Market interventions to improve access to quality medicines and diagnostics:
Generating evidence for malaria medicine policy in the Asia-Pacific region

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March 2014
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Contents

1. Problem statement .................................................................................................................. 3
2. Generating evidence for market intervention policy .............................................................. 4
3. Monitoring market interventions in the Asia-Pacific region ................................................ 5
   3.1 Case Study: Cambodia ..................................................................................................... 5
   3.2 Case Study: Myanmar ...................................................................................................... 9
4. Conclusion .............................................................................................................................. 12
5. References ............................................................................................................................ 14
1. Problem statement

Several countries in the Asia-Pacific region are making progress towards the elimination of malaria, while countries with higher disease burdens prepare to transition from control to elimination-focused strategies. However, the emergence of malaria parasites resistant to artemisinin (the most effective treatment for \textit{Plasmodium falciparum}) in the Greater Mekong Sub-region (GMS) threatens to undermine regional and global progress. The complete elimination of \textit{Plasmodium falciparum} \textit{(P.f)} within the GMS is widely viewed as the only long-term containment solution, and one that is urgently needed to protect the gains made to date. Improved access to quality medicines and diagnostics (and displacement of sub-standard drugs) among at-risk communities is key in this regard.

Despite significant public sector driven gains in recent years (particularly in Tier One resistance containment zones in the GMS and some Asia Pacific Malaria Elimination Network states), access to and utilization of quality malaria medicines and diagnostics within the region remains inadequate (particularly in the private sector where a significant number of people still seek care). It has been suggested that the primary driver of this apparent market failure in the private sector is the way that malaria medicines are financed. As stated by Alphs and Yadav, “...most money comes directly from the individual users at point-of-sale. This financing model favours those [companies] producing cheap (often sub-standard) products. Equally, high quality manufacturers may be discouraged from entering the market.”

The behavior of individual consumers at the point-of-sale is largely governed by availability (of products, services and providers), price and opportunity costs of products and services, and the perceived quality and flexibility of care. In effect, remote rural communities, at most risk of malaria and with the least access to public services, unwittingly fuel a model of which they then become victims; they are forced to simply buy what they can readily access and realistically afford, including partial courses of oral artemisinin monotherapy (oAMT).

A few countries in the region continue to manufacture and export significant quantities of oAMT, suggesting persistent demand and a lack of regulatory control. It is widely acknowledged that oAMT is a serious driver of drug resistance that undermines the economic and health gains associated with the deployment of more expensive Artemisinin-based Combination Therapy (ACT). At present, it is unclear just how widespread oAMT is relative to ACT within the Asia-Pacific region as information on antimalarial commodity markets has, at best, been fragmented and inconsistent.
The lack of reliable, strategic information is a critical gap in current programming within the Asia-Pacific region. Monitoring progress towards the regional malaria elimination goal requires a solid understanding of antimalarial and diagnostic commodity markets (for both *P. vivax* and *P. falciparum* treatment). Without this, policy makers, donors and governments are faced with a significant and dangerous information gap when trying to determine how to improve access to quality commodities, reduce availability and use of oAMT, and monitor market evolution and potential.

Standardized monitoring, for key market indicators, is therefore needed to inform policy, resource allocation, and intervention design for regional malaria elimination efforts. Specifically, this standardized monitoring is needed to:

1. **Provide a regional picture of the total market for malaria products and services** in high priority countries and among key populations, including: all providers carrying commodities and delivering services; the relative market share for each provider type; the supply chain for key malaria-related commodities; and price mark-ups within the supply chain for these commodities.

2. **Monitor the readiness of market components for addressing malaria elimination** within priority countries and resistance containment zones and among key populations, including: availability of key malaria-related commodities and services; consumer price of key malaria commodities and services; and provider qualifications, training and knowledge.

3. **Monitor the performance of market components for addressing malaria elimination** within priority countries and resistance containment zones and among key populations, including: the relative market share for oral artemisinin monotherapy and quality assured artemisinin-based combination therapy; the demand for health services captured through consumer knowledge, attitudes, and health seeking behavior; and the quality of provider service delivery measured against national policies, guidelines and minimum standards.

### 2. Generating evidence for market intervention policy

In 2008, *ACTwatch* (a collaboration between the Bill & Melinda Gates Foundation, London School of Hygiene & Tropical Medicine and Population Services International) was launched that aimed to provide a comprehensive picture of national antimalarial markets and to track key market indicators over time, such as antimalarial (including rapid diagnostic tests) availability, price and market share. *ACTwatch* initially covered Cambodia, Benin, the Democratic Republic of Congo,
Madagascar, Nigeria, Uganda, and Zambia. As evidenced by initial project country selection, market monitoring focused primarily on sub-Saharan African countries with high malaria burden. In these high-burden contexts, ACTwatch has been monitoring antimalarial markets in the context of policy shifts and investments in the scale-up of first-line ACT and malaria rapid diagnostic tests (RDTs). Initial supply chain, outlet and population-based surveys were conducted to provide a comprehensive picture of the total market as well as baseline information on market readiness and performance. Subsequent outlet and population-based surveys and quality of care studies have been implemented to provide trend data in the context of policy, resource allocation, and intervention deployment to reduce morbidity and mortality.

ACTwatch has now become the gold standard source of evidence for policymakers and funders concerned with the health and structure of antimalarial markets. ACTwatch evidence is routinely presented at key malaria fora such as ASTMH (American Society of Tropical Medicine and Hygiene). Perhaps most significantly, ACTwatch methods provided the foundation for the evaluation of the Affordable Medicines Facility-malaria (AMFm), with a significant proportion of the evidence used in the evaluation being directly provided by the ACTwatch project.

The GMS is the global epicenter for artemisinin drug resistant Plasmodium falciparum and the source of the majority of oAMT. As such, it is clear that the Asia-Pacific region (GMS especially), should be considered for regional antimalarial market monitoring. To date, only two countries in the GMS, Cambodia and Myanmar, have seen large-scale outlet surveys conducted to assess the need for, and measure the subsequent impact of, market interventions.

3. Monitoring market interventions in the Asia-Pacific region

3.1 Case Study: Cambodia

Cambodia has been working to improve access to ACT and RDTs in both the private and public sectors since introducing Artesunate and Mefloquine (AS+MQ) as a co-blistered ACT in 2000. Initiated by the European Commission Cambodia Malaria Control Project, in collaboration with the National Centre for Parasitology, Entomology, and Malaria Control (CNM) and the WHO, a nationwide social marketing project was started in recognition of the role of the private sector in 2002 and officially handed over to Population Services International (PSI) in 2003.
The market intervention

The program is composed of the following components which together are designed to ensure patients are informed, providers act in accordance with the national policy and dispense responsibly, and commodities are readily available and affordable.

Early Diagnosis and Treatment (EDAT) Training: A comprehensive, one-day training for private health providers to improve their malaria case management skills was launched in 2004. The curriculum is reviewed annually and adjusted to reflect shifts in the national program and policy including, for example, the discontinuation of chloroquine and the switch of the first line drug from AS+MQ to DHA-pip in 2012.

Medical Detailing: While the EDAT training day provides a solid foundation of knowledge and practical skills, lasting behavior change requires a sustained drip feed of informed supportive supervision. PSI’s Medical Detailers, doctors and pharmacists by training, provide this support through monthly visits to providers at their place of work. Each visit is guided by a behavioral change framework with Quality Assurance checks and balances.

Distribution System: Sales Representatives are on the road seven days a week to ensure that outlets providing malaria case management services across all 20 endemic provinces are fully stocked with RDTs and ACTs (except for Zone 1 where only RDTs are supplied due to there being a different first line drug until 2014). At the end of 2012, as transmission reduced further, PSI tightened the network at the request of CNM to ensure only registered providers were procuring supplies.

Communication campaigns: Communication campaigns to change behaviors and raise awareness among patients were used extensively at the start of the program with a gradual tapering off as caseloads dropped and the focus shifted to ensuring that patients with fever sought care from trained providers promptly.

Tracking changes in the antimalarial market between 2009 and 2013

Between 2003 and 2009, it was only possible to report on the number of ACTs and RDTs sold in the private sector and distributed through the public. There was no reliable information on what other drugs were circulating, or in what quantities.

In 2009, the first ACTwatch outlet survey was carried out and was able to demonstrate that among the total antimalarial volumes sold/distributed nationally, only 6% were oAMTs and 72% were ACTs. A follow up survey in 2011 meant trends could be tracked for the first time. Figure 1 shows
the 2009 and 2011 data from outlets with antimalarials in stock on the day of the survey by sector. The data demonstrates that stocking rates for any antimalarial were consistent in the public sector over two years, but that a drop in availability occurred in the private sector, due to a national stock out. Of primary interest, is the relative drop in availability of oAMT, shown in red, between the public and private sectors. For the public sector, a drop is seen from 2.3% to zero between 2009 and 2011. For the private sector, the decline is much steeper, from 20.3% to 4.2%. Data from the third outlet survey, completed in 2013, is under analysis at the time of writing and is expected to show a further decrease in the availability and market share of oAMT relative to ACT.

Figure 1: Availability of antimalarials among all outlets with antimalarials in stock on the day of survey (2009-2011)

The use of cocktails for the treatment of illnesses is widespread in Cambodia and the 2011 outlet survey results, while generally positive, also revealed the extent to which drug cocktails are used for the treatment of malaria. It should be noted that unpacking the issue of cocktails - defined as the combination of more than one drug - is not straight forward. A full ACT treatment plus paracetamol for example would be an ‘acceptable’ cocktail, while a sub-optimal dose of ACT or oAMT plus vitamin C, would not be. Preliminary analysis on the ingredients of cocktail samples bought during the 2011 Outlet Survey show that they often contain no identifiable antimalarial. In response, a new module on the dangers of providing cocktails was added to the PSI EDAT training.
curricula and the issue is now stressed during the routine visits to providers. Another finding was the relatively low (45%) utilization of RDTs among those reported to have had ‘malaria fever’. In response, intensified medical detailing was employed to encourage correct RDT use and retrieval of the used tests for quality control.

Historically, both the public and private sectors in Cambodia have been affected by intermittent stock-outs of malaria products. But in 2011 the ACT stock out in the private sector lasted over 10 months which was unprecedented. To compound the situation, heavy flooding occurred and the number of migrant workers moving across the country in search of work in newly opened plantations rose, resulting in case loads increasing by 400% in certain areas as compared to records from 2010. The impact of the stock-out was captured by the outlet survey that year and the data can be compared with the 2009 outlet survey when the supply chain was stable, see figure 2.

Figure 2: Total market for antimalarials sold or distributed nationwide by sector (2009 & 2011)

Despite the private sector stock-out, figure 2 illustrates the fact that the volume of any antimalarial (i.e. ACTs and any other drugs) stays the same by sector with 70% and 30% moving through the private and public sectors respectively in both years. What changes is the type of drug available. In 2009, the private sector was fully stocked with AS+MQ (Malarine) which was the first line drug
for *P. falciparum* at the time and represented 31.9% of the total volume of antimalarials in the private sector. Chloroquine, labeled ‘non-artemisinin monotherapy’ made up 18.5%. During the stock-out year of 2011, Malarine ACT availability dropped to 14.1% while chloroquine (the first line drug for *P. vivax* at the time) jumped to 54.2%. In conclusion, it appears there was no change in the relative volume of drugs being dispensed by each sector, but in the absence of AS+MQ, providers turned to what they had on hand, which was chloroquine. An increase in the use of oral artemisinin monotherapies might equally have been expected, and yet the data indicates no rise. It should also be noted that Cambodia has had a ban on the sale of artemisinin monotherapy in place since 2009.

In conclusion, nationally representative *ACTwatch* studies in Cambodia, now stratified to reflect national artemisinin resistance priority zones, continue to inform malaria elimination policies and activities in the country.\textsuperscript{viii, ix}

### 3.2 Case Study: Myanmar

Following an analysis of private sector drug importation records in 2011, it was ascertained that approximately 1.6 million adult equivalent treatment doses (AETD) of oAMT were being imported into Myanmar each year (primarily Artesunate). As a result, the rapid replacement of oAMT with ACT in the private sector became a key objective of the Myanmar Artemisinin Resistance Containment strategy (MARC).\textsuperscript{x}

**The market intervention**

Through a series of rapid surveys it was determined that the private sector supply chain was highly centralized, with one company enjoying 70-80% of the market share for this product, thus presenting the Ministry of Health with a remarkable opportunity. If the company could be persuaded to cease further oAMT imports and switch to a heavily subsidized quality-assured ACT, then a dramatic change in the national market could be achieved. PSI, due to their experience operating at scale in Myanmar’s private sector, was charged with facilitating this process: managing the donor subsidy, commodity procurement and import, onward sales with agreed price points to contracted national distributors, monitoring of supply chains, providing supportive communications and medical detailing interventions and, lastly, generating a comprehensive baseline picture of the private market and measuring impact over time through the utilization of *ACTwatch* surveys.
Quality-assured and highly subsidized ACT first entered the private sector supply chain in October 2012, three months after completion of an ACTwatch baseline outlet survey. In June 2013, the second of a series of annual surveys was conducted to assess impact to date.

**Tracking changes in the antimalarial market between 2012 and 2013**

Over 1.3 million courses of subsidized ACT were distributed through the private sector in Myanmar between October 2012 and December 2013. During a nine-month period (from the time of initial supply to the time of the second ACTwatch outlet survey in June 2013), the availability of ACTs increased exponentially across private sector outlets (27% to 63%). The increase in availability was even more pronounced among priority outlet categories (pharmacies, itinerant drug vendors and general retail stores), from 4.5% to 50.4%, see figure 3.

The outlet survey data also suggested that the Food & Drug Administration’s (FDA) ban on oAMT importation (initially Artesunate and later Artemether) was having some effect, with reduced availability of oAMT observed nationwide (from 51% in 2012 to 36% in 2013).
Although oAMT was still available in many places (as expected), it was extremely encouraging to note that the demand for oAMT (volumes sold during the week before the survey) had dropped sharply. Relative to oAMT, the market share for ACT increased from 3% to 73% among the priority outlet types (those shown previously to account for the majority of national oAMT sales) in nine months, see figure 4.

Figure 4: Ratio of ACT to oAMT sold in private sector priority outlets (2012 & 2013)

Regarding price, 94% of target outlets were reported to be selling full course quality-assured ACT at a price less than or equal to the cost of a typical partial dose of the most common artemisinin monotherapy at baseline.

Further surveys will be conducted in 2014, including outlet surveys, exit interviews and mystery client surveys, with further changes in the national market anticipated. The next stage in the intervention’s evolution is the introduction of subsidized RDTs through the same supply chain, to increase the ratio of confirmed vs. presumptive malaria treatment in this sector. In collaboration with the Global Health Group at the University of California San Francisco, PSI has completed a six-month pilot study to determine demand drivers for RDTs (and appropriate case management) among informal providers and is planning on taking the model to scale in 2014, in close partnership with the Ministry of Health.
At the time of writing, the World Health Organization confirmed that all three first-line ACT treatments for malaria were still effective in Myanmar. While monotherapy replacement will not, alone, contain resistant \( P.f \) malaria within Myanmar, it is hoped that the intervention will, at the very least, buy the public health community valuable time in the fight against artemisinin resistance, whilst helping reduce the burden of disease within the country.

4. Conclusion

Significant progress has been made in recent years in both generalized malaria elimination within the Asia-Pacific region, and \( P.f \) resistance containment within the GMS, largely as a result of coordinated government and civil society action. However, the private sector still plays an important, and in some places dominant, role with regards to fever treatment (especially among remote rural communities). As such, the sector represents both a threat if ignored and an opportunity if adequately managed.

It is increasingly clear that the private sector can be harnessed at various levels to good effect to expand access to quality services and medicines within the Asia-Pacific region. In fact, private sector market interventions have the potential to bring about rapid transformation at significant scale.

The Asia-Pacific region, primarily Viet Nam and PRC, supplies the majority of the world’s raw material needs (\( Artemisia annua \)) for artemisinin-based combination therapies (ACT), and has the potential to increase both output and quality at a time when global demand is growing. Meanwhile, as described, innovative ACT (and RDT) subsidy and supply mechanisms, combined with appropriate supportive interventions, have shown to significantly improve availability, price and market share of quality-assured ACT relative to oAMT.

If nationally representative antimalarial market surveys were conducted in a systematic manner across the region (in both private and public outlets) an evidence base would rapidly establish
whether or not similar interventions are needed elsewhere to mitigate the threat posed by oAMT and sub-standard medicines, whilst boosting commercial demand for quality ACT that is manufactured in the region. Furthermore, should a regional antimalarial subsidy mechanism be deemed necessary, the same market monitoring techniques could be used to assess change over time in the availability, price and market share of ACT and RDTs, including efforts to extend the reach of government and civil society services.
5. References


