GUARD study report

Good Use of Antimalarials and Rapid Diagnostic Tests in Cambodia study report
October 2011

Shunmay Yeung, Clare Chandler, Patricia Tabernero, Mikhael DeSouza, Ouk Rada, Chea Nguon

ACT CONSORTIUM

Contents

Study team....4

Acknowledgements....4

Abbreviations....5

Abstract....6

Background....7

Malaria in Cambodia....7

Malaria treatment and diagnosis....8

Drug resistance....8

Private sector in Cambodia....8

Subsidised ACT and RDT in Cambodia....9

Research questions....10

Methods....11

Study population and sample selection....11

Inclusion Criteria....11

Ethical approval, permissions and consent....11

Study personnel....12

Data collection....12

Census and RDT user assessment....12

Mystery Client Study....12

Focus Group Discussions....13

RDT quality analysis....13

Temperature and Humidity logging....14

Data Entry and analysis....14

Census and RDT user assessment....14

Mystery client study....14

FGD....15

Results....16

Review of the current system for quality assurance of RDTs in private sector....16

RDT selection and procurement....16
In-country supply and stock....16
Census Survey....18
Description of Survey....18
Antimalarials....21
Rapid Diagnostic Tests....23
Buying RDTs....24
RDT quality Testing....29
RDT user assessment....30
RDT temperature and humidity logging....31
Mystery client study....35
Mystery Client description of illness....35
Advising blood tests....35
Selling drugs “for malaria”....35
Focus Group Discussion....37
Discussion....38
Summary of key findings....38
Strengths, limitations and challenges....38
References....44
APPENDIX: FOCUS GROUP DISCUSSION – FULL RESULTS....46
STUDY PARTICIPANTS....46
KEY CONSTRUCTS....48
Selling, not treating....48
Tailoring medicines....51
Showing the parasites....55
Communication and Regulation....59

STUDY TEAM

Shunmay Yeung (PI)

Clare Chandler (Co-PI)

Chea Nguon (Co-PI)

Ouk Rada

Patricia Tabenero

Mikhael DeSouza

Bonnie Cundill

Phoeuk Pisen

Kim Daro

Thearak Muong

Chamnorng Som

Collaborators

Henrietta Allen (Malaria technical advisor, PSI)

Didier Menard (Institut Pasteur – Cambodge)

Harparkash Kaur (LSHTM)

Facundo Fernandez (Georgia Tech)

ACKNOWLEDGEMENTS

This study was jointly funded by the Clinton Health Access Initiative and the ACT consortium which is funded by a grant from the Bill and Melinda Gates Foundation.

We would not have been able to complete the study without the support of numerous people including the administrative staff of the CNM, PSI, ACT consortium and the provincial health departments, operational districts and health centres. We are enormously grateful to all the research assistants, translators and actors who worked tirelessly and with endless enthusiasm. Finally we would like to thank the study participants who generously shared with us their time and thoughts.

ABBREVIATIONS

ACT	Artemisinin Combination Therapy
AMFm	Affordable Medicines Facility malaria
A+M	Artesunate plus Mefloquine (pre-packaged for public sector)
CNM	National Centre for Malaria, Parasitology and Entomology
CS	Census Survey
FGD	Focus Group Discussion
HCCA	Health Centre Catchment Area
LSHTM	London School of Hygiene and Tropical Medicine
MC	Mystery Client
MOH	Ministry of Health
NGO	Non-governmental Organization
OD	Operational District
PHD	Provincial Health Department
PPM	Public-Private Mix
PSI	Population Services International
QA	Quality Assurance
RA	Rapid Diagnostic Test Assessment
RDT	Rapid Diagnostic Test
VMW	Village Malaria Worker

ABSTRACT

Using a mixed methods approach that included quality assessments, a mystery client study and qualitative research, we conducted a comprehensive evaluation of malaria Rapid Diagnostic Tests and in the private sector in 12 health centre catchment areas across Cambodia. In summary, we found that the RDTs collected from drug shops had maintained good quality and that storage and transport conditions were on the whole satisfactory. Uptake of RDTs appeared to highest in the most highly trained providers i.e. "cabinets", and lowest in grocery shops, with pharmacies and drugs shops having some ambiguity around their role. Findings from the focus group discussions and the mystery client study suggest that some of the problems in uptake and interpretation relate to RDTs being on the margins of practice for these providers who see themselves as either providing a diagnosis and cure (*pinit pchier bal*) or simply selling drugs for symptomatic relief (*lout tnam*). Several problems with RDTs were identified in terms of their actual use, in particular relating to interpretation of results, blood safety, and problems related to the buffer and the blood collecting device. In summary this study provides a comprehensive assessment of malaria RDTs in one of the first countries to implement them in the private sector.

BACKGROUND

The detection and effective treatment of malaria have become public health targets across countries affected by malaria facilitated by the availability of Rapid diagnostic tests (RDTs) and artemisinin combination therapies (ACTs) (Bell et al., 2006). However, the assumed technological imperatives of these commodities have not in themselves always brought the desired changes in targeting of treatment (English et al., 2009) or access to effective antimalarial drugs (Cohen et al., 2010; Smith et al., 2009).

In recognition of the important role of the private sector in treatment seeking in many countries (Bennett et al., 1997), interest has arisen in actively engaging them in order to increase access to good quality care for malaria. This includes subsidizing and promoting the sale of good quality ACTs (Arrow et al., 2004; Laxminarayan et al., 2006) and possibly RDTs. However, this raises many questions, particularly over regulation of practices. In many countries the provision of antimalarial drugs and diagnostic services in the private sector is restricted to licensed providers. Proposals therefore to provide these goods through "unlicensed" providers is therefore often met with resistance. Private providers are also assumed to practice with a primary interest in profit, leading to fears of inappropriate use of equipment and drugs (Cross & MacGregor, 2009).

The Affordable Medicines Facility – malaria (AMFm) programme is piloting a manufacture-level co-payment for the purchase of ACTs by governments, NGO's and qualified private importer/distributers in 9 pilot countries[1]. Critics of the AMFm argue that the subsidy will lead to gross overuse of ACTs ,which would be a waste of drugs – and money (Moon et al., 2009). There is therefore interest in also introducing RDTs into the private sector in order to improve targeting and decrease wastage. However, this has been countered by the argument that introducing diagnostic tests and their paraphernalia into drug shops may be delegating health care responsibilities too far to those with little training in managing the tests, let alone non-malarial illnesses (De Allegri et al., 2011). Little is known about how tests may be assimilated into practice by private providers, and how this may affect care provided to their clientele (Adeyi & Atun, 2010).

Cambodia is the first country to have introduced subsidized RDTs and ACTs in the private sector through a social marketing programme that was first piloted by the European Commission -Malaria programme in 2000, and then scaled up and handed over to Population Services International (PSI) in 2003 (Yeung et al., 2011). It therefore offers a unique opportunity to explore some of the issues in practice.

MALARIA IN CAMBODIA

In Cambodia, malaria continues to be an important cause of mortality and morbidity even though the burden of the disease has been declining steadily in the past years. Malaria is transmitted by species of *Anopheles* which breed in the forest. Therefore the most at risk populations are those that live or work in or near the forest, particularly in the border areas of Cambodia with Thailand, Laos and Vietnam. Approximately 3 million people are considered at-risk. Although prevalence rates from 15% up to 40% have been reported in a few villages, rates are generally much lower at around 0%-3% (Incardona et al., 2007; WHO). Overall, malaria incidence in Cambodia was reported to be 4 new cases per 1000 population in 2010, with 135 deaths, according to treated cases in public health facilities (Kingdom of Cambodia Ministry of Health, 2011). Incidence is highest in the Eastern part of the country, with 50-100 new cases per 1000 population in 2010 (ibid). Over 70% of the patients seek treatment outside the public sector, therefore malaria burden estimates which are based on the public health surveillance system significantly underestimate the true burden of disease(CNM, 2009-2014).

[1] Cambodia is one of the pilot countries but has been unable to implement due to delay in international registration of the drug dihydroartemisinin-piperaquine.

MALARIA TREATMENT AND DIAGNOSIS

Since 2000 the national first-line treatment for uncomplicated *P. falciparum* malaria has been co-blistered artesunate and mefloquine although the CNM have wanted to switch to a co-formulated ACT for a number of years. The inability to do so has been in part due to delays in the development and registration of dihydroartemisinin-piperaquine (DHA-PIP), the only realistic alternative to artemether-lumefantrine which has been shown not to be effective in Cambodia. Only in the public sector in Containment zone 1 (described below) is the first-line drug DHA-PIP.

Swift detection of cases, and treatment with a recommended combined therapy for the recommended duration is central to the strategy of the national malaria control programme (Kingdom of Cambodia Ministry of Health, 2011). In recognition that most antimalarial treatments are obtained in the private sector, there has been a programme of subsidizing and social marketing both the first-line ACT and RDT since 2001 (Yeung et al., 2011).

DRUG RESISTANCE

Since the 1950's the Thai-Cambodia border has been at the epicenter of multidrug resistant *P. falciparum* malaria and of much concern there have been recent reports that the parasites in this area have now developed tolerance, or "resistance" to the artemisinin derivatives (Dondorp et al., 2009). The emergence of resistance, is likely to be due to a combination of factors including the widespread use of sub-standard drug regimens, including artemisinin monotherapies and poor quality drugs (Yeung et al., 2008). In response to the threat, a bi-national artemisinin resistance programme was initiated which included the establishment of containment zones (Samarasekera, 2009) and a range of activities to limit the spread of resistance (Dondorp et al., 2010). Containment Zone 1 was defined as the 5 administrative districts in which there was evidence of drug resistance (Pailin, Samlaut and Sampalouen districts in Battambang province, Veal Veng district in Pursat province and Chumkiri in Kampot province). Containment Zone 2 includes the whole province containing the Zone 1 districts and the neighboring provinces and therefore covers the West and North of Cambodia and Zone 3 includes other malaria-endemic provinces ie most of the East. Activities include strengthening and policing of regulation, with the 'justice police' trained to clamp-down on the sale of counterfeit drugs and oral artemisinin monotherapy by private providers (Nariddh, 2011; World Health Organisation, 2011). Particular focus has been paid to private providers in the Containment areas who have been given a number of different messages including instructions not to sell any antimalarial drugs all, to only sell Malarine and only those with a positive test, or to even to refer all suspected cases of malaria.

PRIVATE SECTOR IN CAMBODIA

The private sector in Cambodia includes manufacturers, importers, distributors and wholesalers of drugs and health care products as well as the private providers that are the focus of this report. The term "Private providers" covers a wide-range of provider types, from qualified health care workers such as doctors, nurses and pharmacists, through to grocery shops and so-called mobile providers. Many health care workers are employed in the public health sector and also have their own private clinic, laboratory or pharmacy. As a generalisation, the more qualified or "official" providers tend to cluster in the towns and larger villages whereas in the smaller and more remote villages, the providers tend to be more informal.

Reflecting their wide range of experiences and training, private providers provide a spectrum of products and services; from single tablets of chloroquine within "cocktail packages" of drugs, to diagnosis with RDTs or microscopy and intravenous injections and infusions of quinine and artemisinin derivatives.

The village shop is usually people's first port of call with a subsequent visit to more trained providers for more serious symptoms or where patients have not improved after the initial treatments (Yanagisawa et al., 2004).

The Department of Hospitals is responsible for maintaining a register of licensed clinics and laboratories, and the Department of Drug and Food is responsible for maintaining a register of licensed pharmacies which are categories as "Depot A" or "Depot B" according to the level of qualifications and the products they are permitted to sell. Officially, only registered private providers have the right to sell certain products and provide certain services. Historically however the private sector has been poorly regulated and there are many private providers who operate outside of what they are strictly legally allowed to do.

Currently the relationship between the public and the private sector is undergoing significant change with a number of different initiatives. At the ministerial level, there is a sector-wide public-private partnership (PPP) initiative and decentralisation of the responsibilities from the central Departments to Provincial Health Department and a clampdown on the trade in counterfeit drugs. Within the malaria control programme, as well as the ban on the import and sale of oral artemisinin monotherapies, there have been a number of malaria-specific, district level PPM initiatives which are gradually being scaled up to nationwide.

SUBSIDISED ACT AND RDT IN CAMBODIA

PSI's procures and distributes subsidised specially blister packaged ACT of artesunate and mefloquine branded as Malarine, and a commercially produced RDT re-branded under the name Malacheck. Up until 2009 the RDT was Paracheck® a *P. falciparum* specific test. Since 2010 the RDT has been switched to the Carestart® *P. falciparum* and *non P-falciparum* RDT, but still sold under the name Malacheck. Of note the "new" Malacheck requires only 2 drops of buffer, compared to 6 drops for the original Paracheck® based RDT.

In addition, PSI's social marketing programme also includes the training and support of private providers and a comprehensive behaviour change communications programme which includes mass media, provision of job-aids and mobile video units.

A case study of the social marketing programme has recently been published which includes a description of the available evaluable evidence on its impact on awareness, availability and uptake of RDTs and ACTs (Yeung et al.,2011). Apparent gaps in knowledge include information in relation to how RDTs are used in practice, the quality of RDTs and their use, and a qualitative understanding of how providers perceive them. In this study we address some of these information gaps.

RESEARCH QUESTIONS

This study asks the following research questions:

1. How are RDTs and artemisinin drugs used by private providers, what is their quality and how can a quality control system be designed?
2. How are fevers managed at private providers in terms of use of RDTs, artemisinin based drugs and drug cocktails?

To answer these research questions, we aimed to document the following:

For research question 1,

- To review the current system for quality assurance of RDTs in private sector
- To document the quality of RDTs and artemisinin drugs retrieved from private providers
- To observe whether RDTs are performed correctly
- To suggest ways to assure the quality of RDT use in the private sector

For research question 2,

- To document the availability and uptake of malaria diagnostics including RDTs
- To document the type of treatments sold to febrile clients
- To observe the nature of the interaction between providers and patients
- To explore the rationale for provider's diagnosis and treatment behaviour

METHODS

In order to fulfil the study objectives, a range of methodologies were applied including a census survey of drug outlets, assessment of RDT user performance, RDT quality analysis, temperature and humidity logging, mystery client study and focus group discussions. Except for the temperature and humidity logging of RDTs during transport, the remainder of the study components were carried out in 12 randomly selected Health Centre Catchment Areas. The sample selection and the study components are described in more detail below. In addition stakeholder interviews were carried out with key informants in PSI who are involved in the management of the RDT supply chain and quality assurance.

STUDY POPULATION AND SAMPLE SELECTION

The study was conducted between October 2010 and February 2011, in 12 health centre catchment areas (HCCA)in Cambodia.

The primary sampling unit was the HCCA plus the nearest market town. All health centres that recorded more than 100 malaria cases in the first 6 months of 2009 (the most recent period for which completed data were available) were included in the sampling frame and stratified into either Containment areas (ie Zone 1 or 2) or Non-containment area (ie Zone 3). From each strata 6 health centres and their surrounding catchment area were randomly selected (12 HCAAs in total). The randomised selection process resulted in the following: From Containment areas, one HCAA each from Oddor Meanchey, Siem Riep, Pailin, Battambang, Preah Vihear and Kampot provinces, and in the non-containment area, three from Kratie, and one each from Rattanakiri, Mondulkiri and Kampong Thom provinces.

It was estimated that there would be on average of 15 private providers per HCCA, and that this would result in a sample size of approximately180 providers.

INCLUSION CRITERIA

Any provider who potentially sold medicines or malaria diagnostics was initially visited in order to identify providers who sold antimalarials or RDTs. Attempts were made to distinguish and select only "registered" and "trained" providers. However in most settings, up-to-date lists were not available from local health authorities and therefore all potential providers were included in order to capture more information which would enable later categorisation.

ETHICAL APPROVAL, PERMISSIONS AND CONSENT

Ethical approval for the GUARD study was granted from the National Ethics Committee for Health Research (NECHR) in Cambodia and the London School of Hygiene and Tropical Medicine Ethics Committee, UK(Ref: 5970).

In each study area the Provincial Health Department, Operational District and Health Centre chief were informed about all the study activities and asked to provide lists and or maps of private providers located in their catchment areas.

Individual written consent was obtained in Khmer from the enrolled individuals at the beginning of the census. The provider was given a copy of the signed and dated informed consent form. Each provider was

asked if he agreed to be interviewed on that day, tested for RDT assurance, exchange RDTs or antimalarials and to possibly participate in a Focus Group Discussions.

As per discussion with the Ethics committees, prior informed consent was not obtained for the mystery client study.

STUDY PERSONNEL

The census survey was conducted by three teams, each allocated to four HCCAs. Each team consisted of one driver and three or four surveyors. Field work was supervised by two supervisors who moved between teams and ensured that field work was conducted according to the protocol and answered any queries. The mystery client study was conducted by one team composed of a LSHTM researcher, two translator/research assistants (social sciences graduates), three "mystery client" actors and one driver. The focus group discussions were carried out by one team composed of a LSHTM researcher, two facilitators, both of whom had taken part in the mystery client research and a transcriber.

Training

For the census survey, interviewers participated in one week training that included one day in the field pre-testing the questionnaire. For the mystery client study, the research assistants and mystery client actors participated in a 3 day training including a day in the field pre-testing the data collection tools and de-briefing process. For the Focus Group Discussions, the research assistants were given an additional 3 day training on the objectives and qualitative field and data management methods.

DATA COLLECTION

CENSUS AND RDT USER ASSESSMENT

Data was collected using a structured questionnaire that collected information about the availability of antimalarials and RDTs, as well as opinions and sell-reported practice with regards to antimalarials and diagnosis. All data collection tools were translated into Khmer and back translated to English, piloted and revised a number of times before the final version. At each study location interviewers were provided with the list of private providers as identified by local health authorities. The team attempted to visit all the providers on their list and to identify and visit any other potential providers (of drugs or RDTs) that they found through local enquiry and observation. The location of each outlet was recorded with a hand-held GPS unit. Samples of all artemisinin containing drug were purchased and were sent for laboratory analysis. All eligible providers were invited to participate in an RDT user assessment at the time of the survey. Providers were observed when performing an RDT on a volunteer or a febrile patient in order to assess quality of performance using a standardised checklist.

MYSTERY CLIENT STUDY

The main data collection instruments were a semi-structured debriefing questionnaire and the audio recording of the mystery client actor relaying the story of his interaction with the provider to a research assistant. The interaction itself between the mystery client and the provider was not audio-recorded.

The MC study was conducted in all the selected HCCAs except for in Battambang operational district (OD) due to a road collapsing which made the district inaccessible. The MC study was conducted prior to the census study in 3 ODs and after the census study in the remaining 8 ODs. In addition to the districts included in the Census study, in collaboration with PATH and URC, we conducted additional MC visits in 2

districts, Sala Krau in Pailin (URC) and Sotnikum (Siem Riep) in which these NGOs were conducting pilot studies of PPM for malaria management.

Providers were considered eligible for inclusion in the MC study if according to the census study, they had reported selling ACTs and/or RDTs. Where census information was not available the MC visited all visible providers.

In each HCCA if there were 16 or less eligible providers all were included in the MC study. If there were more than 16 providers then a random selection of 16 were selected from those who with RDTs or ACTs and training, or were on the list provided by PSI. The mystery client actors visited each selected private provider pretending either to be a patient themselves, or a friend or relative of a sick patient. They were instructed to initially only give symptoms of malaria (fever, headache, body pain, chills) and to observe what the provider did and said, before providing more information and buying drugs that were offered. Immediately after the interaction or as soon as possible, the mystery client was debriefed by a research assistant who audio-taped the debriefing and filled in the semi-structured questionnaire. All purchased drugs were sent for laboratory for identification and quality analysis.

FOCUS GROUP DISCUSSIONS

Private providers who had participated in the census survey and mystery client were brought together to discuss their experiences with using medicines and tests for malaria. Focus group discussions (FGDs) were chosen because of the opportunity to observe discussion over the topics of interest between participants, enabling the interpretation of norms and points of derision.

For most districts, all providers who had taken part in both the census and the MC, and who were on the PSI or local authority list, were invited to participated in the FGD. However, in Siem Reap there were too many providers, and a random selection was made. Very large providers (such as hospitals) were excluded as it was felt that they would be unlikely to send a person who was authorized to share information and who was familiar with medical decision making at that practice.

The study co-ordinator invited each provider individually through a visit or telephone call a couple of days prior to the scheduled meeting.

Each FGD was held in a hired room that was not associated with health authorities. Participants were set in a circle, with the facilitator and the note taker within the circle and the LSHTM researcher sitting slightly outside. Stickers with numbers were handed to all participants, offering to the participants to address each other by their number to ensure confidentiality. During the discussion, the facilitator introduced topics in the form of questions, based on the topic guide. The facilitator tried to encourage discussion amongst participants. At the end of the discussion the LSHTM researcher often joined in with the discussion, to probe on some subjects that were discussed.

Three translators (including 2 of the research assistants who participated in the FGDs) carried out the transcriptions and translations. Audio recordings were transcribed in Khmer into Word and then translated into English using meaning-based translation. The translated phrases were inserted immediately after each original Khmer phrase. Another translator then listened to the audio tape and reviewed the transcription and translations. Discrepancies were discussed between the two translators and where uncertainty or disagreement remained, the third translator was consulted.

RDT QUALITY ANALYSIS

Interviews were conducted with PSI staff in November and December 2010 in order to describe the process of quality assurance of RDTs.

To examine the quality of RDTs from the field, the study team exchanged two new boxes of RDTs with two boxes of RDTs from the shelves of 12 purposively selected provider, one in each of the 12 Health Centre Catchment Areas. Providers were selected in order to represent different storage conditions eg pharmacies in a market towns with apparently good storage conditions and drugs shops in remote villages with apparently poorer storage conditions. The collected boxes were labelled with the unique ID code, placed in a zip lock bag, and transported to Institute Pasteur Cambodia in Phnom Penh for analysis.

TEMPERATURE AND HUMIDITY LOGGING

DURING TRANSPORT

On the 30th of November 2010, five data loggers were placed in 5 identified RDT cartons at PSI's main warehouse in Phnom Penh. These cartons followed the normal route of RDT supply from PSI's, to the provincial depots, and then to wholesalers/retailer. It was expected that the 5 cartons would reach their final destination in 1 to 3 months, from where the data loggers would be sent back to PSI's office in Phnom Penh. The warehouse supervisor, was responsible for making sure that the cartons left for their selected destinations, and for recording their daily location until the loggers were returned.

Logger number 1: Sent to Preah Vihear province via Battambang Depot

Logger number 2: Sent to Rattanakiri province via Kampong Cham Depot.

Logger number 3: Sent to Battambang Province

Logger number 4: Sent to Kompong Cham province

Logger number 5: Sent to Koh Kong province directly

IN ROUTINE STORAGE CONDITIONS AT PRIVATE PROVIDERS

In February 2011, data loggers were left in boxes of RDTs at five private providers that were purposively selected to represent different geographic areas and types of shop. At time of writing, 2 of them have been retrieved.

DATA ENTRY AND ANALYSIS

CENSUS AND RDT USER ASSESSMENT

Data was double entered into a pre-designed Epiinfo database then checked for coding errors and consistency. The two data sets were compared and differences checked with the original data form form and in some cases were checked with each provider over the phone. Data cleaning was conducted with double checking of some of the translation of written answers from Khmer to English. STATA 11, (Stata Corp., College Station, TX, USA) was used for data management and analysis.

MYSTERY CLIENT STUDY

Data from the semi-structured questionnaire was handled similarly to the Census survey. In addition the audiotapes of the debriefing sessions were transcribed and then translated into English using meaning based translation. A second questionnaire was then filled in using information from the debriefing note, in order to collate some of the information that was missed in the original semi-structured questionnaire. The data was cleaned and analysed using STATA 11.

FGD

For the Focus Group Discussions, transcripts were read carefully and then coded line-by-line to label ideas emerging from participants and groups. These ideas were grouped into themes which were then developed into concepts through relating themes to literature on Cambodia's social and medical history, particularly relating to malaria, as well as anthropological theory relating to use of medicines, private practices and new technologies. Coding was carried out using NVivo version 8 (QSR International) software. Concepts that draw together different themes that were relevant to the study objectives are narrated in the results section (see appendix for full version).

RESULTS

REVIEW OF THE CURRENT SYSTEM FOR QUALITY ASSURANCE OF RDTS IN PRIVATE SECTOR

RDT SELECTION AND PROCUREMENT

PSI procures RDTs for the social marketing programme according to the procurement requirements of the Global Fund. This process has been fraught with difficulties and resulted in significant delays and a stock out of RDTs (since May 2011). PSI places RDT orders to the manufacturer approximately every two years, according to funding agreements. PSI arranges with the manufacturer for the shipments to be staggered over time usually every 6 months.

Pre- and post-shipment quality tests are conducted. SGS Group is in charge of conducting these tests according to their protocols.

It is clearly specified in the supplier's shipping documents that the goods must be stored in a cool place and normally they are only kept at the airport for less than 24 hours before they are cleared through customs and transferred to the PSI central warehouse in Phnom Penh.

IN-COUNTRY SUPPLY AND STOCK

PSI maintains a buffer stock of about 6 months of RDTs in the country. This stock can be located at the central warehouse, or dispersed through the regional depots. In December 2010, there were 54 RDT boxes in the warehouse (the equivalent of 54,000 RDTs in total). This stock, summed to the stocks in the various depots represents 5.5 months of RDT needs in the country. However since May 2011, due to delays in procurement as described above, there has been a central stock-out of RDTs.

Newly arrived RDTs stay 1-6 months at the central Phnom Penh warehouse, before being transferred to one of three regional depots. The RDTs then stay an average of 1-3 months in the depots before being taken for distribution by the sales-representatives. On average, the transfer of one RDT box from the central Warehouse to the Providers (via the Depots) takes 1.5 months.

The whole supply follows a FEFO model (First Expiry, First Out). Products are "pushed" from the warehouse to the Depot. There are 2 monthly transfers from the Warehouse to the Depot, on the 1st and 3rd week of the month. RDTs are then "pulled" by the providers from the sales-reps. The regional depots make the buffer between the "push" strategy from the warehouse, and the "pull" strategy from the provider.

There are 3 Depots in the country: (Battambang, Siem Riep and Kampong Cham). Some provinces (Ko Kong, Kampong Speu, Takeo, Kampot, Kandal, Sihanoukville) are supplied directly from the central Phnom Penh warehouse, in which case RDTs do not transit via one of the Depots.

Two 3-tonne trucks are used to transfer products from the central warehouse to the depots. A fleet of cars and vans are then used to transfer products from the depots to Sales Representatives houses. Transfers from the Sales Representatives houses to the providers' outlets is done by car or motorbike.

Distribution of RDT cartons is based on batch information, by the PSI Procurement and Logistic Manager, and by the Phnom Penh Warehouse supervisor. To date, there is no "bar-code" supervision of the transfer process.

The central warehouse, but not the depots are air-conditioned and with double ceilings. Cartons are stored 10cm above the ground on wooden pallets, there is at least 60cm between the cartons and the

walls. There are ordinary (ie not minimum/maximum) thermometers in all the rooms, and the ambient temperature is recorded in a log book twice per day.

The weakest points in the supply chain is thought to be are when products are moved from the Regional Depots to the Sales Representatives' houses, and to the providers' outlets, when there is no direct supervision from the PSI logistics department.

CENSUS SURVEY

DESCRIPTION OF SURVEY

In all 430 providers were visited of which 217 were included in the census, 203 sold antimalarial drugs of whom 108 also provided malaria blood tests, and 14 provided only blood tests and no antimalarials. Of the 203 providers who sold antimalarials, 181 sold artemisinin containing drugs. Of the 120 provider who reportedly had RDTs, 74 undertook the RDT user assessments. The study was not powered to detect differences between Zones 1 and 2 but there was a trend towards providers in Zone 1 being more likely to stock RDTs than those in Zone 1 (24/28, 86% compared to 44/150, 54%), and less likely to stock antimalarial drugs (17/28, 86% compared to 81/150, 54%).

Figure 1 summarises the outcome of the screening process overall. In 42% of the outlets surveyed, only 1 person in the outlet reportedly dispensed drugs and/or performed RDTs and in 45% 2 people reportedly carried out these functions.

Table 1provides a breakdown by HCCA which illustrates the variation between sites. Table 2 summarise the number of different types of providers according to the interviewers observations and Table 3 summarises the self-reported qualifications of the providers.

Table 1: Providers selling antimalarials and/or malaria tests, by province and containment zone

Province (District)	No. of providers screened	No. of providers enrolled (% of screened)	No. of providers selling antimalarials (% of enrolled	No. of providers selling tests for malaria (% of enrolled)	No. or providers selling both	No. of providers trained in using RDTs in last 12 months
Kampot (Chumkiri)	13	3 (23%)	1 (33%)	2 (67%)	0	1 (33%)
Battambang	20	9 (45%)	9 (100%)	6 (67%)	6 (67%)	5 (56%)
Pailin	35	16 (46%)	7 (44%)	16 (100%)	7 (44%)	8 (50%)
Oddar Meanchey	58	29 (50%0	29 (100%)	21 (72%)	21 (72%)	11 (38%)
Siem Riep	56	32 (57%)	32 (100%)	5 (16%)	5 (16%)	9 (28%)
Preah Vihear	36	20 (56%)	19 (95%)	18 (90%)	17 (85%)	16 (80%)
Containment zone (1+2)	218	109 (50%)	203 (93%)	122 (56%)	108 (50%)	93 (43%)
Kampong Thom	60	39 (65%)	38 (97%)	27 (69%)	26 (67%)	19 (49%)
Kratie (Kantout)	30	9 (30%)	9 (100%)	3 (33%)	3 (33%)	5 (56%)
Kratie (Rakakandal)	27	14 (52%)	14 (100%)	5 (36%)	5 (36%)	7 (50%)
Kratie (Chhlong)	35	25 (71%)	25 (100%)	7 (28%)	7 (28%)	4 (16%)
Rattanakiri	35	7 (20%)	7 (100%)	2 (29%)	2 (29%)	0
Mondulkiri	25	15 (56%)	13 (93%)	10 (71%)	9 (64%)	8 (57%)
Non-Containment zone	**212**	108 (51%)	**106 (98%)**	**54 (50%)**	**52 (48%)**	**43 (40%)**
Total	**430**	217 (50%)	**203 (93%)**	**122 (56%)**	**108 (50%)**	**93 (43%)**

Figure 1 : Study flow diagram

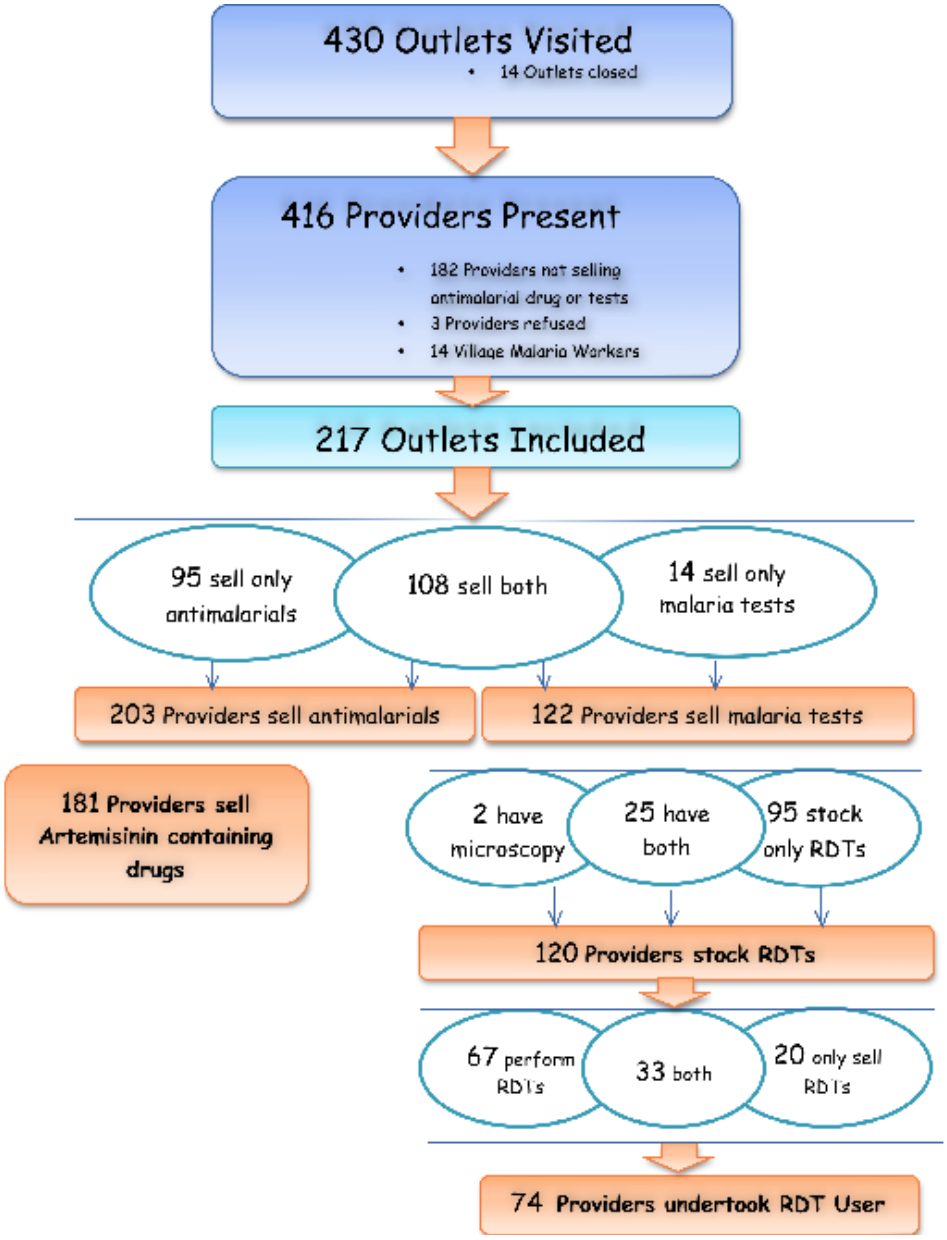


Table 2: Type of outlets by containment area and zone

	Number of Outlets by type (%)						
	Pharmacy	**Cabinet**	**Drug shop**	**Grocery**	**Mobile provider**	**Other**	**Total**
Containment (zones 1 &2)	44 (40%)	22 (20%)	24 (22%)	17 (16%)	0 (0%)	2 (2%)	109
Non-containment (zone 3)	17 (16%)	15 (14%)	17 (16%)	38 (35%)	15 (14%)	6 (6%)	108
Total	**61 (28%)**	**37 (17%)**	**41 (19%)**	**55 (25%)**	**15 (7%)**	**8 (4%)**	**217**

Table 3 : Qualification of providers by containment area and zone

	Type of training or qualification									
Zone	**Phar-macist**	**Doctor**	**Midwife**	**Nurse**	**Medical assistant**	**Informal**	**None**	**Other**	**No information**	**Total**
Containment (zone 1&2)	2 (2%)	4 (4%)	4 (4%)	24 (22%)	10 (9%)	9 (8%)	7 (6%)	10 (9%)	39 (36%)	109
Non-containment (zone 3)	2 (2%)	5 (5%)	6 (6%)	9 (8%)	3 (3%)	11 (10%)	4 (4%)	17 (16%)	51 (47%)	108
Total	**4 (2%)**	**9 (4%)**	**10 (5%)**	**33 (15%)**	**13 (6%)**	**20 (9%)**	**11 (5%)**	**27 (12%)**	**90 (41%)**	**217**

ANTIMALARIALS

Table 5 summarises the type of antimalarials reportedly sold in the last 3 months and antimalarials stocked on the day of the survey. Of note 81% of providers sold Malarine, most of whom had it in stock on the day of the survey. Also of note 12% of providers reported selling artesunate tablets, and 23% reported selling artemether for injection and 33% sold chloroquine. There were reportedly 4 different types of artesunate monotherapy tablets sold of which the "Binhdinh Pharma, Canada was the most popular; and 3 or 4 types of artemether injection with "Rotex Medica" and "Shanghai Pharmaceutical" being the most commonly reported.

Table 4 illustrates the source of drug according to the provider. For Malarine half of providers obtained supplies directly from PSI and the other half from other retailers. (Note: Although 2 providers reportedly obtained supplies of Malarine from the public sector and 1 provider reported obtaining A+M from PSI, we assume these to be errors)

Table 4: Reported source of antimalarials

	Antimalarial		
Source	Malarine	A+M	Other antimalarials
PSI	81 (49%)	1 (4%)	0 (0%)
Other retailer	76 (46%)	15 (58%)	147 (89%)
Public sector	2 (1%)	6 (23%)	5 (3%)
Don't know	6 (4%)	4 (15%)	14 (8%)
Total	165	26	166

When providers were asked which antimalarial drug they sold the most in previous years, Malarine was reportedly the most popular at 133 (66%) of the cases, followed by Chloroquine in 26 (13%) of the cases

Only 37 providers (18 % of the eligible population) reported stocking other antimalarials in previous years that they did not stock now, and half of these (19/38, 51%) reported that the drug they had previously stocked was an artemisinin monotherapy (artesunate). The main reasons for not stocking the drugs anymore were mainly due to stock outs and concerns regarding MoH ban on Artemisinin monotherapies.

Table 5: Type of antimalarials sold and stocked by containment area

	Number of providers selling drug in last 3 months (as % of those selling drugs)				Number of providers stocking drug on day of survey (as % of those selling in last 3 months)			
	All areas N=203	Containment zone N=97	Non-containment zone N=106	P value	All N=203	Containment zone N=97	Non-containment zone N=106	P value
Malarine	165 (81%)	80 (82%)	85 (80%)	0.677	150 (91%)	73 (91%)	77 (91%)	0.672
Chloroquine	67 (33%)	38 (39%)	29 (27%)	0.074	65 (97%)	36 (95%)	29 (100%)	0.137
Artemether for injection	47 (23%)	20 (21%)	27 (25%)	0.413	40 (85%)	17 (85%)	23 (85%)	0.455
A+M	26 (13%)	8 (8%)	18 (17%)	0.063	18 (69%)	7 (88%)	11 (61%)	0.429
Artesunate tablet	25 (12%)	9 (9%)	16 (15%)	0.208	18 (72%)	8 (89%)	10 (63%)	0.766
Artequick	17 (8%)	11 (11%)	6 (6%)	0.144	14 (82%)	10 (91%)	4 (67%)	0.066
Duo-cotexcin	2 (1%)	2 (2%)	0 (0%)	0.137	0	0	0	-
Cotexcin	2 (1%)	2 (2%)	0 (0%)	0.137	2 (100%)	2 (100%)	0 (0%)	0.137
Quinine tablet	14 (7%)	3 (3%)	11 (10%)	0.041	14 (100%)	3 (100%)	11 (100%)	0.041
Quinine injection	7 (3%)	3 (3%)	4 (4%)	0.291	7 (100%)	3 (100%)	4 (100%)	0.791
Artesunate for injection	4 (2%)	2 (2%)	2 (2%)	0.929	1 (25%)	1 (50%)	0 (0%)	0.295
Artemether tablet	2 (1%)	0	2 (2%)	0.174	0 (0%)	0	0	-

RAPID DIAGNOSTIC TESTS

Of the 217 eligible providers, 122 reported providing tests of which 120 provided RDTS. Of the 120 providers selling RDTs, most of these (93%) reportedly sold Malacheck RDTs and most providers (100, 83%) actually performed RDTs on patients ie they did not just sell RDTs to other retailers.

In 41% of the 100 outlets in which RDTs are performed, they are performed by more than one person in the outlet and in 89% of the cases the person is a member of the same family.

Most providers reportedly stocked 1 or 2 boxes ie 10 to 20 RDTs (Figure 2) and for those who performed RDTs, most providers reported performing less than 10 RDTs per week (Figure 3).

Figure 2: Number of boxes of RDTs stocked by provider

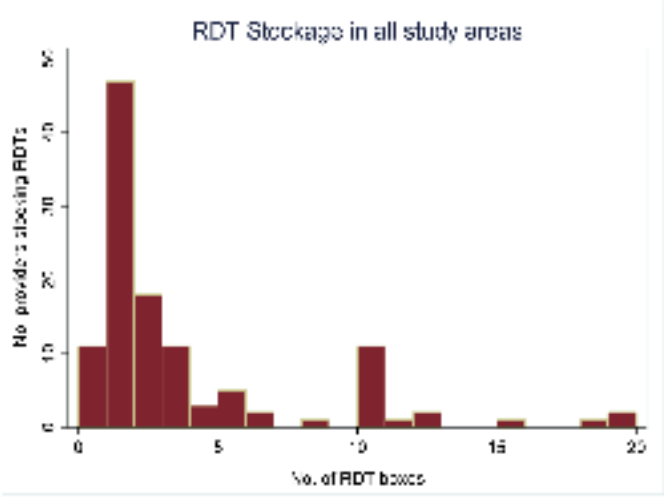
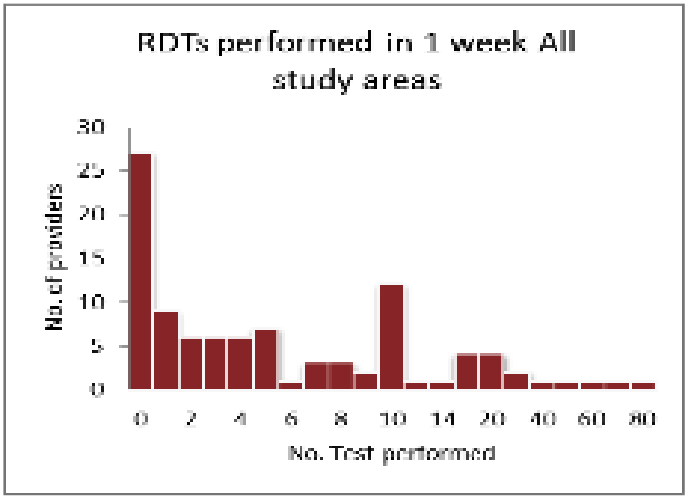


Figure 3: Number of RDTs performed per week by providers



BUYING RDTS

Table 6 shows the source from whom providers reported buying their RDTs. PSI was the source in just over half of cases with other retailers being the reported source in one third.

Table 6: Source of RDTs

Source of RDT	No. providers (% of those who sell RDTs)
PSI	66 (55%)
Another pharmacy	38 (32%)
Health centre	7 (6%)
Wholesaler	5 (4%)
Other	8 (7%)
Don't know	2 (2%)

Problems with RDTs

28% of the providers reported having some kind of problem when performing RDTs. The most common problem reported was a problem with the test result that led the providers to believe that the test was not working and sometimes requiring re-testing. Problems were also reported with interpretation of the results and in collecting blood (Table 7). No association was found between reported problems and frequency of use.

Table 7: Reported problems with RDTs

Problems with RDTs	No. (% of those who perform test)
Unexpected result (RDT "broken", have to test again etc)	11 (11%)
Difficult interpreting result	5 (5%)
Blood collection device	5 (5%)
Time (waiting for result)	2 (2%)
Not enough buffer	2 (2%)
Don't know or missing answer	3 (3%)
No problems	72 (72%)
Total	100

Diagnosis and management of RDT negatives

The most common diagnosis that providers reportedly made in patients who were RDT negative, was typhoid followed by flu and respiratory infections (Table 8). When asked what they would do with such patients only 6% said they would refer elsewhere. The most popular choice of action was to treat with "antiflu" medicines (45%) and/or antibiotics (39%) (Table 9). Of these ß-Lactams were named by half (17/39, 44%) followed by quinolones (8/39, 21%). Surprisingly, providers who mentioned typhoid as a diagnosis did not always mention antibiotics, for example of the 39 providers who mentioned typhoid alone, only 26% mentioned antibiotics (data not shown).

Table 8: The type of illness providers reportedly diagnosing in patients who were RDT negative

Type of illness	No. of providers mentioning illness (% of those who perform RDTs) n=99
Typhoid	66 (67%)
Flu	27 (27%)
Respiratory infection	21 (21%)
Sore throat	11 (11%)
Diarrhoea, vomiting or stomach ache	7 (7%)
Dengue	5 (5%)
"Fever" (Krun Kdaov)	4 (4%)
Other	7 (7%)

*Providers could mention more than one illness, therefore number of treatments exceed the number of providers)

Table 9: Types of medicine reportedly sold to patients who were RDT negative

Treatments mentioned for patients who are RDT negative	No. of providers (% of those who perform RDTs)* n=99
Antipyretic or "antiflu" medication	45 (45%)
Antibiotic(s)	39 (39%)
Cocktails	18 (18%)
Serum	11 (11%)
Treat according to test or symptoms	8 (8%)
Refer to health facility	5 (5%)
Refer to other private provider	1 (1%)

*Providers could mention more than one type of treatment, therefore number of treatments exceed the number of providers)

Training

Of all eligible providers, 93 (43%) reported having training in RDT, with PSI reportedly being the source of training in 58 (62%) of cases. Of the 100 providers who perform RDTs only 63 reported having received training in use of RDTs.

Instructions given on selling or performing RDTs

Providers were asked whether or not they provided any kind of instruction when they sold RDTs to other providers or performed them on patients. Most providers (58%) said that they did not provide any instructions (Table 10) but a quarter reported giving some instruction on use.

Table 10: Instruction given when selling RDTs

	No. of providers (% of those who sell RDTs) n=120
No instruction	32 (26.7%)
Tell them how to use	14 (11.7%)
Demonstrate how to use	6 (5.0%)
Other	3 (2.5%)
No answer	64 (53.3)
Total	**120**

RDT buying and selling prices

Tables 11 and 12 show the reported median prices for buying and selling RDTs by the box of 10, and by single units respectively. The median reported price for buying a box of 10 RDTs was 2500 (n=112) and median reported price for selling 1 box to other providers was 4500 (n=36) median mark-up of 1500 riel (n=35).

This compares to the median price for performing a test as reported as 3000 riel (IQR 2000-3500) with a median absolute mark-up of 2700 riel per test (IQR 1750-3000).

Table 11: Price of buying and selling one box of 10 RDTs: Median, IQR and median mark-up, by province, zone and area (US$1= approx 4000 riel)

Price Paid per box of 10 RDTs		Price in Riels when buying 1 box of RDTs			Price in Riels When Selling 1 box of RDTs to other providers				Absolute markup in Riels per 1 box of			
Province	No. Outlets	Median price per 1 box	1IQ	3IQ	No. Outlets	Median Price per box	1IQR	3IQR	No. Outlets	Markup	1IQR	3IQR
Kampot	2	10000	10000	10000	0	.	.	.	0	.	.	.
Battambang	5	3000	2500	5000	0	.	.	.	0	.	.	.
Pailin	13	3000	2000	6000	3	6000	3000	8000	3	2000	1000	2000
Oddar Meanchey	17	3000	2000	3500	5	2500	2000	3000	5	500	200	1000
Preah Vihear	18	2500	2000	4500	7	4000	4000	6000	7	2000	1000	2000
Kampong Thom	25	2500	2000	3500	13	5000	4000	7000	12	2350	1000	4750
Kratie- Kantout	3	5000	4500	12000	0	.	.	.	0	.	.	.
Kratie- Rakakandal	5	4000	2000	8000	2	3500	3000	4000	2	1500	1000	2000
Kratie- Chhlong	7	2000	2000	5000	3	4000	3000	7000	3	2000	1000	5000
Siem Reap	5	2000	2000	2000	1	8000	8000	8000	1	6000	6000	6000
Ratanakiri	2	5000	5000	5000	0	.	.	.	0	.	.	.
Mondulkiri	10	4000	2000	8500	2	4500	4000	5000	2	2500	2000	3000
Zone 1	20	3500	2000	8500	3	6000	3000	8000	3	2000	1000	2000
Zone 2	40	2500	2000	4000	13	4000	3000	4000	13	1000	500	2000
Zone 3	52	2750	2000	5000	20	5000	3500	6750	19	2000	1000	4500
Containment	60	2500	2000	5000	16	4000	3000	6000	16	1250	750	2000
Non Containment	52	2750	2000	5000	20	5000	3500	6750	19	2000	1000	4500

Table 12: Price of buying and selling single RDTs: Median, IQR and median mark-up, by province, zone and area

Price Paidin Riels per 1 RDT test	Price paid in Riels when buying 1 RDT test				Price in Riels when selling 1 RDT test				Price in Riels when performing 1 RDT test				Absolute markup in Riels between buying 1 Test and Performing			
Province	No. Outlets	Median price in Riels	1QR	3QR	No. Outlets	Median price in Riels	1QR	3QR	No. Outlets	Median Pric	1QR	3QR	No. Outlets	Median markup	1QR	3QR
Kampot	2	1000	1000	1000	0	.	.	.	0	.	.	.	0	.	.	.
Battambang	5	300	250	500	0	.	.	.	2	3250	3000	3500	2	2875	2750	3000
Pailin	13	300	200	600	0	.	.	.	3	2000	2000	3500	3	1600	1100	2700
Oddar Meanchey	17	300	200	350	0	.	.	.	4	2500	1750	3500	3	2500	1650	3700
Preah Vihear	18	250	200	450	4	2000	1500	2500	10	3000	2500	3500	10	2675	2050	3300
Kampong Thom	25	250	200	350	1	1000	1000	1000	1	2000	2000	2000	1	1750	1750	1750
Kratie- Kantout	3	500	450	1200	0	.	.	.	1	2500	2500	2500	1	1300	1300	1300
Kratie- Rakakandal	5	400	200	800	0	.	.	.	0	.	.	.	0	.	.	.
Kratie- Chhlong	7	200	200	500	0	.	.	.	3	3000	3000	5000	3	2800	2600	4500
Siem Reap	5	200	200	200	2	1750	500	3000	1	3000	3000	3000	1	2800	2800	2800
Ratanakiri	2	500	500	500	0	.	.	.	0	.	.	.	0	.	.	.
Mondulkiri	10	400	200	850	0	.	.	.	0	.	.	.	0	.	.	.
Zone 1	20	350	200	850	0	.	.	.	5	3000	2000	3500	5	2700	1600	2750
Zone 2	40	250	200	400	6	2000	1000	3000	15	3000	2000	3500	14	2675	2050	3300
Zone 3	52	275	200	500	1	1000	1000	1000	5	3000	2500	3000	5	2600	1750	2800
Containment	60	250	200	500	6	2000	1000	3000	20	3000	2000	3500	19	2700	1750	3000
Non Containment	52	275	200	500	1	1000	1000	1000	5	3000	2500	3000	5	2600	1750	2800

Other tests

Two thirds of providers who provided RDTs reported not providing any other test, 19 (16%) reported performing Widal test or "test for typhoid" and 15 (12%) reported "other" test (Table 13). Other tests included 4 providers that mentioned Urine Test, 3 providers that mentioned Hepatitis Test, 2 providers mentioned Dengue test.

Of those who had mentioned typhoid as a cause of fever when RDT is negative, 10 perform Widal test. Another 7 providers perform Widal test but didn't mention typhoid as a cause of fever when the RDT was negative.

Table 13: Other tests reportedly offered by providers

	Tests offered by providers who sell malaria tests (%)
None	82 (67%)
Widal/typhoid	19 (16%)
Other	15 (12%)
Haematocrit	8 (7%)
Haemogram	3 (2%)
Don't know	3 (2%)

RDT QUALITY TESTING

Quality of storage

Of 217 providers who sold RDTs, storage conditions were considered adequate (ie clean and dry environment out of direct sunlight) in 193 (89%) and inadequate in 19 (9%). Of these 19, 14 were stored in dirty or dusty conditions, 6 in direct sunlight and 3 were at risk of exposure to water or rain. Of the 217 providers, 39 (18%) had a fan or air-conditioning where the RDTs were stored.

RDT quality analysis

All 12 RDT samples that were collected for quality assurance passed QA assessment according to the WHO protocol performed at the reference laboratory in Pasteur Institute Cambodia. All 12 samples were of the "New" Malacheck. There were samples from three lots in total (5 x lot C101R, 3x lot F10R and 4x lot A201R).

RDT USER ASSESSMENT

In total, sixty eight providers were assessed using the RDT user assessment form. This included 57 of the 100 private providers[2] in the Census survey who reportedly performed RDTs, and an additional 11 village malaria workers. The assessment was opportunistically carried out observing the provider performing RDT testing on a patient in 6 cases (8.8%) and in the remaining was carried out either on the interviewer (12/68, 20%) or another volunteer. No VMWs used gloves or a timer, but they were more likely to write on the RDT and in a register book (Table 14).

Table 14: Results of the RDT user assessment

Step	No. of respondents N=68	Comment
Read expiry date on box	21 (30.9%)	No significant difference between VMW and others
Read instructions before performing test	12 (17.7%)	No significant difference between VMW and others
Used gloves	15 (22.1%)	No VMWs wore gloves
Cleaned the finger with alcohol swab	59 (86.8%)	
Did not use new lancet	2 (2.9%)	
Did not use the blood collection tube	2 (2.9%)	
Blood collected	26 just to the line (38.2%) 25 over the line (36.7%) 16 under the line (23.5%) 1 not observed (1.5%)	No significant difference between VMW and others
Used the correct amount of buffer (2 drops)	59/68 (86.8%)	No significant difference
Used a timer or clock	19/67 (28.4%)	No VMW used timer
Wrote something on the RDT (eg patient details/date)	18/68 (26.5%)	5/11 VMW (p=0.119)
Recorded the patient details or results on register or form	16/68 (23.5%)	6/11 VMW (p=0.008)
Waited less than the recommend 20 minutes (mean 15 minutes)	27/68 (39.7%)	No diff between those who used timer and those that didn't
Disposed of lancet safely	11/68 into sharps box (16.2%) 3/68 into plastic bottle (4.4%) 40/68 into RDT packaging then rubbish bin (58.8%) 12/68 directly into bin (2.9%) 2/68 other (2.9%)	No significant difference between VMW and others

[2] The RDT user assessment was not completed on all providers who perform RDTs. In most cases this was because there was no volunteer available

RDT TEMPERATURE AND HUMIDITY LOGGING

In drugs shops

Figure 4 show the read out from two of the data loggers that were kept in RDT boxes in private providers. They show that the average temperature was maintained just below 30°C (Table 15)

Table 15: Drug shop temperature and humidity logging

Place and time	Temperature average (min and max)	Humidity average (min and max)
Drug shop 1 (rural drug shop) (9/2/11- 19/07/11)	29.1°C (25.5-32.5°C)	73.3% (48.0-88.0%)
Drug shop 2 (urban pharmacy) (17/2/11 – 2/8/11)	28.4°C (22.0-31.5°C)	72.4% (42.4-85.0%)
Mondulkiri	awaited	
Kampong Thom	awaited	
Siem Riep	awaited	

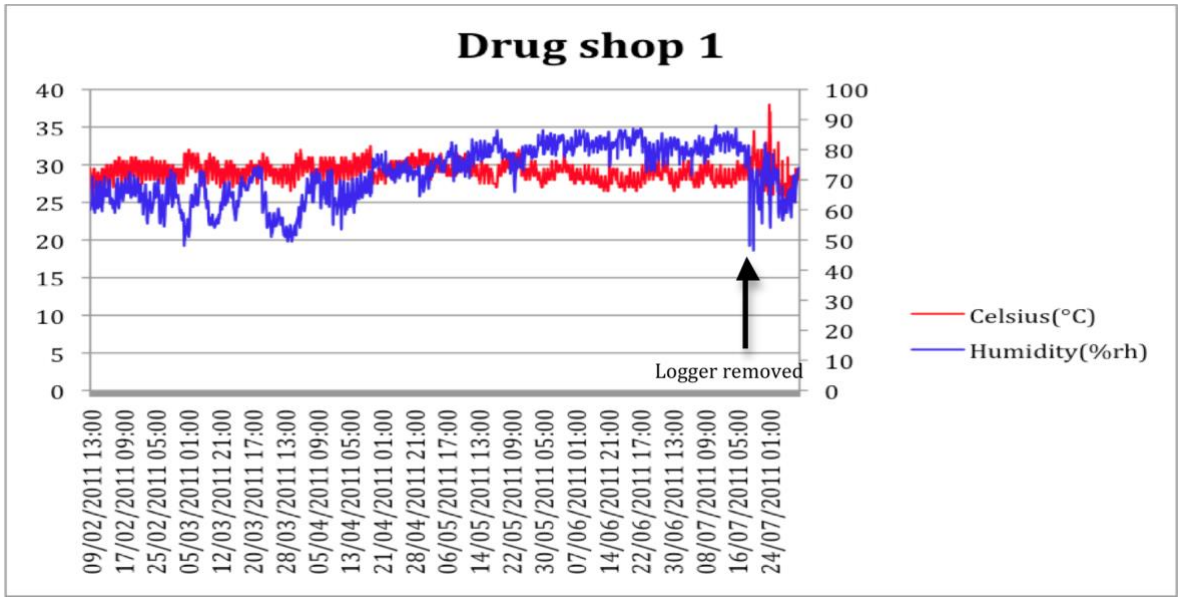
During transport from PSI warehouse to private providers

Figure 5 shows the readout from the data loggers place in RDT boxes in the central warehouse and retrieved from their final destinations. The results are summarized in Table 16. The hottest part of the transport and storage chain appears to be the final journey to the private providers.

Table 16: Transport temperature and humidity logging

Data logger and destination	Temperature average (min and max)	Humidity average (min and max)
Logger 1 – to Preah Vihear	26.3°C (16.5-39.0°C)	61.4% (35.5-79.5%)
Logger 2 – to Rattanikiri	26.8°C (17.0 -41.5°C)	57.2% (24.0 -71.5%)
Logger 3 – to Battambang	26.9°C (22.5 -34.0°C)	59.0% (38.0-74.0%)
Logger 4 – to Kampong Chan	Lost in transit back to Phnom Penh	
Logger 5 – to Ko Kong	Machine error - did not record	

Figure 4: Data logger readouts for temperature and humidity recorded in drug shops



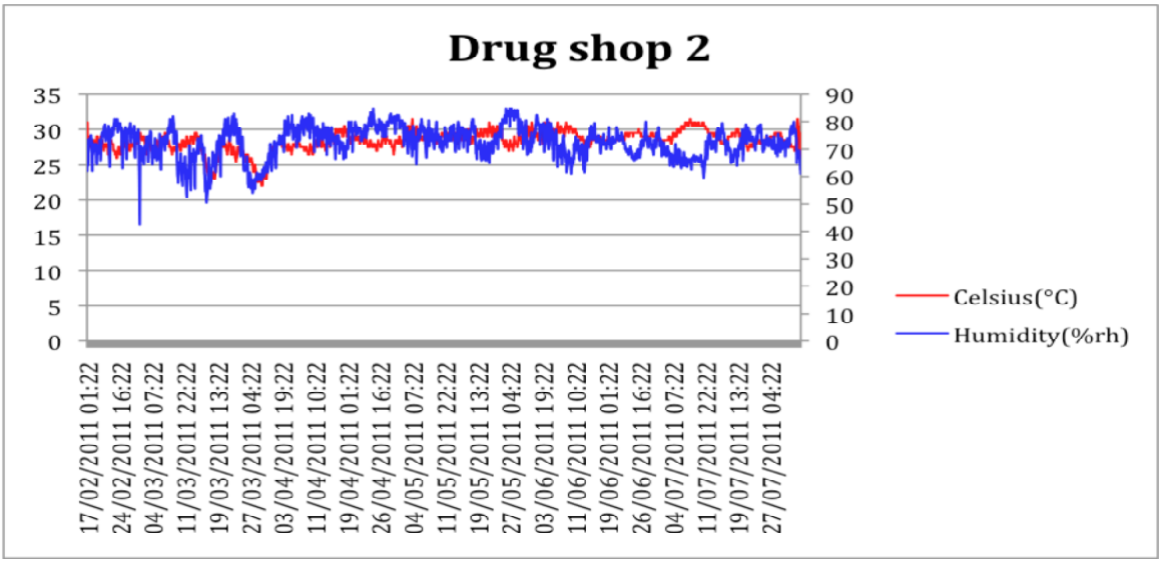
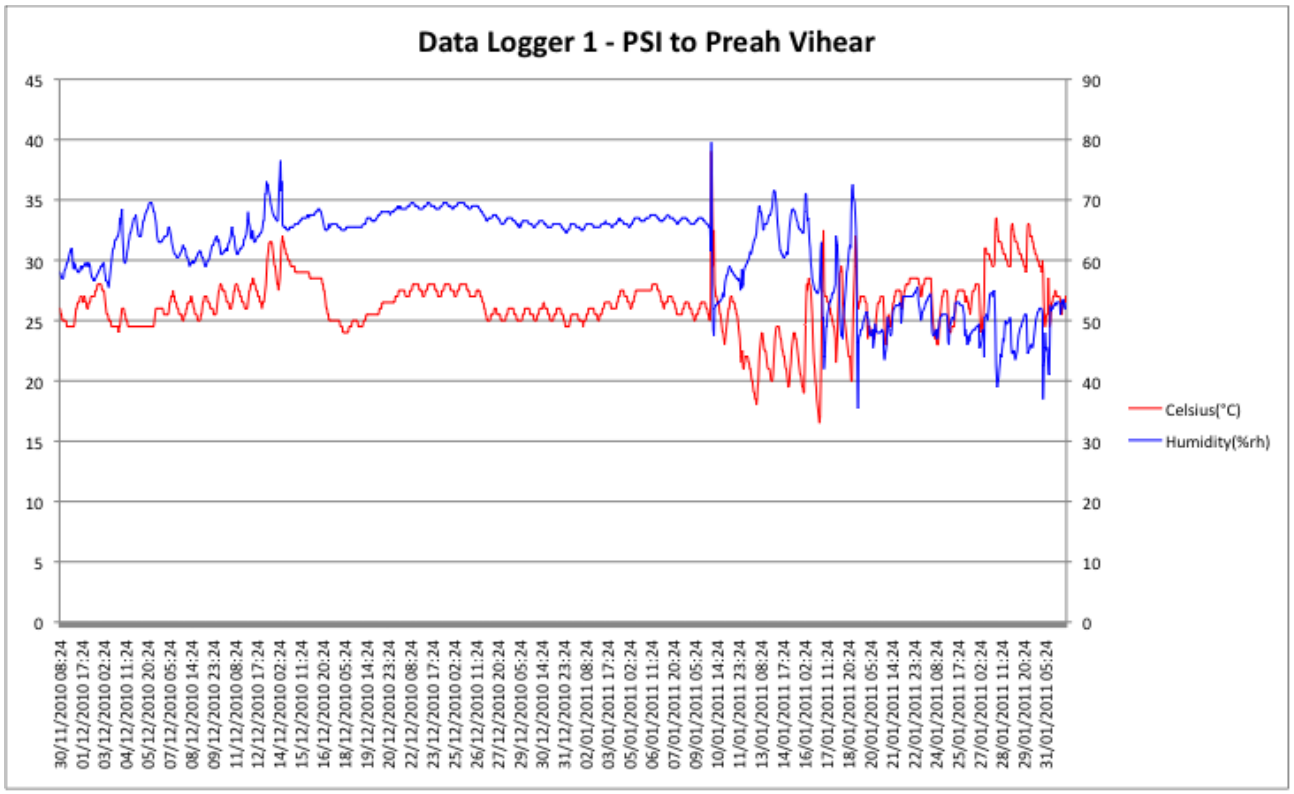
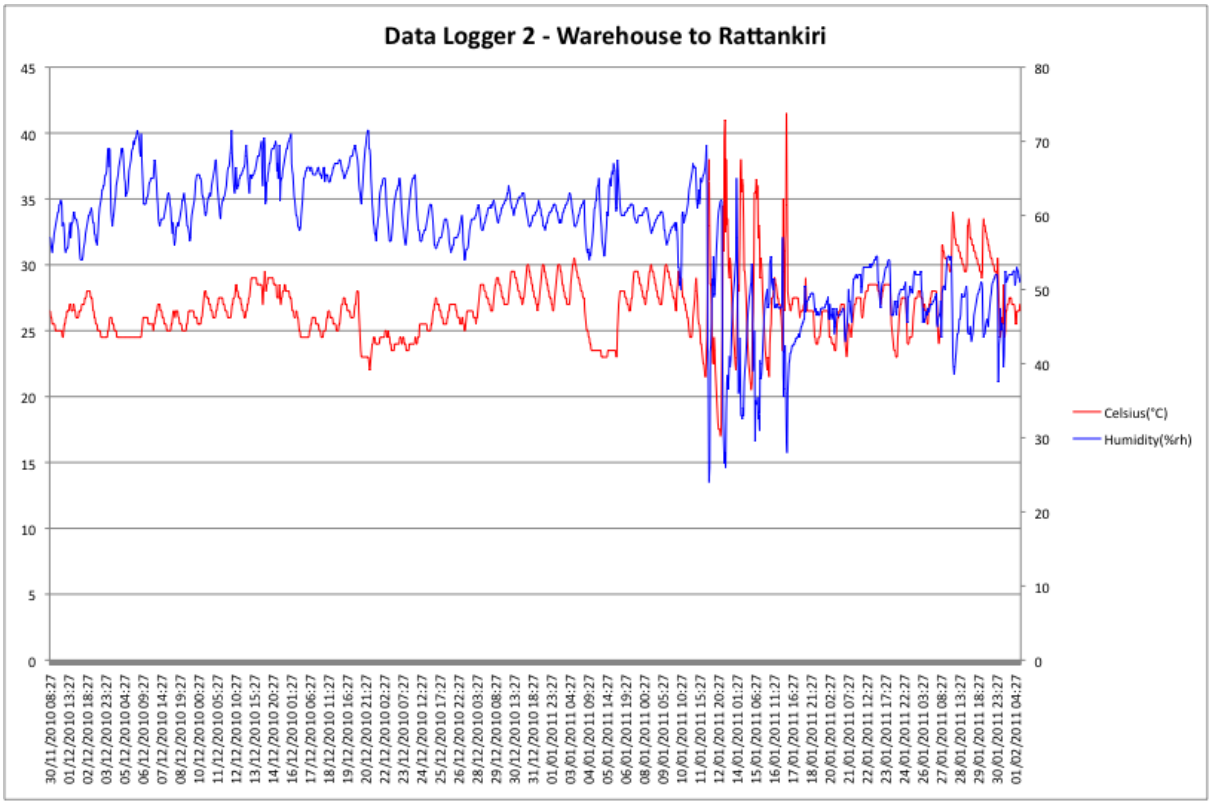
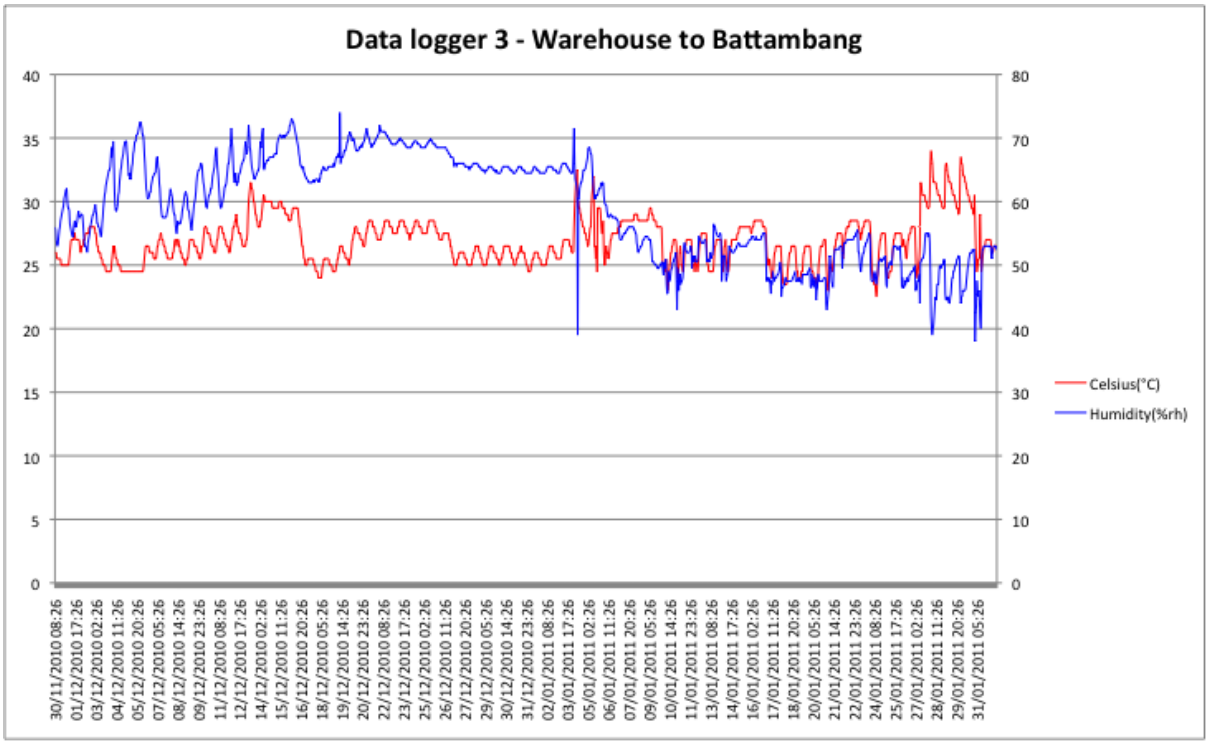


Figure 5: Data logger readouts for temperature and humidity recorded during transport from the central warehouse to the final destinations






Data logger 3 - Warehouse to Battambang
40
35
30
25
20
15
10
5
0
80
70
60
50
40
30
20
10
0
Celsius(°C)
Humidity(%rh)
30/11/2010 08:26
01/12/2010 17:26
03/12/2010 02:26
04/12/2010 11:26
05/12/2010 20:26
07/12/2010 05:26
08/12/2010 14:26
09/12/2010 23:26
11/12/2010 08:26
12/12/2010 17:26
14/12/2010 02:26
15/12/2010 11:26
16/12/2010 20:26
18/12/2010 05:26
19/12/2010 14:26
20/12/2010 23:26
22/12/2010 08:26
23/12/2010 17:26
25/12/2010 02:26
26/12/2010 11:26
27/12/2010 20:26
29/12/2010 05:26
30/12/2010 14:26
31/12/2010 23:26
02/01/2011 08:26
03/01/2011 17:26
05/01/2011 02:26
06/01/2011 11:26
07/01/2011 20:26
09/01/2011 05:26
10/01/2011 14:26
11/01/2011 23:26
13/01/2011 08:26
14/01/2011 17:26
16/01/2011 02:26
17/01/2011 11:26
18/01/2011 20:26
20/01/2011 05:26
21/01/2011 14:26
22/01/2011 23:26
24/01/2011 08:26
25/01/2011 17:26
27/01/2011 02:26
28/01/2011 11:26
29/01/2011 20:26
31/01/2011 05:26

MYSTERY CLIENT STUDY

211 MC interactions were carried out. This included 190 providers covered in the census and 21 others identified at the time of the study (2 in Pailin, 14 in Sotnikum, 1 each in PV, TP, Rattanakiri, Mondulkiri, Kampong Thom). Overall, there were 40 MC interactions in zone 1 (19.0%), 70 (33.2 %) in zone 2 and 101 (47.9%) in zone 3. There were 3 providers who had been included in the census who were selected for the MC study but for whom the MC study could not be completed because they could not be found, were closed or apparently no longer sold drugs.

MYSTERY CLIENT DESCRIPTION OF ILLNESS

In just over half (111, 52.9%) of interactions, MCs presented as patients themselves and in the other half MC's pretended to be a friend or relative of the patient. Initially the MC presented with symptoms of malaria (fever, headache, chills, body ache), sometimes with a story of working in the forest.

After this initial interaction 182 (86.7%) MCs gave more information to try to convince the provider to sell an antimalarial drug and specifically artesunate. Almost half either said that they (or the patient) had had malaria in the past and/or said they had used artesunate in the past and 49 (26.2%) said that they (or patient) had already received a positive test.

ADVISING BLOOD TESTS

88/209 (42.1%) providers advised a blood test, of whom 46/86 (53.5%) offered to perform the test, 26/86 (30.2%) advised going to another place for testing and in 14 cases (16.3%) it was not clear. Providers in the Containment area appeared to be significantly more likely to advise the patient to have a test than outside of the containment area (44.5% versus 28.3%, p=0.002).

There was a trend towards the more trained providers advising and offering tests compared to the relatively less trained providers. Thus 14/25 (56.0%) of cabinets advised a test of whom 11 offered to perform the test, compared to only 3/14 (15.0%) of grocery shops advising a test of whom none offered to perform the test, with pharmacies and drugs shops being somewhere in between. Whether or not the provider had training in using RDTs in the previous 12 months did not appear to be associated with whether or not the provider advised an RDT (data not shown). However for the 35 providers who advised a test for whom information on training was available from the Census study, those who had received training in RDTs were more likely to offer to do the test (13/14, 92.9%) compared to those who had not received training (12/21, 57.1%).

SELLING DRUGS "FOR MALARIA"

After the initial interaction the MC bought some drugs which were apparently intended for "malaria" in only 32/210 (15%) of cases and drugs for something other than malaria in 129/210, 61% of cases. No drugs were initially bought in (27/210) 13% of cases and it was not clear from the debriefing whether or not drugs were initially bought in (22/210) 10% of cases. After the initial interaction 182 MCs then gave more information to convince the provider to sell him an antimalarial, after which 83/182 (45.6%) bought drugs that were apparently for malaria (Table 1). Whether or not a provider sold an antimalarial was not significantly associated with the zone or with the type of provider.

Table 17: Purpose of drugs bought by mystery clients initially and then after more story

Drugs bought	Initially (n=210)	After more story (n=182)
"For malaria" (with or without something else)	32 (15%) of which 10 were Malarine and 5 were artesunate	83 (45.6%) of which 35 were ACT and 18 were artesunate
Not "for malaria"	129 (61%)	7 (4%)
None	27(13%)	91 (50%)
Unclear	22 (10%)	1 (0%)

Although some drugs were sold "for malaria" in some cases the actual drugs that the provider sold did not appear to contain an antimalarial. On inspecting the drugs bought, the provider sold at least one antimalarial in 103 cases and 2 antimalarials in 2 cases. Out of the 107 antimalarials sold, the most popular was a whole blister Malarine (34/107, 31.8%), followed by chloroquine (27/107, 25.2%) and artesunate monotherapy (18/107, 16.8%). (Table 18)

Table 18: Type of antimalarial bought by MC

Name of antimalarial	No. of times bought by MC (n=107)
Malarine	34 (31.8%)
Chloroquine	27 (25.2%)
Artesunate	18 (16.8%)
A+M	11 (10.3%)
Artekin or Artequine	8 (7.5%)
Duocotexcin	3 (2.8%)
Artemether	2 (1.9%)
Other antimalarial	4 (3.7%)

As the MCs had been instructed to try to convince the private provider to sell him an antimalarial, we wanted to be able to make some assessment on how reluctant the provider was to sell antimalarials. The debriefing notes were therefore analysed and a qualitative judgement made on the level of reluctance expressed by the provider. The results are summarised in Table 19.

Table 19: Degree of reluctance of providers to sell antimalarial drugs

	Reluctant to sell any drug N=200	Reluctant to sell any antimalarial N=176*	Reluctant to sell artesunate monotherapy N=85*
Reluctant with or without test	11 (5.5%)	16 (9.1%)	54 (64.3%)
Reluctant without test	12 (6.0%)	92 (52.3%)	19 (22.6%)
Not reluctant	177 (88.5%)	68 (38.6%)	11 (13.1%)

*Interactions in which providers reluctance to sell the item could be assessed

FOCUS GROUP DISCUSSION

A full description of the results of the Focus Group Discussions is given in the Annex. The results are summarized in this section.

We carried out 8 focus group discussions with 52 providers of drugs working in grocery and drug shops, pharmacies and private clinics in 5 provinces to hear about their experiences with recognising, testing and treating for malaria.

Several concepts relevant to the research concern emerged from participants across the different groups. These can be grouped into (1) conceptualisations of the perceived roles of providers, in turn important to understanding (2) the way medicines were used, including ACTs and artemisinin monotherapy, and together important for understanding (3) the way testing in general, and RDTs in particular, are conceived and used.

The roles of providers was prominent in their discussions. A notable distinction was made between the roles of 'selling' *(louk tnam)* and 'treating' *(pinit pchier bal).* A majority considered themselves as providing the former type of service, their role being to distribute drugs, but not to attempt to *cure* individuals of their illnesses. This resulted in dispensing of drugs seen as 'effective' for getting the customer through the illness with few side-effects, including artemisinin monotherapy tablets or injections. By contrast, 'treatment' entailed diagnostic and more intensive curing processes. This included carrying out examinations, batteries of tests and the use of drugs that required the patient to invest more money, energy and time to achieve a cure.

The way to use different medicines was also a popular topic for discussion. Overall, the *modus operandi* could be described as 'tailoring' to the individual case, taking into account their condition and energy levels as well as knowledges about the side-effects of different drugs. This resulted in frequent dispensing of small packets of mixed drugs and tinkering of dosages to lessen the harsh interaction of drugs with the *mero* (akin to the biomedical concept of 'microbes').

Compared with these topics, malaria RDTs were less favoured topics of discussion. This reflected their use on the margins of practice. They were used along with both 'selling' and 'treating' practices, although did not appear central to dispensing decisions for either, situated in a grey area between the two. The principle of testing appeared to be assimilated into practices related to the ideal of *curing* the patient; they *should* be used, or preferably microscopy and other laboratory tests should be used, to show the parasites and other causes of illness, leading to prescription of drugs to cure. However, providers reported reluctance to use RDTs for a number of reasons, identifying problems with the tests not 'showing' malaria, and other logistical issues with the syringes and buffer solution. In Pailin, providers appeared to be more concerned to ensure patients were tested before receiving malaria drugs. Whilst the given rationale for these practices referred to an adjusted version of public health instructions, the regulatory enforcement of drug shops in Zone One may also have affected perception of the use of antimalarial and testing commodities.

FGD Implications: These findings have several implications for programmes interested in incorporating the private sector into strategies to increase access to ACTs together with RDTs. Firstly, it may be most cost-effective to target RDTs to those who consider their role to be 'treatment.' These providers may be more interested in a 'cure' for the patient, identified through a process of seeing the parasites and then cured through taking a full dose of ACT, enduring side effects. In order to improve use of RDTs with these providers, implementers must respond to concerns over logistics, provide reassurances over trusting results, address concerns over identifying typhoid and dengue and focus on facilitating referral for more serious cases. Providers whose principal role is 'selling' should be encouraged to sell over-the-counter drugs to help people in the short term, and to dispense drugs from prescriptions. Referrals should be encouraged and facilitated. Drugs should be regulated at high levels, targeting wholesalers and importers to enforce bans on artemesinin monotherapies. The national first line artemisinin partner drug should be changed from mefloquine to reduce avoidance from side effects.

DISCUSSION

SUMMARY OF KEY FINDINGS

We conducted a comprehensive evaluation of several aspects of RDTs and their use in the private sector in Cambodia. In summary, we found that the quality of the RDTs that we collected were of good quality and that their storage and transport conditions were on the whole satisfactory. Appropriately, uptake appeared to highest in the most highly trained providers i.e. cabinets, and lowest in grocery shops, with pharmacies and drugs shops having some ambiguity around their role. Findings from the focus group discussions and the mystery client study suggest that some of the problems in uptake and interpretation relate to RDTs being on the margins of practice. Providers see themselves as either providing a diagnosis and cure (*pinit pchier bal*) or simply selling drugs for symptomatic relief (*lout tnam*). For the former, RDTs are not always integrated into the practice of diagnosis – in part because the tests only diagnose malaria and not other causes of fever, and because of the uncertainty around how to manage patients who are "RDT negative". For the latter, as they do not see their role as "diagnosing" patients, it is not clear where RDTs fit into their practice.

Several problems with RDTs were identified in terms of their actual use, in particular relating to interpretation of results, blood safety, and problems related to the buffer and the blood collecting device. We also found that it was relatively easy to buy artemisinin containing drugs without an RDT.

Reassuringly, we found good availability of Malarine and lower availability of artesunate monotherapy than reported in past surveys. However, as expected, we identified widespread availability and use of mixtures of drugs, including evidence of split blisters which in effect are equivalent to monotherapies. We also found that a quarter of providers stocked injectable artemether, which is not illegal, but the use of which on its own would be alarming.

The key findings and recommendations arising are discussed in more detail in Table 20.

STRENGTHS, LIMITATIONS AND CHALLENGES

The GUARD study was the first comprehensive evaluation of RDTs in the private sector in a country in which there has been an established programme of subsidised and socially marketed RDTs and ACTs. It therefore provides a unique insight into some of the issues likely to be confronted by other countries considering similar programmes. It employed a range of quantitative and qualitative methodologies in order to provide as complete picture as possible. This included a number of novel approaches such as the mystery client study which will help to establish such methodologies for research in the future. The study was conducted as a close collaboration between the Cambodian National Malaria programme and a multi-disciplinary academic team, with excellent collaboration from PSI and other partners. This helped to ensure the technical quality of the research whilst keeping it closely linked to the priorities for programme implementation. Finally, we were fortunate to have the support of ACT consortium which enabled us to carry out more work than we had originally budgeted for.

However, there are a number of limitations with our project. The initial proposal was funded to conduct the study in 2 areas. However, during the early planning stages it soon became apparent that it would be more interesting and useful to expand this to represent all malaria endemic areas of Cambodia. We therefore expanded to 12 Health centre catchment areas. However, this still represents a relatively small sample size that was not designed to be able to detect significant differences in interesting sub-groups e.g. provider type.

Other limitations related to the timing. The start of fieldwork was somewhat delayed mainly due to delays in obtaining ethical approval. However, the main study was still conducted well within the malaria season. Even so, the study was conducted very early on in the introduction of new (Pf/combo) RDTs. There are three main implications of this timing for the study. Firstly, the results of the RDT quality testing may be better than could be expected if RDTs were stored for much longer, and during the hottest months. Secondly, the RDT user

assessment may reflect poorer use than would be expected after refresher training for the new tests – especially regarding the amount of buffer used. Reassuringly, the majority of providers did use the right number of drops of buffer solution (2 drops) required for the new RDT rather than the 6 drops required for original (Paracheck based) RDT . Thirdly, for the FGDs, our interpretations could have reflected perceptions of original RDTs in cases where respondents were unfamiliar with newer tests. However, most participants who had tests did distinguish the two.

Finally, the scope of the study was always only limited to the private sector, and only from the provider side. It would therefore be of interest to extend some aspects of the study to include public health facilities or village malaria workers, and to also gain more insight into the demand-side.

Table 20: Key findings and recommendations

Domain	Key findings and source (CS- census survey, MC – mystery client, FGD- Focus Group Discussion, RA – RDT assessment)	Recommendations
Diagnosis	• In urban areas the main types of private providers are pharmacies or cabinets (91.8%, 56/61) whereas in rural areas drugs shops and grocery shops predominate (CS) • There seems to be a distinction between selling drugs ("*lout tnam*") versus diagnosing and treating ("*pinit pchier bal*") (MC, FGD) • Out of the 203 providers who had antimalarials, 120 had RDTs (CS) of whom most (100/120) reported performing them. • RDTs seem to be at the margins of practice in the selling of drugs and treatment patients (FGD).Fewer than half of providers advised testing (88/209) when mystery clients presented with malaria symptoms (MC) • Grocery shops were the least likely to report performing RDTs (10/55, 18.2% -CS) and to advise testing (MC). By contrast, cabinets were the most likely to advise and offer a test. For these practices, pharmacies and drugs shops fell in between cabinets and grocery shops. • We found some evidence of willingness of some providers to refer to others (public or private) for diagnosis (FGD, MC) but few providers reported they would refer RDT negative patients elsewhere (CS). • Of providers who have RDTs, 71 (59%) reported having training in last 12 months. • In patients found to be RDT negative, providers most frequently	• Scale up current efforts to strengthen links between public and private providers and strengthen regulation and enforcement. Ensure the registration process for these trained providers is simple and inexpensive. • Clearly differentiate between which providers can diagnose and cure ("*pinit chier bal*") eg cabinets and some pharmacies/drug shops, and those who only sell simple remedies ("*lout tnam*") eg grocery shops and some drug shops. For the latter encourage them to refer to other providers (public and/or private) for diagnosis and treatment. • For those providers who do diagnose and cure (and this may include mobile providers in remote areas without VMWs), they should be given adequate training and monitoring which incorporates diagnosis into their general practice – not just the performance of RDTs. This includes clear guidance to providers on how to manage "RDT negatives" and to clarify the role and limits of microscopy. Emphasize that many fevers are not due to malaria and address concerns over the diagnosis of non-malarial-febrile illness (especially typhoid and dengue) by identifying and communicating diagnostic criteria. • For drug sellers (or those who usually "*lout tnam*") clearly differentiate which drugs can be sold without prescription for symptomatic relief eg paracetemol, vitamins antihistamines, (?chloroquine). Provide training and guidelines on who should refer and strongly encourage and facilitate referral to trained providers for diagnosis and treatment of more serious cases, children, pregnant women. • If microscopy as well as RDT is to be encouraged in the private sector , consider implementing a system for quality control for microscopy. • Median price of test for patient is similar to the RRP of 2900 riel for Malarine.

	named a diagnosis of typhoid (53%) with at least a third of providers saying they would provide antibiotics (CS). • Providers perceived the RDT as less sensitive than microscopy, and not as useful due to only identifying malaria, but useful for using in remote areas (FGD).	Therefore although there is a financial incentive for provider to **sell** test, for patient it is not financially attractive to pay for test. Explore strategies for making RDTs more attractive to patients.
RDT quality and quality assurance	• Current stock out RDTs due to delay in procurement • Currently, there is no routine system for checking quality of RDTs stored under field conditions or for providers to feed back if there are problems (RA) • Quality of RDTs we retrieved (all "new Malacheck") was acceptable (RA) • Providers seemed receptive to having temperature and humidity monitoring and having RDTs taken for QA (RA) • Transport from sales rep house to final destination was the hottest part of journey but is not monitored (RA) • Digital temperature and humidity recorders were easy to use but not so cheap, need to be retrieved and can get lost (RA) **Main problems reported by providers (CS)** • Not sensitive enough/"broken tests"/not showing result clearly/unexpected negative results (CS/FGD) • Insufficient buffer or buffer expires (CS, FGD) • Difficulty in using the blood taking device (CS/FGD)	• GF procurement process needs to be reviewed and rationalised • Consider sampling RDTs on arrival at final destination (because hottest time is during transport) and/or ongoing QA of stored RDTs at different temperature for different length of time– at Institut Pasteur Cambodia reference laboratory • Consider monitoring of temperature and humidity during transport and in sentinel shops? (And consider repeating temperature and humidty monitoring in public sector/VMWs) • Continue the ongoing collection and analysis of used RDTs from private providers. Consider gathering more information relating to RDT and ACT sales. • Provide reassurances over trusting results, e.g. feeding back quality control. Consider feedback mechanism for problem tests (eg freephone telephone number of discussing problems)
RDT user assessment	**RDT user assessment (CS)** • Correct amount of blood only in 38% • Waited full 20 minutes in only 40% • Gloves used by only 22% • Disposed of lancet in sharps box in only 16% • Use correct amount of buffer 88%	• See above recommendation re. the provision of more comprehensive training on the diagnosis and treatment of fever (not just malaria) • Respond to providers concerns over the logistics of tests, e.g. have fewer tests in a pack, make the blood collecting tube more precise, make tests really clear to read. Switch to single packets of RDTs (as planned) • More emphasis on blood safety in particular the safe disposal of lancets including provision of sharps boxes and clear instructions on what should be done with them.

		• In provider training, stress the importance of 1) using a timer and waiting the full 20 minutes, 2) using the correct amount of blood and 3) using the correct amount of buffer. All of these components are very important in obtaining accurate results.

Perceptions about drugs	• Widespread perceptions of side effects of mefloquine leading to deviations from the recommended regime for blister-packed artesunate and mefloquine (FGD, MC)
	• Drug resistance
	  ○ Some awareness of the issue but some confusion in the implications
	• Regulation
	  • Confusion on what provider are not allowed to sell (all antimalarials/artesunate/or Malarine) (FGD, MC)
	  • Lack of clarity is damaging - ?who can and cannot be trained. If not trained but continue to practice.
		• Switch from A+M to other co-formulated drugs eg DHA_piperquine as soon as possible
		• Provide clear guidelines for each zone as to what exactly different types of providers are allowed to sell including list of names and pictures of allowed and/or not allowed drugs

Drug availability and use	• Malarine was the most widely available antimalarial and the most common drug sold to mystery clients.
	• Artesunate availability much less than before suggesting the ban has been effective. However 16.8% of mystery clients managed to buy it.
	• Many providers were reluctant to sell full course of ACT without a test (MC). "Drugs for malaria" were only sold initially to 15% (32/210) of mystery clients presenting with malaria symptoms but if additional information given eg past experience of malaria or reported test result then 44% (80/182) providers sold "drugs for malaria" (without blood test) (MC)
	• Artemether for injection widely available (23% of providers) (CS).
	• Terminology for "cocktails" needs clarification (FGD,
		• Need to collect data on how artemether for injection is being used. If widespread use of artemether on it's own then this is very concerning with regards to impact on artemisinin resistance
		• The practice of selling a mix of drugs ie. "tnam psom" is deeply entrenched. It is very unlikely and may not be necessary that the practice can be changed completely. Instead, it may be better to provide guidance for safe and effective drugs to have in "tnam psom", specifically:
		  ○ What is ok?
		  ▪ Paracetemol, Vitamins (maybe chloroquine?) and possibly antihistamines (depending on symptoms)
		  ▪ Whole blister packages of Malarine or A+M and antipyretics
		  ▪ To tell patients (and for patient so ask) the contents

	MC).Widespread and "normal" practice to give "Tnam psom" = "Drug mix/combination". This term can include the first-line ACT, artesunate and mefloquine. (MC, FGD) . "Ya chut" is used to describe the small pre-packaged packs of medicine, usually for treating non-serious illness eg common cold (MC, FGD) • Widespread practice of cutting blisters in general and some evidence of cutting of A+M and Malarine (MC) • Widespread use of antibiotics for febrile patients (census, MC) • A quarter of providers (54/215) had evidence of providing intravenous medicines or inpatient care. Of these 81.5% (44/54) performed RDTs compared to 34.8% (56/161) of those providers who did not provide inpatient care. (CS)	○ What is not ok? ▪ Artesunate and other antimalarials, ▪ Antibiotics and steroids ▪ Splitting blisters ▪ Unnecessary "serum" infusions ▪ Overdosing on same drug (different formulations of same drug eg paracetemol)

REFERENCES

Adeyi, O., & Atun, R. (2010). Universal access to malaria medicines: innovation in financing and delivery. Lancet, 376, 1869-1871.

Arrow, K.J., Panosian, C.B., & Gelband, H. (2004). Saving Lives, Buying Time. Economics of malaria drugs in an era of resistance. Washington, D.C.: The National Academies Press.

Bell, D., Wongsrichanalai, C., & Barnwell, J.W. (2006). Ensuring quality and access for malaria diagnosis: how can it be achieved? Nat Rev Microbiol, 4, 682-695.

Bennett, S., McPake, B., & Mills, A. (1997). Private Health Providers in Developing Countries. Serving the Public Interest? London: Zed Books.

CNM. (2009-2014). Draft of the National Malaria Control Program Monitoring and Evaluation Plan. National Centre for Parasitology, Entomology and Malaria Control. Ministry of Health, Cambodia

Cohen, J.M., Sabot, O., Sabot, K., Gordon, M., Gross, I., Bishop, D., et al. (2010). A pharmacy too far? Equity and spatial distribution of outcomes in the delivery of subsidized artemisinin-based combination therapies through private drug shops. BMC Health Serv Res, 10 Suppl 1, S6.

Cross, J., & MacGregor, H. (2009). Who Are 'Informal Health Providers' and What Do They Do? Perspectives from Medical Anthropology. IDS Working Paper 334. Brighton: Institute of Development Studies at the University of Sussex.

De Allegri, M., Tiendrebeogo, J., Louis, V.R., Ye, M., & Muller, O. (2011). Measuring the AMFm. Lancet, 377, 810; author reply 810-811.

Dondorp, A.M., Nosten, F., Yi, P., Das, D., Phyo, A.P., Tarning, J., et al. (2009). Artemisinin resistance in Plasmodium falciparum malaria. N Engl J Med, 361, 455-467.

Dondorp, A.M., Yeung, S., White, L., Nguon, C., Day, N.P., Socheat, D., et al. (2010). Artemisinin resistance: current status and scenarios for containment. Nat Rev Microbiol, 8, 272-280.

English, M., Reyburn, H., Goodman, C., & Snow, R.W. (2009). Abandoning presumptive antimalarial treatment for febrile children aged less than five years--a case of running before we can walk? PLoS Med, 6, e1000015.

Incardona, S., Vong, S., Chiv, L., Lim, P., Nhem, S., Sem, R., et al. (2007). Large-scale malaria survey in Cambodia: novel insights on species distribution and risk factors. Malar J, 6, 37.

Kingdom of Cambodia Ministry of Health. (2011). National Strategic Plan For Elimination of Malaria in the Kingdom of Cambodia 2011-2025. Phnom Penh: National Center for Parasitology, Entomology and Malaria Control (CNM).

Laxminarayan, R., Over, M., & Smith, D.L. (2006). Will a global subsidy of new antimalarials delay the emergence of resistance and save lives? Health Aff (Millwood), 25, 325-336.

Moon, S., Pe´ rez Casas, C., Kindermans, J., de Smet, M., & von Schoen-Angerer, T. (2009). Focusing on Quality Patient Care in the New Global Subsidy for Malaria Medicines. PLoS Med, 6, e1000106. doi:1000110.1001371/journal.pmed.1000106.

Nariddh, M.C. (2011). A Day in the Life of a Drug Inspector in Pailin. CONTAINMENT of drug-resistant malaria on the Thai-Cambodian border.

Quarterly Newsletter of the Strategy for the Containment of Artemisinin-Tolerant Malaria Parasites in South-East Asia Project, Available online at http://www.who.int/malaria/diagnosis_treatment/arcp/containment_newsletter_issue2.pdf (accessed 22 June 2011).

Samarasekera, U. (2009). Countries race to contain resistance to key antimalarial. Lancet, 374, 277-280.

Smith, L.A., Jones, C., Meek, S., & Webster, J. (2009). Review: Provider practice and user behavior interventions to improve prompt and effective treatment of malaria: do we know what works? Am J Trop Med Hyg, 80, 326-335.

WHO, W.P.R. WORLD MALARIA REPORT 2010. CAMBODIA. In W.W.P. Region (Ed.),

: WHO Western Pacific Region.

World Health Organisation. (2011). Battling malaria drug resistance along the Thai-Cambodian border. Available online at http://www.who.int/malaria/diagnosis_treatment/arcp/containment_project/en/index.html (accessed 22 June 2011).

Yanagisawa, S., Mey, V., & Wakai, S. (2004). Comparison of health-seeking behaviour between poor and better-off people after health sector reform in Cambodia. Public Health, 118, 21-30.

Yeung, S., Van Damme, W., Socheat, D., White, N.J., & Mills, A. (2008). Access to artemisinin combination therapy for malaria in remote areas of Cambodia. Malar J, 7, 96.

Yeung, S., Patouillard, E., Allen H., Socheat, D. (2011). Socially marketed rapid diagnostic tests and ACTs in the private sector: ten years of experience in Cambodia. Malar J, 10,243.

APPENDIX: FOCUS GROUP DISCUSSION – FULL RESULTS

STUDY PARTICIPANTS

Focus group discussions took place in February 2011. A total of 52 providers participated in 8 focus group discussions held in 8 operational districts across the five provinces included in the wider GUARD project. Most FGDs had 6 to 8 participants, but FGD#6 had only three and unfortunately was not audio recorded due to a technical fault, leaving the information gained as only a summary of the discussion. Each FGD lasted for around two hours.

FGD participant characteristics are shown in Table 21. In each FGD, the participants represented a mix of at least two provider types, including those selling drugs in grocery stores, drug shops, pharmacies and at private clinics. Many participants owned their shop, pharmacy or clinic, whilst others were attendants who worked for others and several were relatives, mostly husbands, wives or siblings. Ages ranged from 23 to 66, with an overall average of 41 years. Around half of the participants were women. Providers had worked in their profession for an average of 9 years, ranging from 1 to 31 years. Around half of all providers had received some form of training, mostly in nursing or midwifery, although three were doctors (in FGDs #3 and #7). Fewer than half of all providers (44%) had attended any malaria or RDT training in the past three years, although some had attended several trainings over this time, especially those in Pailin where one pharmacist had attended 8 trainings over the last three years.

Table 21 Focus Group Discussion Participants

FGD	District	Number of participants	Provider type (n)	Role of providers (n)	Mean Age in years	Number women in group (%)	Mean years as provider	Number providers trained in health care (%)	Number providers attended malaria/RDT trainings in the last 3 years (%)
#1	Kratie	7	Grocery-drug stores (5), mobile providers (2)	Owners (4), relatives (3)	50	4 (57%)	13	1 (14%)	1 (14%)
#2	Kratie	6	Private clinics (3), pharmacies (2), midwife (1)	Workers (4), owners (2)	36	3 (50%)	11	5 (83%)	3 (50%)
#3	Mondul Kiri	8	Grocery-drug stores (5), drug store (1), pharmacy (1), mobile provider (1)	Owners (6), relatives (2)	37	5 (63%)	9	3 (38%)	2 (25%)
#4	Kampong Thom	8	Pharmacies (5), private clinics (3)	Owners (7), Relative (1)	36	2 (25%)	7	6 (75%)	3 (38%)
#5	Kampong Thom	7	Groceries (3), drug stores (3), private clinic (1)	Owners (5), relatives (2)	43	4 (57%)	8	3 (43%)	5 (71%)
#6	Siem Reap	3	Pharmacies (3)	Owners (2), relative (1)	30	2 (67%)	5	1 (33%)	2 (67%)
#7	Siem Reap	6	Pharmacies (4), private clinics (2)	Owners (4), workers (2)	44	5 (83%)	7	4 (75%)	2 (33%)
#8	Pailin	7	Pharmacies (4), private clinic (1), drug store (1), midwife (1)	Owners (5), Workers (2)	44	2 (29%)	10	4 (57%)	5 (71%)

KEY CONSTRUCTS

There were many different ideas discussed in the FGDs across the different areas. However, some key concepts relevant to the research concern emerged from participants across the different groups. The conceptualisations of the role of RDTs hinged on the perceived roles of providers and the way medicines are used. We therefore outline these concepts first, providing context for interpretation of perceptions of RDTs.

The roles of providers was prominent in their discussions. A notable distinction was made between the roles of 'selling' *(louk tnam)* and 'treating' *(pinit pchier bal).* A majority considered themselves as providing the former type of service, their role being to distribute drugs, but not to attempt to *cure* individuals of their illnesses. This resulted in dispensing of drugs seen as 'effective' for getting the customer through the illness with few side-effects, including artemisinin monotherapy tablets or injections. By contrast, 'treatment' entailed diagnostic and more intensive curing processes. This included carrying out examinations, batteries of tests and the use of drugs that required the patient to invest more money, energy and time to achieve a cure.

The way to use different medicines was also a popular topic for discussion. Overall, the *modus operandi* could be described as 'tailoring' to the individual case, taking into account their condition and energy levels as well as knowledges about the side-effects of different drugs. This resulted in frequent dispensing of small packets of mixed drugs and tinkering of dosages to lessen the harsh interaction of drugs with the *mero* (akin to the biomedical concept of 'microbes').

Compared with these topics, malaria RDTs were less favoured topics of discussion. This reflected their use on the margins of practice. They were used along with both 'selling' and 'treating' practices, situated in a grey area between the two. The principle of testing appeared to be assimilated into practices related to the ideal of *curing* the patient; they *should* be used, or preferably microscopy and other laboratory tests should be used, to show the parasites and other causes of illness, leading to prescription of drugs to cure. However, providers reported reluctance to use RDTs for a number of reasons, identifying problems with the tests not 'showing' malaria, and other logistical issues with the syringes and buffer solution. In Pailin, providers seemed more keen than respondents elsewhere to report the need to ensure patients were tested before receiving malaria drugs. Whilst the given rationale for these practices referred to an adjusted version of public health instructions, the regulatory enforcement of drug shops in Zone One may also have affected perception of the use of antimalarial and testing commodities.

SELLING, NOT TREATING

DISTINGUISHING SELLING AND TREATING

Many of the providers who participated in the FGDs described their role as 'selling' *(louk tnam)* rather than 'treating' *(pinit pchier bal).* As concepts, both activities involve some level of history taking and matching drugs to the person's needs ('tailoring'). However, 'treatment' is seen as the use of stronger medicines and also implies a diagnostic process, including physical examination, a scan or blood test, that would usually be carried out by a medic (*kru peet*), often at a health facility.

> 'I am not a *kru peet* (medic) who provides mobile injections like him. I only sell some groceries and make some mixed drugs. I never give treatment.' (FGD#1, P7, untrained husband of grocery shop owner)

This distinction was made repeatedly, and opens a lens through which to understand the roles not only of sellers but of their medicines and of testing. The concept of 'selling' was broad, dispensing drugs for

multiple illnesses, including for malaria and typhoid, often after taking a history of the illness and of the patient themselves and deciding which drug(s) would work well with the illness and the individual.

> 'I ask them in detail before I provide the drug. They said they suspect themselves that they've got typhoid, and then I ask them "how are your shit, watery stool or normal?" Because I give them a drug mix based on the situation, whether they had diarrhoea or were normal. If they got diarrhoea *(reak)*, I would give them the kind of diarrhoea drug. But if they got diarrhoea, and I give the constipated drug, they would be constipated. [All participants laugh]' (FGD#5, P4, female untrained grocery shop owner)

However, 'selling' had its limits. Respondents were clear in identifying practices outside of their knowledge: they saw the process of 'treatment' as the realm of specialists who could perform diagnoses and enable the patient to be cured. Thus, they often talked of trying to refer patients to *kru peet* or health facilities for 'treatment,' but reported that patients rarely followed through, preferring convenient to buy drugs according to their symptoms from the local seller,

> 'Mostly the people here, they want to buy drugs, they do not usually go to hospital. Some people who use to use those drugs, they did not go to the *kru peet* for diagnosis and prescription. In the village, mostly the villagers when they get fever or headache, they say "I have this symptom" and they come to buy [the medicine] by themselves. But we are the seller. We have the pharmacy, we understand. We tell them to go for diagnosis, how to do like this, how to do like that. Because after the discussion and diagnosis, they come to buy drugs so when they take [the medicine] they can be cured according to the prescription. We introduce them like that, [but] some people they do not understand it like this. They say "I want to buy this, I want to buy that," so we are the seller, we follow their needs.'(FGD03, P4, male untrained grocery owner)

ATTENDING TO THE BUYER'S REQUIREMENTS

The purchase of drugs also allowed the patient to remain in control of monetary costs, important for those with little money, and time spent, important for those needing to continue to work through an illness episode,

> 'The patients want a cheap and effective treatment, effective drugs because they are poor. If the doctor has a bit more care to the patients, they could be cured' (FGD#3,P1, male nurse, drug shop owner)

> 'Sometimes they want to go to the hospital too but because of the time ... they want to buy everything in the morning because they are busy with their farming. And sometimes it is about the matter of relationship for example, a person they know that there is a health centre nearby their house but he/she doesn't go there; they come to my house instead because they know me well for a long time.' (FGD#2, P4, female midwife)

Control over which medicines were sold/purchased is jointly held between the provider and client. Providers reported that a client is able to ask for specific drugs, or drugs for specific conditions, unlike at public health centres, where they were at the mercy of the decisions of the health worker. However, the provider held knowledge in terms of which drugs to use, and providers described how they deliberately kept this knowledge to themselves in order to create dependency of the patient upon their specific service,

> 'That they trust us, that is very important. They think that they are not clever and they come to a clever one, so they always come for consulting and visiting us. When they have illness, I provide

drug. If they have fever, flu, we offer them a test. What we are doing is to make them trust us, if they do not trust they will not come to us again.' (FGD#4, P4, male nurse, clinic owner)

P2: The doctors always hide to the patients when they make a cocktail. They do not give the blister of the drug, it is taken out. Because of business, they practice like this.

P3: Sometimes the patients could go to buy the drugs at other places because they have the plastic of the drug

P7: They do not want the patients to know what the drugs are. And they could say this drug is cheap or expensive or a good drug in order to make them not to know the drugs which are provided.

Facilitator: And how about you? What do you want to add?

P6: I am the same as that provider. No one could let the patients go to other shops! [laughter]

P2,P7: We do the same generally. (FGD#3)

That these decisions lay with the buyer when attending a private provider, rather than being in the control of the health worker at a heath centre, was seen by providers as an important value of their service. However, providers were wary of providing 'treatment' to more serious patients when this might have negative consequences for the patient's health and the provider's reputation. One provider described how he got around this by making a contract with a customer in the event of a bad outcome,

'To say frankly, I think that the staff in health centre give poor service. However, they have many works to do with different roles. For example, I am selling drugs, so I could not treat, I could treat when there is necessity. Then, when someone feels very sick, they blame the doctor [at the health centre], this and that. Sometimes there is a serious patient who is needed to go to the hospital, but she/he does not want to go to the hospital. I had an experience with one patient who did not want to go to the hospital. I just asked him to sign on a paper of agreement that there is not any responsibility [on me] for any accident during having treatment.'(FGD#3, P7, female untrained mobile provider)

TREATING FOR A CURE

Providers were also aware that selling rather than treating could be a short-term fix. Many reported advising that if patients want to be cured, a different process must be undertaken, often including diagnostic testing, and the patient must be willing to bear tougher side-effects in order to reach a longer-term cure.

'They take one time and they get side effects, and then they stop taking, I advised them ... It will be cured if we struggle [with the side effect]' (FGD#7,P2, midwife pharmacy owner)

'When humans get that side effect then the *mero* [microbe] will die too. If the human doesn't have the side effect how can the *mero* die?'(FGD#2, chorus of participants: P2, P3, P4, P5 and P6)

Such processes could be undertaken within the roles of some of the providers who participated in the FGDs, pulling 'treatment' into their practice. We observed that some participants who claimed not to

'treat' nonetheless described giving 'strong drugs' such as injections or using diagnostic tests, suggesting a blurring between the roles of 'selling' and 'treating' in practice.

SELLING, TREATING AND DRUG POTENCY

Participants discussed side-effects a lot during the FGDs. Side-effects were feared, and as a consequence, drugs known to have side-effects were also feared, characterized as 'strong drugs.' For malaria, drug mixes were commonly assembled by providers in order to tackle the confluence of symptoms encapsulated within and associated with malaria (chills, fever, headache, weakness). Such mixes of drugs were normalized, considered benign and without consequences of side-effects. Other drugs considered 'normal' or 'simple' included chloroquine, mebendazole, co-trimoxazole and paracetamol. These were used in the first instance for 'normal' illnesses,

> 'For me I have not many, I have only Co-trimoxazole that we used to use in the health centre. So when the patient has this illness [typhoid] we mostly give that drug because it isn't a high anti-biotic, it is simple.' (FGD#2, P4, female midwife)

By contrast, drugs that only treated malaria, particularly mefloquine (one of the two drugs combined in the recommended treatment for malaria, 'Malarine'), were considered very strong. Side-effects described included severe vomiting, dizziness, haemolysis and even death if the patient was not in a state to receive the drug. However, several participants stated that the drug was essential to completely cure malaria; weaker drugs could make the patient feel better but not lead to a long-term cure. Side-effects were also described as an inevitable consequence of the drug interacting with the parasite,

> 'If we use Artesunate or Artemether, it cannot make the illness definitely gone, it will come back in 28 days. That's why we use Mefloquine to avoid the malaria parasite coming back; it can be completely removed.' (FGD#1,P1, male Khmer Rouge trained mobile provider)

> 'In the drug (Malarine) there is Artesunate and Mefloquine, and the one that gives side effect is Mefloquine, for Artesunate it only pauses the *mero* (microbes) from growing. But Mefloquine is the one that kills the *mero*, and during the killing it goes all the way around in human's body. That makes a problem for a person that is weak, for instance, the one who has cardiopathy, and much lack of glucose disease because when it kills the *mero* it makes us even weaker.' (FGD#2, P6, male untrained pharmacy owner)

TAILORING MEDICINES

Of central importance to the practice of the providers who participated in our FGDs was that the medicines dispensed worked well with the patient who would feel better and return to that provider for future illnesses. This involved tailoring medicines to the illness, to the patient's condition and preferences and tinkering doses adding medicines to control anticipated side effects.

TAILORING TO THE ILLNESS

Providers listed the illnesses they commonly see using a combination of symptom and disease terms, including malaria, typhoid, stomach ache, diarrhoea, flu, headache and dengue. Often patients would present with several of these and providers typically described dispensing medicines for each.

> 'Mostly they came to say [they have got] flu, head ache, congestion, tooth ache or something like that. So we make a drug mix for them according to what they told us.' (FGD#1, P4, male untrained grocery shop husband)

For malaria, each symptom reported was catered for, such as temperature reducing medicine, headache medicine, and medicine was also given for the illness of malaria itself. The type of antimalarial dispensed depended in part on the type of malaria perceived, including its particular symptoms and whether the parasites were *P. vivax* or *P. falciparum*. On the whole, participants said chloroquine was suitable for *vivax* malaria, along with mefloquine, nivaquine and quinine (although 'quinine' is also used as a general term for antimlarial drugs), whilst artesunate, artemether, quinine, AQ, A+M (public sector artesunate plus mefloquine) and malarine (private sector artesunate and mefloquine) were popular for *P.faliciparum,*

> 'I only used to use artesunate for normal malaria, and some patients they never take artesunate or mefloquine because they got this illness for the first time but later they take these drugs too. Another thing, for chills, we cannot use artesunate, we give Malarine. For malaria, there are chillsand no chills. The chills one is *vivax* that we have to give mefloquine, and *falciparum* that one we can only give artesunate.'(FGD#2, P5, male nurse, pharmacy owner)

TAILORING TO THE PATIENT'S CONDITION AND PREFERENCES

Patients were considered to respond differently to drugs. Differences to look out for when dispensing drugs included whether the patient was considered to be strong or weak, pre-existing conditions such as heart problems and if the patient was pregnant or of particular age groups, as discussed in FGD#3 by this doctor and mobile provider,

> P2: Drugs sometimes could cure ten patients, and sometimes could cure two patients. It means that there are differences of element in each person.
>
> P7: Yes! [P2] is right. The important [differences] are their illness and their weight. The first is their weight which could tell how the patient [should] take the drug. The second is the type of their illness which lets us know whether the patient is painful around the heart area orhas a mental disorder, and then pregnant, adult or child.

In addition, differences could be observed through response to medicines, which would need to be altered according to the condition of the patient

> 'I treat according to his/her situation, such as giving artemether injection one dose and then control the patient [do a control malaria test] to make sure there is no parasite, so I give the drug [for malaria] but if the patient still has parasites, I continue use the injection drug artemether.' (FGD#2, P2, male midwife, clinic attendant)
>
> 'For example, we inject one box of it [artemether] in the first day, second day, we give two days, and in the fourth day, we give mefloquine if the patient doesn't suffer from the side effect, he can possibly use the drug because of the biological system, but if they are weak, we are afraid to give them mefloquine, we stop giving them anymore.' (FGD#1, P1, male Khmer Rouge trained mobile provider)

Patient preferences were also important in deciding which drugs to dispense, including responding to patient desires for the mode of delivery, particularly injections, specific drug names or specific brands,

> 'My husband has Artemether for treatment and it is an effective drug. And when I took it, even though I am really weak, I did not have any side effect. Artemether injections are the most popular for the children. And when the patients are lazy about taking the pills, they want to use Artemether injection. And if they do not want to inject, they could use Artesunate.' (FGD#3, P7, female untrained mobile provider)

> 'Sometimes the buyers order the drug, if they want Malarine, I would give Malarine, and sometimes they need Quinine, I give Quinine.' (FGD#5, P5, female untrained wife of grocery shop owner)

> 'Sometimes when they believe in mosquitoes "quinine"[3], if we give the drug, quinine, without the mosquito picture, they don't even accept.' (FGD#1, P6, female untrained grocery store owner)

TINKERING TO CONTROL SIDE EFFECTS

In addition to the selection of drugs being tailored to individual patients, providers described altering the quantity and spacing of the drug chosen according to the known side effects of drugs and the condition of the patient. For example, certain strong drugs could be given in smaller doses for a longer period to reduce their 'poison',

> 'But the side effect of Malarine is too much ... I dare not give it like that [according to the instruction] because it is too serious, I normally use the same for three days but I separate it. Nowadays, I use it, but I give some in the morning and some in the evening; it does make the patients relieved.' (FGD#1, P1, male Khmer Rouge trained mobile provider)

For weaker patients or those with pre-existing conditions, dosages recommended by the drug packaging were sometimes considered to be too strong, with potentially serious side effects,

> 'Most people dislike taking Malarine because it has more side effects. Then, we are the seller, we have to reduce to side effects by taking Malarine for more days if we could see that the patients are very weak of power. I reduce the side effect by changing from taking for three days to taking for five days based on the weight and health condition of the patients. That change can[still] cure, and it helps to reduce the side effects. But if we give them 3 days of Malarine base on its instruction, the patients will be having a strong side effect.' (FGD#3, P4, male untrained grocery shop owner)

> 'We keep some of medicine and it is taken only three pills for malaria, so it is not giving the side effect ... I keep the small one [ie artesunate]; sometimes, the patient have no power, so if they take, they will get the side effect.' (FGD#5, P5, female untrained wife of grocery shop owner)

[3] There is some confusion around the use of the word "quinine". Sometimes, "quinine" appears to be used to describe antimalarials in general or chloroquine. The commonly available antimalarial tablet with the picture mosquito is actually chloroquine, and not quinine.

Providers also frequently described adding components to the package of therapy in order to deal with anticipated side effects. These included pharmaceutical additions as well as suggested foods and drinks to take or avoid. For example, drugs to counter the effects of malaria (such as vitamins, although in some cases these were discussed as contraindicated) could be necessary alongside the drug for malaria, such as Malarine,

> 'When they take Malarine, mostly, they vomit. So we have to use a drug that could help them with vomiting and headache.'(FGD#3, P4, male untrained grocery shop owner)

> 'So most of the time when the patients take the Malarine they will vomit, so we have to use B6 [vitamin] to help them. And when the patients have a high temperature, we give Para [paracetamol] to them, so if the patient gets a normal temperature they are able to take Malarine. When the patients still have the high temperature, and they took Malarine, they will have convulsions. The temperature will be higher and higher, and they get diarrhoea. To take B6 in the morning and evening is to help the patient to be fine, and Para for against high temperature.' (FGD#5, P2, male nurse, clinic owner)

For patients with high fever, several providers reported fearing that any treatment at that time could result in worsening of the condition. IV serum was popularly mentioned as a precursor to antimalarial drugs to reduce the shock of the treatment and give the patient strength,

> 'Malaria causes the heat, chills, to lose much water and sugar inside the body, so we have to provide IV fluid; otherwise, the patient would have convulsions.' (FGD#4, P4, male nurse, clinic owner)

> 'And we have to see if the patient is weak we can't give the drug, we have to treat him/her for one or two days at home by giving IV fluid for him, until he becomes better. Then tell him to take the drug.' (FGD#2, P3, male midwife, clinic attendant)

Strength could also be added by taking supplements such as iron and multivitamins,

> 'I give the drug to create cells because when the patients got malaria, they would be deathly pale, so let them take Ferrous or Multi [vitamins] for ten days to create the cells to be normal.' (FGD#5, P2, male nurse, clinic owner)

Curing malaria completely was considered by several providers to require a series of medicines, particularly artesunate followed by mefloquine, resulting in tailoring of the drugs to include those with few side effects while the patient was sickest followed by a powerful drug after a few days to completely cure the patient, rather than the illness recurring again over the next few weeks,

> 'During the last five years, I treated Malaria. First of all, we give artesunate which has 12 pills in a blister to the patients, after they finished them, I give mefloquine too. Four pills of mefloquine, it can be completely cured as well, but we only give in different way. As it provided the serious side effect, we give artesunate first.' (FGD#1, P1, male Khmer Rouge trained mobile provider)

Food and drink were commonly recommended to control side-effects, particularly sweet things to give energy, like coconut juice. Specific recommendations varied between providers,

> 'Malarine is the drug that has side effects as someone has said. Then, after taking it, we should wait for 1 hour before going to have fruit juice or coconut juice immediately. If they can eat something, they will not be dizzy. And if they vomit and you do not provide them the food to increase the energy, for instance, they will be serious and will be cured after up to one month or a

> fortnight, while they are supposed to be cured within one week. According to my husband who has been treating, he always tells the patient to eat to have energy. Even they do not have money, I spend for them. They can pay me back when they have money. Some patients look so pitiful, so they are provided porridge or some delicious food to increase their energy. So they are going to be cured soon.' (FGD#3, P7, female untrained mobile provider)

Controlling side effects through tailoring medicines and tinkering with doses and foods was seen as important part of helping patients to feel better and ensuring continued custom. Custom could also be ensured when, as exemplified above, providers gave services on credit. In addition, providers were afraid of very serious side-effects of drugs, meaning smaller quantities and careful administration were important, especially for very weak patients,

> 'There was a patient who had received a blood test and saw three crosses, but when he took the Malarine, he got convulsions and then died immediately ... He become completely yellow, very serious. I thought that maybe he was asked to take the drug while he was getting too high temperature, I don't know, then the patient convulsed, and then he died after being brought to hospital. And that doctordid not use the drug like he [points at P1] said, they used all the [malaria] drug at first together. The person was a single man, aged similar to you [the facilitator – early 30's]. Maybe the patient had too high temperature and took the drug immediately.' (FGD#1, P6, female untrained grocery store owner)

SHOWING THE PARASITES

In the framework of selling drugs that help the patient versus treating with drugs that cure the patient, testing in general fitted with the latter concept, although RDTs seemed to fit somewhere in between. Providers saw a key benefit of testing as identifying the disease to be treated (for malaria, 'showing the parasites'), so drugs could be targeted more carefully and the patient might get a longer term cure. This mostly applied to microscopy, the benefits of which were broader than RDTs which were restricted to one disease, had some logistical problems and gave less information than microscopy. The advantages of RDTs for rural areas were noted, although the tests were still a financial and time encumbrance in spite of being subsidised and fast, especially for very poor patients who needed to save money and return to work with the help of effective drugs.

TESTING ENABLES PRECISE TREATMENT

Participants reported that testing was an important part of the process of curing an illness: through testing one could find the best treatment,

> 'There is a massive difference in treatment or diagnosis between the past time and right now. Previously, we treated the patients based on their symptoms only. Now, we have a diagnostic test, Malacheck,and the microscope which could show a quick result, and we can provide treatment and serum topping [IV fluid]. In the past, we could help the patients only 80% to 85%. Personally, when I was sick, my uncle, he is a doctor, treated me, [and I] recovered by just telling him the symptoms; however, it is not recovered 100% and it would have impact when we take the wrong drug, he said ... It is better to have a diagnostic test because when there is a typhoid, the test could be matched [to treatment].'(FGD#4, P6, male untrained clinic owner's nephew)

Providers reported wanting to test for multiple diseases, particularly typhoid, malaria and dengue. For this reason, microscopy was considered best to enable treatment, although with some debate amongst participants as to the limits of diseases possible to diagnose by microscopy,

> 'Yes, for instance, it [the microscope] can find typhoid, white cells increasing, laryngitis or inflame sore throat, etcetera[laughter] and it can also find worms in our body. That's the function of it, but Malacheck, that we use only to see malaria.'(FGD#2, P4, female midwife)

Some providers also reported that patients had become more aware of testing, which has become a more central part of the treatment process,

> 'In the last 10 years, quinine was the most popular, which was always asked for. Later and later, I became afraid to give the malaria drug if the patient does not have malaria, since they always ask for malaria drug. Now, my husband is working as a doctor, so the first important thing is to ask them to make a test. If the test [microscopy] gives how many crosses as such, I give the drug base on the result. Because my husband and I have been lived here for 10 years and he had 10 years of treatment, I could say that people here have been improving understanding. When they came to me, they asked me for a test or just say, "now I am sick, I just have a normal fever, running nose.", then I give a drug for flu to them. And if they are still having fever, not better, I have to make them a test immediately.' (FGD#3, P7, female untrained private provider)

Most providers reported relying on microscopy for identifying various causes of illness as part of 'treatment.' However, Malacheck was also seen to be useful, in its ability to extend the possibility of 'treating' people into more remote areas where people could access the test more quickly than going to a laboratory and the test is quick and relatively straight forward to use,

> 'Malacheck is only for rural areas without a laboratory nearby. Or when they go to the forest they bring it along to do themselves ... It saves time, whenever we feel suspect we do the test immediately to see the result not only depending on the laboratory - sometimes it is too far. It is easy to take, we don't to wait long.' (FGD#2, P5, male nurse, pharmacy owner)

> 'It is easy because before we could do the test by machine [Microscope] only, and it was available in a big pharmacy or specialist, but now the test are available based in the community, it is easy and takes less time. (FGD#5, P1, female untrained grocery owner's wife)

> 'I think that now it is easier because we have diagnostic test. It is good to have diagnostic test together with theory of symptoms for knowing the parasite.' (FGD#4, P4, male nurse, clinic owner)

Some participants reported that they believed the Malacheck test to be mostly correct, giving good results according to their experiences,

> 'Nowadays I do believe it because it tells me correctly, if there is malaria I gave malaria drug, the next day, they came and I asked how is the illness, they said it was gone. So it means the test is right. If the test says there is no [malaria], we use the drug for stomach and typhoid, then it works[people recover], so it means the test is correct. When it shows malaria we use malaria drug that we have confidencein, it is always right.' (FGD#1, P2, female grocery owner's wife)

The role of Malacheck was therefore considered to contribute in some cases to the 'treatment' process, but this was overshadowed by other tests, particularly microscopy. The tests were also included within a 'seller' role, particularly useful for rural areas, shifting some 'treatment' capacity into their work.

MALACHECK MAY FAIL TO SHOW THE PARASITES

In discussing RDTs specifically, some participants reported no experience of the tests. At the time of the GUARD Census, 28 (54%) of those participating in FGDs had RDTs available. Those who had used RDTs reported that the new combi-test to detect both *P. falciparum* and *P. vivax* is more useful than the previous *P. falciparum.* only test. However, many providers still expressed disappointment that the test failed to show positive results, often seen as due to a low parasite load (known as fewer 'crosses', a term borrowed from microscopy). Negative RDT results conflicted with expectations built upon clinical experience and results subsequently received from laboratory microscopy,

> 'I have an experience with using Malacheck with one patient when I lived in Kompong Cham. He came from Stung Trang province. I thought he should have malaria because he seemedto have such chills when he came back, but Malacheck could not show there is malaria. So my brother used IV fluid for flu, yet it was not curable. Two hours later, that patient had a high temperature. It means he had a serious malaria, and he had to be sent to provincial hospital ... That patient had 3 crosses when he arrived. He had a high temperature until he was unconscious. I really wondered why that Malacheck I have used for five times could not show the cross [laughter].' (FGD#3, P2, female doctor, grocery shop owner)

> 'There are some cases when we ask the patient to stay in order to extract the blood to the laboratory but they say they are in a hurry so we do the blood test by using it [Malacheck]. But it is difficult too, we can't see [the result as positive, malaria] unless there are two crosses [i.e. more parasites according to microscopy reading]. If there is only one cross we cannot see so it is a bit difficult. It is hard for us to see it in particular, when we do the test for them we cannot see but when they go to another provider [at a laboratory] they can see. So we cannot see it by using this test [Malacheck] while they can find it in the laboratory.' (FGD#2, P4, female midwife)

> 'It shows the result correctly but there is also case like she said, unless there are 3 crosses [many parasites] we can't find the disease. Few parasites are there so we cannot see it.Whenthere are many crosses we can see.' (FGD#2, P2, male midwife, clinic attendant)

Some compared the Malacheck with other tests that were sometimes unreliable, including urine tests for pregnancy,

> 'Sometimes it [Malacheck] has one line, and sometimes it does not have any line, so how could the doctors know that patient has malaria, sometimes they just only say there is not malaria. But that patient had malaria ... Like the test for malaria, a urine test which is used for pregnancy, is hard to get the accurate result. One woman is supposed to be three months pregnant, but the test shows no ... I didnot want to be pregnant. I did four tests already because I was wondered why I was always restless mood, but the test showed no. And I have had a son since that day[Laughter]. Anyway, the test for malaria and urine test are the same.' (FGD#3, P7, female untrained mobile provider)

The unreliable nature of the tests was repeated in the different groups, saying that perhaps 1 or 3 out of 10 tests would not work well. This put off the providers from using the test, especially if they ended up losing patients to other providers,

> 'It even makes us dare not to do the test, for example, in the health centre I work they give a lot of [Malacheck] and when we often cannot see [malaria] so we tell patient to the blood test in laboratory ... And we would like to request to make a better test that can see [malaria] clearly in order not to lose the patients.' (FGD#2, P4, female midwife)

On the whole, microscopy was trusted more than Malacheck, seen to be a poor-man's alternative and a less powerful tool, only identifying *falciparum* or *vivax* malarias and not other important diseases such as typhoid and dengue.

MALACHECK CAN BE TRICKY TO USE

Participants also found the tests themselves to be difficult to use. Table 22 shows the main logistical problems reported by participants with regards to Malacheck. The main logistical problems were problems with the blood-taking device, with the amount of blood dropped in difficult to control, perceived to affect the test's accuracy, and problems with seeing the result. Providers also reported that there were too many RDTs in a pack, which affected whether they would open the pack to rarely use the tests, or buy packs of tests at all.

Table 22. Logistical and Interpretation problems reported with Malacheck RDTs

Problem cited	Number of FGDs	Examples
Blood taking device problems	5	Blood taking device doesn't draw / dispense blood well; too much blood comes out
Stocking problems	4	Too many RDTs in a pack so may expire or waste / run out of buffer with tests remaining
Seeing the result	4	Malacheck doesn't show the result clearly
Expiry problems	3	Sometimes malacheck expire / we don't check date
Buffer problems	2	Find it hard to use correct amount of buffer
Storage problems	2	If it's too hot, Malacheck won't show the result

SOME PREFER NOT TO BE TESTED

The failure of RDTs to show parasites every time and the logistical problems identified with the RDTs were not the only reasons that tests were not incorporated as central to practice in most cases. By and large, providers reported being responsive to patient requirements, and these might include specific preferences for tests or not having tests as well as assessing whether the patient wanted help with a current illness, often seen as minor, or a longer-term cure for an illness that was longer standing or more serious.

Providers perceived that patients who had little money, or time, would prefer not to be tested,

> 'For the fever, the patient would have the blood test to see whether they have parasite of malaria or not. Previously, for example for children, we do the test, but people in this area is a bit saving money, they are afraid of wasting their money in doing the test for one or two illnesses.' (FGD#1, P2, female untrained grocery owner's wife)

> 'If the patient tells us that they have malaria or another fever, firstly, we have to ask them for a test. In the case that they do not agree for having a test since they are busy or just say that they have made a test already, I still sell the drug to them. I have to sell it[Laughter].' (FGD#4, P2, male nurse, pharmacy owner)

In other cases, providers knew that patients simply wanted medicines and not tests, and responded to this requirement, for example by providing their own specific drug mix,

> 'When the patients come and ask for Malarine or chloroquine, I give those drugs to them. For example, when your actors come to my house and ask for Malarine, I just gave Malarine because we could not force them to have diagnostic test.' (FGD#4, P7, male nurse, pharmacy owner) [Note: the participant refers to the previous mystery client component of the research that sent actors to pose as possible malaria patients]

> 'The people when they come to see me, I ask them to have a test. Some people dislike making a test because testing could not see the illness. Then, they came to me and asked me for the drug mix. Another day they came to me again because they were cured by my drug mix. But when they ask for malaria drug, I tell them to make a test and bring a white paper [prescription]. And when the village malaria worker provided the drug to take, they have headache which it makes them not to go there again, better to get the cocktail at my house.'(FGD#3, P1, male nurse, drug shop owner)

COMMUNICATION AND REGULATION

REGULATION SPEAKS LOUDER THAN RATIONALE

In Pailin, respondents were careful to reiterate recent messages stated at meetings held by the MoH about not selling artesunate and that patients should be sent for testing for malaria before giving malaria medicine. Providers were acutely aware of regulatory requirements and consequences for them of traversing these on their business, and repeated these during the focus group discussion.

> 'We are afraid to treat malaria. They come to buy the malaria drug directly, so we have to ask them that did they get a blood test yet? So, if the test shows there is the malaria parasite, my house does not accept [to dispense to] these patients. But if they have already made the test but there was no malaria parasite, then we ask them to bring the result letter to check. If the test result letter does not show the malaria, so we can use the paracetamol or amoxicillin.' (FGD#8, P4, male nurse, pharmacy owner)

> P6: As we sell the drug at home, we just see the symptom and if it is not usual, we send them [to the health centre for testing] and we do not treat them.

> P4: Because we are afraid, as we have processed the business [become registered], if there are some problems with customers or authorities, we will get the problem which affects our business. (FGD#8 with P6 a female midwife and P4 male nurse pharmacy owner)

However, rationales for these regulations were less clearly understood. The 'principle of resistance,' for example, was variously interpreted, being framed as concern for individual patients rather than risks for

the population level, as demonstrated in this discussion amongst two male nurse pharmacy owners in Pailin (FGD#8),

P3: Because Falciparum was resistant. Before, we were able to use artesunate with mefloquine to finish it, and later those drugs are not effective any more to kill malaria (krun chagn), it means the treatment did not kill it all.

P4: I can say that the patient had used one drug for many times. For example, they had treated the malaria (krun chagn) at the first time by taking Malarine, and they were cured at that time, but another time they have malaria (krun chagn) again then they used Malarine again. They often used Malarine, so that's why it is resistant, it means only one patient have used 4 or 5 times, so it is resistant.

P3: it is not our understanding, the national staff, he explained me like that.

P4: this is resistant because the illness or parasite in the body have known the drug and also known the cell.

Elsewhere, providers were also aware of the messages given by the government that artesunate should not be used anymore, and the potential consequences. Some thought the ban was due to fake drugs and licensure issues, others due to resistance. The significance of resistance was interpreted within the framework of curing the illness: individuals who take artesunate inappropriately can suffer from resistance, a condition that meant the malaria would be more difficult to cure, as discussed by providers in FGD#2,

'However, now there is a statement from the Ministry (MoH) not to use Artesunate alone, because it causes resistance. If there is resistance and the patient has malaria (krun chanch) again later it will be difficult to treat ... They completely warn this, they check.' (FGD#2, P5, male nurse, pharmacy owner)

'When they use Artesunate, it means that the *mero*(microbes) will stop for a while, there is no *mero* sign. It becomes normal so that some people think that they are recovered from the illness, but actually the *mero* is not yet killed that's why they recommended to use mefloquine to make the *mero* completely killed. And nowadays, because some of the drug users they just take the drug in advance before they leave for the forest, for instance, that make resistance to the disease, that's why they stop it [Artesunate] from being sold alone.' (FGD#2, P6, male untrained pharmacy owner)

'[Artesunate] was not allowed to sell because it was resistant. It could not cure even if it is taken for 4 or 5 days or one week. But one week later or 10 days later or a fortnight later, the patient starts to have the fever again, and by seeing the test, that patient has malaria again. So mefloquine, which has side effects, is added.' (FGD#3, P3, female untrained grocery shop owner)

ALIGNING TESTING AND MODERN MEDICINE

The rationale for testing was framed by participants within the modern paradigm of finding the *mero* and making prescriptions, in line with the concept of 'treating' rather than selling medicines,

> ‘Unless they go to see the place where they have modern instruments, if they are scanned they would know, so the doctor issues the prescription to them [laughter]’ (FGD#8, P4, male nurse, pharmacy owner)

However, RDTs were still tailored for different uses, with more severe patients requiring microscopy for clearer knowledge and RDTs preferred for non-severe cases, even those who were curious about their parasite status,

> ‘We used the Malacheck when the patients just got high temperature, and they doubt, so I used Malacheck to do the test for them because they just got a higher temperature than normal. We can know about [what to do from] the patient symptoms, but some patients who had serious symptoms, we used the microscope to do the test, to be clear. … [Others] mentioned that they used to get malaria, so they wanted to do the test for malaria, but they had normal temperature, they just want to make the test for malaria. So, I used the malacheck to test them.’ (FGD#8, P2, female nurse, clinic attendant)

Some providers appeared to have aligned themselves with these ‘modern’ ideas, and with the MoH, through valuing registration status and regulations set out through instructions communicated during meetings with MoH staff,

> ‘We are legal shops, we have registration, we follow the Ministry of Health instruction, so we are afraid to give [medicines]’ (FGD#8, P3, male nurse, pharmacy owner)

> ‘But now they came to instruct and CNM, they called to get the meeting, so we cannot do something beside their principles.’ (FGD#8, P6, female midwife)

Whilst being together with the MoH and CNM was important to providers, their relationship with patients appeared differentamongst this group: patients were talked about as ignorant or difficult, and their health outcomes were discussed less than the fear of business outcomes for the provider. When discussing the necessity to dispense only after the patient has a prescription, one provider appeared to abdicate responsibility over the patient’s outcome, leaving this with the prescriber at the health centre,

> ‘we can give the drugs according to the prescription, we just follow the prescription if it is right or wrong, it is the doctors’ response’ (FGD#8, P4, male nurse, pharmacy owner)