to identify people they had been in contact with and places they had visited. They were interviewed to trace their movement (where did they go? at what time? and who did they meet?). We considered a person as a contact if they interacted with the confirmed cases any time between arriving in Cambodia and isolation in hospital.

### How did we collect data?

The Ministry of Health collected all data as part of the national public health response to the COVID-19 pandemic. Additional data on how the primary and secondary cases interacted was collected through phone-interview.

### What did we find?

Twenty-two out of 79 returned travelers tested positive. We called these 22 cases 'primary cases', meaning infected with SARS-CoV-2 at the religious event. Of the 22 primary cases,

14 cases or 63.6% did not develop any symptoms by time they were tested positive SARS-CoV-2. It is possible we would have never known they infected with SARS-CoV-2 if we did not test them.

We identified 501 contacts to the 22 primary cases. Among 501 contacts, ten people (2%) tested positive for SARS-CoV-2. Of these 10 infected people, seven were infected from primary cases who did not develop any sign or symptom.

People in the household of a case were more likely to catch the virus than non-household contacts. In our study, 4 out of 118 household members or 3.4% were tested positive, while 1 out of 60 or 1.7% among non-household contacts tested positive. In households, the spouses had the highest chance to be infected with SARS-CoV-2 from their infected partner. In our study, 3 out of 16 wives tested positive. Children, however, had a much lower chance of catching the virus with 1 out of 60 children testing positive.

Of non-household contacts, people who prayed in a mosque with a case were at risk of getting SARS-CoV-2 (3.3%, 5 out of 153).

## What could our study tell?

Our study found that the people infected with SARS-CoV-2 who do not present signs or symptoms can transmit SARS-CoV-2 to their contacts. It is important that people should all prevent themselves from SARS-CoV-2 infection by avoiding physical contact, talking closer than two meters with people, and doing regular handwashing despite contact with people who do not have any suspected signs and symptoms. Control measures should also include a strategy to prevent SARS-CoV-2 transmission from people who have the virus but do not present any sign or symptom.

Chapter 5

# Appendix 2: Case report form

ឈ្មោះអ្នកបំពេញ:_____លេខទូរស័ព្ទ:_____Case number:_____

Interviewer's name Telephone number

កាលបរិច្ឆេទសម្ភាសន៍ ____/____/20____

Date of interview

**ទំរង់រាយការណ៍ករណីសង្ស័យ ជំងឺរលាកផ្លូវដង្ហើម(COVID-19)**

**Case Report form - suspected case of respiratory infection (COVID-19)**

1. ឈ្មោះ:_____ Patient document number : _____

Name (dossier)

2. អាយុអ្នកជំងឺ: _____ ឆ្នាំ

Age in year

3. ភេទ ❑ ប្រស ❑ ស្រី (ប្រសិនបើស្ត្រី តើមានផ្ទៃពោះឬទេ? ❑មាន ❑មិនមាន ❑មិនដឹង)

Gender Male Female (If female, pregnant? ❑ Yes ❑ No ❑ Unknown)

4. សញ្ជាតិ:_____ 5. មុខរបរ :_____

Nationality Occupation

6. អាស័យដ្ឋាន: ផ្ទះលេខ:_____ ផ្លូវលេខ:_____ ភូមិ:_____ ឃុំ/សង្កាត់:_____

Address: House # street # Village Commune

ខេត្ត/ ក្រុង:_____ លេខទូរស័ព្ទ#1:_____ លេខទូរស័ព្ទ#2:_____

Province/City Telephone # 1 Telephone # 2

7. សូមគូសបញ្ជាក់លក្ខខណ្ឌខាងក្រោម: (ដើម្បីកំណត់និយមន័យករណី)

Please tick the following conditions below ( To define the case)

7.1. សីតុណ្ហភាព _____°C (វាស់ពេលជួបអ្នកជំងឺ)

Curent temperature (Measured when meeting the patient)

7.2. ប្រវត្តិ របស់អ្នកជំងឺក្នុងកំឡុងពេល១៤ ថ្ងៃកន្លងមក

Patient history during the past 14 days

| | | | |
|---|---|---|---|
| 7.2. គ្រុនក្តៅ<br>Fever | ❑មាន<br>Yes | ❑មិនមាន<br>No | ❑មិនដឹង<br>Don't know |
| 7.2.1. ក្អក ឬ ឈឺបំពង់ក ឬ ហៀរសំបោរ<br>Cough or sore throat or runny nose | ❑មាន<br>Yes | ❑មិនមាន<br>No | ❑មិនដឹង<br>Don't know |
| 7.2.2. ហត់ ឬ ពិបាកដកដង្ហើម<br>Breathing difficulty | ❑មាន<br>Yes | ❑មិនមាន<br>No | ❑មិនដឹង<br>Don't know |

7.2.3. ថ្ងៃ/ខែ/ឆ្នាំ ចេញរោគសញ្ញាដំបូង: ____/____/20____

Date of first symptom(s)

8. អ្នកជំងឺបានធ្វើដំណើរមកពីប្រទេសចិន ឬ ប្រទេសដែលកំពុងមានករណី

ក្នុងពេល ១៤ ថ្ងៃមុនចេញរោគសញ្ញា: ❑មាន ❑មិនមាន ❑មិនដឹង

The patient came from China OR country with presence of confirmed cases within 14 days before symptoms:

**If NO/DK >>> Go to Q 9**

8.1. ថ្ងៃ/ខែ/ឆ្នាំមកដល់ប្រទេសកម្ពុជា: ____/____/20____

Date of arrival to Cambodia:

8.2. ច្រកព្រំដែនមកដល់ប្រទេសកម្ពុជា:_____

Port of entry at arrival to Cambodia

8.3. លេខជើងហោះហើរមកប្រទេសកម្ពុជា:

| Flight number to Cambodia | From | To |
|---|---|---|
| Flight 1._____ | មកពី_____ | ទៅ_____ |
| Flight 2._____ | មកពី_____ | ទៅ_____ |
| Flight 3._____ | មកពី_____ | ទៅ_____ |

8.4. មកជាមួយនរណាខ្លះ?

| Who did you come with? Name | Relationship |
|---|---|
| 1._____ | ត្រូវជា_____ |

2._____ ត្រូវជា_____

3._____ ត្រូវជា_____

9. បាននៅក្បែរ ឬ ប៉ះពាល់អ្នកជំងឺរលាកផ្លូវដង្ហើមស្រដៀងផ្តាសាយ១៤ ថ្ងៃមុននេះ

Have you been near or in contact with a person who presented flu-like symptoms for the last 14 days

❑មាន ❑មិនមាន ❑មិនដឹង **If NO/DK >>> Go to Q 10**

Yes No Don't know

9.1. បាននៅក្បែរ ឬ ប៉ះពាល់អ្នកជំងឺនៅទីកន្លែងណា:_____

Specify the place?

10. បាននៅក្បែរ ឬ ប៉ះពាល់សត្វ ១៤ ថ្ងៃមុននេះ

Have you been near or in contact with sick or dead animals for the past 14 days?

❑មិនមាន ❑ សត្វក្នុងស្រុក ❑សត្វព្រៃ ❑មិនដឹង **If NO/DK >>> Go to Q 11**

No Domestic animal Wild animal Don't know

10.1. បាននៅក្បែរ ឬ ប៉ះពាល់សត្វនៅទីកន្លែងណា:_____

Has been near or in contact with animals anywhere

10.2. ក្នុងនោះមានសត្វ ឈឺ ឬ ងាប់ ដែរឬទេ? ❑មាន ❑មិនមាន ❑មិនដឹង

Any sick or dead animals among those animals? Yes No Don't know

11. កំពុងមានបញ្ហាសុខភាព ❑មាន (សូមគូស ✓ រាល់ចំលើយដែលមាន) ❑មិនមាន ❑មិនដឹង

Current health problem Please tick all available answers **If NO/DK >>> Go to Q 12**

❑ Heart disease ❑ Lung disease ❑ Neurologic disease ❑ Blood disease

❑ Kidney disease ❑ Liver disease ❑ Diabetes ❑ Cancer

❑ TB ❑ HIV/AIDS ❑ Malnutrition ❑ Obesity

❑ Other_____

12. វត្ថុវិភាគដែលបានស្រង់យកនិងបញ្ជូនទៅមន្ទីរពិសោធន៍ (សូមគូស ✓ រាល់វត្ថុវិភាគដែលមាន)

Sample(s) collected and sent to laboratory (Please tick all available samples)

❑ តម្បារច្រមុះ/ បំពង់ក ❑ ឈាម-សេរ៉ូម ❑ ផ្សេងទៀត (Other)_____

Nasal swap/throat Blood - serum

ថ្ងៃ/ខែ/ឆ្នាំ ____/____/____ ឈ្មោះអ្នកស្រង់: _____ លេខទូរស័ព្ទ: _____

Date of sampling Name of sample collector Phone number

12.1. កន្លែងយកវត្ថុវិភាគ ❑មន្ទីរពេទ្យ/ គ្លីនិក ❑នៅផ្ទះ

Place of sampling Hospital/Clinic Home

12.2. បញ្ជូនវត្ថុវិភាគទៅមន្ទីរពិសោធន៍ឈ្មោះ _____ ថ្ងៃ/ខែ/ឆ្នាំ ____/____/____

Samples sent to laboratory (name) Date

13. ការគ្រប់គ្រងនឹង ព្យាបាលនៅមន្ទីរពេទ្យ (សូមគូស ✓ បញ្ជាក់ )

Patient management and treatment (please tick)

13. អ្នកជំងឺសម្រាក់ក្នុងបន្ទប់ដាច់ដោយឡែក ❑មាន ❑មិនមាន

Patient placed in a separate room Yes No

13.1. Intubation with assisted ventilation ❑មាន ❑មិនមាន ❑មិនដឹង

Yes No Don't know

13.2. Continuous positive airway pressure (CPAP) ❑មាន ❑មិនមាន ❑មិនដឹង

Yes No Don't know

13.4. Only medication:_____

14. សរុបស្ថានភាពរបស់អ្នកជំងឺ: Summary of patient's status

❑ កំពុងនៅផ្ទះ Staying at home

❑ កំពុងសំរាកនៅមន្ទីរពេទ្យ ឈ្មោះមន្ទីរពេទ្យ:_____

Staying at the hospital Hospital name

ថ្ងៃ/ខែ/ឆ្នាំចូលសំរាកពេទ្យ:____/____/20____

Day / Month / Year of admission

15. ការបញ្ជូន ❑មាន ❑មិនមាន **If NO >>> Go to Q 16**

Patient transfer Yes No

15.1. បញ្ជូនពី ឬ ចេញពី: _____ ថ្ងៃ/ខែ/ឆ្នាំ ____/____/20____
Transferred/discharge from (name of hospital/clinic) Date

15.2. ត្រៀមបញ្ជូនទៅ: _____ ថ្ងៃ/ខែ/ឆ្នាំ ____/____/20____
Prepare for transfer to (name of hospital/clinic) Date

16. ស្ថានភាពសុខភាព: ❑ជាសះស្បើយ ❑ធូរស្រាល ❑ធ្ងន់ធ្ងរ ❑ស្លាប់
Health status Recovery Relieved Serious Died

**If Died >>> Go to Q 17**

**If recovery, relieved and serious>>> Go to Q 18**

17. ក្នុងករណីអ្នកជំងឺបានស្លាប់ In case of death

17.1. ថ្ងៃ/ខែ/ឆ្នាំ Date of death

17.2. នៅកន្លែងណា? ❑ នៅផ្ទះ ❑ មន្ទីរពេទ្យ/ គ្លីនិក
Place of death Home Hospital/Clinic

17.3. ស្លាប់ដោយរលាកផ្លូវដង្ហើមស្រួចស្រាវ ❑មែន ❑មិនមែន
The patient died of acute respiratory infection

18. រោគវិនិច្ឆ័យគ្លីនិកចុងក្រោយ (សូមគូស √ រាល់ជំងឺដែលមាន)
Latest Clinical Diagnosis (Check all that apply) _____

# Annex 3: Questionnaire

**Quantitative Interview with confirmed cases**

| No | Question | Answer |
|---|---|---|
| Case ID | Case ID nCovid_____ | |
| Q1 | At what grade did you complete at school? | Grade_____ |
| Q2 | What is your job? | _____ |
| Q3 | Do you live in a concrete house or wood house? | 1. Concrete house<br>2. Wood house<br>3.Other(specify ) |
| Q4 | Do you use air conditioner at home? | 1. Yes<br>2. No |
| Q5 | How many household members do you have? | _____ |
| Q6 | On what date did you fly to Malaysia? | DD____MM_____2020 |
| Q8 | When did you come back? | DD____MM_____2020 |
| Q9 | Have you had any of the following symptoms during isolation at hospital? | 1. Fever<br>2. Cough<br>3. Runny nose<br>4. Sore throat<br>5. Difficult to breath<br>6. Loss of taste/smell<br>7. Fatigue<br>8. Body pain<br>9. Diarrhoea<br>10. Other(specify) |

Q10. In the information you provided the health department earlier it is mentioned you had close contact with XX people. May you tell us a bit more detail what kind of interaction did you had?

| Contact ID | Relationship with the case (e.g. wife, son, friend, roommate) | Physical or non-physical contact (<2 meter) | Duration of interaction (<2 meter) | Type of interaction (e.g. same household, travelling in the same car, chatting in open air) |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |

**Qualitative Interview with confirmed cases**

Q1 How many days were you in Malaysia?

Q2 How many people flew to join the event with you in Malaysia? Who are they?

Q3 How did you reach there from airport? Who was with you?

Chapter 5

Q4 Where did you stay when you were in Malaysia? Did you stay at the same place the whole time?

Q5 Who did you stay with?

- Was this in the same room?
- What was the ventilation like in this room?
- Was anybody showing symptoms in the room?

Q6 How did you travel to and from the event? Who did you travel with?

Q7 May you describe your main activities in Malaysia? Please give as much details as possible.

- First day: …….
- Second day: ……
- .
- .
- Last day: ……

Q8 Did you wear a mask of face covering? When? What type of covering?

- Were there hand washing facilities at the event? How many times a day did you use them?
- Were you aware of COVID-19 before you travelled/before the event?
- Did you take extra measures to protect yourself from COVID-19 in Malaysia? If yes, why? If not, why not?

Q9 When you arrived home from Malaysia, did you stay home for 14 days in case you had COVID-19?

- Did you do somethings to preventing your household members from COVID-19? If yes, what did you do? If not, why?

Q10 When/If you developed symptoms – what measures did you take to stop others getting sick?

- When you had symptoms – did you
  - Go to the market
  - Go to the mosque
  - Go to your neighbour's house
  - Go to see family / friends
  - Go to work
  - Share a sleeping area

    Other

# Chapter 6 : Teaching

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# Prologue

## Rationale

This chapter demonstrates how I fulfill the two MAE program teaching requirements. First, it requires that MAE students to choose a lesson they learned from the field (LFF) and then teach a small learning group of MAE students within the cohort (MAE19). Each learning group member participates in the LFFs of other members within the group. Second, the MAE program requires that students form a small teaching group, choose a topic, and teach first-year MAE students (MAE20). In addition to the required teachings, I will also demonstrate in this chapter my contribution to local capacity building.

## Lesson learned from the field

Sharing a lesson learned from the field (LFF) allows a small group of MAE students to learn from each other. I was the third person sharing my LFF in my group. I shared my experience in doing contact tracing in Cambodia. In my group, I had other members:

- Laura Goddard, placement at Darwin Public Health Unit, Top End Health Service, Northern Territory, Australia,

- Elenor Kerr, placement at Queensland Health in Australia, The Pasteur Institute Cambodia in Cambodia, Doherty Institute, and Victorian Department of Health and Human Services in Australia, and

- Hannah Vogt, placement at Metropolitan Communicable Disease Control at North Metropolitan Health Service, and Communicable Disease Control Directorate at the Department of Health in Western Australia

I chose this topic based on an informal discussion during the first session shared by Laura Goddard. Other team members expressed their interest in *“something about Cambodia”.* In April 2020, it was a time that Coronavirus Disease 2019 (COVID-19) was a common topic to discuss. I was supporting Cambodia’s Communicable Disease Control Department (CCDC) to do contact tracing. I thought this could be *“something about Cambodia”* I should share.

The purpose of my LFF was to help peers understand contact tracing in a low resource setting like Cambodia as it was different from that of the settings they were working in Australia. The specific objectives of LFF were to (1) understand the rationale of contact tracing, (2) describe the steps of contact tracing in Cambodia, and (3) challenges and lessons learned in contact tracing in Cambodia. The session lasted an hour and was conducted through Zoom teleconference.

I used the “debriefing” method (1, 2) to share and examine what I had been doing using slide presentations (Annex 1). I introduced Cambodia’s situation and my experience doing contract tracing and asked other group members to share their situation and experience. We had a lively discussion. The discussion was around how a COVID-19 patient’s privacy was disclosed, difficulty balancing between keeping a patient’s privacy and ability to identify the contacts, and using the “demonstrating” method (1, 2) to train other contact tracers. I encouraged the discussion by asking questions to the group members to share their experiences and opinions. Everyone was enthusiastic about sharing what they had been doing and their views. No pre-reading was provided as some of us were members of the COVID-19 response team needing time for emergency activities.

I did not conduct a formal evaluation at the end of my session, however my understanding from our discussion there were areas which should be improved, such as adding a practical exercise. By having an exercise, I would have given my teammates time to think, so they could have provided better answers and therefore would have developed a deeper understanding of my topic.

## Teaching first-year MAE student

I joined a group of three MAE students for first-year student teaching, having Vannida Douangboupha (National Centre for Laboratory and Epidemiology in Vientiane, Laos), Kushani Marshall (National Center for Immunization Research and Surveillance), and myself. As the COVID-19 pandemic disrupted the usual learning process, the MAE program allowed us to choose one of our Lesson Learned from the Field (LFF) among our team to teach the first-year students. I took part in all processes, including identifying the teaching topic, discussing and creating the teaching plan, creating slide presentations, commented on the evaluation form, and took part in teaching.

Our team decided to use Vannida's LFF entitled "How to create a knowledge, attitude, and practice survey." It was a 30-minute teaching session through Zoom teleconference. The objectives of that teaching were: (1) explain what a knowledge, attitude & practice (KAP) survey is, (2) explain why we use KAP surveys, and (3) learn how to develop KAP survey questions. The slide presentation used for this teaching is in Annex 2 of this chapter.

The 30 minutes were split into 10 minutes for teaching or three minutes for each team member, eight minutes for students doing their tasks, eight minutes for students presenting their team's task, and four minutes for all students filling an online evaluation form. The lesson plan can be found in Annex 3 of this chapter.

Our team used the "collaborating" method (1, 2), meaning students actively discussed in their group and presented the result of the discussion with the larger group. We started by introducing the theory and an example. Our first member, Kushani, presented the global picture and Laos's dengue epidemiology. I covered the second section introducing "what the KAP is," "why we use KAP," and "how we use KAP." Vannida covered the last section demonstrating how KAP was used in dengue in Laos and gave the assignment to the students.

A link to an online survey was sent to all students for feedback. We encouraged them to complete the form immediately after the teaching was finished. When we got a result, my team and I spent the time to discuss the evaluation results and lessons learned from the teaching. Overall, the students indicated that the teaching was well planned and organized, useful in improving knowledge on KAP surveys, and also useful in improving skills to develop KAP survey questions. According to the feedback, the explanation we provided was clear for the majority of the students. The main criticism we received was that the session was a bit rushed at the ends.

## Additional teaching experience

As part of capacity building, I provided two other trainings. First, I trained in creating smartphone-based data collection form using Kobo Toolbox software (https://www.kobotoolbox.org) for the Cambodian National Institute of Public Health staff. Second, I trained contact tracers at the provincial and district level to respond to the spread of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

### *Kobo Toolbox Training*

Kobo Toolbox (https://www.kobotoolbox.org) is an open-source solution and provide free server and storage. Individual researchers or research institute can easily register and use it. It is designed to support data collection in limited resource settings.

Due to the increasing demand for smartphone/tablet-based forms for data collection, I was informally invited to provide training on creating a smartphone/tablet-based data collection form at the National Institute of Public Health (NIPH), Ministry of Health, Cambodia. Ten staff of NIPH attended the training. It was a one-day training on Saturday, 20 July 2019. I used the “demonstrating” method (1, 2). I started by asking participants to identify the online data and discussed the advantages and disadvantages of non-commercial platforms. I showed them all the steps from having a questionnaire in Microsoft Word to have an electronic form in smartphone. Next, participants learned to do each step by themselves including creating a user account on Kobo Toolbox. They learned to create a short data collection form in Excel and uploaded the form to the Kobo Toolbox server, downloaded the form to use in smartphone. I was with them to support them when they had questions. The training helped them to understand the whole process to have an electronic form in smartphone. However, they have to practice to get more familiarity.

### *COVID-19 Contact Tracing Training*

In response to COVID-19 in Cambodia, I spent four months, from March 2020, to support Cambodia’s Communicable Disease Control (CCDC). I was involved with contact tracing and surveillance between the country’s 2nd and 124th cases.

I shared my contract tracing experience with the Rapid Response Team (RRT) in other provinces to support actual contract tracing and COVID-19 preparedness. In the provinces where the COVID-19 cases were detected, with the CCDC team, we provided a short contract tracing training using the “demonstrating” method (1, 2). This method mixes the theory and the demonstration of how we do things. We presented participants with the rationale and process of contract tracings. We help them get familiar with the existing materials and reporting flow. We demonstrated the actual activities in their areas. RRT teams learned it, and they were confident in doing it in a short time. We left them after two to three days.

In provinces where the COVID-19 case has not yet been identified, we could discuss the first part-- the rationale, process of contract tracings, materials used-, but unable to demonstrate the actual activities.

From my four-month involvement, I supported CCDC to provide the training to 84 RRT and health staff in 12 provinces in Cambodia. We provided training to three RRT leaders and members in Kampong Cham on the 11 March, 75 RRT leaders, RRT members, and health staff from 10 provinces on the 19 March 2020 in Phnom Penh, and six RRT leader and members in Kep province on 21 March 2020.

Photo 1: COVID-19 laboratory and contact tracing on 19-20 March at the National Institute of Public Health, Cambodia

## Lesson Learnt

From this teaching experience, I learned that:

- The teaching plan is useful to control the teaching process. The lesson plan helps us decide what is necessary to talk to achieve the teaching objectives in the

permitted time. Practice teaching using our lesson plan, again and again, allow us to reduce unnecessary content. During the actual teaching, it helps us to overcome nervousness if we are new to teaching.

- Different contexts need different teaching methods. In my case, I used a different types of approaches, including the “debriefing” method for a small group learning that all members were knowledgeable about the topic and could share their opinion contributing to learning, “demonstrating” method to train RRT team as they needed to learn the actual activities urgently, and “collaborating” to teach students who have varied background and expertise.

- Hands-on training may be suitable in emergency situations. In an emergency, people are overwhelmed with competing priorities. The teaching should be focused on what is critical to know and worth spending time with.

# Reference

1. Wikipedia. Teaching method: Wikipedia; 2020 [updated 28 November 2020. Available from: https://en.wikipedia.org/wiki/Teaching_method.

2. Eric Gill. What is Your Teaching Style? 5 Effective Teaching Methods for Your Classroom: Resilent Educator; 2020 [Available from: https://resilienteducator.com/classroom-resources/5-types-of-classroom-teaching-styles/.

# Annex 1: Slide presentation used for Lesson Learned from the field

## Contact Tracing of the Confirmed COVID-19 Cases in Cambodia

By Srean Chhim

LFF session on 17 APR 2020

Acknowledgement : Slides on steps of contact tracing was created by **Michael Kinzer,** MD, MPH, USPHS
Global Health Protection Program Director, US Centers for Disease Control and Prevention (CDC) Cambodia

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## Background

- This LFF is to help MAE students to understand the contact tracing process and its relevant activities in Cambodia- a low resource setting.
- The content is based on my three-month experience involving contact tracing in Cambodia.

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## Objective

- At the end of this LFF, the learning members will be able to:
  - Understand the rational of contact tracing in Cambodia
  - Describe the steps of contact tracing in Cambodia
  - Challenges and lesson learned in contact tracing

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## Rational of contact tracing

- In context of Cambodia, contact tracing is possibly the most crucial to slow down the virus spread before COVID-19 vaccine and treatment are available

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## Cambodia context of COVID-2

- Cambodia detected a first case of COVID-19 on 27 Jan 2019
- By 13 Apr 2020, Cambodia had 123 confirmed cases (out of 5276 tests)
  - 85/123 cases (~69%) were imported cases
  - 36/123 cases (~29%) were locally transmitted cases
  - 2 are under investigation (no epi-link so far, potential local transmission)

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## Steps of contact tracing

- Identification of the cases
- Finding contacts
- Quarantine the high risk contacts

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## Step 1. A Suspect Case is Identified

- Suspect Case Definition:
  - Fever OR symptoms AND travel outside of Cambodia OR contact with a confirmed case
  - Hospitalized pneumonia patient without another diagnosis
- Laboratory Request Form (LRF) completed and sent with sample
- Sample and isolate at home or hospital until result is available
  - 1 person, 1 room, 1 bathroom
  - Choose the location where this is most practical

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## Step 2. A test result is reported

- Negative and NOT a contact
  - Release from isolation
  - No further follow-up
- Negative and a contact
  - Continue normal contact follow-up for 14 days
- Positive
  - Confirmed case
  - Isolate in hospital or home (can be with other confirmed cases)
  - Begin contact tracing

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## Step 3. Contact Tracing

- Contact Tracing Lead interviews case with the Case Report Form (CRF) within 24 hours of positive result
  - Scan and send CRF to CCDC Surveillance Team Lead
- Establish movements and exposures since 14 days before test result, or arrival date in Cambodia
- Finalize contact list on the basis of the interview within 48 hours of positive result using Contact Tracing Form (CTF)
  - Scan and send CTF to CCDC Surveillance Team Lead

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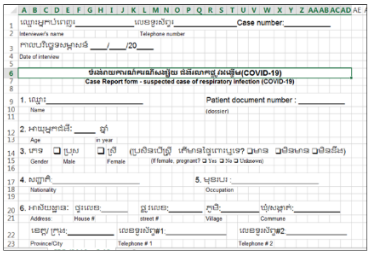
## Case Report Form


Case number:
Case Report form - suspected case of respiratory infection (COVID-19)
Patient document number :

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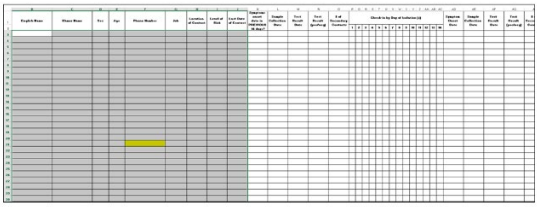
## Contact Tracing Form



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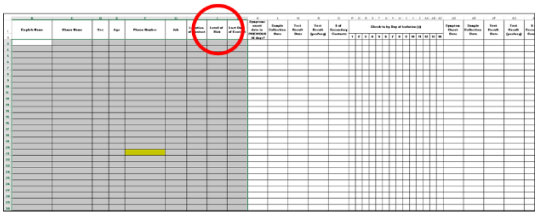
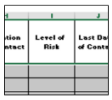
## Contact Tracing Form



12

## Step 4. Determine Level of Risk

- High Risk
  - Unprotected household contacts
- Medium Risk
  - Airplane passengers within 2 rows
  - Unprotected exposure closer than 2 meters for more than 10 minutes
- Low Risk
  - Any other indoor exposure

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## Why level of risk of the contact is important?

| Activities | Risk level of contact | | |
|---|---|---|---|
| | High | Medium | Low |
| Quarantine for 14 days from the date of last contact with the case | Yes, at hospital or home | Yes, at home | No |
| Symptom follow-up for 14 days by phone-call | Yes | Yes | Yes |
| Testing for COVID-19 if a contact had a symptom during symptom follow up | Yes | Yes | Yes |
| Testing for COVID-19 at day 13 of quarantine | Yes | No | No |

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## Step 5. Plan for Contact Tracing

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## Contact Tracing for HIGH RISK

- What was date of last exposure?
- Hospital or home isolate for 14 days after last exposure
  - 1 person, 1 room, 1 bathroom
- Daily symptom checking
- Test for COVID19:
  1. Start of isolation
  2. For any symptoms
  3. End of isolation

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## Contact Tracing for MEDIUM RISK

- What was date of last exposure?
- Home isolation for 14 days after last exposure
  - 1 person, 1 room, 1 bathroom
- Daily symptom checking
- Test for COVID19: For any symptoms

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## Contact Tracing for LOW RISK

- What was date of last exposure?
- Symptom checking for 14 days after last exposure
- No isolation
- Test for COVID19: For any symptoms

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## Example – Household Contacts

- 1 wife, 2 children
  - Close contact indoors, shared meals, bathing, and sleeping quarters
  - HIGH RISK
  - Isolate at home or hospital for 14 days: until 28MAR
  - Test immediately
  - Test for symptoms
  - Test after 14 days on 28M

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## Example – Office Contacts

- 20 co-workers
- 17 more than 2 meters, less than 10 minutes
  - LOW RISK
  - 17 co-workers self-monitor for 14 days until 28MAR
  - Test only for symptoms
  - No isolation
- 3 in the same room
  - Closer than two meters, more than 1
  - MEDIUM RISK
  - **Isolate at home** until 28MAR
  - Test only for symptoms

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## Example – Social Contacts

- 5 people at a restaurant where he ate
  - More than 2 meters, less than 10 minut
  - LOW RISK
  - 5 people self monitor for 14 days until 26MAR, test only for symptoms
- 3 people in the car on 13MAR
  - Less than 2 meters, more than 10 minutes
  - MEDIUM RISK
  - **Isolate at home** until 27MAR
  - Test only for symptoms

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## Example – Final Contact List

- 31 contacts
  - 3 HIGH risk
  - 6 MEDIUM risk
  - 22 LOW risk
- Contact Tracing Lead
  - Assign callers
  - Follow test results
  - Confirm symptom status each day
  - Get started!

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## Challenges and Lessons learned

- No/invalid contact information
  - Keep trying different way, not always success
- No collaboration from the from the confirmed cases
  - Identify their boss or a high rank official to talk to the cases (not always success)
- Panic health staff
  - We go to the site and spent two to three days with them (mostly susses)

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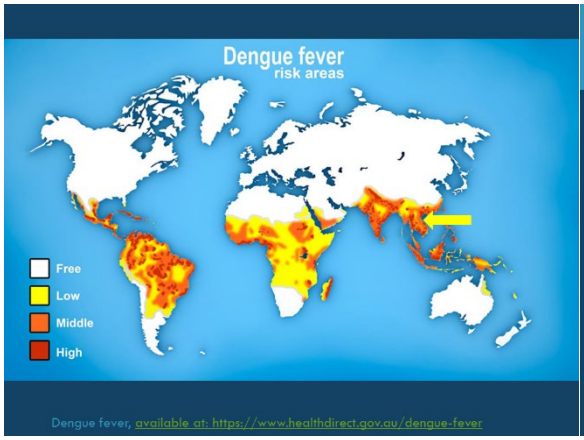
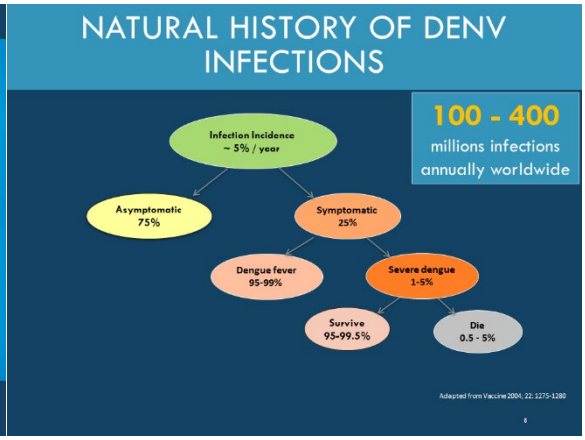
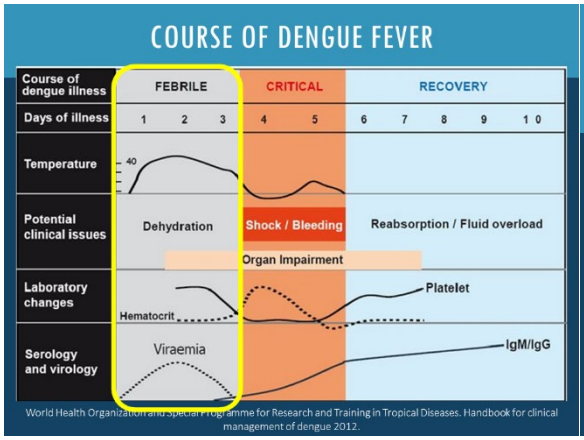
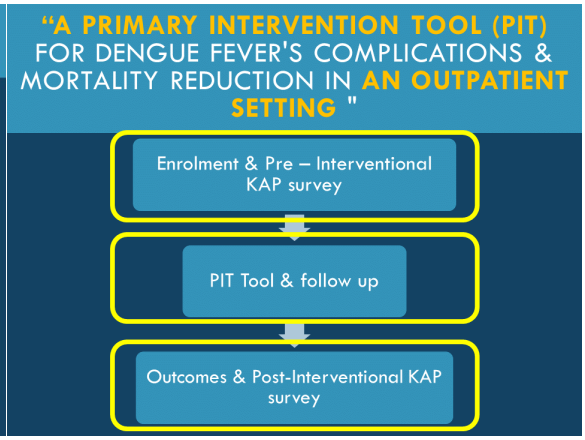
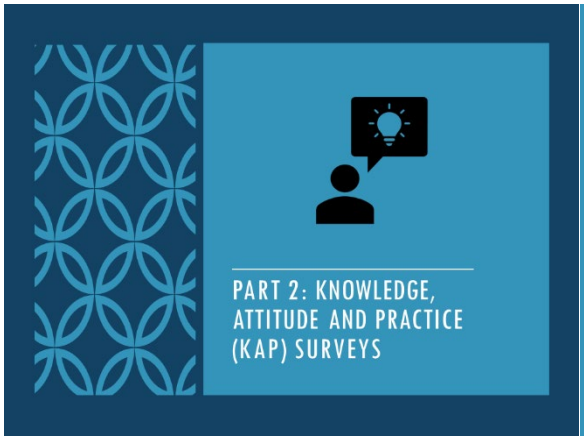
# Annex 2: Slide presentation used for teaching first-year MAE student

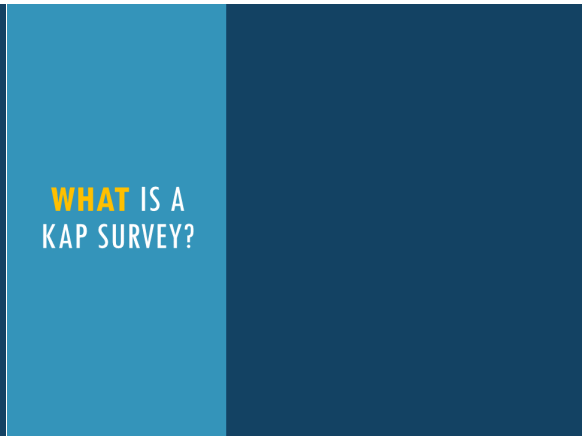

Dengue fever
risk areas
Free
Low
Middle
High
Dengue fever, available at: https://www.healthdirect.gov.au/dengue-fever


NATURAL HISTORY OF DENV INFECTIONS
100 - 400
millions infections annually worldwide
Infection Incidence ~ 5% / year
Asymptomatic 75%
Symptomatic 25%
Dengue fever 95-99%
Severe dengue 1-5%
Survive 95-99.5%
Die 0.5 - 5%


COURSE OF DENGUE FEVER
Course of dengue illness
FEBRILE
CRITICAL
RECOVERY
Days of illness
1 2 3 4 5 6 7 8 9 10
Temperature
40
Potential clinical issues
Dehydration
Shock / Bleeding
Reabsorption / Fluid overload
Organ Impairment
Laboratory changes
Hematocrit
Platelet
Serology and virology
Viraemia
IgM/IgG
World Health Organization and Special Programme for Research and Training in Tropical Diseases. Handbook for clinical management of dengue 2012.


"A PRIMARY INTERVENTION TOOL (PIT) FOR DENGUE FEVER'S COMPLICATIONS & MORTALITY REDUCTION IN AN OUTPATIENT SETTING "
Enrolment & Pre – Interventional KAP survey
PIT Tool & follow up
Outcomes & Post-Interventional KAP survey


PART 2: KNOWLEDGE, ATTITUDE AND PRACTICE (KAP) SURVEYS


WHAT IS A KAP SURVEY?

**WHAT IS A KAP SURVEY?**

A study of a specific population to collect information on:

Knowledge (what is **known**)

**WHAT IS A KAP SURVEY?**

A study of a specific population to collect information on:

Knowledge (what is **known**)

Attitude (what is **believed**)

**WHAT IS A KAP SURVEY?**

A study of a specific population to collect information on:

Knowledge (what is **known**)

Attitude (what is **believed**)

Practices (what is **done**)

**WHY USE A KAP SURVEY?**

**WHY USE A KAP SURVEY?**

To help identify **knowledge gaps**, **cultural beliefs** & **behavioural patterns**

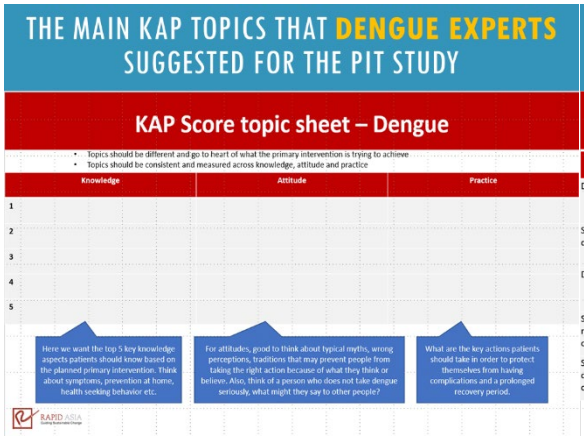
**WHY USE A KAP SURVEY?**

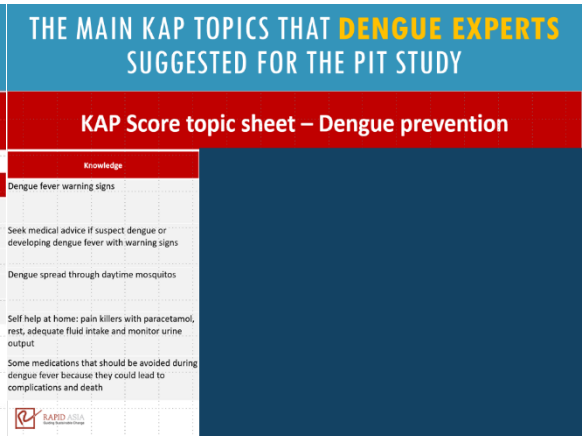
To help identify **knowledge gaps**, **cultural beliefs** & **behavioural patterns**

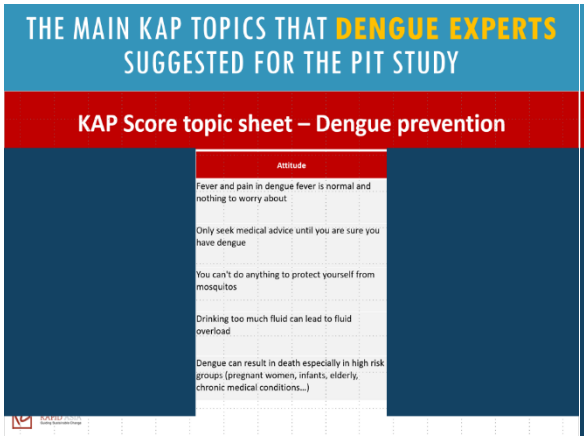
To deepen the understanding of **commonly known information**, **attitudes**, & **factors** influencing behaviour

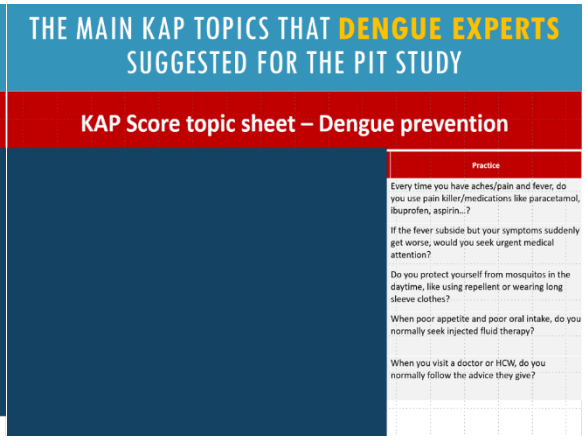

WHY USE A KAP SURVEY?
To help identify knowledge gaps, cultural beliefs & behavioural patterns
To deepen the understanding of commonly known information, attitudes, & factors influencing behaviour
To generate baseline levels (in terms of knowledge, attitudes & practice) & measure changes resulting from interventions.


PART 3: DEVELOPING KAP SURVEY QUESTIONS


THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY
KAP Score topic sheet – Dengue
Topics should be different and go to heart of what the primary intervention is trying to achieve
Topics should be consistent and measured across knowledge, attitude and practice
Knowledge
Attitude
Practice
1
2
3
4
5
Here we want the top 5 key knowledge aspects patients should know based on the planned primary intervention. Think about symptoms, prevention at home, health seeking behavior etc.
For attitudes, good to think about typical myths, wrong perceptions, traditions that may prevent people from taking the right action because of what they think or believe. Also, think of a person who does not take dengue seriously, what might they say to other people?
What are the key actions patients should take in order to protect themselves from having complications and a prolonged recovery period.


THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY
KAP Score topic sheet – Dengue prevention
Knowledge
Dengue fever warning signs
Seek medical advice if suspect dengue or developing dengue fever with warning signs
Dengue spread through daytime mosquitos
Self help at home: pain killers with paracetamol, rest, adequate fluid intake and monitor urine output
Some medications that should be avoided during dengue fever because they could lead to complications and death


THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY
KAP Score topic sheet – Dengue prevention
Attitude
Fever and pain in dengue fever is normal and nothing to worry about
Only seek medical advice until you are sure you have dengue
You can't do anything to protect yourself from mosquitos
Drinking too much fluid can lead to fluid overload
Dengue can result in death especially in high risk groups (pregnant women, infants, elderly, chronic medical conditions...)


THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY
KAP Score topic sheet – Dengue prevention
Practice
Every time you have aches/pain and fever, do you use pain killer/medications like paracetamol, ibuprofen, aspirin...?
If the fever subside but your symptoms suddenly get worse, would you seek urgent medical attention?
Do you protect yourself from mosquitos in the daytime, like using repellent or wearing long sleeve clothes?
When poor appetite and poor oral intake, do you normally seek injected fluid therapy?
When you visit a doctor or HCW, do you normally follow the advice they give?

## THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY

**KAP Score topic sheet – Dengue prevention**

| | Knowledge | Attitude | Practice |
|---|---|---|---|
| E.g. | Dengue fever warning signs | Fever and pain in dengue fever is normal and nothing to worry about | Every time you have aches/pain and fever, do you use pain killer/medications like paracetamol, ibuprofen, aspirin...? |
| | Seek medical advice if suspect dengue or developing dengue fever with warning signs | Only seek medical advice until you are sure you have dengue | If the fever subside but your symptoms suddenly get worse, would you seek urgent medical attention? |
| | Dengue spread through daytime mosquitos | You can't do anything to protect yourself from mosquitos | Do you protect yourself from mosquitos in the daytime, like using repellent or wearing long sleeve clothes? |
| | Self help at home: pain killers with paracetamol, rest, adequate fluid intake and monitor urine output | Drinking too much fluid can lead to fluid overload | When poor appetite and poor oral intake, do you normally seek injected fluid therapy? |
| | Some medications that should be avoided during dengue fever because they could lead to complications and death | Dengue can result in death especially in high risk groups (pregnant women, infants, elderly, chronic medical conditions...) | When you visit a doctor or HCW, do you normally follow the advice they give? |

## CREATE A KNOWLEDGE QUESTION

**Knowledge**

Dengue fever warning signs

a. What are the early warning signs of severe dengue fever? **(Single)**

| | |
|---|---|
| Sudden high fever | 1 |
| Severe stomach pain and persistent vomiting | 2 |
| Red eyes and joint pain | 3 |
| Not sure | 4 |

## CREATE AN ATTITUDE STATEMENT

**Attitude**

Fever and pain in dengue fever is normal and nothing to worry about

K2a To what extent do you agree or disagree with the following? **(Single)**

| | | Disagree Completely | Disagree to some extent | Agree to some extent | Agree completely | Not sure |
|---|---|---|---|---|---|---|
| A | Fever and pain in dengue fever is normal and nothing to worry about | 1 | 2 | 3 | 4 | 5 |

## CREATE A PRACTICE QUESTION

**Practice**

Every time you have aches/pain and fever, do you use pain killer/medications like paracetamol, ibuprofen, aspirin...?

a. When you experience severe aches, pain or high fever, do you normally take pain killers like Ibuprofen, aspirin or diclofenac....? **(Single)**

| | |
|---|---|
| Most of the time | 1 |
| Sometimes | 2 |
| Rarely | 3 |
| Never | 4 |

## GROUP WORK (06 minutes)

**Develop** KAP survey questions

**1** knowledge

**1** attitude

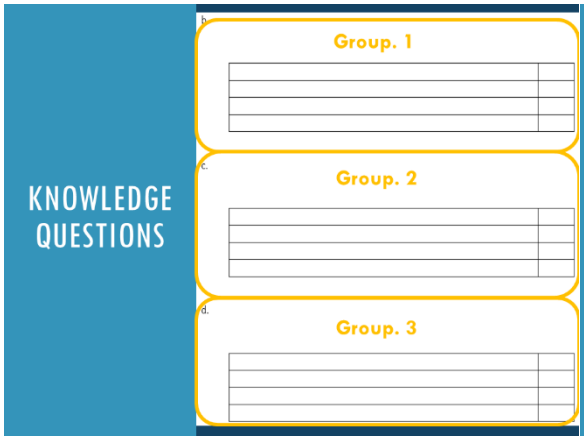
**1** practice

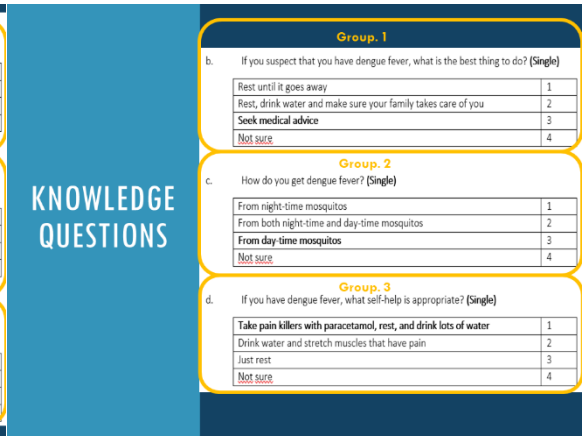
Based on the given main KAP topics relevant to the Primary Intervention Tool Study

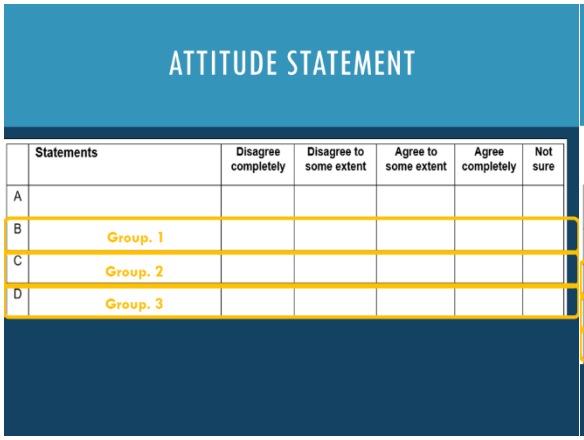
## THE MAIN KAP TOPICS THAT DENGUE EXPERTS SUGGESTED FOR THE PIT STUDY

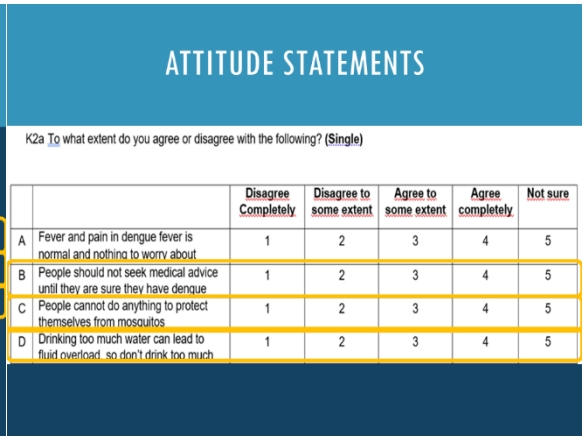
**KAP Score topic sheet – Dengue prevention**

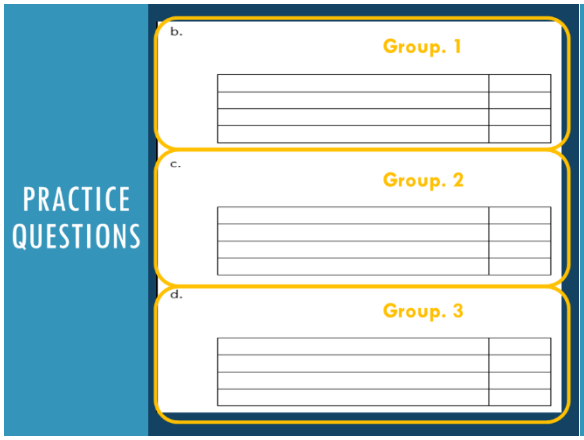
| | Knowledge | Attitude | Practice |
|---|---|---|---|
| | Dengue fever warning signs | Fever and pain in dengue fever is normal and nothing to worry about | Every time you have aches/pain and fever, do you use pain killer/medications like paracetamol, ibuprofen, aspirin...? |
| Gr. 1 | Seek medical advice if suspect dengue or developing dengue fever with warning signs | Only seek medical advice until you are sure you have dengue | If the fever subside but your symptoms suddenly get worse, would you seek urgent medical attention? |
| Gr. 2 | Dengue spread through daytime mosquitos | You can't do anything to protect yourself from mosquitos | Do you protect yourself from mosquitos in the daytime, like using repellent or wearing long sleeve clothes? |
| Gr. 3 | Self help at home: pain killers with paracetamol, rest, adequate fluid intake and monitor urine output | Drinking too much fluid can lead to fluid overload | When poor appetite and poor oral intake, do you normally seek injected fluid therapy? |
| | Some medications that should be avoided during dengue fever because they could lead to complications and death | Dengue can result in death especially in high risk groups (pregnant women, infants, elderly, chronic medical conditions...) | When you visit a doctor or HCW, do you normally follow the advice they give? |

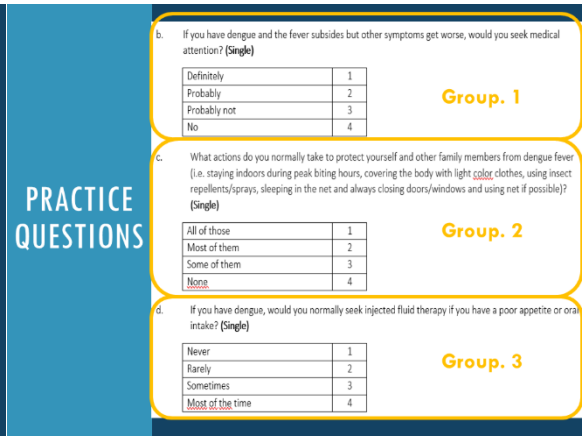

KNOWLEDGE QUESTIONS
Group. 1
Group. 2
Group. 3

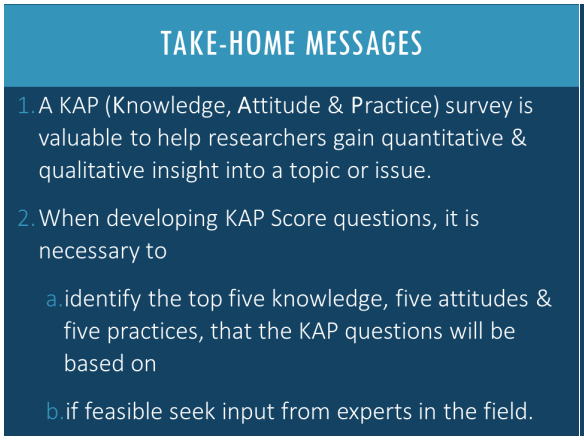

KNOWLEDGE QUESTIONS
Group. 1
b. If you suspect that you have dengue fever, what is the best thing to do? (Single)
Rest until it goes away 1
Rest, drink water and make sure your family takes care of you 2
Seek medical advice 3
Not sure 4
Group. 2
c. How do you get dengue fever? (Single)
From night-time mosquitos 1
From both night-time and day-time mosquitos 2
From day-time mosquitos 3
Not sure 4
Group. 3
d. If you have dengue fever, what self-help is appropriate? (Single)
Take pain killers with paracetamol, rest, and drink lots of water 1
Drink water and stretch muscles that have pain 2
Just rest 3
Not sure 4


ATTITUDE STATEMENT
Statements
Disagree completely
Disagree to some extent
Agree to some extent
Agree completely
Not sure
A
B Group. 1
C Group. 2
D Group. 3


ATTITUDE STATEMENTS
K2a To what extent do you agree or disagree with the following? (Single)
Disagree Completely
Disagree to some extent
Agree to some extent
Agree completely
Not sure
A Fever and pain in dengue fever is normal and nothing to worry about 1 2 3 4 5
B People should not seek medical advice until they are sure they have dengue 1 2 3 4 5
C People cannot do anything to protect themselves from mosquitos 1 2 3 4 5
D Drinking too much water can lead to fluid overload, so don't drink too much 1 2 3 4 5


PRACTICE QUESTIONS
b.
Group. 1
c.
Group. 2
d.
Group. 3


PRACTICE QUESTIONS
b. If you have dengue and the fever subsides but other symptoms get worse, would you seek medical attention? (Single)
Definitely 1
Probably 2
Probably not 3
No 4
Group. 1
c. What actions do you normally take to protect yourself and other family members from dengue fever (i.e. staying indoors during peak biting hours, covering the body with light color clothes, using insect repellents/sprays, sleeping in the net and always closing doors/windows and using net if possible)? (Single)
All of those 1
Most of them 2
Some of them 3
None 4
Group. 2
d. If you have dengue, would you normally seek injected fluid therapy if you have a poor appetite or oral intake? (Single)
Never 1
Rarely 2
Sometimes 3
Most of the time 4
Group. 3


TAKE-HOME MESSAGES
1. A KAP (Knowledge, Attitude & Practice) survey is valuable to help researchers gain quantitative & qualitative insight into a topic or issue.
2. When developing KAP Score questions, it is necessary to
a. identify the top five knowledge, five attitudes & five practices, that the KAP questions will be based on
b. if feasible seek input from experts in the field.


QUESTIONS? COMMENTS?
Thank you
Evaluation: Survey Monkey
https://www.surveymonkey.com/r/L5NGQCB

# Annex 3: Teaching session outline

| | |
|---|---|
| Date of session | Friday 28 August 2020 |
| Leads | Kushani, Srean, Vannida |
| Topic | How to create knowledge, attitude, and practice (KAP) survey questions using KAP Score model |
| Session Outlines | What is a KAP (Knowledge, Attitude and Practice) survey?<br>When would you use a KAP survey?<br>KAP examples<br>What is the KAP Score model?<br>When would you use a KAP Score Model?<br>Introduce the dengue scenario<br>Students practice developing KAP survey questions based on the top five dengue KAP from dengue experts.<br>Students report back on their KAP survey questions and provide useful feedback and tips.<br>Wrap up and evaluation. |
| Learning Objectives | Students are able to:<br>Explain what a KAP survey is and when to use it.<br>Explain what a KAP Score model is and when to use it.<br>Practice developing KAP survey questions and apply these to a real-life scenario |
| Teaching | Introduce KAP surveys as a useful tool to help researchers to gain quantitative and qualitative insight into a topic/issue.<br>Based on the given scenario, guide students to develop KAP Score questions and agree on tips on developing KAP score questions, including<br>identify the top five knowledge, five attitudes, and five practices, where the KAP questions will be based on<br>if feasible, seek input from experts in the field |
| Activity & Assessment | Students will be divided into groups of 3-4 to develop one knowledge, one attitude, and one practice question. These should be based on the provided scenario and the top five dengue KAP from dengue experts.<br>Each group will present their KAP survey questions back to the class, and students will be asked to provide feedback on each group's suggestions. |
| Time | 3 mins – intro to KAP surveys and examples<br>3 mins – intro to KAP Score model and explanation<br>3 mins – intro to the scenario<br>8 mins – each group develops 3 KAP survey questions based on the scenario<br>8 mins – feedback of KAP survey questions to groups, wrap up and evaluation |