Cost-effectiveness analysis of malaria rapid diagnostic test incentive schemes for informal private healthcare providers in Myanmar: Supporting Information

Ingrid T. Chen¹, Tin Aung², Hnin Nwe Nwe Thant², May Sudhinaraset¹, James G. Kahn¹

¹ University of California, San Francisco ² Population Services International, Myanmar

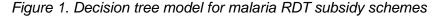
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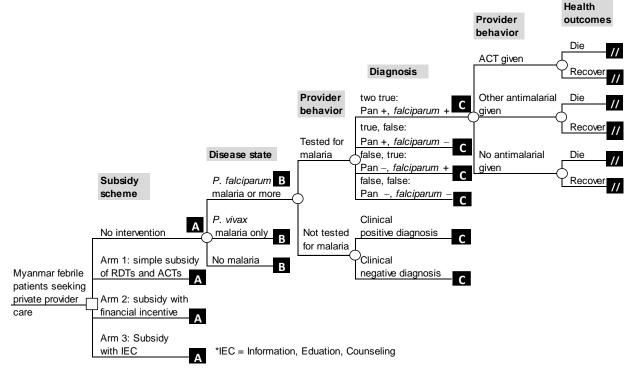
1. Decision Tree Overview

<u>Concepts</u>

We designed a decision tree using a spreadsheet in Microsoft Excel, 2010. A decision tree consists of decision nodes (denoted by squares) and chance nodes (denoted by circles). Each branch that arises from a chance branch is mutually exclusive of other branches, and the combined possibilities from each node must be collectively exhaustive such that branch probabilities add to 1. A decision tree that compares health service delivery options conventionally starts with each incentive method denoted as a decision option.

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.





Decision Tree Design:

In the beginning of the decision tree, each subsidy method is represented as a decision We use 'no intervention' as a base case for reference. For each subsidy scheme, we use a conventional decision tree structure for diagnostic tests, which starts with the true disease state as the first chance node. Our disease states are: *P. falciparum* malaria or more (including *P. vivax*), *P. vivax* malaria only, and no malaria, as we assume that all non-*falciparum* malaria is *P. vivax* malaria.

For each disease state, we then use a chance node for whether the provider uses an RDT. If the patient is tested with an RDT, there will be four possible test results for the combined pan *Plasmodium* test and *P. falciparum* diagnostic test: ++, +-, -+, and --. The probability of each result depends on whether the test result is true or false: a true positive corresponds to test sensitivity, false negative to (1 – sensitivity), true negative to specificity, and false positive to (1 – specificity). If the provider does not use an RDT, the resulting clinical diagnosis will be positive or negative for malaria. We assume that the pan *Plasmodium* test and

P. falciparum test performance is independent: failure to detect malaria with the pan *Plasmodium* PLDH antigen-detecting test is uncorrelated with failure to detect malaria with the *P. falciparum* HRP2 antigen-detecting test.

Each test result then leads to one of three treatment possibilities that are chosen by the provider. The provider sells subsidized ACTs, other antimalarials, or no antimalarial to the patient. After each treatment, the patient either lives or dies, which is a terminal node represented by "//". If the patient lives, morbidity associated with illness is accounted for in quantified health outcomes.

Data Inputs

There are three types of data inputs described below. The actual sources of data are described in section 4 (Data Inputs).

Probability Data

A probability value is assigned to each node. Each decision node is assigned a probability of 1, and each chance node is assigned a total probability of 1. Since chance nodes encompass a mutually exclusive and collectively exhaustive set of possible actions, the sum of probabilities that emerge from each chance node adds to 1.

The probability of occurrence for each path leading to a terminal node is calculated as the product of probabilities of every chance node from the decision node to that terminal node. The probability of occurrence is used to weight the associated costs (measured in USD) and health outcomes (measured in DALYs) of each path.

Cost Data

Cost data is incorporated at every applicable node and measured in USD. The exchange rate used is 907 Kyats / dollar, the official rate on May 1st 2013. Exchange rates in the model can be changed and updated easily. The total cost associated with each path is weighted by probability, and the sum of weighted costs for each decision node is the total cost for that decision node.

Health Outcome Data

The health outcome that corresponds to every terminal node is quantified in DALYs. Life years lost to mortality are calculated by subtracting the mean life expectancy from the average age of malaria-induced death and applying a 3% discount rate to each year in the future. Discounting is typically used in CEA to account for the fact that people tend to value events in the present more than in the distant future. For surviving patients, the morbidity of those who do not recover immediately will be calculated by dividing the average duration of illness by the DALY weight for the illness. The health outcomes associated with each path are weighted by probability, and their sum for each decision node represent the total DALYs incurred for that decision node.

Comparison of Intervention Arms

Once probabilities, weighted costs, and weighted health outcomes are established, the sum of weighted costs and health outcomes for each decision node (subsidy scheme) are used to compare the three intervention arms and the base case (no intervention). We compare the subsidy methods by ordering the approaches from least to most expensive. The subsidy methods were first obtained incrementally. The incremental cost-effectiveness ratio (ICER) for each intervention is obtained by the following formula:

ICER = <u>(Cost of intervention – cost of next less expensive approach)</u> (DALYs with intervention) – (DALYs with next less expensive approach)

Extended dominance

In this study, we found that increasing programmatic interventions led to increases in costs that were compensated by larger increases in effects. This led to decreasing ICERs. This is called "extended dominance", where a combination of 'no intervention' and the last intervention (arm 3) is more cost-effective than the intermediate interventions (arm 1). The proper comparison is thus each intervention versus the reference, not versus the next-least expensive option. The formula used in this case:

Cost per DALY averted vs baseline = _	(Cost of intervention – cost of no intervention)
(1	DALYs with intervention) – (DALYs from no intervention)

2. Model assumptions

The purpose of this study is to inform policy-makers on scale-up methods, so we deliberately do not account for malaria transmission (from untreated cases) or the likelihood of selection of resistance in this model. The model applied the following assumptions based on the rationale detailed below.

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

Rationale: During the Artemisinin Monotherapy Replacement (AMTR) program mystery client survey in late 2012 which recorded fever drug stocks four months after ACT rollout, only 4.3% provider-recommended fever drugs were artemisinin monotherapies. By contrast, 54.1% of provider-recommended fever drugs were quality-assured ACTs. The replacement of artemisinin monotherapies with ACTs is well underway, and monotherapies in Myanmar have been banned since December 31st 2012.¹ 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 ACTs).

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 ACTs. We validated this assumption during interviews with private providers, where all outlets had the subsidized Supa Arte product in stock, none of which had expired.

3. The subsidized RDTs are stored properly and can be accurately characterized by reported sensitivity and specificity measurements.²

Rationale: Although high heat or humidity can compromise the quality of RDTs. Intervention provider training sessions emphasized how to properly store RDTs and to check for expiration dates. Interviews with private providers will also check the expiration dates of any RDTs in stock.

4. ACTs and RDTs 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 leaders 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%.³

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

Rationale: the 2012 mystery client survey for the AMTR project shows that 97% of qualityassured ACTs 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 ACTs. 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 ACTs 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 ACTs.

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 ACTs 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 ACTs 3) the design of the ACT packaging includes two written Burmese reminders to complete a full course of ACTs: one on the front of the cardboard envelope and a second below the pills inside the envelope. The RDT 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 AMTR mystery client survey showed that only 8% of fever diagnoses were treated with non-artemisinin antimalarials. We chose quinine or chloroquine based on in-depth interview stock audit data from the pilot study, triangulated with conversation with PSI Myanmar program staff. 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 PSI Myanmar program officers suggested that 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.⁴ 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 and primaquine therapy.⁴

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

Rationale: A 2012 mystery client survey at PSI Myanmar 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, the 2012 PSI mystery client survey shows that only 0.4% of providers administered more than one drug at a given time.

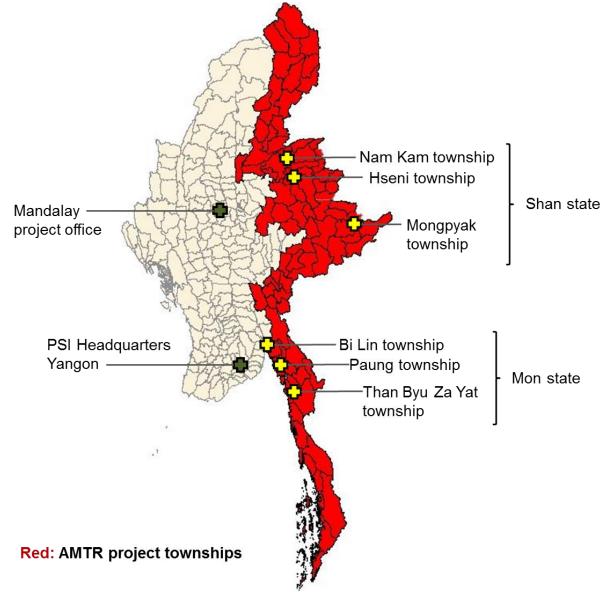
3. Intervention details

The pilot study took place from May to September, 2013. The 631 outlets enrolled were in the RDT pilot study (Table 1). The pilot study townships are shown in the map in Figure 2, of which Artemisinin Monotherapy Replacement (AMTR) outlets targeted for RDT scaleup are shown in red.

State	Township	Intervention arm
Mon	Paung	Arm 1: simple subsidy
Mon	Bi Lin	Arm 2: subsidy with financial incentive
Mon	Than Byu Za Yat	Arm 3: subsidy with Information, education and counseling (IEC)
Shan	Mongpyak	Arm 1: simple subsidy
Shan	Nam Kam	Arm 2: subsidy with financial incentive
Shan	Hseni	Arm 3: subsidy with IEC
Total outlets enrolled	631	

Table 1. Outlets reached by RDT pilot study.





4. Input data sources

A combination of finance/account records and management information systems (MIS) data from PSI Myanmar, mixed methods data from the RDT pilot study (household surveys, interviews with private providers, mystery client visits, stock audit data from supply points), and a review of published scientific literature were used as detailed below.

Study Population and Epidemiology

The study population was defined as the number of patients that seek private provider care at all outlets enrolled in the RDT pilot study from May to September, 2013. Study population data was derived from malaria epidemiology and provider assessments from other PSI Myanmar programs and a review of published scientific literature.

Malaria Epidemiology and Provider Assessments from PSI Myanmar

PSI Myanmar has detailed Management Information System (MIS) data on malaria RDT uptake as well as provider-reported RDT test results and patient demographics. The data is a part of the PSI Sun Primary Health (SPH) social franchising brand for private providers throughout rural Myanmar.⁵ We also used SPH monitoring mechanisms to estimate baseline provider knowledge levels of RDT use. A patient simulation known as the Sustained Quality study in 2011 used direct observation, clinical vignettes, and medical mannequins to assess provider understandings of malaria diagnosis and treatment before and after a single RDT training session (time points: 6 and 12 months post training). The study assessed provider knowledge levels in the following categories: medical history taking, looking for signs of severe malaria, checking for vital signs, malaria drug history, RDT performance, proper referral to higher level facilities, and drug prescription and information.

RDT Pilot Study Data

The RDT pilot study used four analytical methods: 1) household surveys, 2) interviews with private providers, 3) mystery client visits, and 4) stock audit data from supply points. Each method was used to evaluate RDT uptake and intervention effectiveness. The household surveys measured RDT uptake at a community / patient level before and after the intervention. The interviews with private providers explored provider attitudes to RDT use at the end of the pilot study and also included a survey of antimalarial and RDT stock and prices. Mystery clients presented with an alleged fever to providers that are enrolled in the pilot study as an additional measure for RDT uptake in the beginning and end of the pilot study. Stock audit data monitored RDT and ACT use, which was possible through the program requirement that used RDTs be returned to supply points for resupply. Providers were instructed to record the date, result of the test, and patient age / gender on each test. A comparison of RDT results with ACT sales suggested whether ACTs are being sold as recommended (for *P. falciparum* malaria only).

Cost Data from PSI Myanmar

Cost data was derived from PSI Myanmar finance and account records, and the exchange rate used is 907 Kyats / dollar, the official rate on May 1st 2013.⁶ Cost-effectiveness analysis from a societal perspective included operational costs to PSI Myanmar, commodity costs across the supply chain, as well as time and commodity costs to the patient and provider.

Operational costs were informed by PSI Myanmar finance and account data. To allow for the prediction of long-term operational costs, we defined operational costs in two categories: the cost of program initiation and the cost of recurrent program activities.

Program initiation consisted of staff training sessions, provider recruitment activities, and community education sessions on the utility and availability of subsidized RDTs. Community education sessions were considered to be a program initiation cost because once all intervention areas were reached, community education was considered complete and sessions were no longer continued. PSI program staff members expect that for scale-up, six months of community education sessions are sufficient to reach communities throughout the intervention

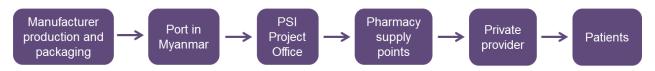
areas. Staff training sessions are also a program initiation cost: PSI training program designers expect the initial staff training session to be much more involved and costly than additional refresher training sessions which take place every 6-12 months. Refresher training costs were not included in this analysis. The costs of research and preparation required for program initiation were also excluded.

Recurrent program activities included all field activities and office support required for program rollout. 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 evaluative methods (i.e. mystery client visits) since research evaluative methods do not represent scale-up practices.

For both program initiation and recurrent program activities, the RDT pilot study had three types of operational costs: 1) overhead costs for PSI Myanmar, 2) staff costs, and 3) program materials and supplies. All costs were scaled to estimate the monthly operational costs for each arm of the RDT pilot study.

Commodity costs were mapped across the supply chain, starting from manufacturing and ending at the patient's drug or RDT purchase (Figure 2). Costs included product costs and delivery costs. RDT costs from manufacturing to pharmacy supply point delivery were recurrent operational costs. RDT purchases from pharmacy supply points to private outlets are provider costs, and individual RDT purchases from private informal outlets are patient costs.

Figure 2. Malaria RDT supply chain for RDT pilot study



Patient and provider commodity costs were estimated through data from PSI programmatic activities as well as staff consultation. There were two sources of baseline data that are available from the AMTR program evaluation in late 2012: a full stock audit and a mystery client survey. The RDT program is nested within the AMTR program, which has been delivering subsidized ACTs to 6,865 private outlets throughout eastern Myanmar since September 2012. The AMTR stock audit reached 1,159 private outlets that were enrolled to purchase subsidized ACTs, recording all available antimalarials and RDTs. The mystery client survey reached 446 private providers to establish baseline provider behavior for patients that present with fever. The mystery client survey also recorded antimalarial and RDT stock and prices, the proportion of providers that used RDTs, the drugs recommended for sale to the patient, and the level of provider instruction to the patient on ACT use. Patient and provider time costs were estimated through informal discussion with PSI Myanmar staff members. Patient traveling costs are estimated from a similar CEA in scientific literature. We excluded the potential lost income from healthcare seeking and illness due to the unavailability of data.

Health Outcome Data

Health outcomes were quantified in Disability Adjusted Life Years (DALYs), with a 3% discount rate applied.

5. Data Input values and rationale

Subject	Input value	Source(s) and/or rationale
Percentage of P. falciparum /		Reference 7, WHO SEARO data: 70% P. falciparum in
<i>P. vivax</i> malaria	65%	2006.
	falciparum	National Malaria Control Program estimate in August
		2012 from PSI Myanmar: 68%
	35% vivax	PSI Myanmar program staff: 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 RDTs showed <i>P. falciparum</i> and mixed
		Plasmodium infections, while 45% of these RDTs
		showed <i>P. vivax</i> only.**
		Estimate based on the above: 65%
Proportion of febrile cases in	8%	PSI Myanmar MIS data:* 7.2%
population that are malaria		Pilot study stock audit data: 8.56% of fever cases tested
		were malaria according to returned RDTs**
Average number of febrile	20	PSI Myanmar MIS data estimated 20 per month.
patients that visit one private		Pilot study stock audit data showed that 1-4 RDTs were
provider per month		used by each provider per month. Baseline uptake
		levels are between 9-16% (Table 6), therefore the
		estimated number of clients is between 1/16% and
		4/9%: 6 to 44.

Table 2. Malaria epidemiology and care-seeking behavior

* MIS data is from SPH interventions from July to October 2012 in the same Mon state townships as the RDT 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.

** Returned RDTs 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.

Su	Subject		Source(s) and/or rationale			
Case fatality Given ACT		0.0001	Very low probability			
rates for <i>P. falciparum</i> malaria*	Given chloroquine or quinine	0.007	Assumption because of high rates of chloroquine resistance ⁸			
	Given no antimalarial	0.03	Ref. 9, hospital case fatality rate in Bago Myanmar: 2.7% for uncomplicated <i>P. falciparum</i> malaria, 22% for cerebr Ref. 10: 3% case fatality rate for <i>P. falciparum</i> malaria ceastern border of Myanmar.			
Case fatality	Given ACT	0.0001	Very low probability: blood-stage parasites cleared			
rates for <i>P.</i> vivax*	Circli Circli		Ref. 11, Published materials on <i>P. vivax</i> treatment rates with chloroquine in Papua.			
	Given no antimalarial	0.01	Ref.12: the case fatality rate for multidrug resistant <i>P. vivax</i> malaria in Papua was 1.4%. We estimate a slightly lower rate because patients can seek retreatment for drug sensitive <i>P. vivax</i> malaria.			
Case fatality rate for non- malarial febrile illnesses*	Given ACT or other antimalarial	0.002	Ref. 13: mortality analysis from hospital and village records in Bago, Myanmar. 40% of febrile deaths are non-malarial. Triangulated with PSI MIS data from Bago: 8% of fevers are malaria. Malaria is 17.5x more deadly than other fevers.			

Table 3. Case fatality rates

Given no antimalarial	0.0016	Ref. 14: WHO burden of disease in Myanmar: categorized febrile illnesses treatability with antibiotics in appendix B to estimate 2/3 nonmalarial fevers are treatable with antibiotics. Ref. 15: confirms that a large proportion of non-malarial fevers in neighboring country Laos are treatable with antibiotics.
		Assumption 12, 30% of no antimalarial administration is an antibiotic. We estimate that 2/3*30% (= 20%) of nonmalarial fevers get treated properly, the remaining 80% suffer the same fatality rate as those given ACT or other antimalarial.

Table 4. Health outcomes

	Subject	Value	Source and Comments			
		Surviv	al			
Average duration effective treatmer	of malaria illness without ht	1 week	Ref. 16: 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 n	nalaria	0.2	On a scale of 0 to 1: ref. 17.			
Average duration illness	of non-malarial febrile	1 week	Assumption			
DALY weight of n	on-malarial fever	0.18	Estimate based on Ref. 18, Global Burden of Disease: infectious diseases assigned 0.21 DALY weight for acute, 0.053 for moderate.			
	Mortality					
Mean life expecta	ancy in Myanmar	62	Took the average of three data points: 64.7: Ref. 19, World Bank data. 56: Ref. 20, Global Burden of Disease. 64.2: Ref. 21, Global Burden of Disease.			
Average age of m intervention town	nalaria-induced death in ships*	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 n	on-malarial febrile death	30	MIS data from 4,853 confirmed negative malaria			
in Myanmar			cases.			
DALYs incurred	No discount rate	33.00	Calculated as years of life lost - (DALY weight of			
non-malarial 3% discount rate fever death		21.07	non-malarial fever * 1 week of illness)			

*Data only available from intervention townships in the Mon state

Table 5.	Diagnostic	Test	Characteristics
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Subj	ject	Value	Source(s) and/or rationale		
RDT sensitivity	P. falciparum	100% (FR	Ref. 2: Foundation for Innovative New Diagnostics (FIND)		
and specificity	sensitivity	and SD)	WHO RDT data, at 200 parasites / μL.		
	P. falciparum	97% (FR			
	specificity	and SD)	SD = Standard Diagnostics Ag Pf Pv, Korea. Given		
	Pan	92%	during the first 2 months of the RDT pilot study.		
	plasmodium	(estimate)			
	sensitivity		FR = First response Pf Pan from Premier Medical		
		100%	Corporation, India. Given during the last 4 months of the		
		(SD)	RDT pilot study.		
		88% (FR)			
	Pan	98%			
	plasmodium	(Estimate)			
	specificity				

		95% (SD) 100% (ER)	
Clinical diagnostic result	Clinical positive diagnosis Clinical negative diagnosis	(FR) 0.50 0.50	The data used does not indicate whether the provider believes if the patient has malaria or not. Therefore, the corresponding prescription probabilities for clinical positive and negative diagnoses are the same. The values in this field do not affect 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 ACTs or
			antimalarials for alleged fever.

Su	bject		Source							
		No	Arm 1	Arm 2	Arm 3					
		intervention								
Diagnostic method										
Clinical diagnosis		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. ⁺				
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)	HH survey (weighted data, denominator only includes private informal provider types in study).				
			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: clients do not have malaria.				
	Other antimalarial	0.03 0.06 (MC 2012) 0.003 (HH) n=1	0.07 0.14 (MC 2013) 0.008 (HH) n=1	0.07 0.11 (MC 2013) 0.009 (HH) n=1	0.07 0.13 (MC 2013) 0.014 (HH) n=2	Value used: an average between 2013 mystery client and household				
	No antimalarial	0.92 0.24 (MC 2012) 0.992 (HH) n=383	0.81 0.753 (MC 2013) 0.992 (HH) n=119	0.81 0.879 (MC 2013) 0.991 (HH) n=107	0.74 0.625 (MC 2013) 0.986 (HH) n=139	survey data.				

Oliveration	AOT	0.05	0.40	0.40	0.40	,
Clinical -	ACT	0.05	0.12	0.12	0.19	
malaria		0.7 (MC 2012)	0.107 (MC	0.105 (MC	0.25 (MC	
		0 (HH) n=0	2013)	2013)	2013)	
			0.13 (HH)	[0.13] (HH)	[0.13] (HH)	
	Othor	0.02	n=16	n=0	n=0 0.07	
	Other	0.03	0.07	0.07		
	antimalarial	0.06 (MC	0.14 (MC	0.11(MC	0.13 (MC	
		2012)	2013)	2013)	2013)	
		0.003 (HH) n=1	0.008 (HH)	0.009 (HH)	0.014 (HH)	
	No	0.92	n=1 0.81	n=1 0.81	n=2 0.74	
	antimalarial					
	anumaianai	0.24 (MC 2012) 0.992 (HH)	0.753 (MC 2013)	0.879 (MC 2013)	0.625 (MC 2013)	
		n=383	0.992 (HH)	0.991 (HH)	0.986 (HH)	
		11=303	n=119	n=107	n=139	
RDT Pan	ACT	0.75 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	Prescriptions
+	ACT	0 (HH) n=0	0.857 (MC	0.972 (MC	0.978 (MC	for 'no
+ falciparum		0 (111) 11–0	2013)	2013)	2013)	intervention'
•			Correct	Correct	Correct	are informed by
+			treatment	treatment	treatment	the PSI SPH
			MC = 0.857	MC = 0.972	MC = 0.978	patient
			* 0.914 =	* 0.861 =	* 0.889 =	simulation
			0.78	0.84	0.87	assessment,
	Other	0.05 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	2011,
	antimalarial	0.50 (HH) n=1	0.05	0.05	0.05	estimated for
	No	0.2 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	arms 1-3.
	antimalarial	0.50 (HH) n=1	0.17	0.11	0.08	
RDT Pan	ACT	0.5	0.10	0.10	0.10	Qualitative
+		0.6 (SPH)	1.0 (HH	(HH n=0)	(HH n=0)	interviews
falciparum		1.0 (HH) n=2	n=1)			show that
-	Other	0.25	0.45	0.45	0.45	typically other
	antimalarial	0.2 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	antimalarials or
		(HH n=0)				antibiotics are
	No	0.25	0.45	0.45	0.45	given for vivax
	antimalarial	0.2 (SPH)	(HH n=0)	(HH n=0)	1.0 (HH) n	malaria.
		(HH n=0)			= 1	
RDT Pan -	ACT	0.75	(HH n=0)	(HH n=0)	(HH n=0)	Assuming
falciparum		(SPH)	0.857 (MC	0.972 (MC	0.978 (MC	same
+		0 (HH) n=0	2013)	2013)	2013)	prescriptive
			Correct	Correct	Correct	behavior as
			treatment	treatment	treatment	Pan +
			MC = 0.857	MC = 0.972	MC = 0.978	falciparum +,
			* 0.914 =	* 0.861 =	* 0.889 =	as qualitative
	Other		0.78	0.84	0.87	in-depth
	Other	0.05 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	interviews
	antimalarial	0.50 (HH) n=1	0.05	0.05	0.05	show that
	No	0.2 (SPH)	(HH n=0)	(HH n=0)	(HH n=0)	providers understand that
	antimalarial	0.50 (HH) n=1	0.17	0.11	0.08	
						falciparum +
						should be troated with
						treated with ACTs
RDT Pan -	ACT	0.4 (SPH)	0.057 (MC)	0.083 (MC)	0.022 (MC)	Results taken
falciparum		(HH n=0)	(HH n=0)	(HH n=0)	(HH n=0)	directly from
-	Other	0.02 (SPH)	0.029 (MC)	0.056 (MC)	0.089 (MC)	mystery client
	antimalarial	(HH n=0)	(HH n=0)	(HH n=0)	(HH n=0)	providers that
	No	0.58 (SPH)	0.914 (MC)	0.861 (MC)	0.889 (MC)	used RDTs.
	antimalarial	1.0 (HH n=8)	1.0 (HH n =	1.0 (HH n =	1.0 (HH n =	
	anumaianal	1.0 (11111=0)	1.0 (HH II = 4)	12)	13)	
		1		14)	13/	

* Numbers adjusted to be the same as no intervention due to small sample sizes

** 70% use of ACTs is an average value between the Mon and Shan state results from the 2012 mystery client survey. We scale the mystery client prescription of other antimalarials and no antimalarial (antibiotic and antipyretic) to a 70% ACT uptake.

*** Numbers adjusted to match arm 1 since no data available for arms 2 and 3

**** Lowered estimate of actual ACT use because the 2012 mystery client survey took place 4 months after ACTs were first introduced, possibly leading to temporary overuse.

RDT Costs

RDT commodity costs include the cost of subsidy and are separated as costs to the donor, provider and patient (Table 6). The RDT commodities used are: Standard Diagnostics (SD) Bioline Ag Pf Pv from Korea (used in the first 2 months of the intervention) and First Response, Premier Medical Corporation from India (used in the last 4 months of the intervention). The cost of RDT distribution across the supply chain is detailed in Table 7. Calculations for RDT costs are based on product markup costs between distribution stages, estimated to be: 3% from wholesale to retail, 20% from retail to distributor, and 100% from vendor to patient based on discussion with PSI program staff managers (Table 8). Estimates are indicated by red text while hard numbers are denoted by black text.

Perspective	No intervention	Arm 1	Arm 2	Arm 3
Societal*	\$1.16	\$0.68	\$0.80	\$0.68
Donor	\$0.00	\$0.36	\$0.48	\$0.36
Provider	\$0.48	\$0.11	\$0.09	\$0.11
Patient	\$1.16	\$0.32	\$0.32	\$0.32

Table 6. RDT costs from a societal perspective

*Societal = donor costs + patient costs.

Table 7. RDT	distribution acro	oss	the s	supply a	chain
				-	

Distribution stage	Delivery Cost	Comments
	(USD)	
Manufacturer to PSI	\$0.01 per unit	\$3,269 for 400,000 units. Accounted for in RDT unit
headquarters		costs.
PSI headquarters to project	\$61.77 per	Accounted for in recurrent program costs
office	month	
PSI project office to supply	N/A	For the pilot study, RDTs were transported in the
point		backpack of Jr. Health Service Officers.
Supply point to private provider	\$11.02 per	For the pilot study, resupply was done by both Product
	provider per	Promoters and providers. Stock audit data showed
	month	that 22 – 47% of RDTs sold were returned. Accounted
		for in provider travel costs and provider time costs.
Provider to patient	\$3.50 per	Patient travel estimates were not included in the
	patient	analysis (estimate from reference 19).

Table 8. RDT cost calculations across the supply chain

		Cost at Le		Source / triangulated data			
	Wholesale*		Retail	Vendor	Consu-		
	Cost per package	Shipping	Total			mer	
No interven- tion	\$0.47	\$0.01	\$0.48	\$0.48	\$0.58	\$1.16	Cost per RDT kit is \$0.41, cost per pair of gloves is \$0.06. Field staff estimated
Arms 1 or 3	\$0.47	\$0.01	\$0.48	\$0.12	\$0.18	\$0.32	consumer price \$1.10 Qualitative demographics: average price to providers, \$0.11, consumer price: \$0.30. MC survey: average cost of RDT was \$0.35
Arm 2**	\$0.56	\$0.01	\$0.57	\$0.09	\$0.15	\$0.32	

* Cost per packet includes cost per unit, packaging and labor.

** Arm 2 prices reflect that for every 5 RDTs purchased at retail, the donor has to provide 1 for free.

Drug Costs

Table 9 summarizes drug costs: when the cost of marketed drugs could not be obtained, we use wholesale drug prices to estimate the cost to the patient. Product markup costs between distribution stages are estimated to be: 3% from wholesale to retail, 20% from retail to distributor, and 67% from vendor to patient based on estimates from PSI program staff managers. Unsubsidized drugs are considered to be patient costs while the donor cost of subsidized ACTs is also calculated (Table 10).

Table 9. Drug Costs

Commodity	Patient Cost	Source
ACT	\$0.53	Table 10, Provider in-depth interview demographic data, Mystery Client Survey 2012, discussion with PSI Program manager
Quinine and chloroquine	\$0.55	Quinine and chloroquine prices based on in-depth interview demographics and mystery client survey. No prices given for chloroquine, quinine costs \$1.65. Mystery clients paid between \$0.22 to \$1.76. The mode in the mystery client was \$0.55
Antibiotics ⁺	\$0.93	Table 11: antibiotic prices based on wholesale costs from PSI social franchising account records
Antipyretics	\$0.44	Personal purchase of 8 paracetemol tablets in the Shan state.
Cost of "no antimalarial" calculation	\$0.58	Table 11: calculated according to 70% administration of antipyretics and 30% of antibiotics

Subsidized ACTs are sold as four products: Supa Arte 1, 2, 3 and 4. The Supa Arte products, marketed from Ipca laboratories limited in India, contain various doses of artemether and lumefantrine targeting different age ranges. We scaled the percentage of use for each Supa Arte product according to the percentage of individuals within each age range that were tested for malaria in the Mon state from July to October, 2012 to obtain a weighted average cost of an ACT (Table 10). The exchange rate used is the rate at the time of purchase: 845.94 Kyat/dollar.

Table 10. Calculation of average Supa Arte cost to intervention patients

Supa Arte Product	Age range	# of tablets*	Wholesale price (USD)	Percentage of malaria patients in age range **	Weighted costs per patient on average
1	N/A	N/A	\$0.53	6.3%	\$0.03
2	N/A	N/A	\$0.95	22.2%	\$0.21
3	N/A	N/A	\$1.36	16.8%	\$0.23
4	N/A	N/A	\$1.70	54.7%	\$0.93
Total		<u> </u>			\$1.40

* Each tablet contains 20 mg of artemether and 120 mg of lumefantrine.

** Based on percentage of RDTs used by SPH providers in the Mon State from July-October, 2012.

To obtain societal drug costs, consumer or unit costs were obtained where available. Markup rates throughout distribution were used to estimate societal costs (Table 11). Wholesale costs include the cost of commodity, packaging materials, and packaging labor. All costs up to the retail level are donor costs, while costs to vendors and customers are at the provider and patient costs, respectively.

Commodity		Cost at Lev	el of Di	stributio	n (USD)		Source / triangulated data
	Wholesale			Retail	Ven-	Consu-	
	Cost per unit	Packaging and labor	Total	*	dor	mer	
ACT	N/A	N/A	\$1.40	\$0.28	\$0.31	\$0.52	Qualitative demographics: Vendor cost, \$0.31 consumer price \$0.52. MC survey, \$0.53 average consumer price (range 0 - \$1.10).
Other anti- malarials	N/A	N/A	\$0.25	\$0.26	\$0.32	\$0.63	\$1.65. MC survey avg \$0.63, range \$0.22 to \$1.76
Antibiotics ⁺	\$0.37	\$0.08	\$0.45	\$0.46	\$0.56	\$0.93	PSI social franchising account records
Antipyretics	N/A	N/A	\$0.21	\$0.22	\$0.26	\$0.44	Purchase of 8 paracetemol tablets in the Shan state
No anti- malarial			\$0.28	\$0.29	\$0.35	\$0.58	Assumed 70% antipyretics, 30% antibiotics

Table 11. Commodity costs across the supply chain

* ACTs are subsidized

⁺ Averaged between pneumox 125 and pneumox 250 amoxicillin products.

Patient and provider time and travel costs

Table 12 describes annual patient and provider time and travel costs. Travel costs are detailed in table 13 (patient travel not included in this analysis, estimated to be \$504,000 annually). Time costs are detailed in table 14. Provider time is counted as a time cost because the provider is a client of the program.

Table 12. Provider time and travel costs for RDT intervention (annu	Jal)
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Costs for RDT intervention, 600 providers	Fi	irst year red	Comments		
	No intervention	Arm 1	Arm 2	Arm 3	
Patient and provider time costs	\$0	\$53,366	\$53,366	\$64,498	Time spent administering RDT, visiting supply point
Provider travel costs	\$0	\$79,344	\$79,344	\$79,344	Monthly travel cost per provider to reach supply point estimated to be \$11.02 per provider per month

Table 13. Patient and provider travel costs

Commodity	Patient Cost	Source
Patient travel	\$3.50 per patient per visit, not	Travel cost: reference 21: cost study from Taikkyi
time	included in analysis	township Myanmar, 2004.
Provider travel	\$11.02 per provider per	Estimated by PSI program staff members, assuming
to the supply	month. Scaled to 600	providers visit supply points once a month.
point	providers: \$79,334 annually	

Table 14. Patient and provider time costs

	Monthly income (USD)	RDT time cost*	Additional costs	Source / triangulated data
Provider	\$138.04	\$0.29	Time cost for provider visits** Arms 1 and 2: \$0.32 per provider per month. \$192 for 600 providers. Arm 3: \$1.29 per provider per month. \$774 for 600 providers per month. \$6.90 per provider = \$4,140 for 600 providers	In-depth interview demographics provide provider monthly salary. The range was between \$22.05 and \$330.76. Reference 40 estimates \$200/month salary. Product promoters estimated each support visit is 30-60 minutes. Monthly visit to supply points: assuming 1 day per visit.
Patient	\$92.00	\$0.19	· · ·	Assuming patient makes 2/3 of what a provider makes.

*Assuming each RDT takes 20 minutes to conduct and each provider works 40 hours per week. ** Provider visit time estimated to be 45 minutes per visit.

6. One-way sensitivity analysis

Table 15. One-way sensitivity analysis for parameters that affect cost

Parameter description							
	low, high	high	change in costs	in costs per 1,000 people	justification		
Arm 1 program costs per febrile individual (base case \$3.61)	2, 10	\$393,041, \$1,545,041	\$1,152,00 0	\$8,000	Estimated from half of current range to 2.5x		
Arm 2 program costs per febrile individual (base case \$3.61)	2, 10	\$393,469, \$1,545,469	\$1,152,00 0	\$8,000	more		
Arm 3 Program Costs per febrile individual (base case \$4.23)	2, 10	\$412,656 , \$1,564,656	\$1,152,00 0	\$8,000			
Probability of using RDT for Arm 2 (base case 0.02)	0, 0.65	\$622,580 , \$744,847	\$122,267	\$849	From below base case to mystery client levels (0.64)		
Number of febrile patients seeking care per private sector provider per month, No intervention (base case 20)	1, 40	\$4,850, \$858,996	\$854,146	\$5,932	Based on discussion with PSI Myanmar employees		
Probability of using RDT for Arm 1 (base case 0.02)	0, 0.65	\$622,152 , \$730,487	\$108,335	\$752	From below base case to mystery client levels (0.64)		
Probability of using RDT for Arm 3 (base case 0.08)	0.02, 0.65	\$725,217, \$821,005	\$95,788	\$665			
Cost of no antimalarial (same across all arms), No intervention (base case 0.58)	0.3, 1	\$60,212, \$152,172	\$91,960	\$639	From cost of 5 paracetemol tables (\$0.30) to above antibiotic (\$0.93)		
Probability of no antimalarial administration for clinical diagnosis, arm 2 ^{**} (base case 0.81)	0.5, 0.93	\$673,152 , \$608,222	\$64,929	\$451	From below mystery client survey levels (0.63) to		
Probability of no antimalarial administration for clinical diagnosis, arm 1 ^{**} (base case 0.81)	0.5, 0.93	\$672,295 , \$607,366	\$64,929	\$451	household survey levels (0.99, but fixed variable** makes 0.93		
Probability of no antimalarial administration for clinical diagnosis, arm 3 ^{**} (base case 0.74)	0.5, 0.93	\$768,360 , \$707,406	\$60,954	\$423	maximum possible value for analysis)		
Probability of ACT administration for clinical diagnosis, no intervention** (base case 0.19)	0.05, 0.4	\$614,916 , \$667,765	\$52,849	\$367	Wide estimate including household survey (0.13) and mystery client (0.25) with small samples		
Cost of ACT (same across all arms), arm 3 (base case \$1.65)	0.5, 2.5	\$704,153 , \$756,651	\$52,498	\$365	Commodity base cost (\$0.53) to cost without subsidy (\$2.50)		
Probability of using RDT for No Intervention (base case 0.02)	0.02, 0.11	\$96,996 , \$123,553	\$26,557	\$184	Household survey (0.02) to mystery client (0.11)		

Cost of other antimalarial (same across all arms), arm 1 (base case	0.18, 1.65	\$730,476 , \$745,824	\$15,348	\$107	Minimum cost to mystery clients
\$0.55)					(\$0.22) to ACT societal cost (\$1.65)
Cost of RDT, arm 3 (base case \$0.68)	0.36, 1.2	\$730,653, \$740,330	\$9,677	\$67	Donor cost (\$0.36) to societal cost without subsidy (\$1.16)
RDT time cost (same across all arms), arm 3 (base case \$0.29)	0.18, 0.75	\$730,883, \$737,450	\$6,566	\$46	Estimate
Probability of ACT administration for pan -, falc – test result, arm 3** (base case 0.022)	0.02, 0.4	\$734,318, \$738,424	\$4,107	\$29	Mystery client (0.02) to no intervention SPH survey (0.4)
Cost of RDT no intervention, arm 3 (base case \$1.16)	0.36, 1.2	\$94,692, \$97,111	\$2,419	\$17	Donor cost (\$0.36) to societal cost
Cost of RDT arm 1 (base case \$0.68)	0.36, 1.2	\$624,564, \$626,983	\$2,419	\$17	without subsidy (\$1.16)
Cost of RDT arm 2 (base case \$0.80)	0.36, 1.2	\$625,075, \$627,494	\$2,419	\$17	
Probability of ACT administration for pan -, falc – test result, arm 2** (base case 0.083)	0.02, 0.4	\$626,172, \$627,199	\$1,027	\$7	Mystery client (0.02) to no intervention SPH
Probability of ACT administration for pan -, falc – test result, arm 1** (base case 0.057)	0.02, 0.4	\$625,386, \$626,412	\$1,027	\$7	survey (0.4)
Specificity of P. falciparum RDT arm 3 (base case 0.97)	0.92, 0.98	\$734,834, \$734,240	\$593	\$4	Estimate within referenced ranges for other brands
Probability of ACT administration for pan +, falc – test result, arm 3** (base case 0.1)	0.1, 0.5	\$734,339, \$734,551	\$211	\$1	Household survey (0.1) to SPH survey for no intervention (0.6)
Probability of other antimalarial administration for pan +, falc – test result, arm 3** (base case 0.45)	0.25, 0.45	\$734,448, \$734,312	\$136	\$1	No intervention (0.25) to present value (0.45)
Percentage of febrile illnesses that are malaria, no intervention (base case 8%)	0.03, 0.2	\$96,958, \$97,087	\$130	\$1	Wide range estimate
Probability of ACT administration for pan +, falc + test result, arm 3** (base case 0.87)	0.75, 0.9	\$734,267, \$734,358	\$91	\$1	No intervention (0.75) to above present value
Probability of ACT administration for pan -, falc + test result, arm 3** (base case 0.87)	0.75, 0.9	\$734,293, \$734,351	\$58	\$0	
Probability of ACT administration for pan +, falc – test result, arm 2** (base case 0.1)	0.1, 0.5	\$626,342, \$626,395	\$53	\$0	Present value to result in no intervention (0.5)
Probability of ACT administration, pan +, falc – test result, arm 1** (base case 0.1)	0.1, 0.5	\$625,486, \$625,538	\$53	\$0	
Specificity of pan plasmodium RDT (base case 0.98)	0.95, 1	\$734,362, \$734,324	\$37	\$0	Range of reported specificity for the two commodities used for intervention

Probability of other antimalarial	0.25,	\$625,513,	\$34	\$0	No intervention
administration for pan +, falc – test	0.5	\$625,479			value (0.25) to
result, arm 1*** (base case 0.45)					above present
Probability of other antimalarial	0.25,	\$626,369,	\$34	\$0	value
administration arm 2*** (base case	0.5	\$626,335			
0.45)					
Sensitivity of P. falciparum RDT	0.95,	\$734,314,	\$25	\$0	Estimate within
arm 3 (base case 1)	1	\$734,339			range of reported
					sensitivity for other
					brands
Percentage of falciparum vs vivax	0.3,	\$96,974,	\$25	\$0	Wide estimate to
malaria arm 3 (base case 65%)	0.7	\$96,999			account for
					changing
					epidemiology
					given targeting of
					falciparum malaria
					in Myanmar
Probability of other antimalarial	0.02,	\$734,360,	\$24	\$0	No intervention
administration for pan -, falc - test	0.1	\$734,336			(0.02) to above
result, arm 3* (base case 0.089)					present value
Probability of ACT administration	0.75,	\$625,481,	\$23	\$0	No intervention
for pan +, falc + test result, arm 1**	0.9	\$625,504			(0.75) to above
(base case 0.78)					arm 3 value (0.87)
Probability of ACT administration	0.75	\$626,329,	\$23	\$0	
for pan +, falc + test result, arm 2^{**}	0.9	\$626,351			
(base case 0.84)		* ***	.		
Probability of ACT administration	0.75,	\$625,483,	\$14	\$0	
for pan -, falc + test result, arm 1**	0.9	\$625,497			
(base case 0.78)	0.75	¢000.004	¢ 4.4	¢0	
Probability of ACT administration	0.75,	\$626,334,	\$14	\$0	No intervention
for pan -, falc + test result, arm 2**	0.9	\$626,348			(0.02) to above
(base case 0.84) Probability of other antimalarial	0.02,	\$626,345,	\$6	\$0	arm 3 value (0.09) No intervention
administration for pan -, falc – test	0.02,	\$626,339 \$626,339	φO	φU	(0.02) to above
result, arm 2* (base case 0.056)	0.1	φ020,339			present value
Probability of other antimalarial	0.02,	\$625,486,	\$6	\$0	
administration for pan -, falc – test	0.02,	\$625,480	ΨΟ	Ψ	
result, arm 1* (base case 0.03)	0.1	ψυ20,400			
Sensitivity of Pan Plasmodium	0.85,	\$734,338,	\$3	\$0	Estimate within
RDT (base case 0.92)	0.00,	\$734,341	ΨŪ	ΨŪ	range of reported
		φ, ο ι, ο τ ι			sensitivity for other
					brands
Probability of other antimalarial	0.05,	\$734,339,	\$1	\$0	From base case
administration fo pan +, falc + test	0.13	\$734,338	.	T -	(0.05) to highest
result, arm 3* (base case 0.05)		,			possible value
Probability of other antimalarial	0.05,	\$734,339,	\$1	\$0	with ACT kept
administration for pan -, falc + test	0.13	\$734,338	*		constant*
result, arm 3* (base case 0.05)	-	. ,			
Probability of other antimalarial	0.05,	\$625,486,	\$1	\$0	
administration for pan +, falc + test	0.2	\$625,485			
result, arm 1* (base case 0.05)		. ,			
* Holding ACT constant	1	1	1	1	

 * Holding ACT constant
** Holding other antimalarial constant
*** Holding no antimalarial constant
Note: intervention arm shown is the one that affects costs the most when cost changes are similar across arms.

Table 16. One-way sensitivity analysis on parameters that affect health outcomes

Parameter description	Input Iow, high	DALY low, high	Abs. change in DALYS	Change in DALYs per 1000 people	Range justification
Probability of death for nonmalarial fever given no antimalarial, no intervention (base case 0.0016)	0.001, 0.05	8,626, 133,491	124,865	867	From below base case to high virulence (more
Probability of death for nonmalarial fever given ACT (base case 0.002)	0.001, 0.05	8,659, 33,101	24,442	170	than untreated P. falciparum, 0.03)
Number of febrile patients seeking care per private sector per month (base case 20)	1, 40	508, 20,310	19,802	138	Based on discussion with PSI Myanmar employees
Percentage of febrile illnesses that are malaria (base case 8%)	0.03, 0.2	6,931, 17,893	10,962	76	Wide range estimate
Probability of death for nonmalarial fever given other antimalarial (base case 0.002)	0.001, 0.05	8,957, 18,803	9,846	68	From below base case to high virulence (more than untreated P. falciparum, 0.03)
Discount rate, arm 3 (base case 3%)	0, 0.05	16,408, 7,801	8,607	60	From none to highest discount rate typically published
Probability of death for falciparum malaria given no antimalarial, no intervention (base case 0.03)	0.005, 0.04	6,286, 11,702	5,416	38	Wide range estimate to capture low to high virulence
Life expectancy in Myanmar, no intervention (base case 62)	50, 80	7,846, 12,392	4,546	32	Wide range estimate to capture potential future development
Age of malaria death, no intervention (base case 30)	5, 45	11,342, 7,866	3,476	24	Wide range estimate
Probability of using RDT for Arm 2 (base case 0.02)	0, 0.65	9,777, 7,227	2,549	18	From below base case to mystery client levels (0.64)
Probability of using RDT for Arm 1 (base case 0.02)	0, 0.65	9,777, 7,378	2,399	17	
Probability of using RDT for Arm 3 (base case 0.08)	0.02, 0.65	9,386, 6,992	2,394	17	
Percentage of <i>P. falciparum</i> vs <i>P. vivax</i> malaria, no intervention (base case 65%)	0.3, 0.7	8,473, 10,395	1,922	13	Wide estimate to account for changing epidemiology given targeting of falciparum malaria in Myanmar
Probability of no antimalarial administration with clinical diagnosis, arm 1** (base case 0.81)	0.5, 0.93	8,337, 10,232	1,895	13	From below mystery client survey levels (0.63)
Probability of no antimalarial administration with clinical diagnosis, arm 2** (base case 0.81)	0.5, 0.93	8,332, 10,227	1,895	13	to household survey levels (0.99, but fixed variable**
Probability of no antimalarial administration with clinical	0.5, 0.93	8,165, 9,944	1,779	12	makes 0.93 maximum possible

diagnosis, arm 3** (base case 0.74)					value for analysis)
Probability of death for falciparum malaria given ACT, arm 3 (base case 0.0001)	0.0001, 0.04	9,158, 10,825	1,667	12	Wide range to account for potential worst case scenarios of complete drug resistance
Probability of death for vivax malaria given no antimalarial, no intervention (base case 0.01)	0.001, 0.02	9,404, 10,990	1,586	11	Wide range estimate to capture fatality probabilities for P. vivax malaria
Probability of ACT administration for clinical diagnosis, no intervention*** (base case 0.19)	0.05, 0.4	10,011, 8,469	1,542	11	Wide estimate including household survey (0.13) and mystery client (0.25) with small samples
Probability of death for falciparum malaria given other antimalarial, arm 2 (base case 0.007)	0.005, 0.04	9,675, 10,091	416	3	Wide range to account for potential drug resistance
Probability of using RDT for No Intervention (base case 0.02)	0.02, 0.11	10,155, 9,823	332	2	Household survey (0.02) to mystery client (0.11)
Weeks of febrile illness for nonimmediate recovery, arm 3 (base case 1)	0.5, 2	9,094, 9,287	193	1	Based on conversation with PSI Myanmar employees
DALY weight of nonmalarial fever, arm 3 (base case 0.18)	0.05, 0.4	9,087, 9,277	190	1	Wide range estimate to capture a range of virulence for nonmalarial fevers
Probability of death for vivax malaria given ACT, arm 3 (base case 0.0001)	0.0001, 0.01	9,158, 9,326	168	1	Wide estimate to account for potential drug
Probability of death for vivax malaria given other antimalarial, arm 3 (base case 0.0001)	0.0001, 0.01	9,150, 9,238	89	1	resistance
Probability of ACT administration, Pan + falc + test result, arm 3** (base case 0.87)	0.75, 0.9	9,204, 9,147	57	0	No intervention (0.25) to above present value
Probability of ACT administration, Pan – falc – test result, arm 3** (base case 0.022)	0.02, 0.4	9,158, 9,201	43	0	Mystery client (0.02) to no intervention SPH survey (0.4)
Probability of ACT administration, Pan + falc – test result, arm 3** (base case 0.1)	0.1, 0.5	9,158, 9,133	25	0	Household survey (0.1) to near SPH survey for no intervention (0.6)
Probability of other antimalarial administration, Pan + falc + test result, arm 3* (base case 0.05)	0.05, 0.13	9,158, 9,135	23	0	From base case (0.05) to highest possible value with ACT kept constant*
Probability of ACT administration Pan + falc + test result, arm 1** (base case 0.78)	0.75, 0.9	9,706, 9,692	14	0	No intervention (0.75) to above arm 3 value (0.87)

Drobobility of ACT administration	0.75	0 707	14	0	
Probability of ACT administration Pan + falc + test result, arm 2**	0.75, 0.9	9,707, 9,693	14	U	
(base case)	0.9	9,095			
Probability of other antimalarial	0.05,	9,703,	11	0	From base case
administration Pan + falc + test	0.03,	9,692		U	(0.05) to highest
result, arm 1* (base case 0.05)	0.2	0,002			possible value with
					ACT kept constant*
Probability of ACT administration	0.02,	9,697,	11	0	Mystery client
Pan – falc – test result, arm 2 (base	0.4	9,707		•	(0.02) to no
case 0.083)**	0.1	0,101			intervention SPH
Probability of ACT administration	0.02,	9,702,	11	0	survey (0.4)
Pan – falc – test result, arm 1**	0.4	9,713		•	
(base case)	••••	0,110			
Sensitivity of P. falciparum RDT,	0.95,	9,168,	10	0	Estimate within
arm 3 (base case 1)	1	9,158	-		range of reported
		,			sensitivity for other
					brands
Probability of other antimalarial	0.02,	9,150,	9	0	No intervention
administration, Pan – falc – test	0.1	9,159			(0.02) to above
result, arm 3* (base case 0.089)					present value
Probability of other antimalarial	0.05,	9,698,	7	0	From base case
administration Pan + falc + test	0.15	9,691			(0.05) to highest
result, arm 2* (base case 0.05)					possible value while
					keeping
					ACTconstant*
Probability of ACT administration	0.1,	9,703,	6	0	Present value to
Pan + falc – test result, arm 1**	0.5	9,697			result in no
(base case 0.1)					intervention (0.5)
Probability of ACT administration,	0.1,	9,698,	6	0	
Pan + falc – test result, arm 2**	0.5	9,692			
(base case 0.1)					
Probability of ACT administration	0.75,	9,162,	4	0	No intervention
Pan – falc + test result, arm 3**	0.9	9,157			(0.75) to above
(base case 0.87)					present value
Sensitivity of Pan Plasmodium RDT,	0.85,	9,160,	4	0	Estimate within
arm 3 (base case 0.92)	1	9,156			range of reported
					sensitivity for other
					brands
Specificity of P. falciparum RDT,	0.92,	9,161,	4	0	Estimate within
arm 3 (base case 0.97)	0.98	9,157			referenced ranges
		0.455			for other brands
Specificity of pan plasmodium RDT,	0.95,	9,160,	3	0	Range of reported
arm 3 (base case 0.98)	1	9,157			specificity for the
					two commodities
					used for
					interventino

* Holding ACT constant ** Holding other antimalarial constant *** Holding no antimalarial constant Note: intervention arm shown is the one that affects DALYs the most when DALY changes are similar across arms.

7. Results beyond first year of intervention

Results presented in the main text of the paper focus on the first year of the intervention. For recurrent years, costs are lower as staff will not need new training, community outreach will not be performed, and less providers will have to be recruited. Costs for the first year and subsequent years is shown in the tables below.

Scenario (societal)		Total cost	-	Drug and RDT costs (scaled to uptake)		Patient and provider	Provide r travel costs ⁺⁺
			Total	(RDT Donor only)	commodity costs	time costs	
No interventio	n	\$96,996	\$95,614	\$0	\$0	\$1,382	\$0
Arm 1: simple	First year cost	\$625,486	\$103,658	\$1,037	\$387,735	\$54,748	\$79,344
subsidy	Recurrent annual cost	\$566,152	\$103,658	\$1,037	\$328,401	\$54,748	\$79,344
Arm 2: subsidy with	First year cost	\$626,342	\$104,087	\$1,382	\$388,163	\$54,748	\$79,344
financial incentives	Recurrent annual cost	\$567,008	\$104,087	\$1,382	\$328,829	\$54,748	\$79,344
Arm 3: subsidy with	First year cost	\$734,339	\$119,127	\$4,147	\$476,973	\$58,896	\$79,344
IEC	Recurrent annual cost	\$675,005	\$119,127	\$4,147	\$417,639	\$58,896	\$79,344

Table 17. Annual commodities, programmatic expenses, time and travel cost

*Includes time spent conducting RDT, and provider time for monthly supply point visit based on wages, as providers were not compensated by the programme. **Patient travel costs were excluded and the same across each arm, estimated to be \$504,000 per arm.

Table 18. Cost-effectiveness ratios from a societal perspective

Subsidy	Total	Added	Total	DALYs	Incremental	Cost per			
scheme	costs	costs vs	DALYs	averted	cost per DALY	DALY averted			
		prior	<u>incurred</u>	<i>vs</i> prior	averted vs	vs no			
		strategy		strategy	prior strategy	intervention			
	Year 1								
No intervention	\$96,996		10,155						
Arm 1: Simple subsidy	\$625,486	\$528,490	9,703	452	\$1,169	\$1,169			
Arm 2: Subsidy with financial incentive	\$626,342	\$857	9,698	5	\$185	\$1,159			
Arm 3: Subsidy with IEC	\$734,339	\$107,997	9,158	540	\$200	\$639			
		Y	ear 2 and aft	ter					
No intervention	\$96,996		10,155						
Arm 1: Simple subsidy	\$566,152	\$469,156	9,703	452	\$1,038	\$1,038			
Arm 2: Subsidy with financial incentive	\$567,008	\$857	9,698	5	\$185	\$1,029			
Arm 3: Subsidy with IEC	\$675,005	\$107,997	9,158	540	\$200	\$580			

*PSI operational costs. Exchange rate used: 907 Kyat/USD, 1 May 2013.

8. Supporting information references:

- Give Well: Containment of artemisinin resistance in eastern Myanmar (PSI Myanmar project) <u>http://www.givewell.org/PSI-Myanmar-Artemisinin-Resistance-Containment</u> (accessed July 13, 2013).
- 2. Foundation of Innovative New Diagnostics, <u>http://www.finddiagnostics.org/resource-</u> <u>centre/reports_brochures/malaria-diagnostic-test-report.html</u> (Accessed February 7, 2013).
- Zhou M., Liu Q., Wongsrichanalai C., Suwonkerd W., Panart K., Prajakwong S., Pensiri A., Kimura M., Matsuoaka H., Ferreira M.U., Isomura S., Kawamoto F. High prevalence of *Plasmodium malariae* and *Plasmodium ovale* in malaria patients along the Thai-Myanmar border, as revealed by acridine orange staining and PCR-based diagnoses. *Tropical Medicine and International Health* 1998, **3**: 304-312.
- Takeuchi R., Lawpoolsri S., Imwong W., Kobayashi J., Kaewkungwal J., Pukrittayakamee S., Puangsa-art S., Thanyavanich N., Maneeboonyang W., Day N. P. J., Singhasivanon P. Directly-observed therapy (DOT) for the radical 13-day primaquine treatment of *Plasmodium vivax* malaria at the Thai-Myanmar border. *Malaria Journal* 2010, **9**:308.
- 5. Lwin, M. M., Sudhinaraset, M., San, A. K., Aung, T. Improving malaria knowledge and practices in rural Myanmar through a village health worker intervention: a cross-sectional study. *Malaria Journal* 2014, **13**:5.
- Oanda currency converter. <u>http://www.oanda.com/currency/converter/</u> (accessed July 13, 2013).
- 7. WHO SEARO 2006. <u>http://www.who.int/malaria/publications/country-profiles/2008/mal2008-myanmar-en.pdf</u> (Accessed December 8, 2012).
- Myint, H.Y., Adjuik, M., Olliaro, P., Pukrittayakamee, S., Looareesuwan, S., Hien, T.T., Farrar, J., Nosten, F., Day, N.P., White, N.J. In vivo assessment of drug efficacy against Plasmodium falciparum malaria: duration of follow-up. Antimicrobial Agents and Chemotherapy 2004, 48:4271-80.
- 9. Ohnmar, Tun-Min, May-Aye-Than, San-Shwe, Wai-Wai-Mying, Chongsuvivatwong, V. Access to a blood test and antimalarials after introducing rapid diagnostic tests in rural Myanmar: initial experience in a malaria endemic area. *International Health* 2010, **2**:275-281.
- Richards A. K., Banek K., Mullany L. C., Lee C. I., Smith L., Eh Kalu Shwe Oo, Lee, T. J. Cross-border malaria control for internally displaced persons: observational results from a pilot programme in eastern Burma/Myanmar. *Tropical Medicine and International Health* 2009, **14**:512-521.
- 11. Price, R.N., Douglas, N.M., Anstey, N.M. New developments in Plasmodium vivax malaria: severe disease and the rise of chloroquine resistance. Current Opinion in Infectious Disease 2009, 5:430-5.
- 12. Tijtra E., Anstey N.M., Sugiarto P., Warikar N., Kenangalem E., Karyana M., Lampah D. A., Price, R. N. Multidrug-resistant *Plasmodium vivax* associated with severe and fatal malaria: a prospective study in Papua, Indonesia. *Plos Medicine* 2008, **5**: e128.
- 13. Ohnmar, Tun-Min, San-Shwe, Than-Win, Chongsuvivatwong, V. Effects of malaria volunteer training on coverage and timeliness of diagnosis: a cluster randomized controlled trial in Myanmar. *Malaria Journal* 2012, **11**:309.
- 14. WHO Global Burden of Disease Death Estimates 2008 <u>http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html</u> (Accessed February 10, 2013).
- Mayxay M., Castonguay-Vanier J., Chansamouth V., Dubot-Pérès A., Paris D. H., Phetsouvanh, Tangkhabuanbutra J., Douangdala P., Inthalath S., Souvannasing P., Slesak G., Tongyoo N., Chanthongthip A., Panyanouvong P., Sibounheuang B., Phommasone K., Dohnt M., Phonekeo D., Hongvantong B., Xayadeth S., Ketmayoon P., Blacksell S. D., Moore C. E., Craig S. B., Burns M., Sonnenburg F., Corwin A., Lamballerie X., González I. J., Christophel E. M., Cawthorne A., Bell D., Newton P. N. Causes of non-malarial fever in Laos: a prospective study. *The Lancet* 2013, **1**:e46-54.

- 16. Ejov M. N., TUn T., Aung S., Lwi S., Sein K. Hospital-based study of severe malaria and associated deaths in Myanmar. *Bulletin of the World Health Organization* 1999, **77**: 4.
- 17. Lopez A.D., Mathers C.D.. Measuring the global burden of disease and epidemiological transition: 2002-2030. *Annals of Tropical Medicine and Parasitology*, 2006, **100**:481-499.
- Murray, C.J.L., Lopez A. D., Black, R., Mathers, C. D., Shibuya, K., Ezzati, M., Salomon, J. A., Michaud, C. M., Walker, N., Vos, T. Global burden of disease 2005: call for collaborators. *The Lancet* 2007, **370**:109-110.
- 19. The World Bank Myanmar. <u>http://data.worldbank.org/country/myanmar</u> (Accessed July 19, 2013).
- Salomon, J. A., Wang, H., Freeman, M. K., Vos, T., Flaxman, A. D., Lopez, A. D., & Murray, C. J. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden Disease Study. *The Lancet*, 2013, **380**:2144-2162.
- Wang, H., Dwyer-Lindgren, L., Lofgren, K. T., Rajaratnam, J. K., Marcus, J. R., Levin-Rector, A., Murray, C. J. et al. Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2013, **380**:2071-2094.
- 22. Cho-Min-Naing, Gatton M. L. Costs to the patient for seeking malaria care in Myanmar. *Acta Tropica* 2004, **92**:173-177.