Improving Malaria Treatment Practices in Myanmar: An Evaluation of Provider Incentives to Increase the Uptake of Malaria Rapid Diagnostic Tests in the Private Sector

Population Services International/Myanmar

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Table of Contents

| Abbreviations | 4 |
|--|----|
| Executive Summary | 5 |
| Background | 6 |
| Burden of Malaria | |
| Management of Malaria | |
| Rapid Diagnostic Tests | |
| | |
| Program Description | |
| Myanmar Artemisinin Resistance Containment (MARC) | |
| Scope of Work | |
| Intervention: Phase One | |
| Specific Aims and Objectives | 10 |
| Methods | 11 |
| Household Survey Methods | 11 |
| Mystery Clients Data | |
| Qualitative Interviews: Providers and Phase One Operations and Management | 13 |
| RDT-Derived Data | |
| Stock Resupply | |
| | |
| Results Impact of Interventions: RDT Use, Quality, and Provider Experiences | |
| Impact of RDT Roll-out by Intervention Arm | |
| Quality of RDT Use: Mystery Client Findings | |
| Provider Experiences: Qualitative Interviews | |
| Programmatic, Operations and Management Results | |
| Stock Resupply Data: Distribution and Use of RDT | |
| Operations and Management Qualitative Interviews: Challenges and Opportunities | |
| Cost-Effectiveness Analysis Across Three Arms | |
| Limitations of the Study | |
| Conclusions and Recommendations | 20 |
| Conclusions | |
| Recommendations | |
| | |
| Cost-Effectiveness Implications | |
| Demand Creation | |
| Training of Providers | |
| Targeting Provider Types | 31 |
| References | 32 |
| Tables and Figures Used in Report | 34 |
| Table 1: Number of providers trained on RDT use by outlet type, township, and study arm of | |
| Phase One | _ |
| Table 2: Number and type of outlets for mystery client assessment of RDT use by region | 34 |
| Table 3: Cost-effectiveness ratios compared to 'no intervention' from a societal perspective | |
| Table 4: Annual costs separated as commodities, programmatic expenses, time and travel | |

| _ | Figure 1: RDT use pre- and post- roll-out from household survey |
|------|--|
| | Figure 2: Provider compliance with proper testing and diagnosis standards |
| - | Figure 3: Proportion of providers proposed mRDT to malaria suspected patient |
| | Figure 4: Mystery clients – percentage of providers who propose blood test at his/her own facility by arm |
| _ | Figure 5: Mystery clients - percentage of providers properly treating and correctly reading results by arm |
| | Figure 6: Mystery clients - percentage of providers properly treating and correctly reading results by provider type |
| | Figure 7: Number of RDTs distributed by arm40 |
| | Figure 8: Ratio of ACTs and RDTs distributed |
| | Figure 9: Number of outlets returning used RDT by outlet type |
| | Figure 10: Number of outlets returning any used RDT kit by outlet type41 |
| - | Figure 11: Returned RDT results by arm |
| Addi | tional Figures43 |
| _ | Figure 1: Test results of returned RDTs according to provider results |
| | Figure 2: Test results of returned RDTs according to MIS officer results and consistency with provider results |
| Appe | endix: Cost-Effectiveness Analysis44 |

3

Abbreviations

| ACT Artemisinin combination therapy AMT Artemisinin monotherapy AMTR Myanmar Artemisinin Resistance Containment BCC Behavioral change communication DALY Disability-adjusted life year FGD Focus group discussion GHG Global Health Group GPARC Global Plan of Artemisinin Resistance Containment GPS Global Positioning System GRS General retail store JHSO Junior Health Service Officer HH Household IDI In-depth interview IDV Itinerant drug vendor IEC Information education communication IPC Interpersonal Communicator IRS Indoor residual spraying LLIN Long-lasting insecticidal nets MARC Myanmar Artemisinin Resistance Containment MC Mystery client MDR Medical drug representative MIS Management Information System NMCP National Malaria Control Programme PP Product Promoter PSHi Private Sector Healthcare Initiative PSI Population Sciences International RDT Rapid diagnostic test SPH Sun Primary Health WHO World Health Organization UCSF University of California San Francisco | l | |
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| IDI In-depth interview IDV Itinerant drug vendor IEC Information education communication IPC Interpersonal Communicator IRS Indoor residual spraying LLIN Long-lasting insecticidal nets MARC Myanmar Artemisinin Resistance Containment MC Mystery client MDR Medical drug representative MIS Management Information System NMCP National Malaria Control Programme PP Product Promoter PSHi Private Sector Healthcare Initiative PSI Population Sciences International RDT Rapid diagnostic test SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | JHSO | Junior Health Service Officer |
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| PP Product Promoter PSHi Private Sector Healthcare Initiative PSI Population Sciences International RDT Rapid diagnostic test SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | MIS | Management Information System |
| PSHi Private Sector Healthcare Initiative PSI Population Sciences International RDT Rapid diagnostic test SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | NMCP | National Malaria Control Programme |
| PSI Population Sciences International RDT Rapid diagnostic test SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | PP | Product Promoter |
| RDT Rapid diagnostic test SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | PSHi | Private Sector Healthcare Initiative |
| SPH Sun Primary Health SQH Sun Quality Health WHO World Health Organization | PSI | Population Sciences International |
| SQH Sun Quality Health WHO World Health Organization | RDT | Rapid diagnostic test |
| WHO World Health Organization | SPH | Sun Primary Health |
| | SQH | Sun Quality Health |
| | WHO | World Health Organization |
| | UCSF | |

Executive Summary

In 2006, Myanmar had the highest malaria mortality in the Greater Mekong Sub-region, and is the only country where incidence of confirmed cases has increased since 1998. Nearly 80% of the population in Myanmar is at risk for malaria, with 68% of cases due to *P. falciparum* and 32% due to *P. vivax*. Artemisinin combination therapy (ACT) is recommended as first-line treatment for malaria caused by *P. falciparum*. With widespread drug resistance to artemisinin monotherapy (AMT) for treating *P. falciparum*, treatment guidelines have rapidly developed to replace AMT with ACT. However, indiscriminate deployment of ACT to treat suspected rather than confirmed cases may lead to drug resistance, rendering ACT ineffective. Rapid diagnostic tests (RDTs) for malaria have been shown to be safe, feasible, and effective at reducing inappropriate treatment for suspected malaria.

Population Services International/Myanmar worked in partnership with the University of California, San Francisco (Global Health Group – Private Sector Healthcare Initiative (PSHi)) to evaluate to the optimal incentive system to drive informed demand and appropriate use of RDTs among private providers. The pilot study targeted the informal private sector – pharmacists, itinerant drug vendors, and general retailers – because they were responsible for the majority of the AMT market share.

Evaluation of these three arms examined the relative importance of a cost subsidy, versus subsidy with material and commodity incentive, versus cost subsidy with intensive supervision. All three arms were potentially scalable using an existing and highly efficient ACT supply chain, but differed markedly with regards to cost efficiency. The overarching objectives of this study were to document RDT use and examine whether financial incentives or information, education and communication strategies, increased uptake of RDTs and quality of services by informal providers in Myanmar.

The study used a number of data sources – household quantitative surveys, RDT-derived data, resupply stock data, mystery client visits, qualitative data collection with program staff and providers, and program costing data – to make recommendations to scale-up the RDT program among private providers in Myanmar.

This study demonstrated that introduction of RDTs in the informal sector in Myanmar is feasible, and resulted in increased RDT use in the community and improved clinical diagnostic practices. Results also indicate that Arm 3 (education and counseling) led to the largest increases in RDT use, and greatest likelihood that proper treatment would follow RDT results. Arm 2 (incentives) had a nearly equivalent effect on RDT volume, and a positive, but lower, effect on quality. Both interventions were cost-effective, according to WHO standards.

Based on these findings, we recommend an introduction of a combined intervention, incorporating both the education and counseling components of Arm 3, and the financial incentives of Arm 2. Given what is known about the development of, and adherence to, standard operating procedures for basic clinical services, we feel that after approximately 6 months, the program could progressively reduce the frequency of counseling support visits with little or no effect on quality. Cost-effectiveness, demand creation, and training recommendations are also discussed.

Background

Burden of Malaria

The global burden of malaria has been significantly reduced in the past decade. Between 2000 and 2010, malaria mortality decreased by 26% globally (1). Improvements are primarily a result of large scale-up of programs focused on monitoring, treatment, and diagnosis. South East Asia is the second most severely affected region in the world after sub-Saharan Africa. While 90% of malaria deaths occur in sub-Saharan Africa (1), South East Asia faces unique challenges. The local epidemiology of malaria is complex with numerous vectors. Only 53% of estimated malaria cases are due to *P. falciparum*, with a significant number also the result of *P. vivax* (2). Moreover, drug resistance is a significant concern. Four countries in South East Asia – Cambodia, Thailand, Vietnam, and Myanmar – have shown *P. falciparum* resistance to artemisinins (2).

In 2006, Myanmar had the highest malaria mortality in the Greater Mekong Sub-region, and is the only country where incidence of confirmed cases has increased since 1998 (3). Myanmar has a total population of over 47 million, which accounts for approximately one-fifth of the area's population, and yet more than half of malaria cases and about three-quarters of malaria deaths occurred in Myanmar in 2006 (3). Nearly 80% of the population in Myanmar is at risk for malaria, with 68% of cases due to *P. falciparum* and 32% due to *P. vivax* (2).

Management of Malaria

Early diagnosis of febrile illness and treatment with correct antimalarial combination therapy are critical steps for proper and timely identification and management of malaria. The current first-line treatment for *P. falciparum* malaria is artemisinin combination therapy (ACT). Until recently, artemisinin in Myanmar was mostly marketed as artemisinin monotherapy (AMT). The sale of AMT are largely linked to the emergence of artemisinin drug resistance, of which the spread threatens global malaria control efforts. Treatment guidelines have rapidly developed to replace AMT with ACT, and significant global efforts are underway in order to mitigate the threat of artemisinin drug resistance.

In order to reduce the misuse of artemisinin drugs, a proper diagnosis is required. Indiscriminate deployment of ACT to treat suspected rather than confirmed cases may lead to drug resistance, rendering ACT ineffective. Implementation of universal diagnostic testing could help to drastically relieve the global requirements of antimalarial treatment (2) if widely available and inexpensive.

Rapid Diagnostic Tests

Rapid diagnostic tests (RDTs) for malaria have been shown to be safe, feasible, and effective at reducing inappropriate treatment for suspected malaria. Numerous studies have shown a decrease in overuse of and overtreatment with ACT after implementation and scale-up of RDTs (4, 5, 6, 7, 8, 9). Diagnosis with RDT combined with other malaria control interventions such as ACT as first-line treatment, indoor residual spraying (IRS), and distribution of long-lasting insecticidal nets (LLIN), may succeed in decreasing the burden of malaria in many settings worldwide (10).

Many patients initially seek care for fever or other ailments at drug shops, retail vendors, and low-level health facilities. For example, of the febrile population in the Shan Special Region II Myanmar who sought treatment, the proportion accessing the retail sector (79.6%) was significantly higher (P<0.0001) than accessing the public sector (10.6%) (11). Since many patients initially seek care in drug and retail shops, introducing RDTs in the informal sector has the potential for significant gains and positive impact on malaria diagnosis and management.

Previous programs have shown that implementation and use of RDTs is feasible at low-level health care facilities (12) and with drug shops (13), although improved targeted malaria treatment is needed. Community health workers and volunteers are able to correctly and safely administer RDTs and even improve early, well-targeted ACT treatment at a community level (14, 15, 16, 17). Patients and community members believe diagnostic testing is useful and are curious about the results (18), and despites some fears, introduction of RDTs in drug shops is highly accepted (19). RDTs also have the potential to be cost-effective by improving treatment and health outcomes for non-malarial febrile illness and savings in antimalarial drug costs (20) in both private and public sectors (21). Compared to scaling up other diagnostic tests such as microscopy, RDTs are more cost-effective (22).

7

Program Description

Myanmar Artemisinin Resistance Containment (MARC)

The Myanmar Artemisinin Resistance Containment (MARC) framework was developed between 2010 and 2011 with the aims of preventing or delaying the spread of artemisinin resistant parasite and reducing the transmission, morbidity, and mortality of *P. falciparum* (23). The MARC framework follows the WHO Global Plan of Artemisinin Resistance Containment (GPARC). Donors have invested \$40 million for the subsidy of RDTs and ACT, and the National Malaria Control Programme (NMCP) along with implementing partners commenced actions in July 2011 (23).

As a key implementing partner of MARC, Population Sciences International (PSI) Myanmar is involved in: (a) supporting aggressive generalized control efforts within already identified containment zones; and (b) the rapid replacement of artemisinin monotherapy (AMT) in the informal, largely unregulated, private sector throughout the country (utilizing an existing, highly centralized, supply chain). One of the major objectives of MARC is to strengthen and improve access to and use of early diagnosis and quality treatment (23). With the support of the Myanmar Ministry of Health, PSI Myanmar commenced deployment of RDTs in the informal private sector in early 2013 (Phase One), with anticipated rapid scale-up following in 2014 (Phase Two).

Phase One is now complete. The results detailed in this report will help to ascertain the optimal incentive system to drive informed demand and appropriate use of RDTs among private providers with little to no experience of diagnostic testing (primarily in three outlet types already shown to have the majority of the AMT market share – pharmacies, itinerant drug vendors (IDVs), and general retailers (GRS).

Scope of Work

In order to complete all actions needed for Phase One, PSI Myanmar worked in partnership with the University of California, San Francisco (Global Health Group – Private Sector Healthcare Initiative (PSHi)). The Global Health Group PSHi contributed expert input to study design, development of field guides and study instruments, and lead the analysis and interpretation of data. PSI Myanmar oversaw all data collection activities, management, and program implementation.

Intervention: Phase One

Prior to deployment of RDTs, PSI Product Promoters (PPs) identified and mapped all outlets supplying antimalarials in the operational zone. PSI PPs visited all outlets involved in Phase One RDT deployment for a minimum of once every 2-3 months. Shortly before RDT deployment, PSI trained providers from Phase One outlets (outlet types described below) on RDT use, interpretation, and safe disposal. At the time of the training, all attendees received:

- An initial free supply of RDTs (box of 10 individual government approved combo test kits)
- A disposable sharps box for used lancets

• A collapsed stack of 20 boxes for used RDTs (with separate compartments for *P. falciparum*, *P. vivax*, mixed infections, negative, and invalid tests)

Three incentive models for driving demand among providers were evaluated. In all cases, initial supply of RDTs was free and provided at the training sessions. Resupply was provided through pharmacies supplied directly by PSI (Phase One only). The three models are as follows:

Arm 1

RDT resupply at approximately \$0.18/RDT, upon receipt of a box of used RDTs

Arm 2

- RDT resupply at approximately \$0.18/RDT, upon receipt of a box of used RDTs
- 'Financial' incentive in the form of 'free/promotional' ACT AETD¹ or RDT kits, or every 5 RDTs purchased at resupply

Arm 2

- RDT resupply at approximately \$0.18/RDT, upon receipt of a box of used RDTs
- Monthly intensive support visit to all target outlets (with one-on-one discussion, behavioral change communication (BCC), information, education, and communication (IEC), provision of materials, and visits to recent patients)

Evaluation of these three arms examined the relative importance of a cost subsidy, versus subsidy with material and commodity incentive, versus cost subsidy with intensive supervision. All three were potentially scalable using an existing and highly efficient ACT supply chain, but differed markedly with regards to cost efficiency.

Geographic Scale and Outlet Types

A total of 6 townships received RDTs in Phase One. The interventions specifically targeted three types of private providers: providers in general retail stores (GRS), itinerant drug vendors (IDVs), and medical drug representatives (MDRs). In this report, MDRs are also sometimes referred to as 'pharmacists' given the nature of their work. These three types of providers are typically the first point of care for fever patients in many parts of Myanmar; therefore, training on RDTs may be particularly important for these types of outlets. GRS are small shops in the communities, typically selling a variety of goods, including products not health-related. IDVs often serve as the village doctor, with some IDVs traveling to people's homes for care ranging from maternal and child health services to malaria diagnosis and treatment. While IDVs may not have received formal health training, most typically have some experience in health delivery. Most IDVs operate from their homes. Finally, MDRs are similar to pharmacists, knowledgeable about basic drugs and treatments.

Commodity Supply

PSI supplied quality assured, highly subsidized ACT for nationwide distribution to AA Medical Products Ltd in the first instance, as they enjoyed the most market share for antimalarials across Myanmar. While initial stocks (seed stock) of RDTs were provided to the outlet providers directly

¹ Adult Equivalent Treatment Dose

(following training on use), subsequent stocks were accessed through their usual drug commodity supply points. Typically, but not solely, pharmacies act as lower level 'wholesalers' to other outlets (particularly IDVs, GRS, and private clinics). Pharmacies also provide some direct treatment to patients.

Specific Aims and Objectives

The overarching objectives of this study were to document RDT use and examine whether financial incentives or IEC strategies increased uptake of RDTs by informal providers in Myanmar.

<u>Aim 1</u>: To assess whether RDT use increased following the introduction of RDTs in PSI pharmacies, grocery retail shops, and itinerant drug vendors.

<u>Aim 2</u>: To examine whether financial incentive schemes or information, education, and communication strategies increased RDT uptake among PSI pharmacies, grocery retail shops, and itinerant drug vendors.

<u>Aim 3</u>: To examine whether financial incentive schemes or information, education, and communication strategies best improves quality of treatment following diagnosis.

Aim 4: To examine the most cost-effective intervention arm.

Methods

The 18-month study included the roll-out of RDTs and two provider incentive interventions to six townships in Myanmar. RDT roll-out was assessed over the course of four months. We used the following methods to assess the aims and objectives: 1) household surveys; 2) mystery clients; 3) RDT-derived data; 4) stock resupply data; and 5) qualitative interviews with providers and Phase One operations and management staff.

We carried out the study in three different types of intervention areas: i) with no specific intervention, except for PSI RDTs availability in pharmacies and drug shops (Arm 1); ii) with financial incentives to providers (Arm 2); and iii) with BCC/IEC to providers (Arm 3). We included six townships in the study, with two townships per arm. We purposefully selected the townships to include areas where PSI RDT supplies were available among pharmacists and drug vendors, and areas with similar risk of malaria. The selected townships were similar in terms of socioeconomic status, level of migration, access to roads, population size, male-to-female ratio, and presence of health centers.

<u>Table 1</u>: Number of providers trained on RDT use by outlet type, township, and study arm during Phase One

| Townships | General Retail Store (GRS) | Itinerant Drug Vender (IDV) | Medical Drug Representative (MDR) | Total |
|----------------------|-------------------------------|--------------------------------|---|-------|
| Bilin (Arm 2) | 91 | 40 | 14 | 145 |
| Hseni (Arm 3) | 79 | 14 | 1 | 98 |
| Monghpyak (Arm 1) | 32 | 50 | 0 | 82 |
| Namkhan (Arm 2) | 103 | 15 | 5 | 119 |
| Paung (Arm 1) | 83 | 31 | 18 | 132 |
| Thanbyuzayat (Arm 3) | 11 | 27 | 17 | 55 |
| Total | 399 | 177 | 55 | 631 |

Household Survey Methods

We conducted pre- and post- roll-out household surveys in the six townships to gauge the change in RDT use in the target population. We collected baseline data one month after the introduction of RDTs in all townships for all 3 Arms. One month later, we rolled out the interventions of IEC (Arm 3) and provider financial incentives (Arm 2) in two townships each in four communities. At the end of the four months, we conducted a follow-up household survey to assess differences in RDT uptake by intervention arm (Aim 2). To reduce potential confounding, the interventions were implemented in townships matched on the community-level characteristics of population size, male-to-female gender ratio, geographic area, and socioeconomic status.

For survey implementation, we enumerated and screened all households in the selected townships for inclusion. Inclusion criteria were: 1) having a member of the household who had a fever in the last three weeks, had either taken an antimalarial drug, or who had symptoms consistent with malaria (24); and 2) living in an area where PSI supplies RDTs in pharmacies and drug shops.

Once a household was determined eligible for the study, the head of the household answered questions on basic demographic characteristics (including household socioeconomic status), recent episodes of fever among household members, antimalarial drug use, RDT knowledge and use, RDT test results if applicable, and where they obtained the RDT.

The main outcome of interest from the household survey data was the proportion of RDT use (defined as the proportion of RDT use per population treated for malaria or fever in the past 2 weeks). In total, we completed 832 household surveys with fever cases. All analyses were carried out in Stata 12MP and weighted by population.

Mystery Clients Data

Participants

We enrolled 631 owners or workers at private outlets who PSI had trained on providing RDT services across the six townships in the Mon and Shan States. Table 1 shows the number of provider outlets included in the sampling frame of the study. In total, we trained 399 GRS owners/workers, 177 IDVs, and 55 MDRs on using RDTs.

Sampling Strategy

We used stratified random sampling to select provider participants for the mystery client assessment, with stratification by intervention arm and provider type (GRS, IDV, MDR). From the list of all 631 providers (Table 1), we randomly selected 20 providers of each provider type and intervention arm to be enrolled, with the exception of the MDRs where fewer than 20 per cell were to be enrolled. The final study sample included 171 providers as shown in Table 2.

Data Analysis And Outcome of Interest

The outcome of interest comprised five key steps in conducting and interpreting a RDT for malaria.

- 1. <u>Propose to give RDT test</u>: Providers who proposed and performed RDT at their facility (n=171).
- 2. <u>Use antiseptic in preparation for finger prick</u>: The researcher who accompanied the mystery client noted whether the provider used antiseptic or not. The RDT kit is supplied with an antiseptic pad inside and could be easily seen as the provider unpacked the kit for use (n=116).
- 3. Read the result correctly: Providers who accurately read a negative test, assuming that all mystery clients did not have malaria (n=116).
- 4. Show the result to the client: Providers who showed the result to the client (n=116).

5. <u>Provide treatment correctly according to the result</u>: Providers gave quality assurance ACT for a malaria positive client and refrained from giving any antimalarial drugs for a negative client (n=171).

Table 2: Number and type of outlets for mystery client assessment of RDT use by region

| Townships | General Retail Stores (GRS) | Itinerant Drug Venders (IDV) | Medical Drug Representatives (MDR) | Total |
|--------------|--------------------------------|---------------------------------|--|-------|
| Bilin | 13 | 14 | 12 | 39 |
| Paung | 12 | 11 | 17 | 40 |
| Thanbyuzayat | 2 | 9 | 17 | 28 |
| Monghpyak | 4 | 19 | 0 | 23 |
| Hseni | 19 | 5 | 1 | 25 |
| Nankhan | 10 | 2 | 4 | 16 |
| Total | 60 | 60 | 51 | 171 |

Mystery clients received intensive training by study personnel on the clinical scenario and completing the assessment form. The mystery client assessments were conducted between 26 August and 1 September 2013. The mystery client presented at the outlets saying that s/he had fever that s/he thought was like a malaria fever that s/he had on a previous occasion. The provider could then propose a RDT on site, not propose a RDT at all, or propose a RDT at a different location. If the provider did not automatically propose a RDT at his or her own shop, the mystery client was trained to ask for a RDT [see Appendix 1]. The researcher accompanied the mystery client to the outlet as a friend from town, but did not speak or engage with the provider. The researcher observed everything the outlet provider did and completed the record form after leaving the outlet. All data were analysed in Stata MP12, stratified by provider type and intervention arm. Results were calculated unweighted, except for the overall score, which was calculated as weighted average.

Qualitative Interviews: Providers and Phase One Operations and Management

Provider Interviews

We used purposeful sampling to select providers for in-depth interviews (IDIs), 10 from each study arm, for a total of 30 interviews. IDIs focused on decision making regarding testing and treatment, attitudes towards RDTs, malaria and malaria treatment, and attitudes towards the program and PSI Myanmar. The main outcomes of interest were identification of the motivators and barriers to carry out testing with RDTs at the retail outlet.

Phase One Operations and Management

Informal focus group discussions (FGDs) were conducted with implementation staff. These FGDs examined the implement challenges and successes. Three types of field staff were interviewed:

- 1) Interpersonal Communicators (IPCs): IPCs are responsible for educating rural populations on malaria prevention and treatment, especially the importance of getting tested before taking malaria treatment.
- 2) Product Promoters (PPs): PPs are responsible for training informal providers on the use of RDT and supervising RDT services provided by providers.
- 3) Junior Health Service Officers (JHSOs): JHSOs are responsible for advocacy, monitoring and supervision of IPCs and PPs' activities in their assigned township.

Three FGDs were conducted with each type of field staff, and eight IPCs, eight PPs and six JHSOs participated in the informal discussions.

RDT-Derived Data

Each stack of collapsible RDT collection boxes given to an individual provider also carried a unique identifier code that matches or references the Global Positioning System (GPS) coordinates associated with that particular outlet. Providers were instructed to mark the used RDT with the age, weight, and gender of the patient/consumer. Therefore, collected RDTs (once checked by PSI field supervisors) provided information regarding positivity rates and incidence over time (across age, weight, and gender groups) throughout the area of operations, by outlet type, and for individual providers.

Stock Resupply

RDT resupply occurred primarily through pharmacy-type outlets where private providers typically access ACT (although for Phase One, PSI supplied the initial RDTs directly to outlets rather than through the private distribution chain for ACT). Pharmacy-type supply points checked the number of RDTs returned and mark the boxes accordingly, retaining them for later collection by PSI field staff. The indicators of interest from the stock resupply data included: ratio of RDTs used to ACTs dispensed, number of ACTs used (monthly purchase data), and monthly average ACTs purchase volume in intervention versus control outlets.

Results

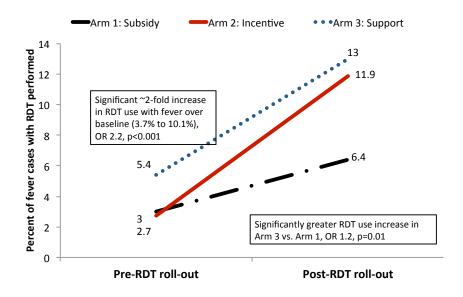
This section presents findings in three parts. The first examines: i) the overall impact of rolling out RDTs to informal providers (based on household surveys); ii) quality of provider use of RDTs (how many providers proposed RDTs and treated correctly based on mystery clients); and iii) provider acceptability and experiences with RDTs (based on provider qualitative interviews). The second part presents how many RDTs were distributed, used, and returned based on stock resupply data and the results of RDTs based on returned RDT kits. This section also covers qualitative interviews with program operations management and staff, including their challenges and recommendations. The third part presents the cost-effectiveness of the programs, building on data presented in the previous section.

Impact of Interventions: RDT Use, Quality, and Provider Experiences

Impact of RDT Roll-out by Intervention Arm

We conducted household surveys to test the intervention arms before and after the roll-out of RDTs. Figure 1 indicates that averaged across all three intervention arms, there was a significant increase of RDT use with fever patients post-RDT roll-out (10.1%) compared to baseline (3.7%) (p<0.001). By logistic regression analysis, respondents were over twice as likely to receive a RDT when they went to a provider with a fever compared to baseline (p<0.001). At baseline, there were no statistically significant differences across the three arms in regards to RDT use (Arm 1=3%, Arm 2=2.7%, and Arm 3=5.4%); however, post-RDT roll-out, those in the Arm 3 catchment area were most likely to receive a RDT when presenting with fever (13%) compared to Arm 1 (6.4%) (p=0.01). Arm 2 demonstrated similar results to Arm 3 with 11.9% of fever patients receiving a RDT by their providers.

Figure 1: RDT use pre- and post- roll-out from household survey



Quality of RDT Use: Mystery Client Findings

Overall Performance of Study Participants

Figure 2 illustrates the proportions of providers who performed the five key steps. Overall, 65% of providers proposed a RDT without prompting. Of the providers who performed a RDT, 95% used an antiseptic, 94% read the results correctly, 85% showed the client results, and 84% gave a correct treatment. Of all the providers, 40% performed all five steps.

Proposing RDT Before Treatment

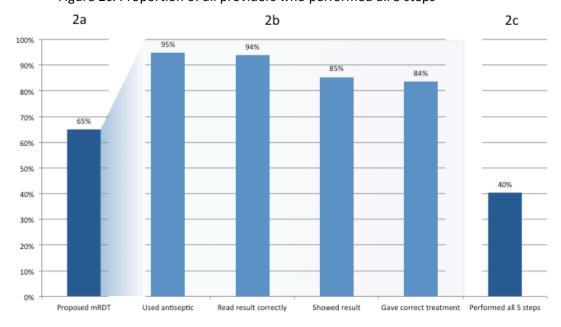
The first step in performing a RDT is that the provider has to propose or recommend the patient to undergo the test before taking malaria drugs. The proportion for the first step "Propose to perform a test for malaria" was calculated among all providers in the study (N=171), whereas the proportions for the remaining 4 steps were calculated on the 116 who actually performed the test. In this study, 65% of providers proposed a RDT before giving treatment, with 56.1% proposing the RDT at their own facility and an additional 8% referring clients to other facilities for the test (Figure 3). When stratified by intervention arm, providers in Arm 3 were most likely to propose a blood test at their own facility: 64% compared to 49.1% and 55.2% in Arm 1 and Arm 2, respectively (Figure 4).

Figure 2: Provider compliance with proper testing and diagnosis standards

Figure 2a: Proportion of all providers who proposed RDT

Figure 2b: Proportion of those, who complied with follow-up steps

Figure 2c: Proportion of all providers who performed all 5 steps



Mystery clients were trained to prompt the providers who failed to propose a RDT by saying that they have heard of a test for malaria. An additional 18 providers who failed to propose a RDT originally agreed to perform the test. When prompted for a RDT, providers in Arm 3 were almost

twice as likely to perform the test after requesting compared to Arms 1 and 2 (92.9% vs 54.4% and 56.9%, respectively). By provider type, IDVs were more likely to propose a RDT (65%) compared to GRS providers and MDRs (53.3% and 52.9%, respectively) [16]. The remaining four key steps in the process of conducting and interpreting a rapid diagnostic test for malaria were calculated among those who actually performed the test.

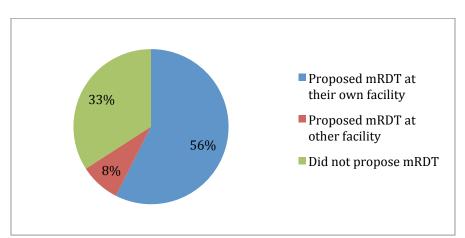
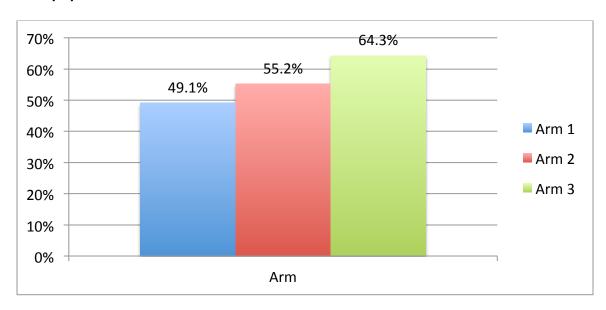


Figure 3: Proportion of providers who proposed a RDT to malaria suspected patients

<u>Figure 4</u>: Mystery clients – percentage of providers who propose blood test at their own facility by arm



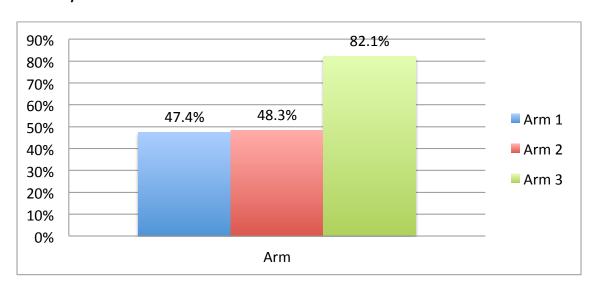
Provider Use of Antiseptic, Read Result Correctly, Show Result

Overall, providers who actually performed the test did well on indicators relating to antiseptic use, reading the result, and showing the result to the client. Over 90% of providers from all outlet types used antiseptic for finger prick, 85.3% showed results, and 94% read results correctly. There were no significant differences across intervention arms or provider type.

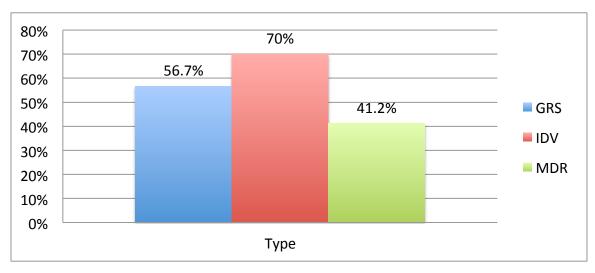
Correct Treatment

We were interested in the percentage of providers who correctly treated after reading RDT correctly. There were significant differences across intervention arms and by provider type. Providers in Arm 3 were significantly more likely to correctly treat after using a RDT at 82.1% compared to Arm 1 (47.4%) and Arm 2 (48.3%) (Figure 5). Moreover, IDVs were also significantly more likely to correctly treat after RDT use (82.1%) compared with GRS providers (56.7%) and MDRs (41.2%) (Figure 6).

<u>Figure 5</u>: Mystery clients – percentage of providers properly treating and correctly reading results by arm



<u>Figure 6</u>: Mystery clients – percentage of providers properly treating and correctly reading results by provider type



Provider Experiences: Qualitative Interviews

Challenges of Using RDTs: Quality, Demand, Access, and Patient Experiences

Quality of the RDTs was a concern for providers. Half of the providers mentioned they doubted the results.

MDR, Arm 2: "I was wondering – can the blood test results be wrong? I used four tests, and all were negative, but I suspected that one was positive. I didn't give malaria drugs at the time, only normal drugs. The patient didn't get better. The next day I gave quinine and artesunate. Only then did he get better. I wonder if the blood test strip was correct or not. Have you had any experience with this?"

A few mentioned that if a patient had taken malaria medication previously, the test result was negative. Several providers had missing buffers in their kits and a few providers had inconclusive or unclear test results (for example, line between *P. falciparum* and *P. vivax*, or no lines at all).

Many providers said there was little demand for testing with RDTs; several providers had never even used one RDT. Generally providers believed there were few malaria patients. Instead of testing every fever case presenting, they tested only when they suspected malaria, such as in cases with fever with chills, high fever that comes and goes, previous history of malaria, or the resident area of the patient.

Provider qualification was an issue. Some providers lacked confidence in performing the test. Providers described that if a patient wanted to be tested, they would go to a midwife, health clinic, or doctor, rather than their shop. This theme was particularly significant in certain types of providers.

GRS, Arm 1: "Keep in mind I am not a doctor and do RDT by looking at the book."

How comfortable the provider felt in testing depended on the type of provider. Providers who only sold drugs were not as comfortable and capable of using RDTs. GRS providers and MDRs were much more likely to doubt their own qualifications as a provider compared to IDVs. In the following quote, "sayer-ma" refers to an IDV.

MDR, Arm 2: "Because they are just selling drugs. They don't do that [RDT]. Maybe they don't want to do it because it's painful for the patient or the patient doesn't want to do it. These are possibilities. Maybe the patient doesn't want to do it because they aren't Sayer-ma. They only focus on selling drugs."

The majority of providers did not feel restocking was an issue, mainly because the trip was short or not too far, the price was fixed, they had other staff to help, and/or most importantly, the PP or a SPH staff restocked for them. For those who said restocking was a challenge, distance, inconvenience (lack of time and staff), and unreliable transportation were the main reasons.

Very few providers mentioned that patients disliked testing, although some patients expressed fear of the needle and blood. Yet with thorough explanation of the purpose and procedure of the test, most patients accepted.

Benefits: Provider Empowerment and Patient-Provider Relationships

There was universal acceptance of RDT among all types of providers. Providers felt empowered in their work because they did not have to refer patients to be tested. The test was quick and easy, patients could get their results immediately, and providers could properly diagnose and treat.

MDR, Arm 2: "It's good if I have the blood test strip because previously I just gave out medicine based on guessing. Now, because I have the test strip, it's more accurate. I can know the result and if the patient has malaria I can give Supa-Arte. If there's no malaria, I won't give it to them."

Providers also described an improved patient-provider relationship. Patients trusted the providers more and wanted to know their results. Some providers even mentioned that patients preferred to come to their shops compared to hospitals or doctors.

MDR, Arm 3: "If I send these patients to the hospital, they don't want to go. They rely on me, so I want to help them. It's better if I have a device to diagnose their illness. That's my wish. I want to be able to help using my skills."

GRS, Arm 3: "Many people recover because I give them good medicine. They tell me that if they go somewhere else, they don't get better."

Intervention Experiences: Education and Counseling, and Financial Subsidies

All providers appreciated the training being done at their shop or home, and that they received handouts and reminders of the RDT instructions. Most providers welcomed the follow-up visits while a few were indifferent. No one disliked them. They appreciated the opportunity to ask questions, review steps, discuss difficulties (i.e. accuracy of test), and restock. Typically the visits took about 30 minutes. In all three arms, the providers liked the number of visits and expressed that the level of support was sufficient (note: number of visits does not necessarily follow assigned arm; see "study limitations" below).

When asked what the buying price for a RDT should be, generally providers found the buying price of 150 kyats (or 250 or 300 if used RDT was not returned) to be very reasonable and cheap. They believed the test to be worth more and were aware how highly subsidized it was. They encouraged the price to remain low so they could charge the patient very little or even give it for free. Providers sold a RDT for 200, 300, 400, or 500 kyats, or for free (i.e. patient could not afford it, or if the test result was positive, the provider only charged for medication). Providers believed the patients could afford these prices. If patients went elsewhere to get tested, the RDT would cost much more (between 1000-5000 kyats).

When asked if lowering the cost of the RDT (both buying and selling) would increase use, overwhelmingly providers did not believe a lower price would increase use. What was more important was demand creation and awareness.

GRS, Arm 1: "Price doesn't necessarily equate to use. People will use it when they need it. If people need it for their health, I think they will use it. I think of the price is lower, people will trust it less. If the provider knows how to explain it well, people will accept it."

Programmatic, Operations and Management Results

Stock Resupply Data: Distribution and Use of RDT

Programmatic results, including how many RDTs were distributed and used, were collected from stock resupply data. Results of used RDTs were also collected. In total, 6,573 RDTs were distributed, 6,397 ACTs were distributed, and 2,046 used RDTs were returned to the supply point.

Arm 2 distributed the greatest numbers of both RDTs and ACTs. Arm 2 distributed 3,551 RDTs compared to Arm 3 (n=1,777) and Arm 1 (n=1,245) (Figure 7). Similarly, the number of ACTs distributed was greatest in Arm 2 (n=3,390) compared to Arm 1 (n=1,846) and Arm 3 (n=1,161) [Figure 10]. The ratio of ACTs to RDTs distributed was calculated to assess the level of ACTs given RDTs availability in the community under the assumption that ACT use should not exceed RDT use given that treatment should only follow testing. Arm 3 had the best ratio of 0.65 – in other words, for every 100 RDTs distributed, 65 ACTs were prescribed. This compares to a ratio of 1.48 in Arm 1 and 0.95 in Arm 2 (Figure 8).

While RDT distribution was greatest in Arm 2, Arm 3 had the most RDTs returned to the supply point (n=832 compared to 775 in Arm 2 and 439 in Arm 1) (Figure 9). This represents 91 outlets in Arm 3, 83 outlets in Arm 2, and 52 outlets in Arm 1 (Figure 10). By provider type, GRS had the greatest number returning RDTs. In Arm 3, 43 GRS providers returned RDTs compared to 32 IDVs and 16 MDRs (Figure 11).

Figure 7: Number of RDTs distributed by arm

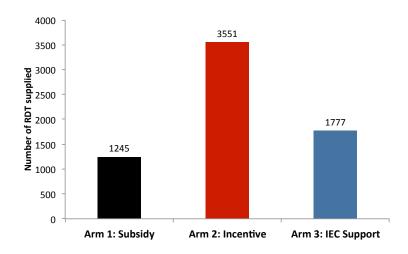


Figure 8: Ratio of ACTs and RDTs distributed

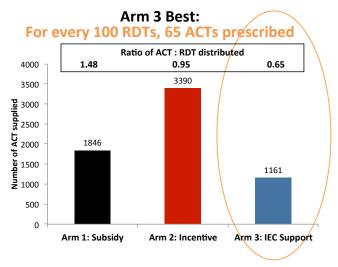


Figure 9: Number of outlets returning used RDTs by outlet type

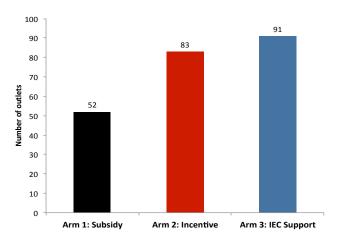


Figure 10: Number of outlets returning any used RDT kit by outlet type

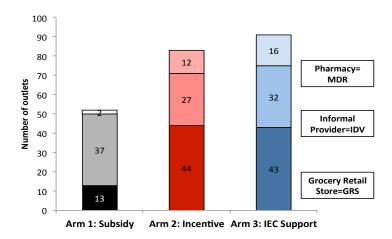
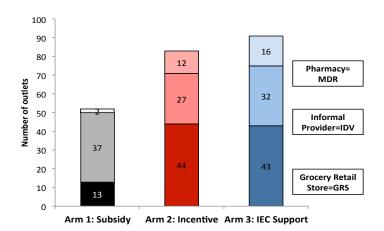


Figure 11: Returned RDT results by arm



By examining returned RDT kits, we also obtained malaria results. Figure 12 displays test results by intervention arm. In Arm 1, there was almost three times as much P. vivax diagnosed by RDT compared to P. falciparum (7.3% vs. 2.1%). In the other two arms however, P. falciparum was slightly more common than P. vivax – Arm 2 found 5.7% compared to 5.4%, and Arm 3 found 1.3% compared to 0.8%. We also examined the consistency of provider results and Management Information System (MIS) officer results (Figure 13). There was high internal consistency of test result readings across all three arms – 88.4% in Arm 1, 80.4% in Arm 2, and 82.6% in Arm 3. Levels of invalid results were low with some variation by intervention arm – 0.7% in Arm 1, 2.7% in Arm 2, and 0.8% in Arm 3.

Operations and Management Qualitative Interviews: Challenges and Opportunities

In addition to restock RDT data, we conducted focus group discussions (FGDs) with the Operations and Management team rolling out Phase One. FGDs were held with interpersonal communicators (IPCs), product promoters (PPs), and junior health service officers (JHSOs), all PSI Myanmar employees. These informal FGDs highlighted the challenges and opportunities with the intervention to inform programmatic scale-up.

Challenges: Incentives, Distance and Travel Costs, Program Acceptability, and Capacity

The most common challenge mentioned was the expectation of incentives from community members during community outreach events. While IPCs would bring promotional items to events, often they would not have enough for all attendees (i.e. 35 incentives for 100 people). All attendees expected to receive an incentive and were upset when only those who answered questions received an incentive or promotional item.

This misunderstanding interfered with recruitment for events. IPCs originally asked villagers to help recruit other villagers, but once incentives were not provided for all, this became a challenge. IPCs started recruiting from outlets with the help of midwives and Sun Primary Health (SPH) staff and/or with the help of village heads who would go to individual households to recruit; ultimately these sessions were smaller so everyone could receive an incentive.

IPC staff expressed that villagers have expectations of receiving incentives based on previous experience with other organizations.

IPC staff: "Because it is becoming like a custom to expect incentives or promotional items after the health sessions because other organizations are also doing that. When they [IPC staff] show up to the village and explain the activities, villagers want to know what the promotional item will be. Because other organizations give bed nets, they expect them."

While this challenge was more common with IPC staff, PP staff also had limited amount of promotional items during their follow-up visits and would prioritize giving items to outlets returning many used RDTs.

The second most common challenge was issues with distance and travel. Many different forms of transportation were used, and in order to reach certain outlets or villages, staff worked very long days and often spent overnight in a village.

Road conditions were often a problem. The rainy season made work harder or even impossible, both in reaching villages and recruiting community members.

Safety was another frequent concern.

JHSO staff: "Before they travel [JHSO staff] have to get information from the village fast about the safety of travel. Sometimes due to security problems they cannot travel to some villages."

Some staff mentioned acceptability of the program as a challenge. PPs described that the bigger outlets, especially GRS providers, were sometimes too busy to accept the program and were not interested. GRS providers were also less likely to travel out into the community in order to access hard-to-reach clients.

PP staff: "Because they [informal providers] travel to other villages, they are moving and seeking out the sick people so they get more chances to do the RDT tests. And they also do the tests if they suspect someone needs it. But this is different from the GRS because they are stationed in one place and are only in charge of his or her village."

Community acceptance was sometimes difficult. While local authorities typically gave permission to conduct health education events for the community, they only did so verbally. Without local township authority documented with a formal letter, some communities were not accepting of the community outreach events, and sessions were not approved or stopped. Approval from the Township Medical Authority was also sometimes not accepted.

Both PPs and IPCs were asked for health advice on topics outside malaria, such as other illnesses, reproductive health, and diarrhea. Understandably, they were not trained or able to provide the information requested.

One PP mentioned the challenge of training providers who were illiterate and had trouble interpreting the results of the tests. Another PP described the challenge that not all providers speak their language and a translator was required during follow-up visits.

Benefits and Opportunities

Despite issues with community recruitment and some GRS providers, many staff described how community members were excited to have visitors from urban areas and how outlets were cooperative. While traveling to remote villages was a common challenge for staff, staff also expressed that this was a benefit by enabling providers in those areas to test patients who otherwise would not have been reached.

JHSO staff: "Because in villages there are gold mines, but it is difficult to access. But they [JHSO staff] can reach the informal providers and give RDT and train them. The strength is that the informal providers can travel to remote regions."

The frequent visits to providers helped to encourage and reinforce proper use of RDTs.

PP staff: "Because they [PP staff] frequently visit the outlets, the outlets are more willing to do testing but previously the outlets were not as willing to do testing. Now due to the frequent visits, the outlets are doing blood testing."

Cost-Effectiveness Analysis Across Three Arms

The cost-effectiveness of the simple RDT subsidy (Arm 1), subsidy with financial incentives (Arm 2) and subsidy with IEC (Arm 3) was modeled using a decision tree (see Appendix: Cost-Effectiveness Analysis). This model predicted the annual scale-up cost for each intervention arm in US dollars, as well as the disability-adjusted life years (DALYs) averted in each arm as compared to the baseline scenario, 'no intervention.' The purpose of the model is to inform programmatic scale-up, and assumptions are detailed in the Appendix.

This analysis was conducted from a societal perspective, which included operational costs to PSI Myanmar, commodity costs across the supply chain, as well as time and commodity costs to the patient and provider.

Results from a Societal Perspective

Results are shown in Table 3, which reflect the society cost to enroll 600 providers per year for each intervention and DALYs <u>incurred</u> (meaning a lower number is better). A detailed list of cost and health outcome model inputs is shown in the Appendix, and a breakdown of programmatic costs, commodity costs, time, and travel costs is shown in Table 4.

We estimated upper and lower bound ranges for the cost-effectiveness of each intervention arm because malaria endemicity is quickly dropping in Myanmar, and only 8% of fever cases are malaria. Thus, despite a large number of houses screened in the household survey, very few individuals had fever in the past 2 weeks, and even less were tested with a RDT. We used the percentage of individuals who received a RDT test as a lower bound though this number should

be interpreted with caution because the pilot study did not enroll all providers in the community. For example, if only 2% of household survey individuals received a RDT, it is likely that many of them did not receive the RDT from a provider enrolled in the pilot study. We used this conservative estimate (2% in this example, actual numbers shown in the Appendix) as the lower bound. For the upper bound, we used mystery client survey results, which only included providers receiving the intervention. The mystery client survey results were likely to be an inflation of the actual RDT uptake because the mystery client scenario included that they suspected themselves of having malaria. Given the provider's interest in business and customer satisfaction, they were much more likely to use a RDT if the client stated s/he believed s/he had malaria. The upper and lower bound estimates are shown in Table 3, although the lower bound is highlighted to be more likely given the bias that is introduced in the mystery client survey.

Importantly, regardless of whether the upper or lower bound is used to predict the costs and health outcomes, either results showed consistently that IEC (Arm 3) lead to better results than a financial incentive (Arm 2), which also lead to better results than Arm 1 (simple subsidy). There were also added costs associated with the improved health outcomes for each arm.

Cost Data from PSI Myanmar

Costs are presented annually, and first-year costs were higher due to the costs to initiate the program. Program initiation consisted of staff training sessions, provider recruitment activities, and community education sessions on the utility and availability of subsidized RDTs. Recurrent program activities included all field activities and office support required for program roll-out. Field activities included the management and delivery of provider visits and community education sessions, and office support included administrative and managerial staff members. We excluded the cost of pilot study evaluation methods (i.e. mystery client visits) since research evaluative methods do not represent scale-up practices.

<u>Table 3</u>. Cost-effectiveness ratios compared to 'no intervention' from a societal perspective (Costs are denoted as lower or upper bounds of RDT uptake)

| Subsidy Scheme | Annual Total | Added Costs | Total | DALYs Averted | Cost Per DALY | | |
|------------------|------------------|---------------------------|-------------|------------------------|---------------------------------|--|--|
| | Costs | Versus No Intervention | DALYs | Versus No Intervention | Averted Versus No Intervention | | |
| | | intervention | | intervention | No intervention | | |
| Year 1 | | | | | | | |
| No intervention | (\$600,995.92, | | (10,154.95, | | | | |
| | \$627,552.78) | | 9,822.93) | | | | |
| Arm 1: Simple | (\$1,129,485.59, | (\$528,489.67, | (9,702.95, | (452.01, | (\$1,169.21, | | |
| subsidy | \$1,211,153.74) | \$583,600.96) | 7,894.66) | 1928.27) | \$302.66) | | |
| Arm 2: Subsidy | (\$1,130,342.27, | (\$529,346.34, | (9,698.31, | (456.64, | (\$1,159.22, | | |
| with financial | \$1,246,966.31) | \$619,413.53) | 7,266.58) | 2556.34) | \$242.30) | | |
| incentive | | | | | | | |
| Arm 3: Subsidy | (\$1,238,339.34, | (\$637,343.42, | (9,157.99, | (996.96, | (\$639.28, | | |
| with IEC | \$1,315,881.94) | \$688,329.16) | 7,219.75) | 2603.17) | \$264.42) | | |
| Year 2 and after | Year 2 and after | | | | | | |
| No intervention | (\$600,995.92, | | (10,154.95, | | | | |
| | \$627,552.78) | | 9,822.93) | | | | |

| Arm 1: Simple | (\$1,070,151.59, | (\$469,155.67, | (9,702.95, | (452.01, | (\$1,037.94, |
|----------------|------------------|----------------|------------|----------|--------------|
| subsidy | \$1,151,819.74) | \$524,266.96) | 7,894.66) | 1928.27) | \$271.88) |
| Arm 2: Subsidy | (\$1,071,008.27, | (\$470,012.34, | (9,698.31, | (456.64, | (\$1,029.28, |
| with financial | \$1,187,632.31) | \$560,079.53) | 7,266.58) | 2556.34) | \$219.09) |
| incentive | | | | | |
| Arm 3: Subsidy | (\$1,179,005.34, | (\$578,009.42, | (9,157.99, | (996.96, | (\$579.77, |
| with IEC | \$1,256,547.94) | \$628,995.16) | 7,219.75) | 2603.17) | \$241.63) |

Exchange rate used: 907 Kyat / USD, May 1st 2013.

<u>Table 4</u>. Annual costs separated as commodities, programmatic expenses, time and travel (Based on lower bound of RDT uptake)

| Scenario (societal) | | (including costs (scaled to uptake excluding time | | Program costs excluding commoditi es, time | Time costs | Travel costs | | |
|------------------------|------------------------------|---|----------------------|--|------------|-----------------|-----------------|---------------|
| | | | Total | (RDT Donor only) | and travel | | Provider | Patient |
| No inte | rvention | \$600,995.92 | \$95,6 13.52 | \$0 | \$0 | \$1,382.40 | \$0 | \$504,00 0 |
| Arm 1 | First year cost | \$1,129,485.5 9 | \$103, 658.1 9 | \$1,036. 80 | \$387,735 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,070,151.5 9 | \$103, 658.1 9 | \$1,036. 80 | \$328,401 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| Arm 2 | First year cost | \$1,130,342.2 7 | \$104, 086.8 7 | \$1,382. 40 | \$388,163 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,071,008.2 7 | \$104, 086.8 7 | \$1,382. 40 | \$328,829 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| Arm 3 | First year cost | \$1,238,339.3 4 | \$119, 126.7 4 | \$4,147. 20 | \$476,973 | \$58,895.6 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,179,005.3 4 | \$119, 126.7 4 | \$4,147. 20 | \$417,639 | \$58,895.6 0 | \$79,344 .00 | \$504,00 0 |

^{*}Assuming that at baseline, provider costs are not accounted for. Baseline societal costs therefore comprise of patient costs.

Limitations of the Study

- (1) <u>Intervention study limitations</u>: We note potential variability in the intensity and consistency of the interventions in different areas. For example, the number of visits to providers often depended on how far they were from main road. Another example is that some providers received incentives not in the form of extra RDTs but rather with umbrellas, lamps, jackets, or other tokens of appreciation, as is common practice in the trade. We are unable to quantify such potential differences.
- (2) <u>Stock resupply data</u>: Our data were based on collaborating supply points; however, these points may not have exclusive distribution to providers in the study. We were unable to identify or quantify all other sources of RDTs.
- (3) <u>Household surveys</u>: Our assessment of RDT use in the target area depended on two cross-sectional surveys at two time points. Because these are not longitudinal, we are unable to determine true changes in individual practices.
- (4) <u>Qualitative data collection</u>: These interviews were not necessarily representative or inclusive of all provider and staff views.
- (5) <u>Mystery clients</u>: A major limitation in assessing quality of RDT use was that all mystery clients were malaria negative. Thus the study cannot examine the quality of the providers' service regarding malaria positive clients.
- (6) <u>Cost-effectiveness analysis</u>: The data was based on household surveys, mystery clients, and a literature review, triangulated with qualitative interviews where necessary. Therefore the limitations reflected in those sections of the pilot study also apply to the cost-effectiveness analysis. Sensitivity analysis assessed the relative contributions of each area of uncertainty to model outcomes:
 - (6a) The level of uncertainty in the level of RDT uptake in each arm (household surveys and mystery client survey) impact the health outcomes, with a higher uptake leading to improved health outcomes across the range of uncertainty.
 - (6b) The derived nature of provider behavior for positive malaria diagnoses (based on negative diagnosis from mystery client survey) did not have a significant impact on cost or health outcomes.

Also, the model lacked precision for non-malarial fevers. We considered all non-malarial fevers to be an average of febrile WHO Global Burden of Disease illnesses in Myanmar; therefore there was a range of uncertainty behind the DALY treatment outcomes for non-malarial fevers. The model was intended for programmatic use and was unable to predict the selection for drug resistance due to inherently wide ranges of uncertainty in the probability of selection for resistance.

Conclusions and Recommendations

Conclusions

Use of RDT

Introducing RDTs through informal providers in Myanmar is feasible, and in this pilot study, led to increased uptake of RDTs in the community. Of our three study arms, Arm 3 (education and counseling) increased RDT use the most, with only slightly lower results for Arm 2 (incentive). Arm 1 (subisdy alone) led to lower uptake rates.

Quality 1. Use of RDTs and ACTs

While Arm 2 (financial incentive) led to the largest number of RDTs distributed, the high rates of ACTs also sold by Arm 2 providers suggest (but do not alone confirm) a focus on sales rather than proper use and prescription. Arm 3 providers (education and counselling) distributed fewer ACTs than RDTs, as would be expected, given inevitable negative RDT results.

Quality 2. Proper Procedures

Mystery client visits showed that providers often proposed a RDT, and that correct treatment was given after using a RDT. The ability of providers to perform and interpret a RDT was quite high despite general lack of formal health training. The current PSI Myanmar training program appears able to effectively provide the relevant information and skills.

Providers in Arm 3 (education and counseling) were most likely to initially propose a RDT to a suspected malaria patient at their own facility. Providers in Arm 3 were almost twice as likely as providers in the other two arms to treat correctly after using a RDT.

Provider Type

Provider type was associated with notable differences in both distribution and quality. Based on stock resupply data, GRS providers were the most likely to return any RDT kit – yet there are significantly more GRS providers compared to the other types of providers in the Mon and Shan State. Itinerant drug vendors (IDVs) were more likely than other types of providers to propose a RDT and treating correctly following the RDT results.

Recommendations

Arm 3 (education and counseling) led to the largest increases in RDT use, and greatest likelihood that proper treatment would follow RDT results. Arm 2 (incentives) had a nearly equivalent effect on RDT volume, and a positive, but lower, effect on quality. Both interventions were cost-effective, according to WHO standards.

Based on these findings we recommend an introduction of a combined intervention, incorporating both the education and counseling components of Arm 3, and the financial incentives of Arm 2. Given what is known about the development of, and adherence to, standard operating procedures for basic clinical services, we feel that after approximately 6

months the program could progressively reduce the frequency of counseling support visits with little or no effect on quality.

Cost-Effectiveness Implications

Annual program costs from Arm 1, Arm 2, and Arm 3 were \$387,735, \$388,163, and \$476,973 for year 1, and \$328,401, \$328,829, and \$417,639 for subsequent years, respectively. We expect that these will be slightly reduced during program roll-out because of efficiencies such as motorcycle purchases and amortized staff training. Health impact were calculated as ranges, and compared to baseline, are expected avert 452 – 1928 DALYs for Arm 1, 457-2556 DALYs for Arm 2, and 997 – 2603 DALYs for Arm 3. As discussed previously, the actual numbers for DALYs averted (higher numbers are better) are expected to fall within this range. Importantly, comparing the lower bound estimates shows that Arm 3 leads to the best health outcomes. Comparing the higher bound estimates shows that arms 2 and 3 both lead to significant health benefits compared to Arm 1. Therefore, we recommend Arm 3 as the priority intervention. If possible, a hybrid approach combining arms 2 and 3 would provide further benefit.

Effects of Expected Environmental Change

Programmatic cost-effectiveness is driven by RDT uptake, the case fatality rates of febrile illnesses (in particular non-malarial fevers), and the number of individuals that seek care in the informal private sector. Also undiagnosed fevers are better off treated presumptively as malaria, which is no longer the practice based on lowering endemicity of malaria.

Our cost-effectiveness models are based on current disease patterns. As malaria endemicity decreases, the overall cost-effectiveness of the integrated RDT and treatment program will decrease, and PSI Myanmar will eventually need to introduce protocols for proper case management of non-malarial febrile illnesses.

Cost of RDT

The success of an expanded program will depend on ongoing subsidy of RDT to providers. Most providers did not mention the price of RDT as either a motivation or challenge for their work. Because of the fixed and reasonable price, providers had the flexibility to sell the RDT at a price patients can afford, or even give the RDT for free.

Demand Creation

Although not the primary focus of this study, we found evidence that PSI Myanmar can improve patient demand for RDTs using mass media and interpersonal communication activities. More efforts to increase awareness of RDT with community members, village heads and providers would help to improve RDT acceptance and use. Where possible this should be undertaken.

Training of Providers

While providers had few suggestions on how to improve the initial training, there were certain skills and knowledge of topics they lacked. The following topics should be included and/or reviewed more thoroughly in the training:

- 1. Prevalence and incidence of malaria
- 2. RDT reliability (sensitivity and specificity); issues of quality
- 3. What treatment to give if patient tests positive
 - a. specifically, what to do if test is positive for *P. vivax*
 - b. importance of selling and prescribing full course of treatment
- 4. How to interpret results
 - a. specifically, what to do when all 3 lines appear
- 5. What to do if patient tests negative
 - a. what drugs to prescribe, when to refer, etc.
- 6. Providers should practice on an actual person
 - a. especially true with GRS providers and IDVs who may lack a health background

All of the providers appreciated the follow-up visits they received, along with the promotional items distributed. A visit 1 to 2 times a month by program staff is integral for the success of future programs.

Targeting Provider Types

PSI Myanmar should target IDVs given their existing capacity in the community, and should better train GRS providers given the potential for these providers to reach a wider population.

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Tables and Figures Used in Report

Table 1: Number of providers trained on RDT use by outlet type, township, and study arm during Phase One

| Townships | General Retail Store (GRS) | Itinerant Drug Vender (IDV) | Medical Drug Representative (MDR) | Total |
|----------------------|-------------------------------|--------------------------------|---|-------|
| Bilin (Arm 2) | 91 | 40 | 14 | 145 |
| Hseni (Arm 3) | 79 | 14 | 1 | 98 |
| Monghpyak (Arm 1) | 32 | 50 | 0 | 82 |
| Namkhan (Arm 2) | 103 | 15 | 5 | 119 |
| Paung (Arm 1) | 83 | 31 | 18 | 132 |
| Thanbyuzayat (Arm 3) | 11 | 27 | 17 | 55 |
| Total | 399 | 177 | 55 | 631 |

Table 2: Number and type of outlets for mystery client assessment of RDT use by region

| Townships | General Retail Stores (GRS) | Itinerant Drug Venders (IDV) | Medical Drug Representatives (MDR) | Total |
|--------------|--------------------------------|---------------------------------|--|-------|
| Bilin | 13 | 14 | 12 | 39 |
| Paung | 12 | 11 | 17 | 40 |
| Thanbyuzayat | 2 | 9 | 17 | 28 |
| Monghpyak | 4 | 19 | 0 | 23 |
| Hseni | 19 | 5 | 1 | 25 |
| Nankhan | 10 | 2 | 4 | 16 |
| Total | 60 | 60 | 51 | 171 |

Table 3: Cost-effectiveness ratios compared to 'no intervention' from a societal perspective (Costs are denoted as lower or upper bounds of RDT uptake)

| Subsidy Scheme | Annual Total Costs | Added Costs Versus No | Total DALYs | DALYs Averted Versus No | Cost Per DALY Averted Versus | | |
|------------------|-----------------------|--------------------------|----------------|----------------------------|---------------------------------|--|--|
| | | Intervention | | Intervention | No Intervention | | |
| Year 1 | | | | | | | |
| No intervention | (\$600,995.92, | | (10,154.95, | | | | |
| | \$627,552.78) | | 9,822.93) | | | | |
| Arm 1: Simple | (\$1,129,485.59, | (\$528,489.67, | (9,702.95, | (452.01, | (\$1,169.21, | | |
| subsidy | \$1,211,153.74) | \$583,600.96) | 7,894.66) | 1928.27) | \$302.66) | | |
| Arm 2: Subsidy | (\$1,130,342.27, | (\$529,346.34, | (9,698.31, | (456.64, | (\$1,159.22, | | |
| with financial | \$1,246,966.31) | \$619,413.53) | 7,266.58) | 2556.34) | \$242.30) | | |
| incentive | | | | | | | |
| Arm 3: Subsidy | (\$1,238,339.34, | (\$637,343.42, | (9,157.99, | (996.96, | (\$639.28, | | |
| with IEC | \$1,315,881.94) | \$688,329.16) | 7,219.75) | 2603.17) | \$264.42) | | |
| Year 2 and after | | | | | | | |
| No intervention | (\$600,995.92, | | (10,154.95, | | | | |
| | \$627,552.78) | | 9,822.93) | | | | |
| Arm 1: Simple | (\$1,070,151.59, | (\$469,155.67, | (9,702.95, | (452.01, | (\$1,037.94, | | |
| subsidy | \$1,151,819.74) | \$524,266.96) | 7,894.66) | 1928.27) | \$271.88) | | |
| Arm 2: Subsidy | (\$1,071,008.27, | (\$470,012.34, | (9,698.31, | (456.64, | (\$1,029.28, | | |
| with financial | \$1,187,632.31) | \$560,079.53) | 7,266.58) | 2556.34) | \$219.09) | | |
| incentive | | | | | | | |
| Arm 3: Subsidy | (\$1,179,005.34, | (\$578,009.42, | (9,157.99, | (996.96, | (\$579.77, | | |
| with IEC | \$1,256,547.94) | \$628,995.16) | 7,219.75) | 2603.17) | \$241.63) | | |

^{*} Exchange rate used: 907 Kyat / USD, May 1st 2013.

Table 4: Annual costs separated as commodities, programmatic expenses, time and travel (Based on lower bound of RDT uptake)

| Scenario (societal) | | Total cost (including commodities) | ommodities) costs (scaled to commodities) uptake excluding time costs | | Program costs excluding commoditi es, time | Time costs | Travel costs | |
|------------------------|------------------------------|--|---|------------------------|--|-----------------|-----------------|---------------|
| | | | Total | (RDT Donor only) | and travel | | Provider | Patient |
| No inte | rvention | \$600,995.92 | \$95,6 13.52 | \$0 | \$0 | \$1,382.40 | \$0 | \$504,00 0 |
| Arm 1 | First year cost | \$1,129,485.5 9 | \$103, 658.1 9 | \$1,036. 80 | \$387,735 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,070,151.5 9 | \$103, 658.1 9 | \$1,036. 80 | \$328,401 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| Arm 2 | First year cost | \$1,130,342.2 7 | \$104, 086.8 7 | \$1,382. 40 | \$388,163 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,071,008.2 7 | \$104, 086.8 7 | \$1,382. 40 | \$328,829 | \$54,748.4 0 | \$79,344 .00 | \$504,00 0 |
| Arm 3 | First year cost | \$1,238,339.3 4 | \$119, 126.7 4 | \$4,147. 20 | \$476,973 | \$58,895.6 0 | \$79,344 .00 | \$504,00 0 |
| | Recurren t annual cost | \$1,179,005.3 4 | \$119, 126.7 4 | \$4,147. 20 | \$417,639 | \$58,895.6 0 | \$79,344 .00 | \$504,00 0 |

^{*}Assuming that at baseline, provider costs are not accounted for. Baseline societal costs therefore comprise of patient costs.

Figure 1: RDT use pre- and post- roll-out from household survey

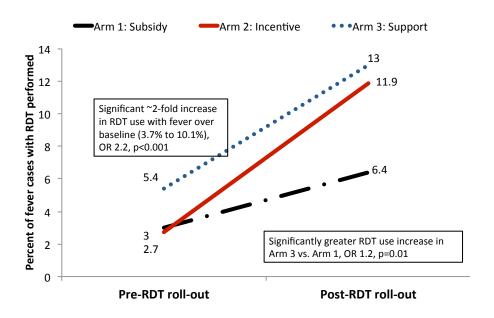
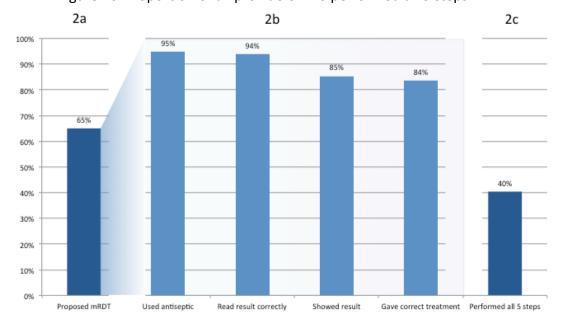


Figure 2: Provider compliance with proper testing and diagnosis standards

Figure 2a: Proportion of all providers who proposed RDT Figure 2b: Proportion of those, who complied with follow-up steps Figure 2c: Proportion of all providers who performed all 5 steps





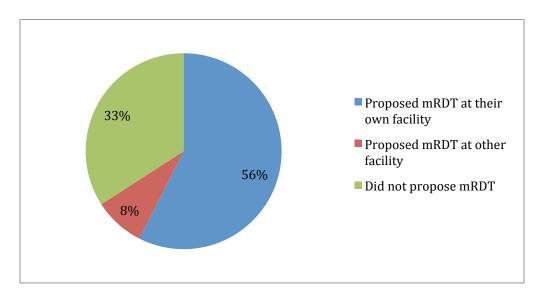


Figure 4: Mystery clients – percentage of providers who propose blood test at his/her own facility by arm

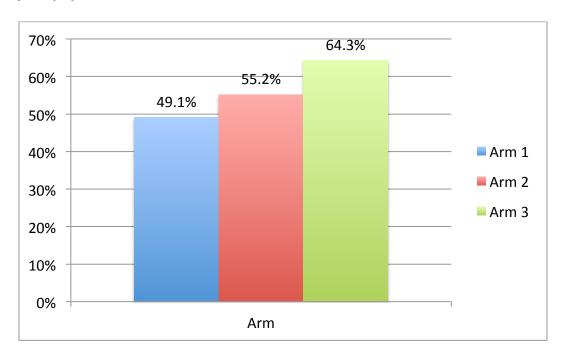


Figure 5: Mystery clients - percentage of providers properly treating and correctly reading results by arm

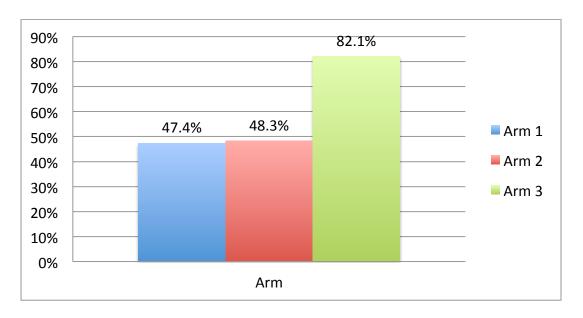


Figure 6: Mystery clients - percentage of providers properly treating and correctly reading results by provider type

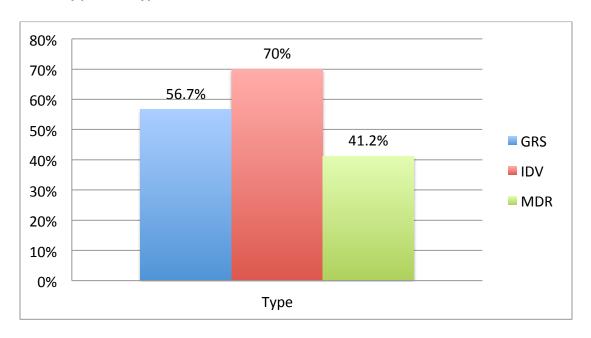


Figure 7: Number of RDTs distributed by arm

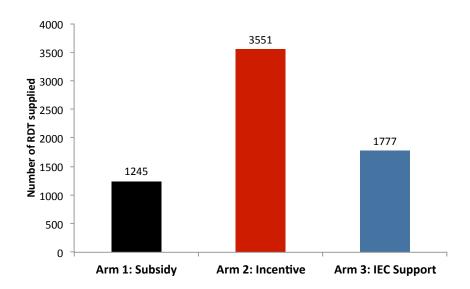


Figure 8: Ratio of ACTs and RDTs distributed

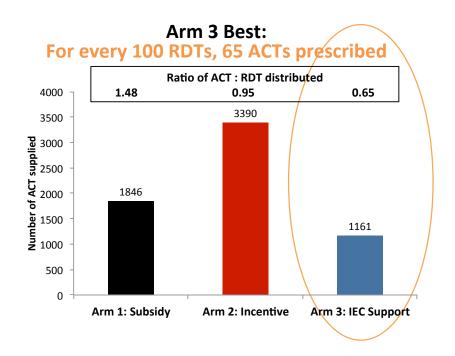


Figure 9: Number of outlets returning used RDT by outlet type

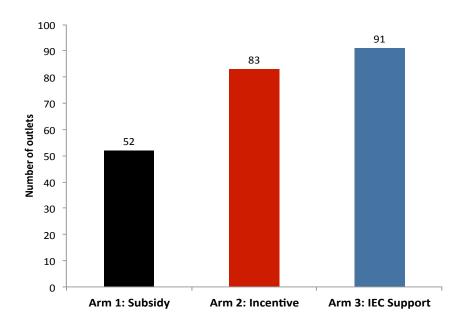


Figure 10: Number of outlets returning any used RDT kit by outlet type

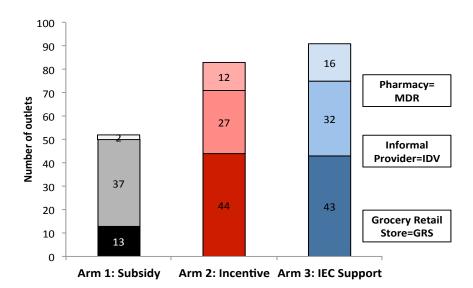
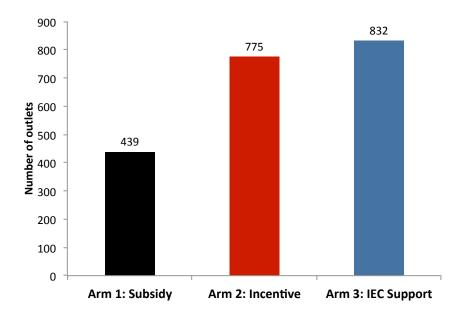


Figure 11: Returned RDT results by arm



Additional Figures

Figure 1: Test results of returned RDTs according to provider results

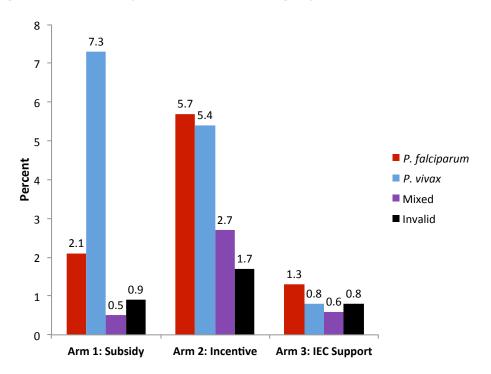
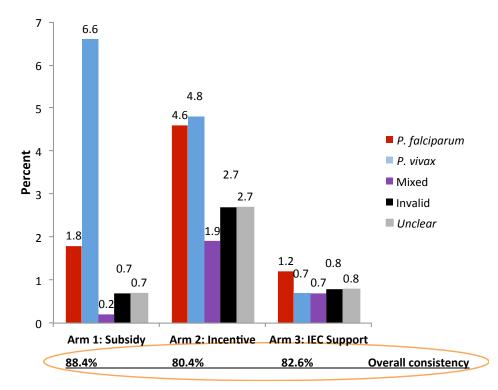


Figure 2: Test results of returned RDTs according to MIS officer results and consistency with provider results

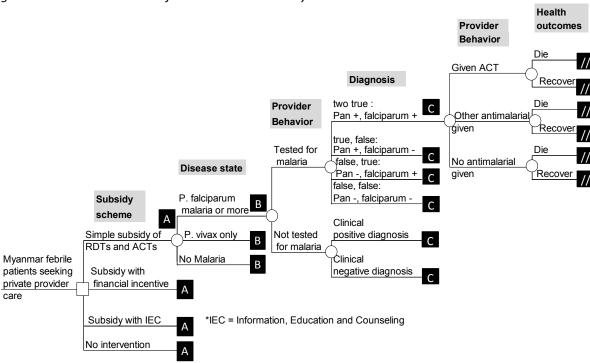


Appendix: Cost-Effectiveness Analysis

A. Decision Tree Model Design

We constructed a decision tree in Microsoft Excel 2010 to estimate the incremental cost-effectiveness ratio between three pilot study subsidy schemes: simple subsidy, subsidy with financial incentives, and subsidy with information, education and counseling. The decision tree is a flow chart that aims to encompass all possible courses of action within a chosen population (Figure 1). The population for this study comprises of febrile patients in six townships within Myanmar's Mon and Shan states that seek healthcare within the informal private sector from May to September. By following the decision tree from left to right, each pathway of action is represented by a terminal node (denoted '//'). The decision node represents subsidy schemes while chance nodes are categorized as: disease state, provider behavior, diagnosis, and health outcomes. Each subsidy method is represented as a decision and 'no intervention' is used as a base case for reference.

Figure 1. Decision tree model for malaria RDT subsidy schemes



Model inputs include programmatic costs (in dollars) and Myanmar malaria epidemiology data. Data sources include finance/account records and management information systems data from Population Services International Myanmar, a review of published scientific literature, and data from the pilot study. The pilot study was implemented between April and September 2013, using household surveys, interviews with private providers, mystery client visits, and stock audits to assess the uptake and accuracy of malaria rapid diagnostic test use for each subsidy scheme. Model outcomes assess the proportion of properly treated *Plasmodium falciparum* malaria, quantifying improperly treated fevers in disability-adjusted life years. Cost-

effectiveness is reported as the cost US dollars per disability-adjusted life year averted for each intervention, as compared to no intervention.

B. Model Limitations and Assumptions

Model Limitations

While the model estimates comparative costs and health outcomes between intervention arms for the selected population, it does not explore the probability for malaria transmission or the likelihood of selection for resistance. Therefore this model is intended for programmatic use to predict the cost and clinical impact on the intervention on individuals, and does not model malaria transmission at a population level.

Assumptions

The model applies the following assumptions based on the rationale detailed below.

1. Artemisinin monotherapy is crowded out by quality-assured ACT.

Rationale: During the AMTR mystery client survey in late 2012 which recorded fever drug stocks four months after ACT roll-out, only 4.3% provider-recommended fever drugs were artemisinin monotherapies. By contrast, 54.1% of provider-recommended fever drugs were quality-assured ACT. The replacement of artemisinin monotherapies with ACT is well underway, and monotherapies in Myanmar have been banned since December 31st 2012.²⁸ The 2013 mystery client survey affirms that no artemisinin monotherapies were prescribed to any mystery clients. Qualitative demographics also showed that very few outlets still stocked monotherapies (2/31, who were also selling ACT).

2. All medicine is of high quality: there are no counterfeits or expired drugs.

Rationale: artemisinins are the most common counterfeit durgs,¹⁷ and all studied providers are receiving subsidized quality-assured ACT. This assumption was validated through mystery client survey data, which showed that all outlets visited use Supa Arte, which is the subsidized ACT, and none of the antimalarial drugs in stock were expired.

We seek to validate this assumption during interviews with private providers, which includes antimalarial stock data including expiration dates. If expired medicine is common, the model will be updated.

3. The subsidized RDT are stored properly and can be accurately characterized by reported sensitivity and specificity measurements.²⁹

Rationale: Although high heat or humidity can compromise the quality of RDT, it is not feasible for us to conduct the necessary laboratory tests to assess RDT quality. Provider training sessions emphasize how to properly store RDT and to check for expiration dates. Interviews with private providers will also check the expiration dates of any RDT in stock.

4. ACT and RDT are distributed through the same channels as all medicines considered in the decision tree model: antipyretics, antibiotics, and non-artemisinin antimalarial monotherapies.

Rationale: there is no data available to track the distribution of other products within the informal private sector. We used estimates provided by program staff leader Hnin Hsu Hsu Khin at PSI Myanmar to predict price mark-ups between from wholesale to retail to provider to the patient.

5. Either P. falciparum or P. vivax malaria is present in all malaria infections.

Rationale: *P. malariae* and *P. ovale* parasites are technically difficult to differentiate from *P. vivax* parasites. WHO reports on the malaria burden in Myanmar do not account for *P. malariae* and *P. ovale* because they are considered to be rare, and furthermore can be treated with therapeutics that effectively treat *P. vivax* malaria. Both *P. malariae* and *P. ovale* parasites can be detected by the Pan *plasmodium* RDT test so even if these parasites are present without *P. vivax* infection, the model results will be unaffected. A report in 1998 showed that the prevalence of *P. malariae* at the Thai-Myanmar border was 24.3%, which is much higher than the Myanmar department of health estimate of 0.1%.³⁰

6. Subsidized ACT are sold only as a full course of therapy.

Rationale: the 2012 mystery client survey for the AMTR project shows that 97% of quality-assured ACT were sold as full courses of therapy. This fact attests to the success of the AMTR project strategy to discourage providers from cutting the blister packets of subsidized ACT. Providers were previously known to cut blister packets of artemisinin monotherapy prior to sale, so the AMTR package design team intentionally nested the blister packet in a cardboard envelope that was sealed with a sticker, making it very difficult to cut the full course of ACT into pieces. Results from the 2013 Mystery Client survey in the pilot study affirm that all courses of ACT prescribed were full courses.

7. Patients adhere to a full 3-day course of subsidized ACT.

Rationale: the AMTR project uses a multipronged approach to encourage the completion of three-day ACT regimens: 1) the price of a full course of ACT is set to match the price of partial courses of artemisinin monotherapy that patients afford 2) both provider support visits and community outreach programs emphasize the importance of completing a full course of ACT 3) the design of the ACT packaging includes two written Burmese reminders to complete a full course of ACT: one on the front of the cardboard envelope and a second below the pills inside the envelope. The M-ROSE household surveys will confirm whether this assumption is accurate: otherwise the model will be updated accordingly.

8. 'Other antimalarial' refers to the use of quinine or chloroquine.

Rationale: The 2012 mystery client survey showed that only 8% of fever diagnoses were treated with non-artemisinin antimalarials. We chose quinine or chloroquine through in-depth interview stock audit data from the pilot study and consultation with PSI Myanmar program managers. Interestingly, none of the providers screened carried primaquine, which is the only drug combination capable of clearing hypnozoites, the latent liver stage of *P. vivax* infections.

9. Drug adherence to chloroquine and injectable quinine is high given the short course of therapy.

Rationale: Consultation with Hnin Su Su Khin, the AMTR head program officer stated the patients seeking private sector care typically adhere to the first 2-3 days of a drug regimen. Pilot study qualitative demographic data shows that most providers who carry quinine carry it as an injectable solution. The injection is available as a single dose, and orally administered chloroquine is available as a three-day course of therapy.

10. P. vivax malaria does not relapse.

Rationale: The complexity of relapse and unavailability of epidemiological data prevent the accurate prediction of *P. vivax* relapse. A full course of primaquine is required to ensure the clearance of hypnozoites, the parasite stage responsible for the relapse of *P. vivax* malaria. Relapse rates depend on the duration of fever before initial treatment, the type of treatment used, the level of parasitemia, and the level of patient drug adherence.³² Relapse rates are also likely to be low within the 1-month time frame considered by the model: a study at the Thai-Myanmar border showed a 28-day relapse rate of 3.4% for self-administered therapy and 0% for directly-observed chloroquine and primaguine therapy.³²

12. 'No antimalarial' refers to the use of antipyretics 70% of the time and antibiotics 30% of the time.

Rationale: The 2012 mystery client survey showed that when antimalarials were not prescribed for fevers, 50% of cases were treated with antibiotics and the other 50% with antipyretics. However, more recent household surveys at PSI Myanmar showed that the vast majority (90% estimated) of providers administered antipyretics to patients presenting with a fever. We therefore assume that patients receive antipyretics 70% of the time.

13. Only one type of medication is prescribed at any given time.

Rationale: While some providers in Myanmar are known to administer "machine gun therapy" by prescribing multiple drugs (correspondence with Dr. Tin Aung), the 2012 mystery client survey shows that only 0.4% of providers administered more than one drug at a given time.

C. Model Input Data

The model input data is presented in four sections: epidemiological data, probability data, cost data, and health outcomes. We detail the source of each data point and rationalize the estimates where applicable. Epidemiology data focuses on malaria epidemiology in the intervention townships. Probability data is organized as: 1) case fatality rates, 2) diagnostic test characteristics, and 3) provider behavior. Costs are characterized as: 1) operational costs 2) commodity costs and 3) time costs. Health outcomes are contingent on pilot study results to translate the number of malaria cases properly tested and treated into DALYs averted for each intervention arm.

Malaria Epidemiology

Table X describes model epidemiology data inputs and sources and/or rationale.

Table X. Model epidemiology data inputs

| Subject | Input value | Source(s) and/or rationale |
|--|-------------|--|
| Percentage of <i>P. falciparum / P. vivax</i> malaria | 65% | Reference 33, WHO SEARO data: 70% <i>P. falciparum</i> in 2006. |
| | falciparum | National Malaria Control Program estimate in August 2012 from Ko Htet, PSI Myanmar: 68% |
| | 35% vivax | Hnin Su Su Khin PSI Myanmar: falciparum rates have declined to nearly 60% in the Mon state due to high NGO presence |
| | | Pilot study stock audit data: 55% of returned malaria positive RDT showed <i>P. falciparum</i> and mixed Plasmodium infections, while 45% of these RDT showed <i>P. vivax</i> only.** |
| | | Estimate based on the above: 65% |
| Proportion of febrile cases in population that are malaria | 8% | PSI Myanmar MIS data:* 7.2% Pilot study stock audit data: 8.56% of fever cases tested were malaria according to returned RDT** |
| Average number of febrile | 20 | PSI Myanmar MIS data* estimated 20 per month. |
| patients that visit one private provider per month | | Pilot study stock audit data showed that 1-4 RDT were used by each provider per month. Baseline uptake levels are between 9-16% (Table 5), therefore the estimated number of clients is between 1/16% and 4/9%: 6 to 44. |

^{*} MIS data is from SPH interventions from July to October 2012 in the same Mon state townships as the M-ROSE study. The sample includes 3769 patients that were tested for malaria within 24 hours of the onset of fever. MIS data from the Shan state was not available.

Probability Data

Table X describes input probability data for case fatality rates and diagnostic test characteristics, and table X describes input probability data for provider behavior at baseline and for each intervention.

Table X. Model probability data inputs: case fatality rates and diagnostic test characteristics

| Subject | | Value | Source(s) and/or rationale |
|---|------------------------------|--------|--|
| Case fatality ra | tes | | |
| Case fatality | Given ACT | 0.0001 | Very low probability |
| rates for <i>P.</i> falciparum malaria* | Given chloroquine or quinine | 0.007 | Assumption because of high rates of chloroquine resistance |
| | Given no antimalarial | 0.03 | Reference 34, hospital case fatality rate in Bago Myanmar: 2.7% for uncomplicated <i>P. falciparum</i> malaria, 22% for cerebral. Reference 35: 3% case fatality rate for <i>P. falciparum</i> malaria on |

^{**} Returned RDT were both read by providers (the results were recorded on the RDT using a black permanent marker) as well as PSI staff. The reads between provider reports and PSI staff showed high concordance, and we chose to use provider reports since the rate of false positive RDT test results increases past the recommended 20-minute readout.

| | | | eastern border of Myanmar. | | | |
|-----------------------------|---------------------------|--------------------|---|--|--|--|
| Case fatality | Given ACT | 0.0001 | Very low probability: blood-stage parasites cleared | | | |
| rates for P. | Given | 0.0001 | Section 5.3. Assumption 10: good drug adherence. Less | | | |
| vivax* | chloroquine or | | chloroquine-resistant <i>P. vivax</i> parasites than <i>P. falciparum</i> . | | | |
| | quinine | 0.01 | | | | |
| | Given no | 0.01 | Reference 36: the case fatality rate for multidrug resistant <i>P.</i> | | | |
| | antimalarial | | vivax malaria in Papua was 1.4%. We estimate a slightly lower rate because patients can seek retreatment for drug sensitive | | | |
| | | | P. vivax malaria. | | | |
| Case fatality | Given ACT or | 0.002 | Reference 37: mortality analysis from hospital and village | | | |
| rate for non- | other | | records in Bago, Myanmar. 40% of febrile deaths are non- | | | |
| malarial febrile illnesses* | antimalarial | | malarial. Triangulated with PSI MIS data from Bago: 8% of fevers are malaria. Malaria is 17.5x more deadly than other | | | |
| 1111103303 | | | fevers. | | | |
| | Given no | 0.0016 | Reference 38: WHO burden of disease in Myanmar: | | | |
| | antimalarial | | categorized febrile illnesses treatability with antibiotics in | | | |
| | | | appendix B to estimate 2/3 non-malarial fevers are treatable | | | |
| | | | with antibiotics. Reference 39: confirms that a large proportion of non-malarial | | | |
| | | | fevers in neighboring country Laos are treatable with | | | |
| | | | antibiotics. | | | |
| | | | Section 5.3. Assumption 12, 30% of no antimalarial | | | |
| | | | administration is an antibiotic. | | | |
| | | | We estimate that 2/3*30% (= 20%) of non-malarial fevers get | | | |
| | | | treated properly, the remaining 80% suffer the same fatality rate as those given ACT or other antimalarial. | | | |
| Diameter 1 | h | | Tute as those given her or other antimalaria. | | | |
| Diagnostic test c | _ | | | | | |
| RDT sensitivity | P. falciparum | 100% (FR | Reference 29: Foundation for Innovative New Diagnostics | | | |
| and specificity | sensitivity P. falciparum | and SD) 97% (FR | (FIND) WHO RDT data, at 200 parasites / μL. | | | |
| | specificity | and SD) | SD = Standard Diagnostics Ag Pf Pv, Korea. Given during the | | | |
| | Pan | 92% | first 2 months of the RDT pilot study. | | | |
| | plasmodium | (estimate) | | | | |
| | sensitivity | | FR = First response Pf Pan from Premier Medical Corporation, | | | |
| | | 100% | India. Given during the last 4 months of the RDT pilot study. | | | |
| | | (SD) | | | | |
| | | 88% (FR) | | | | |
| | Pan | 98% | | | | |
| | plasmodium | (Estimate) | | | | |
| | specificity | 050((8=) | | | | |
| | | 95% (SD) | | | | |
| | | 100% (FR) | | | | |
| Clinical | Clinical | 0.50 | The data used does not indicate whether the provider believes | | | |
| diagnostic result | positive | | if the patient has malaria or not. Therefore, the corresponding | | | |
| | diagnosis | 0.50 | prescription probabilities for clinical positive and negative | | | |
| | | 0.50 | diagnoses are the same. The values in this field do not affect | | | |
| | Clinical | 0.50 | - | | | |
| | negative diagnosis | 0.30 | results and we use a provisional 50% probability of positive or negative diagnosis. | | | |

| | Actual values likely range between 24 and 82% according to |
|--|---|
| | mystery client surveys. |
| | |
| | At baseline, in 2012, 82% of mystery clients receiving clinical |
| | diagnosis were treated with ACT or other antimalarials. |
| | However, the 2013 mystery client survey only showed 24-37% |
| | of individuals received ACT or antimalarials for alleged fever. |

Table X. Model probability data inputs: provider behavior (Bolded numbers are used as inputs)

| Subject | del probability dat | Probability | | ' | | Source |
|---------------------|------------------------|---|---|--|---|---|
| | | | Arm 1 | Arm 2 | Arm 3 | |
| Diagnostic m | ethod | | | | | |
| Clinical diagno | osis | 0.98 (HH) 0.89 (MC 2012) | 0.98 (HH) 49.2 (MC 2013) | 0.98 (HH) 36.4 (MC 2013) | 0.92 (HH) 41.5 (MC 2013) | Baseline: 2012 mystery client survey. HH survey (weighted data, denominator only includes private informal provider |
| RDT | | 0.02 (HH, n = 1) 0.11 (MC 2012) | 0.02 (HH, n = 0) 50.8 (MC 2013) | 0.02 (HH, N = 0) 63.6 (MC 2013) | 0.08 (HH) 58.5 (MC 2013) | types in study. This is a lower bound estimate since in reality not all of those provider types within the community were enrolled in the pilot study, so the actual percent uptake of RDT would be higher). Arms 1 and 2 are speculated due to low sample size numbers, since the difference between no intervention, Arm 1, and Arm 2 was not statistically significant |
| Prescription | | | | | | |
| Diagnosis | Medicine prescribed | | | | | |
| Clinical malaria | ACT | 0.05 0.7 (MC 2012) 0 (HH) n=0 | 0.12 0.107 (MC 2013) 0.13 (HH) n=16 | 0.12 0.105 (MC 2013) [0.13] (HH) n=0 | 0.19 0.25 (MC 2013) [0.13] (HH) n=0 | 2012 Mystery client survey* 2013 Mystery client survey: these clients do not have malaria Value used: an average |
| | Other antimalarial | 0.03 | 0.07 0.14 | 0.07 0.11 | 0.07 | between 2013 mystery client and household survey data. For no |

| | No antimalarial | 0.003 (HH) n=1 0.92 0.24 (MC 2012) 0.992 (HH) n=383 | 0.008 (HH) n=1 0.81 0.753 (MC 2013) 0.992 (HH) n=119 | 0.009 (HH) n=1 0.81 0.879 (MC 2013) 0.991 (HH) n=107 | 0.014 (HH) n=2 0.74 0.625 (MC 2013) 0.986 (HH) n=139 | intervention, lowered estimate of actual ACT use because the 2012 mystery client survey took place 4 months after ACT were first introduced, possibly leading to temporary overuse. Arm 2 had no data so we matched values with Arm 1. |
|------------------------|-----------------------|--|---|---|--|--|
| RDT Pan + falciparum + | Other antimalarial | 0.75 (SPH) 0 (HH) n=0 | (HH n=0) 0.857 (MC reading test 2013) Correct treatment MC = 0.857 * 0.914 = 0.78 (HH n=0) 0.05 | (HH n=0) 0.972 (MC reading test 2013) Correct treatment MC = 0.972 * 0.861 = 0.84 (HH n=0) 0.05 | (HH) N=139 (HH n=0) 0.978 (MC reading test 2013) Correct treatment MC = 0.978 * 0.889 = 0.87 (HH n=0) 0.05 | Prescriptions for 'no intervention' are informed by the PSI SPH patient simulation assessment, 2011. The numbers for intervention arms are derived based on mystery client surveys. Since all tested individuals do not have malaria, provider behavior for those who would have malaria is inferred by how accurately the provider read the test results and provided the correct diagnosis. |
| RDT Pan + falciparum - | No antimalarial | 0.2 (SPH) 0.50 (HH) n=1 | (HH n=0) 0.17 | (HH n=0) 0.11 | (HH n=0) 0.08 | We are inferring that Pan + falciparum + and Pan - falciparum + (only possible via test error) leads to the same prescriptive behavior, since in-depth interviews with providers showed that they understood ACT were for falciparum malaria only. Qualitative interviews show that typically other |
| jaicipul alli - | Other antimalarial | 0.6 (SPH) 1.0 (HH) n=2 0.25 | 1.0 (HH n = 1) | (HH n=0) | (HH n=0) | antimalarials or antibiotics are given for vivax malaria. |

| | | 0.2 (SPH) | (HH n=0) | (HH n=0) | (HH n=0) | |
|---------------------------|--------------------|-----------------------------------|--|--|---|--|
| | | (HH n=0) | | | | |
| | No antimalarial | 0.25 | 0.45 | 0.45 | 0.45 | |
| | | 0.2 (SPH) (HH n=0) | (HH n=0) | (HH n=0) | 1.0 (HH) n = 1 | |
| RDT Pan - falciparum + | ACT | 0.75 (SPH) 0 (HH) n=0 | (HH n=0) 0.857 (MC 2013) Correct treatment MC = 0.857 * 0.914 = 0.78 | (HH n=0) 0.972 (MC 2013) Correct treatment MC = 0.972 * 0.861 = 0.84 | (HH n=0) 0.978 (MC 2013) Correct treatment MC = 0.978 * 0.889 = 0.87 | |
| | Other antimalarial | 0.05 (SPH) 0.50 (HH) n=1 | (HH n=0) 0.05 | (HH n=0) 0.05 | (HH n=0) 0.05 | |
| | No antimalarial | 0.2 (SPH) 0.50 (HH) n=1 | (HH n=0) 0.17 | (HH n=0) 0.11 | (HH n=0) 0.08 | |
| RDT Pan - falciparum - | ACT | 0.4 (SPH) (HH n=0) | 0.057 (MC) (HH n=0) | 0.083 (MC) (HH n=0) | 0.022 (MC) (HH n=0) | |
| | Other | 0.02 | 0.029 | 0.056 | 0.089 | |
| | antimalarial | (SPH) | (MC) | (MC) | (MC) | |
| | No antimalarial | (HH n=0) 0.58 | (HH n=0) 0.914 | (HH n=0) 0.861 | (HH n=0) 0.889 | |
| | No diffillialarial | (SPH) | (MC) | (MC) | (MC) | |
| | | 1.0 (HH n=8) | 1.0 (HH n = 4) | 1.0 (HH n = 12) | 1.0 (HH n = 13) | |

Costs

Costs are summarized in tables X (direct program, time and travel costs) and X (commodity costs). There are no capital costs required or investments (vehicles) in the pilot study.

Table X. Direct program costs for RDT intervention (annual)

| Costs for RDT intervention, 600 providers | First year cost | | | Comments | |
|---|--------------------|-----------|-----------|-----------|---|
| | No intervention | Arm 1 | Arm 2 | Arm 3 | |
| Personnel | | | | | |
| Interpersonal communicators | | \$34,599 | \$34,599 | \$34,599 | Role in first 6 months. Salary, travel costs |
| Jr. Health Service Officers | \$0 | \$17,568 | \$17,568 | \$17,568 | Manage and oversee field activities |
| Product promoters | \$0 | \$31,374 | \$31,374 | \$62,748 | Recruit and visit providers. Arm 3 costs are higher due to more visits from product promoters |
| Office personnel | \$0 | \$79,186 | \$79,186 | \$79,186 | Finance, administration in office |
| Supplies | | | | | |
| Incentives for providers | \$0 | \$17,784 | \$17,784 | \$17,784 | Incentives for providers to join: lamp, jacket, T-shirt, and timer. |
| Commodities | \$95,614 | \$103,658 | \$104,087 | \$119,127 | Cost of RDT, ACT, and other drugs (societal) |
| Materials for providers | \$0 | \$19,656 | \$19,656 | \$19,656 | Materials to run intervention: marker pen, sharps containers, zipper bags, box for disposables |
| Materials for product promoters | \$0 | \$324 | \$324 | \$324 | A backpack and flipchart for RDT materials |
| Services | | | • | | |
| Field staff training | | \$6,951 | \$6,951 | \$6,951 | Hotel, materials, & supplies for training of new product promoters and interpersonal coordinators |
| Field staff transport: monthly office visits | \$0 | \$30,834 | \$30,834 | \$53,028 | Higher price of Arm 3 results because there are more product promoters |
| Motorcycle taxi | \$0 | \$39,202 | \$39,202 | \$59,402 | Field activities used motorcycle taxis in pilot. NB: will cost less during scale-up, when motorcycles will be purchased. Higher price in Arm 3 due to increased provider visits |
| PSI Overhead | \$0 | \$5,329 | \$5,329 | \$5,329 | Building rental, electricity, phone, internet, |

| | | | | | computers, printers |
|--------------------------|----------|-----------|-----------|-----------|-----------------------------|
| Shipping logistics | \$0 | \$1,271 | \$1,271 | \$1,271 | Shipping and import permits |
| Total | | | | | |
| Total, year 1 | \$95,614 | \$387,735 | \$388,163 | \$476,973 | |
| Non-recurrent, year 1 | \$0 | \$59,334 | \$59,334 | \$59,334 | |
| Recurrent annual | \$95,614 | \$328,401 | \$328,829 | \$417,639 | |

Table X. Time and travel costs for RDT intervention (annual)

| Costs for RDT intervention, 600 providers | First year recu | urrent costs | Comments | | |
|---|-----------------|--------------|-----------|-----------|---|
| | No intervention | Arm 1 | Arm 2 | Arm 3 | |
| Time costs: Provider | \$0 | \$53,366 | \$53,366 | \$64,498 | Time spent administering RDT, visiting supply point |
| Travel costs: patient and provider | \$504,000 | \$583,344 | \$583,344 | \$583,344 | Travel cost per patient to reach the clinic, and for provider to reach supply point |
| Total Other Costs | \$504,000 | \$636,710 | \$636,710 | \$647,842 | |

Table X. Summary of non-programmatic costs to the donor, provider and patient

| | | Cost (USD) | Cost (USD) | | | | |
|--------------------|---|------------|------------|------------|---------|------------------|--|
| Cost category | Cost category | | | Provider | Patient | Societal (Total) | |
| RDT cost per unit, | No interventio | n | \$0 | \$0 | \$1.16 | \$1.16 | |
| including delivery | Arm 1 | | \$0.36 | \$0.11 | \$0.32 | \$0.68 | |
| | Arm 2 | | \$0.48 | \$0.09 | \$0.32 | \$0.80 | |
| | Arm 3 | | \$0.36 | \$0.11 | \$0.32 | \$0.68 | |
| Drug costs | Subsidized ACT | | \$1.12* | \$0 | \$0.53 | \$1.65 | |
| | Chloroquine ar | nd quinine | \$0 | \$0 | \$0.55 | \$0.55 | |
| | Antibiotics** | | \$0 | \$0 | \$0.93 | Weighted average | |
| | Antipyretics** | | \$0 | \$0 | \$0.44 | \$0.58 | |
| Time and travel | RDT time (per | RDT) | \$0 | \$0.29 | \$0.19 | \$0.48 | |
| costs | Product promoter support visit (time for providers annually) | Arm 1 | \$0 | \$192.00 | \$0 | \$192.00 | |
| | | 2 | \$0 | \$192.00 | \$0 | \$192.00 | |
| | | 3 | \$0 | \$774.00 | \$0 | \$774.00 | |
| | Provider travel to supply point (for 600 providers per year) | | \$0 | \$6,612.00 | \$0 | \$6,612.00 | |
| | Provider time visit supply po 600 providers | nt (for | \$0 | \$4,140.00 | \$0 | \$4,140.00 | |

| Patient travel to clinic | \$0 | \$0 | \$3.50 | \$3.50 |
|--------------------------|-----|-----|--------|--------|
| (per patient) | | | | |

^{*}Donor price of subsidized ACT calculated from appendix D table A5 = (wholesale price – sale to retailer)

Health Outcomes

Health outcomes are measured as DALYs incurred. Immediate recovery corresponds to no DALYs incurred: table 13 describes the quantification of all other health outcomes.

Table X. Calculation of health outcomes

| Subject | bject | | Source and Comments | | | |
|---|-----------------------------------|----------------|---|--|--|--|
| Survival | | | | | | |
| Average duration of effective treatmen | of malaria illness without t | 1 week | Ref. 41: hospital-based records indicate that most individuals check into the hospital 5-8 days of malarial illness with signs of severe malaria. | | | |
| DALY weight of ma | laria | 0.2 | On a scale of 0 to 1: reference 42. | | | |
| Average duration of | of non-malarial febrile illness | 1 week | Assumption | | | |
| DALY weight of no | n-malarial fever | 0.18 | Estimate based on Ref. 43, Global Burden of Disease: infectious diseases assigned 0.21 DALY weight for acute, 0.053 for moderate. | | | |
| Mortality | Mortality | | | | | |
| Mean life expectar | ncy in Myanmar | 62 | Took the average of three data points: 64.7: Ref. 44, World Bank data. 56: Ref. 45, Global Burden of Disease. 64.2: Ref. 46, Global Burden of Disease. | | | |
| Average age of malaria-induced death in intervention townships* | | 25 | MIS data from PSI Myanmar from 374 confirmed positive malaria cases. | | | |
| DALYs incurred | No discount rate | 38.00 | Calculated as years of life lost - (DALY weight of | | | |
| malaria death | 3% discount rate | 22.82 | malaria * 1 week of illness) | | | |
| Average age of non-malarial febrile death in Myanmar | | 30 | MIS data from 4,853 confirmed negative malaria cases. | | | |
| DALYs incurred non-malarial fever death | No discount rate 3% discount rate | 33.00 21.07 | Calculated as years of life lost - (DALY weight of non-malarial fever * 1 week of illness) | | | |

^{*}Data only available from intervention townships in the Mon state

Sensitivity Analysis

We perform sensitivity analysis to assess how the intervention costs and health outcomes change as a function of uncertainty in input values. One-way sensitivity analysis was conducted on each input value. The significant results, denoted by [LIMITS] are shown in table X.

Table X. One-way sensitivity analysis results that affect cost or DALY outcomes

| - table in a y constantly and you reconstant appear cost of 2 i.e. cateconics | | | | | | |
|---|------------|-----------|-------------------|-------------------|------------------|--|
| Inputs varied | Range that | Is cost | If sens. to cost, | Are the DALYs | If yes to DALYs, | |
| | input was | sensitive | how much does | incurred | how much do | |
| | varied | to this | cost vary as a | sensitive to this | DALYs respond to | |

⁺ Assuming a study population of 12,000 patients per month: 600 providers, 20 febrile patients per month.

^{** &#}x27;No antimalarial' refers to antibiotics 30% of the time and antipyretics 70% of the time.

| | | | input? | response to range varied? | input? | range varied? |
|--|--|------------------|----------------|------------------------------|---|---|
| RDT Uptake | | | | | | |
| RDT uptake No Intervention | | 0.02-0.11 | Yes | \$26,557 for no intervention | Yes - higher uptake leads to less DALYs | Negative 332 DALYs for no intervention |
| RDT uptake Arm 1 | | 0.0-0.65 | Yes | \$108,335 for Arm 1 | Yes - higher uptake leads to less DALYs | Negative 2,399 DALYs for Arm 1 |
| RDT uptake Arm 2 | | 0.0-0.65 | Yes | \$122,267 for Arm 2 | Yes - higher uptake leads to less DALYs | Negative 2,549 DALYs for Arm 2 |
| RDT uptake Arm 3 | | 0.02-0.65 | Yes | \$95,788 for Arm 3 | Yes - higher uptake leads to less DALYs | Negative -2,394 DALYs for Arm 3 |
| Provider Behav | vior | | | | | |
| Differing drug a | dministra | ation after RD | Г | | | |
| Pan - | Arm 1 | 0.02-0.40 | Yes | \$1,027 | Yes- higher | 10.8 DALYs |
| Plasmodium - ACT for Arm 1 | Arm 2 | 0.02-0.40 | | \$1,027 | uptake leads to MORE DALYs | 10.8 DALYs |
| (other antimalarial constant) | Arm 3 | 0.02-0.40 | | \$4,107 | | 43.1 DALYs |
| Differing drug a | dministra | ation after clin | ical diagnosis | | | |
| Clinical diagnosis, | Arm 1 | 0.05-0.40 | Yes | \$52,849 | Yes | Negative 1,542 DALYs |
| give ACT (other | Arm 2 | 0.05-0.40 | | \$52,849 | | Negative 1,542 DALYs |
| antimalarial constant) | Arm 3 | 0.05-0.40 | | \$49,614 | | Negative 1,448 DALYs |
| Clinical diagnosis, | Arm 1 | 0.50-0.93 | Yes | Negative \$64,929 | Yes, higher uptake leads to | 1,895 DALYs |
| give No antimalarial (Other | Arm 2 | 0.50-0.93 | | Negative \$64,929 | more DALYS | 1,895 DALYs |
| antimalarial constant) | Arm 3 | 0.50-0.93 | | Negative \$60,954 | | 1,779 DALYs |
| Health Outcom | es | | | | | |
| Differing Health | Outcom | es: Death | | | | |
| _ | Death from <i>falciparum</i> malaria given ACT | | No | \$0 | Yes - increasing death rates lead to more DALYs | Positive 1,666 for Arm 3, less for others |
| Death from falciparum malaria given other antimalarial | | 0.005-0.04 | No | \$0 | Yes | Positive 416 DALYs for arms 1 and 2, less for others |
| Death from <i>falciparum</i> malaria given no antimalarial | | 0.005-0.04 | No | \$0.00 | Yes | Positive 5,416 DALYs for no intervention, less for others |

| Death from viv | | 0.0001- | No | \$0.00 | Yes | Positive 167 DALYs |
|--------------------|-------------------|-------------|-----|--------------------|-----|---------------------------------|
| malaria given ACT | | 0.01 | | | | for Arm 3, less for |
| | | | | | | others |
| Death from vivax | | 0.0001- | No | \$0.00 | Yes | Positive 89 DALYs |
| malaria given o | other | 0.01 | | | | for Arm 3, less for |
| antimalarial | _ | | | | | others |
| Death from viv | /ax | 0.001-0.02 | No | \$0.00 | Yes | Positive 1,586 |
| malaria given i | | | | | | DALYS for on |
| antimalarial | | | | | | intervention, less |
| | | | | | | for others |
| Death from no | ın- | 0.001-0.05 | No | \$0 | Yes | Positive 24,442 for |
| malarial fever | | 0.001 0.03 | 110 | | 163 | Arm 3, less for |
| ACT | Biveii | | | | | others |
| Death from no | m- | 0.001-0.05 | No | \$0.00 | Yes | Positive 9,946 for |
| malarial fever | | 0.001-0.03 | NO | 30.00 | 163 | Arm 3, less for |
| other antimala | _ | | | | | others |
| | | 0.001.0.05 | No | ¢0 | Vaa | |
| Death from no | | 0.001-0.05 | No | \$0 | Yes | Positive 124,865 for |
| malarial fever | given no | | | | | no intervention, less |
| antimalarial | 15 | | | | | for others |
| Differing Costs | s (Same ac | | | | | |
| Cost of ACT | | \$0.50-2.50 | Yes | \$52,498 for Arm | No | 0 |
| | | | | 3, less for others | | |
| Cost of RDT | Arm 1 | \$0.36-1.20 | Yes | \$2,419 | No | 0 |
| (societal, | | | | | | |
| financial | Arm 2 | \$0.36-1.20 | Yes | \$2,419 | No | 0 |
| incentive | | | | | | |
| present in | Arm 3 | \$0.36-1.20 | Yes | \$9,677 | No | 0 |
| Arm 2) | | , | | | | |
| Cost of other | | \$0.18-1.65 | Yes | \$15,348 for Arm | No | 0 |
| antimalarial | | 30.18-1.03 | 163 | 3, less for others | INO | U |
| | +:0 / | \$0.30-1.00 | Vos | \$91,960 for no | No | 0 |
| Cost of antibio | itic / | \$0.30-1.00 | Yes | | INO | U |
| antipyretic | | | | intervention, less | | |
| DDT.: | | 60.40.0.75 | | for others | A1 | |
| RDT time cost | | \$0.18-0.75 | Yes | \$6,566 for Arm | No | 0 |
| | | | | 3, less for others | | |
| Patient travel | cost | \$0-\$3.50 | Yes | \$504,000, same | No | 0 |
| | | | | for all | | |
| Differing Costs | s for Speci | fic Arms | | | | |
| Arm 1 operation | onal | \$2-10 | Yes | \$1,152,000 | No | 0 |
| program costs | program costs per | | | | | |
| febrile individual | | | | | | |
| Arm 2 operational | | \$2-10 | Yes | \$1,152,000 | No | 0 |
| program costs per | | | | | | |
| febrile individual | | | | | | |
| | Arm 3 operational | | Yes | \$1,152,000 | No | 0 |
| program costs per | | \$2-10 | | | | |
| febrile individual | | | | | | |
| Differing Mala | | miology | | | | |
| Number of feb | | 5-40 | Voc | \$1,100,148 for | Voc | Positivo 17 771 |
| | | 3-40 | Yes | Arm 3, less for | Yes | Positive 17,771 DALYs for no |
| patients seekii | patients seeking | | | ATTIT 5, 1855 TOT | | DALTS IUI IIU |

| private care / provider / month | | | others | | intervention, less for others |
|---|-----------------------------|-----|---------------------------------------|-----|--|
| Percentage falciparum vs vivax malaria | 0.3-0.7 (falciparu m) | Yes | \$301 for Arm 3, less for others | Yes | Positive 1,922 DALYs for no intervention, less for others |
| Percentage febrile illnesses that are malaria | 0.03-0.20 | No | \$1,163 for Arm 3, less for others | Yes | Positive 10,962 DALYs for no intervention, less for others |
| Life expectancy in Myanmar | 50-80 | No | \$0 | Yes | Positive 4,546 DALYs for no intervention, less for others |
| Average age of malaria death | 5-45 | No | \$0 | Yes | Negative 3,476 DALYs for no intervention, less for others |
| Discount rate | 0.0-0.05 | No | \$0 | Yes | Negative 8,607 DALYs for no intervention, less for others |