DISCUSSION PAPER

Distribution of Artemisinin-Based Combination Therapies through Private-Sector Channels

Lessons from Four Country Case Studies

Oliver Sabot, Shunmay Yeung, Franco Pagnoni, Megumi Gordon, Nora Petty, Kristen Schmits, and Ambrose Talisuna

1616 P St. NW
Washington, DC 20036
202-328-5000   www.rff.org

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Distribution of Artemisinin-Based Combination Therapies through Private-Sector Channels:
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Abstract

Substantial progress has been made in delivering ACTs through public health systems, but high prices have kept ACTs from those buying antimalarials in pharmacies or shops—the majority of patients in Africa. This paper reports on the delivery of highly subsidized ACTs through the private sector in Tanzania, Kenya, Cambodia, and Senegal, providing insight into how the new Affordable Medicines Facility-malaria will work. In Tanzania, the location of the only project specifically designed as an AMFm-like subsidy, uptake of ACTs increased significantly (from less than 1 to 42 percent). In Kenya, ACT uptake had increased from 15 to 42 percent 15 months after the intervention began. In Cambodia, ACT awareness increased, but supply remained irregular. In Senegal, the full range of ACT packs for different age groups was still unavailable in most private shops. Private sector subsidies can increase ACT availability but countries must take into account local malaria epidemiology and treatment-seeking behavior as well as health systems, regulatory frameworks, and consumer preferences.

Key Words: malaria, Africa, treatment, ACT, antimalarials, subsidies

JEL Classification Numbers: I10, I18

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Introduction

Since the 1970s, prompt treatment with chloroquine (CQ) and other simple and inexpensive therapies has been a cornerstone of malaria control efforts around the world. By 2000, however, chloroquine-resistant malaria parasites were pervasive throughout many countries, rendering the drug largely ineffective and contributing to increased mortality in some areas (World Health Organization/UNICEF 2003). In response, many governments switched national first-line treatment policy to sulfadoxine-pyrimethamine (SP) (East African Network for Monitoring Antimalarial Treatment 2003), but resistance to SP rapidly emerged soon after its introduction, jeopardizing not only patients with clinical illness but also the intermittent presumptive treatment strategy for pregnant women (Farooq and Mahajan 2004).

In response to this crisis, the World Health Organization changed its guidelines to recommend artemisinin-based combination therapies (ACTs) as first-line malaria treatment in 2001 because of their high efficacy and ability to limit the development of further resistance. The subsequent launch of the Global Fund to Fight AIDS, Tuberculosis, and Malaria began providing countries with the financial confidence needed to switch to these more expensive therapies. Today, nearly all malaria endemic countries have adopted ACTs as first-line treatment. With funding from the Global Fund, the U.S. President's Malaria Initiative, the World Bank, and others, many of these countries have made substantial progress in delivering ACTs to patients through public health systems (UNICEF/Roll Back Malaria Partnership 2007). However, because of their considerably higher cost (10 to 40 times higher than CQ), few who seek treatment in the private sector are accessing ACTs, but are instead continuing to purchase suboptimal therapies such as SP and CQ or antipyretics (Laxminarayan, R. et al. 2006).

Treatment-seeking patterns differ substantially between countries, and robust evidence to define the patterns is scarce. Studies indicate, however, that most patients seek treatment in the private rather than the public sector (McCombie 1996; Yeung and White 2005). Numerous factors drive this use, including the distance to, long wait times at, and poor availability of drugs in public sector facilities, all of which are related to the fundamental strength of the health system (Foster 1995; Brugha and Zwi 1998). Private-sector treatment sources vary considerably between and within countries, ranging from private hospitals and clinics to one-room drug shops to general stores and medicine peddlers (McCombie 1996). Moreover, relatively little data exist on the supply and demand of antimalarials in the private sector, inhibiting the development of effective, evidence-based interventions. As a result, despite the important role of the private sector in providing treatment, few large-scale efforts have been launched to increase ACT access through this channel.

In response to low ACT access and the threat of artemisinin resistance, an Institute of Medicine committee recommended, in 2004, the creation of a global subsidy to make ACTs available through both the public and private sectors at the same price as CQ and other common therapies (Institute of Medicine 2004). By reducing the price of the drugs at the manufacturer level, ACTs will flow through the same channels used to distribute those other therapies, thereby dramatically increasing access to ACTs and correspondingly reducing use of artemisinin monotherapies—and the development of artemisinin resistance—and other suboptimal drugs (Roll Back Malaria Partnership 2007). This concept was later further developed by the Roll Back Malaria Partnership into a potential new global mechanism known as the Affordable Medicines Facility—malaria (AMFm). The AMFm was recently approved by the governing Board of the

Global Fund and will be launched in an initial set of countries in 2009 (Global Fund To Fight AIDS 2008).

As the AMFm has been developed and debated over the past year, numerous questions about its impact have been raised. Will a subsidy be passed through to consumers or absorbed by middlemen? What interventions must be implemented within countries to ensure uptake and quality of ACTs, and what interventions will enhance its effectiveness? How will a subsidy affect vulnerable groups, notably young children and the poor? Most important, will a subsidy available to the private sector dramatically increase overall coverage of ACTs for people with malaria in high burden countries? Models have provided guidance, but policymakers are also interested in empirical evidence for additional answers (Laxminarayan et al. 2006). No studies, however, have yet been published on the distribution of subsidized ACTs in the private sector, and initiatives with other therapies, such as CQ, are often not relevant because the cost of the drug was not subsidized (Roll Back Malaria/Malaria Case Management Working Group 2005).

In recent years, a number of countries have developed or launched initiatives to distribute subsidized ACTs through the private sector. These efforts are typically small, either geographically or in the type of outlet involved, but they can provide valuable lessons to guide the design and launch of AMFm. This paper presents the available data and associated lessons from a subset of these programs.

As shown in table 1, ACT subsidies are planned or have been put in practice in 12 countries in sub-Saharan Africa and Asia. Data are not available in most countries on the outcomes, however, either because evaluation is not yet completed or because it was not built into the project. Of the four countries where results are available, two, Kenya and Tanzania, were designed as pilot projects and thus have substantial baseline and postintervention data. Cambodia was the first to introduce an ACT subsidy in the private sector and, though an explicit evaluation was not conducted, data from surveys before and during implementation provide useful insight. Last, a single survey, with limited but useful data, was conducted during a subsidy initiative in Senegal. Experiences in these countries cannot answer all relevant questions about private-sector ACT interventions. The studies in this paper focus primarily on ACT stocking, uptake, and pricing. The programs differ widely, each with unique distribution systems, retail outlets, accompanying interventions, pricing, country settings and evaluation methodologies. These differences made it impossible to robustly compare outcomes, but key findings did emerge that can inform both policy and research priorities.

Tanzania

In Tanzania, more than 90 percent of the population is at risk for malaria. There are an estimated 14 to 18 million clinical cases of the disease each year, causing 100,000 deaths (Tanzania National Malaria Control Programme 2007). Up to half of Tanzanians seek treatment for malaria from private sector sources, including private health facilities, registered pharmacies, small drug stores (*duka la dawa baridi)*, and general stores (Goodman 2004; Tanzania National Malaria Control Programme 2007). With more than 8,000 outlets nationwide, *duka la dawa baridi* have been documented as the most common source for antimalarials in the private sector (Tanzania Food and Drug Authority 2007). In response to high rates of resistance to chloroquine and other therapies, Tanzania switched its national guidelines for first-line malaria treatment to ACT, specifically artemether-lumefantrine (AL), in 2006. ACTs are classified as prescription-only medications and are therefore not sold legally through *duka la dawa baridi* and general stores, which are restricted to sales of over-the-counter medication; the availability of ACTs has remained largely limited to health facilities and registered pharmacies (Kachur et al. 2006).

In October 2007, the Tanzanian Ministry of Health and Social Welfare (MOHSW) and the Clinton Foundation HIV/AIDS Initiative (CHAI) launched a pilot ACT subsidy project to evaluate a new approach to increasing ACT access in the private sector. Specifically, the pilot was designed to assess the impact of a subsidy on price and uptake of AL and the effect of a suggested retail price (SRP) on those outcomes. The pilot is being implemented in three rural districts where malaria transmission is stable. Districts were selected to be roughly representative of the country and have comparable basic socioeconomic and malaria-related indicators. Key indicators considered in the selection process included population size, access to public and private health facilities, employment in agriculture, use of bed nets, and access to anti-malaria treatment. The 2002 national census and the 2004–2005 Demographic and Health Survey served as the primary sources for these data (Mbogoro 2002; National Bureau of Statistics, ORC Macro 2005).

Each district was randomly assigned one of the three study groups. Kongwa, in the center of the country, and Maswa, in the northwest, are the intervention areas and receive both subsidized AL and a varying package of support. Shinyanga Rural district, also in the northwest, where only monitoring and evaluation are conducted, serves as a control. The Tanzania Food and Drug Authority granted provisional over-the-counter status for AL so that it could be sold through *duka la dawa baridi* in Kongwa and Maswa.

AL is sold to private outlets at highly subsidized prices in the intervention areas by the following means: CHAI sells AL to an established national pharmaceutical wholesaler at 88 percent below the manufacturer's price (about $0.12 compared to $1 under usual wholesale conditions). The wholesaler then uses existing distribution channels, including sale to regional distributors, to deliver the AL to *duka la dawa baridi* in the two intervention districts. The packages destined for Kongwa district include on the packaging a suggested retail price (SRP) of $0.25 for a pediatric dose and $1 for an adult dose.[1] In addition, Population Services International (PSI) distributes a package of educational material before and during drug distribution to generate demand for subsidized AL and to improve the quality of care patients receive from *duka la dawa baridi*. The package includes behavior change campaign materials related to prompt treatment, proper use of AL, shopkeeper training, AL storage and dispensing, and simplified dosing instructions that use pictures and the local language, Kiswahili. In Kongwa, campaign materials also alert consumers to the recommended price levels.

Methodology

A baseline dataset was established in all three districts before implementation in August 2007. Similar data have been collected on a quarterly basis since initiation of distribution. Datasets were collected and analyzed in November 2007 and March 2008.

To eliminate the potential for sampling error, an attempt was made to include every *duka la dawa baridi* in the three districts in each data collection exercise. However, a *duka la dawa baridi* may not have been included in certain data collection exercises if it was closed on the day it was visited or the owner refused to participate (for retail audits only). Every government and NGO health facility within ten kilometers of a *duka la dawa baridi* was included in the public/NGO facility audits, as long as a staff member was available to answer the survey questions. Four methods were used to gather data to evaluate the pilot project's impact:

1. *Exit interviews*—Trained data collectors positioned themselves near an operating *duka la dawa baridi* and administered a structured questionnaire to consenting customers who

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[1] Prices were set on a per pill basis so as not to create incentives for customers to buy an inappropriate dose for their age group. Thus, all prices are based on 50 Tanzania Shillings (TSH) per pill, about US$0.04. The final SRP created through this process is 300 TSH or roughly US$0.25 for the 5- < 15 kg dose consisting of 6 pills, 600 TSH (US$0.50) for the 15- < 25 kg dose consisting of 12 pills, 900 TSH (US$0.75) for the 25- < 35 kg dose consisting of 18 pills, and 1200 TSH (US$1) for the 35+ kg dose consisting of 24 pills.

had purchased an antimalarial or antipyretic. The questionnaire sought information about product selection as well as perceptions and price paid for antimalarials.

2. *Retail audits*—Data collectors recorded the total volume of antimalarials and antipyretics stocked in the shop and interviewed the owner about new purchases or disposals (for example, of expired products) in the past month. This information was compared to the volume stocked at the shop one month beforehand to arrive at the total sales.

3. *Mystery shoppers*—Data collectors posing as young adults seeking treatment for themselves or their young child (encounters are equally divided between the two scenarios) visited shops and purchased antimalarials according to a set algorithm.

4. *Public facility audits*—All public facilities were visited and data captured from official records on volumes of AL dispensed and stock-outs during the preceding period.

The GPS coordinates of all shops were recorded using Garmin Etrex handheld equipment, enabling data to be linked to each shop between collection periods. These coordinates were also used to analyze key outcomes by shop location and competition level. Each shop was assigned a competition index (CI) based on the number of others within one kilometer, with categories ranging from 0 to 5. This assumes that a provider's customers come from the area within a given radius. Thus a shop with no competitors in the radius was classified in category 0, and one with four fell into category 4 (see table 2). GPS maps reveal that the competition index is highly correlated with population density, with higher levels of competition typically found in towns and village centers.

Results

Stocking and Availability of ACT

At baseline, in August 2007, no outlets were stocking AL or any other ACTs. By the November 2007 retail audit, one month after the launch of subsidized AL distribution, 87 of 159 (55 percent) *duka la dawa baridi* in Kongwa and Maswa were stocking AL. That number remained about the same after five months (60 percent of 146 shops). The percentage of shops stocking AL was slightly higher in Kongwa than Maswa in both periods (62 percent in Kongwa compared to 51 percent in Maswa in November, and 63 percent compared to 57 percent in March). In addition, the higher the competition index, the greater the percentage of shops that were stocking AL, and the trend was significant ($\chi^2(1) = 20.855$, $p < 0.001$): 80 percent in CI categories 4 and 5 had AL in stock in March compared to 38 percent in categories 0 and 1. Stocking of the most common alternative antimalarial, SP, declined in Maswa ($p < .001$) from 88

percent of outlets in November to 69 percent in March, and in Kongwa from 83 percent to 69 percent of outlets (not significant). Only 6 percent of shops in all districts stocked an artemisinin monotherapy and no subsidized AL was found in stock in the control district.

Uptake of Subsidized AL

In March, 290 consumers were interviewed after purchasing antimalarials in Kongwa (106 interviewees) and Maswa (184 interviewees). Of these 290 consumers, 44 percent (40 percent in Maswa and 52 percent in Kongwa) bought AL, a significant increase over the less than 1 percent at baseline. The proportion of interviewed consumers who were seeking treatment for children under five and who purchased subsidized AL rose from 40 percent (23 of 58) in November to 62 percent in March (50 of 81). By comparison, the proportion purchasing AL in the control district remained constant from baseline at less than 1 percent. Retail audits indicate that total monthly sales of subsidized AL increased from 1,663 in November to 8,932 in March, causing AL's share of overall antimalarial sales to grow correspondingly from 6 percent to 31 percent. The majority of subsidized AL sales, however, continue to be in more densely populated areas: in March, 68 percent were by stores in CI categories 4 and 5.

In both intervention districts (see table 3), subsidized AL has increasingly replaced other common therapies. In Maswa, purchases of SP and AQ by consumers purchasing for themselves or another adult declined from 67 percent to 38 percent and from 25 percent to 17 percent, respectively, between August and March (see table 3). In the control district, purchasing patterns have remained largely consistent from the baseline, with no interviewed consumers obtaining AL and the majority buying SP (75 percent) or AQ (21 percent) in March. Sales of artemisinin monotherapies were minimal in all districts, with only 49 doses (0.3 percent) sold in the month preceding the March collection.

Price

Consumers interviewed in November and March bought subsidized AL at the SRP in Kongwa, and at lower prices in Maswa. Prices reported for other anti-malarials in November and March remained consistent from baseline, with the median price for a full adult dose of SP at 500 and 600 TSH in Maswa and Kongwa ($0.42 and $0.50), and AQ at 400 and 425 TSH ($0.33 and $0.35). In comparison, consumers paid $0.51 on average for subsidized AL in March, which is

95 percent less than the benchmark retail price of roughly $10.[2] No evidence has been found of retailers engaging in price gouging: no consumer has paid more than $1, the SRP for an adult dose, for a subsidized ACT. There was no significant correlation between the price consumers paid for antimalarials, including subsidized AL, and the competition index category of the store ($F = 0.579$, $p = 0.678$).

The SRP reduced the price variation of subsidized AL, but the price of adult doses was nearly double the market rates charged in Maswa. Almost all (93 percent) consumers in Kongwa paid exactly the recommended price for subsidized AL. In contrast, consumers paid between 300 and 900 TSH ($0.25 and $0.75) for an adult dose and between 200 and 800 TSH ($0.17 and $0.67) for an infant dose in Maswa.

Consumer Purchasing Behavior

The majority of consumers (69 percent) seeking treatment from *duka la dawa baridi* in all three districts purchased antimalarials for themselves or another adult. The proportion purchasing treatment for children under five rose significantly in both Maswa (from 11 percent to 31 percent) and Kongwa (10 percent to 26 percent) between August and March ($p < 0.01$). This proportion remained roughly constant at about 20 percent in the control district over the same period, which is nearly twice as high as the baseline proportion in Kongwa and Maswa. The most common reason for purchasing subsidized AL cited by consumers in March was the perception that they are the most effective products to cure malaria (29 percent), up from 12 percent in November. Other frequently given reasons include having a prescription (21 percent) and the seller's recommendation (17 percent). Most interviewed consumers (88 percent) who purchased subsidized AL bought a full dose for the reported age of the patient. Significantly fewer ($p < 0.01$) buying SP and AQ bought an appropriate dose (76 percent and 78 percent respectively).

Discussion

The Tanzania pilot is the only project to date specifically designed to test the impact of a subsidy introduced at the top of the usual private sector supply chain. In most other projects, either government or NGOs complement or manage the distribution of AL by the private sector.

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[2]As observed in private pharmacies in Dar es Salaam. No ACTs from originator manufacturers were found in study districts.

In Tanzania, PSI conducted communications activities in the intervention districts, but otherwise had no contact with supply chain. It replicates the AMFm model in many respects but one important difference is that it selected a single wholesaler to distribute subsidized ACTs and AMFm would be much more expansive, including all distributors and outlets. Other limitations include the small area, relatively short implementation time, and the collection of data at providers only (rather than at household level).

The initial results relating to AL uptake and price are promising. After five months of implementation, just under half of all consumers visiting *duka la dawa baridi* are buying AL rather than older therapies. This shift is more pronounced for those seeking treatment for children under five, at nearly two-thirds. Purchase of AL in the control district has remained negligible since baseline.

Consumers are now paying the same price or less for AL as they were for SP and other common alternatives. No evidence was found of price gouging for subsidized AL as it moved through the supply chain. The World Health Organization defines access to essential medicines as encompassing greater availability, reduced prices, better geographical access, and increased acceptability of the product (WHO 2004). As a result, according to this definition, though overall ACT coverage in the districts was not captured in this study, the subsidy has substantially increased access to AL.

The pilot has also highlighted several challenges that should be taken into consideration in the design of similar interventions. Although more than half of the shops in the intervention districts stocked the product within the first month, by the second data collection, that supply had increased very little. The shops that do stock the product are clustered in population centers. By contrast, fewer than a third of the shops defined by the competition index as more remote stocked it in March, whereas nearly two-thirds (62 percent in March) stocked other antimalarials, such as SP. This suggests that a primary driver of the lower ACT supply is the distribution chain used in the pilot. Whereas dozens of wholesalers and distributors sell other antimalarials, only one wholesaler and two distributors officially distribute subsidized AL. Because remote shops have higher costs to obtain drugs (i.e., travel to town centers) and limited capital to make bulk purchases, they are particularly affected. The lower supply may also be affected by demand factors such as less awareness of the new product among businesses and consumers in remote areas. It will therefore be important to observe whether the trend continues as the project progresses.

Experience also indicates that applying an SRP can help control retail prices but can also be counterproductive if not calculated carefully. All but six (93 percent) consumers and mystery shoppers in Kongwa district paid the SRP for subsidized AL, but prices in Maswa varied. At the same time, however, consumers paid substantially more for the adult dose in Kongwa, suggesting that the SRP is set above the rate that the market would set. This illustrates the challenges of arriving at an SRP that is both affordable for customers and profitable for businesses, and suggests that detailed analysis of the supply chain and demand elasticity should be conducted before setting such prices for larger subsidy initiatives. With financing from the Global Fund, Tanzania is now aiming to expand the distribution of subsidized AL to the entire country over the next two years. The results of the pilot are a basis for cautious optimism that the initiative will have a considerable impact on ACT coverage and malaria mortality.

Kenya

Kenya is a malaria endemic country, with 77 percent of the population at risk of the disease. About one-quarter of hospital deaths and 40 percent of outpatient consults are attributable to malaria (WHO 2003). As part of its overall malaria control strategy, the Kenyan government adopted artemether-lumefantrine (AL) as the first-line treatment for uncomplicated malaria in 2006, introducing the drug to government health facilities free of charge in July of that year. Since then, a nationwide campaign employing mainly radio and television spots has been conducted to inform the public on the importance and proper use of AL.

A substantial number of Kenyans seek treatment for malaria outside the formal public health system. According to one recent household survey, of the 90 percent of caregivers who took some action to treat a child's fever within 48 hours of symptom onset, 47 percent first sought treatment in the private retail sector. In total, only 23 percent were treated with an antimalarial within 48 hours and only 10 percent received AL as recommended. As expected, the majority of AL (95 percent) was dispensed from public health facilities, though a July 2007 survey showed that 34 percent of government health facilities (GHF) had run out of the drug in the preceding six months (Amin et al. 2007).

In an effort to increase access to ACTs, an initiative was launched in 2007 to make AL available through private shops in targeted rural areas. These Community and Family Wellness (CFW) shops, which operate through a franchising system organized by the Sustainable

Healthcare Foundation (SHEF), are staffed by a trained health worker and provide a range of health services in the community.[3] As part of this initiative, AL is distributed to CFWs from the government central medical stores and administered free of charge to patients with uncomplicated malaria after confirmation by an RDT. Patients must pay $0.65 for a consultation and RDT before receiving AL for confirmed malaria. Patients with a negative RDT are either screened for other diseases (such as ear infections, measles, or an upper respiratory tract infection) at CFW clinics or referred to GHF for further assessment. To inform potential scale-up of the approach, impact and quality of ACT distribution were documented and evaluated.

Methodology

The intervention was implemented in Central Kenya, where malaria is holo-endemic. Nine CFW shops in three districts participated in the study: five in Embu, three in Kirinyaga, and one in Mbeere. These shops were selected by SHEF from a total of 36 on the basis of high malaria morbidity and disease burden (after a parasitological survey to determine malaria prevalence), capacity of the shop to assimilate new products, and current business performance. The participating shops were upgraded to clinics through the recruitment of a qualified nurse (if the owner was not already a nurse) to dispense ACTs. Given the prescription-only status of AL, the Pharmacy and Poisons Board mandated that CFW clinics were supervised monthly by pharmacy assistants to monitor appropriateness of drug use.[4]

Quantitative and qualitative household surveys were performed at baseline (December 2006) and after 15 months of the intervention (March 2008) to assess the quality of care provided by CFW clinics and consumer uptake and perception of subsidized ACTs. Household recall interviews were conducted to explore health-seeking behaviour of patients of all ages in cases of suspected malaria episodes within the previous two weeks (425 patients at baseline, 1143 at evaluation). To complement the household surveys, in-depth interviews were conducted with franchisees and other stakeholders and gender-specific focus group discussions were carried out

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[3] A franchise arrangement with the Kenya-based NGO Sustainable Healthcare Foundation (SHEF) provides quality-assured drugs and other essential health products to the outlets. SHEF establishes uniform, affordable prices for tests and procedures—and provides those for ACTs, in conformity with Kenyan government guidelines, at no cost. SHEF also provides training and supervision to shop owners and health-care providers. The SHEF franchising system started in 1999 with 11 drug shops and is currently running 65 outlets in 10 districts of Kenya. There is a target of expanding the program to 225 outlets by 2012.

[4] Currently, AL is still a prescription only medicine in Kenya, but the Ministry of Health is considering moving it to an over-the-counter medicine.

with caregivers and the general population. Purposive sampling was used to select the respondents based on whether they had experienced malaria-like symptoms in the past month.

Results

Health-Seeking Behavior

At baseline, 97 percent of the 425 interviewed patients with symptoms of malaria in the previous two weeks had been treated with an antimalarial. This did not change. The percentage of patients seeking treatment from public health facilities, however, increased from 60 percent (95 percent CI 55–65 percent) at baseline to 69 percent (95 percent CI 66–72 percent) following the intervention, while those accessing treatment through the private sector declined from 50 percent (95 percent CI 45–55 percent) to 39 percent (95 percent CI 36–41 percent) over the same period.

ACTs at Private Clinics

CFW clinic registers show that as of September 2007, nine months after the launch of the initiative, 2,086 patients with a positive RDT were treated at the nine target clinics. The RDT positivity rate of patients seeking treatment at CFW clinics during this period was 36 percent. An additional 288 patients referred from GHFs with evidence of parasitological positivity were provided with AL at the CFW clinics (see table 3).

ACTs to Treat Malaria

Before the intervention, most of the 414 patients who sought treatment for malaria symptoms and received an antimalarial were treated with either SP (32 percent) or amodiaquine (27 percent), with only a few receiving AL (15 percent) or chloroquine (2 percent) (table 4). Fifteen months into the intervention, AL had become the most commonly obtained product, with 457 of the 1,092 (42 percent) interviewed patients receiving it. Of those, 393 (86 percent) obtained the drug from GHFs, 42 (9 percent) from CFW clinics, and 23 (5 percent) from other sources. These figures represent significant increases in both overall use of AL to treat malaria ($p < .001$) and the proportion of patients who accessed AL from public facilities ($p < .001$).

Adherence to Treatment

There was no significant difference between the proportion of patients who took AL the same or next day at baseline (34 percent, CI 23–46 percent) and following the intervention (47 percent, CI 42–51 percent). Similarly, no significant difference in promptness of treatment was

found between patients obtaining AL from CFW clinics and public facilities (40 percent versus 47 percent).

According to household interviews, 94 percent of the 457 patients who received AL before the evaluation received the correct dosage, and 91 percent reported taking the correct dose of AL twice a day for three days. This was not verified by observation of packages or other methods. However, 9 percent of the respondents acknowledged that they did not follow the nurse's prescription. The reasons cited included improved symptoms, pill burden, a complex dosage schedule, lack of a paediatric formulation, and forgetfulness. No significant difference in reported adherence to the AL treatment schedule was observed between patients having obtained AL from GHF and from CFW clinics.

Quality of Care at Clinics

All CFW clinics reported full adherence to stipulated treatment guidelines. A higher proportion of patients treated at CFW clinics (71 percent, CI 58–85 percent) received AL based on their weight in accordance with national guidelines compared to patients treated at public facilities (52 percent, CI 47–57 percent). According to women participating in focus group discussions, the CFW clinics took special care to weigh the children, while other facilities often assessed weight using antenatal cards. Adherence to another treatment guideline, observance of the first treatment dose, was also higher at CFW clinics than public facilities (60 percent, CI 45–74 percent versus 37 percent, CI 32–42 percent).

Access to Clinics by Age

Although the small number of observations prevents robust analysis of the difference in ACT access by age, the data indicate a trend towards greater use of CFW clinics by older children and adults. Of the 42 patients receiving AL from CFW clinics at evaluation, the majority (88 percent) were children over five or adults, and only a few were children under five (12 percent). Children under five, however, made up 20 percent of those receiving AL from other sources.

ACT and RDT Acceptability and Cost

Almost all malaria patients who sought treatment at the CFW clinics (98 percent) reported that they intended to use AL in the future. In interviews, the large number of pills and recommended dietary requirements (i.e., taking pills with fatty foods) were the two primary obstacles cited.

CFW clinics were instructed to provide AL free but to charge the patient $0.65 for consultation and RDT. No data were collected on the actual compliance with this policy. Interviews revealed that patients viewed the consultation fee as a payment for the medicines. More than half reported that they paid for the drugs. Of those who reported paying, 70 percent perceived the price to be fair or cheaper than expected. Many respondents, however, expressed concerns about the cost of the RDT, particularly in the case of a negative test when further testing was required. As a result, some respondents reported purchasing drugs from other private outlets to avoid the testing costs.

In-depth interviews with CFW clinic health providers revealed that patients at times questioned the accuracy of RDTs, claiming that they later tested positive for malaria through microscopy conducted elsewhere. Some interviewees also raised concerns that RDTs were HIV tests and that their status would be available to the CFW staff without their knowledge.

Discussion

Subsidized ACTs were introduced into CFW clinics on a small scale to better understand the potential impact on patients who seek malaria treatment in the private sector and to inform the potential of this model and similar approaches in other countries. Overall, the distribution of ACTs through CFW clinics were found to have contributed to less than 10 percent of the increase in total ACT coverage observed after 15 months of intervention. Although important, this contribution is relatively minor in the face of targets of reaching more than 80 percent of patients with ACT treatment. There are several potential explanations for this modest impact.

First, access to antimalarial treatment was relatively high at baseline (60 percent) and increased during implementation (to 69 percent) as the result of an intense health education and medicine distribution campaign of the Kenyan government. The impact of private sector treatment interventions will always partly depend on conditions and developments in the public sector. Second, the cost of care at CFW clinics may have played a role. CFW clinics required an RDT at a cost of $0.65 before providing treatment, whereas in government facilities RDTs are not administered to children and care for children under five is supposed to be free of charge. This may have contributed to the lower use of CFW clinics for malaria treatment for young children. In addition, as common alternative antimalarials cost substantially less than this consultation fee (e.g., one study found SP sells for $0.38 on average), some patients may have sought treatment from other private retailers (Amin and Snow 2005).

A third factor contributing to the modest impact of the intervention was the limited number of included outlets. Only nine CFW shops (25 percent) were provided with subsidized ACTs versus an estimated 214 public and mission health facilities and hundreds of other private retail outlets in the districts (Noor 2008; Amin and Snow 2005). As such, the CFW clinics are less accessible and accordingly treat a minority of cases. Last, and in contrast to the comprehensive campaign that promoted AL at government facilities, no widespread communication was conducted to increase awareness of ACT availability in CFW clinics. Awareness that ACTs were available in the private sector may therefore have been low outside of the communities immediately surrounding the clinics.

This evaluation does show that CFW clinics are capable of providing high quality care for malaria patients. Key practices that contribute to proper dosing and adherence were regularly followed and compliance with national treatment guidelines was greater than at public facilities. In addition, though the impact of RDT provision on treatment was not part of the evaluation, the data clinic records provided suggest that a substantial number of patients tested negative and either received other care or were referred to a public facility. This is in contrast to most private shops and public facilities in Kenya and other countries, which usually treat presumptively, leading to considerable provision of drugs to patients without clinical malaria (Hamer et al. 2007). Overall, however, this experience suggests that if Kenya wants to substantially increase ACT use among patients seeking malaria treatment outside the public sector, CFW clinics will need to be complemented by distribution through more prevalent private outlets.

Cambodia

In Cambodia, malaria remains a health risk for an estimated 2 million people (14 percent of the population) who live or work near the thick tropical forests. Despite increased coverage of control measures in recent years, more than 60,000 cases were reported in the public health system alone.

Cambodia was the first country to switch to an ACT, a loose combination of artesunate and mefloquine (AS+MQ), in 2000 (World Health Organization 2002). The combination was co-blistered and packaged locally in different age-weight packages for adults and children and provided for free through public health facilities as A+M. To reach the most remote and affected populations, trained community-based volunteers called Village Malaria Workers (VMWs) provide free diagnosis with RDTs and treatment with A+ M in 400 endemic villages, mainly in Eastern Cambodia.

The majority of patients in Cambodia, however, seek treatment for fever outside of the public health system, with more than 70 percent visiting private providers instead (National Institute for Public Health 2005; Yeung et al. 2008). The private sector is poorly regulated and consists of a wide range of formal and informal outlets of varying quality. Diagnosis is often presumptive and there is widespread availability of artemisinin monotherapies and sub-standard and fake drugs (Rozendaal 2001; Newton et al. 2003; Dondorp et al. 2004; Yeung et al. 2008). To address this situation, the European Commission initiated a social marketing program in 2000 to sell subsidized AS+MQ. A P. falciparum-specific RDT was also socially marketed and sold separately in boxes of ten at a subsidized price. This program began as a two-district pilot in 2002 before scaling up to reach 17 endemic provinces and being transferred to the NGO Population Services International (PSI) and financed by a grant from the Global Fund in 2003. In 2004, sales were briefly interrupted as the brand names were changed (to Malarine® for ACTs and Malacheck® for RDTs) and prices reduced.

PSI is responsible for the procurement, blister-packaging, and marketing of Malarine and Malacheck. PSI-trained sales representatives directly distribute the products to a network of wholesalers in 17 out of 20 malaria endemic provinces. Both registered and unregistered private providers can purchase supplies from PSI representatives or wholesalers. PSI also trains private providers on appropriate diagnosis and treatment as well as on communication and education through mobile video unit shows, mass media, and special events, among others.

Methodology

There were no formal evaluations and no baseline survey before the ACT/RDT social marketing program. The results presented have therefore been drawn from a number of surveys conducted by different investigators before and after the nationwide scale-up and from discussions with key informants. Methodologies differed between surveys, making it important to exercise care in the interpretation of results.

In 2002, before the social marketing program was launched nationally, two cross-sectional studies had been undertaken on community drug usage in malaria endemic provinces. The first, conducted by the Mahidol-Oxford Tropical Medicine Research Unit (MORU) in conjunction with the Cambodia National Malaria program (CNM), compared access to AS+MQ in areas with and without supporting interventions (Yeung et al. 2008) and included interviews with 316 respondents with a recent history of fever. The second, the Cambodian Drug Usage Survey (CDUS), aimed at documenting knowledge related to drug usage and behavior of providers and consumers. It included 1,277 household respondents and 156 drug outlets, of

which 49 were in villages and 107 in markets (Cambodia National Malaria program/Cambodia Ministry of Health 2003).

Since the nationwide scale-up of subsidized ACTs in 2003, a number of surveys have been conducted, by PSI and other institutions. One, in 2004, was the Cambodia Malaria Baseline Survey (CMBS), in which a wide range of malariometric data were collected from household and drug outlets, including some information on the availability and use of antimalarial drugs. A stratified multistage sampling design divided the country into three domains by epidemiological features. Clusters were stratified by risk of malaria according to distance from forest. Selection of drug outlets was opportunistic. Of 90 village outlets and 45 market outlets, 80 villages and 43 markets were sampled. Of these, 61 were pharmacies or drug shops, 54 were general stores, six were drug sellers in an open market, and two were private clinics (National Institute for Public Health 2005).

Two survey reports are available from PSI: a 2006 TRaC (Tracking Results Continuously) survey and a 2007 MAP (Measuring Access and Performance) survey. The TRaC study consisted of a cross-sectional household survey conducted in June and July 2006. Stratified multistage sampling was used to collect data from 675 respondents living in villages classified under three domains (high, medium, and low risk of malaria) within the 17 provinces targeted by the social marketing program. The focus of the study was to investigate behaviors related to ITN use and diagnostic blood testing for malaria among residents of malaria endemic areas (Population Services International 2006).

Unlike the other surveys, the MAP study, conducted in September 2007, used Lot Quality Assurance Sampling (LQAS), in which the key outcome is whether a certain threshold has been reached (in this case whether at least 50 percent of shops in a community stock the ACT product). Nineteen communes[5] from each of the three domains within PSI's 17 target provinces were randomly selected and all eligible health[6] and nonhealth[7] outlets in the selected communes

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[5] Cambodia is divided into 1,621 administrative units, called *communes*, which usually represent four to seven villages.

[6] Malarine and Malacheck are supposed to be sold only in health outlets. PSI defines health outlets as those that "specialize in selling health products. They include drug stores, cabinets, pharmacies, clinical pharmacies, SQHN clinics, and mobile providers."(Population Services International 200X).

[7] PSI defines nonhealth outlets as those that "typically sell a combination of products from household items to groceries. They include grocery/convenience stores, village shops, market stalls, and mobile net sellers." (Population Services International 200X).

were audited for the presence of malaria-related products marketed by PSI, including Malarine and Malacheck. Additional information was also collected on a range of quality standards (Population Services International 2008).

Results

Availability and Supply of AS+MQ

From 2003 to 2006, PSI sales to private providers increased from 30,242 to 241,936 packs per year. In 2007, PSI sold 162,364 packs (14 percent for children under five and the remainder for adults), a 33 percent reduction in sales over the previous year. Data on the actual distribution and volume of sales from retail outlets to consumers are not available.

In 2004, a year after the nationwide launch of Malarine, the CMBS found that 22 percent of the sampled private sector outlets sold the adult doses, 6 percent sold the child doses, and 11 percent stocked Malacheck.

The 2007 MAP survey found that 44 percent of sampled communities met the LQAS threshold (at least 50 percent of shops stocking the product) for the adult AS+MQ dose, with penetration generally highest in high-risk areas (55 percent of communities). By comparison, 17 percent of communities met the threshold for the child dose, with few differences across the three risk areas. Few mobile providers were found selling Malarine. Malacheck market penetration was on average 42 percent among private outlets. Most pharmacies, cabinets, and drug stores but fewer mobile providers from medium and low risk areas sold the product.

The presence of expired stocks of either ACTs or RDTs was rare and products were usually stored correctly. However, stock-outs of both Malarine and Malacheck were common. Of the communities that met the stocking threshold, 60 percent reported a stock out of Malarine for adults and children. A stock-out is defined as at least one day without the product in the three months before the survey. The MAP report states that while the survey was being conducted, PSI's central warehouse was out of stock, which may have had an impact on availability among retailers. Information gathered through interviews indicates that delays in central-level procurement were another factor.

Cost of First-Line Drug and RDTs

In September 2004, after PSI conducted a willingness-to-pay study, the printed recommended retail price (RRP) for Malarine was reduced from 7500 riel ($1.88) for the adult

dose and 4500 riel ($1.13) for the child dose to 2500 riel ($0.63) for a dose of either. The RRP for Malacheck is 1000 riel ($0.25).

The current recommended price for retail outlets to buy from wholesalers, distributors or sales agents is $0.55 per dose of Malarine and $0.22 per Malacheck test. The 2007 MAP study found that, in practice, there are large variations in prices retailers pay for the product. Outlets paid an average price of $0.75 (range $0.50 to $2.00) per dose of adult Malarine and $0.69 (range $0.50 to $2.00) per dose of child Malarine, 36 percent and 25 percent higher, respectively, than the recommended price. Malacheck was purchased for an average of $0.29 (range $0.19 to $1.25) per test.

In turn, retailers often sold the products to consumers above the RRP, charging an average price of $1.07 (range $0.63 to $3.75) for adult doses of Malarine and $0.95 (range $0.63 to $2.50) for child doses. Malacheck was sold at a mean price of $0.37 ($0.25 to $1.25).

Patient Awareness

Shortly after the nationwide launch of Malarine, 24 percent of household respondents in the CDUS claimed that they had heard of the drug. In the following year, 46 percent of CMBS household respondents reported that they heard of either Malarine or A+M**.**

Artemisinin Drug Usage

Results from both of the two drug usage studies conducted in 2002 indicate that fewer than 10 percent of febrile patients who sought treatment in the private sector received AS+MQ at the time. Use of artemisinin monotherapies was common and constituted more than 70 percent of treatment with artemisinin-based products.

The 2007 MAP study showed that of the 517 outlets surveyed, the most commonly stocked antimalarial was tetracycline (41 percent)[8], followed by artesunate monotherapies (19 percent). Of the 104 surveyed outlets that sold drugs in "cocktail" packages (a mixture of several loose drugs), 45 percent included artesunate and 13 percent contained artemether. Mefloquine was included in 21 percent. The study also showed that almost one-third of private providers had sold Malarine tablets individually by either removing or cutting tablets from the blister pack (29 percent for the adult doses and 26 percent for the child doses).

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[8] Tetracycline is usually used as an antibiotic but has antimalarial properties and in Cambodia is the recommended second-line treatment in combination with quinine.

Diagnosis

In the 2002 surveys, household respondents reported that only 18 percent of interactions between private providers and patients with recent fever resulted in a biological diagnosis. In the 2006 PSI TRaC study, 64 percent (n = 309) of respondents reported taking a diagnostic blood test the last time they had symptoms, and 34 percent reported generally ("always/often") doing so. Because the 2006 PSI study included consultations with public as well as private providers, and during this time there was an increase in diagnosis in the public sector, these two sets of results are not directly comparable.

Discussion

Cambodia was the first country to pilot and then scale up the provision of subsidized ACTs in the private sector. It did not, however, collect and analyze formal baseline and follow-up data, which limited any comprehensive evaluation of the program. However, a number of studies and surveys have been conducted before and during the program. General conclusions are possible, but survey sampling strategies differed and were not necessarily representative of the country or of malaria-endemic areas. In particular, the private drug outlets in the CMBS study were convenience sampled, introducing potential bias, and the outlets in the MAP study were sampled using the LQAS technique.

Awareness of Malarine and Malacheck among providers and consumers appears high, following several years of social marketing activities. Market penetration rates, however, are only just above 40 percent for Malarine and Malacheck. Supplies of the products are irregular and provider stock-outs frequent (Population Services International 2008). Further research is needed to clarify the extent to which low stocking levels are attributable to difficulties obtaining supplies versus a lack of consumer demand. The observed trend that providers consistently sell both ACTs and RDTs above their RRP likely reduces the equity of access and may be driven by a number of factors. First, because the products were available for several years at substantially higher prices before PSI reevaluated the pricing, providers and consumers may still associate the products with these price levels and charge or pay accordingly. Second, the irregular supply may have enabled providers to charge more when products are available assuming adequate demand. Last, consumers' price elasticity for the products may be higher than estimated or the providers' margin from the RRP is limited, enabling them to generate greater revenue by selling fewer products at higher prices.

Malaria transmission in much of Cambodia is very low with a yearly decline in cases of *P. falciparum* (Cambodia National Malaria Program/Cambodia Ministry of Health/and partners

2008). Most fevers, especially in western Cambodia, where drug resistance is worst, are not due to falciparum malaria, and therefore do not need to be treated with artemisinin drugs. Although RDTs have been marketed for several years, availability and uptake of biological diagnosis is still low. The MAP study found that the strongest determinant of a patient with fever using a diagnostic test for malaria was being offered a test by the provider. This suggests that ensuring an adequate and reliable supply of affordable RDTs and properly training and motivating providers to dispense them are essential. In addition, further operational research to assess and explore ways to increase the proper usage of RDTs is warranted given the poor adherence to guidelines observed in other settings (Reyburn et al. 2007).

Given the challenges in stocking and uptake of ACTs and the apparent declining incidence of malaria, the most effective way of increasing access to high quality ACTs and diagnosis may be to provide both at no cost through trained village volunteers (Yeung et al. 2008). This scheme is now being expanded to include lower transmission areas and should be thoroughly evaluated to ensure maximum coverage and efficiency in light of the low parasite prevalence rates. Regardless of progress in this initiative, however, a large proportion of patients will continue to seek treatment in the private sector. With use of artemisinin monotherapies at these outlets high, and with resistance to artemisinin apparently emerging in the region, it is imperative that a comprehensive approach to private antimalarial treatment in Cambodia be implemented in the near future (2007).

Senegal

Malaria is endemic throughout Senegal. An estimated 1.5 million cases occur each year, accounting for 30 percent of outpatient visits and 25 percent of hospital deaths in children under five (Senegal National Malaria Control Program 2006; President's Malaria Initiative 2008). There are signs, however, that recent efforts by government and partners have yielded positive outcomes: although malaria-related morbidity has not changed between 2000 and 2005, the proportion of attributable infant mortality dropped from 30.2 percent to 20.7 percent (Republic of Senegal 2007).

In 2005, Senegal changed its first-line treatment for uncomplicated malaria to the ACT artesunate-amodiaquine (AS+AQ). In April 2006, with support from the Global Fund, the government medical stores (Pharmacie Nationale d'Approvisionement—PNA) procured its first consignment of 3 million courses of AS+AQ for national distribution that year. In January 2007, it received a second consignment of 3 million for the following year. The number of doses exceeds estimated malaria cases because a large number of fever cases were treated as suspected

malaria (Republic of Senegal 2007). Treatment for malaria occurs primarily in the public sector, where an estimated 75 percent of patients seek treatment from public facilities (Thior 2008). In line with the cost-recovery system for essential medicines in the country, public facilities charge 600 F CFA ($1.29) for an adult dose of AS+AQ and 300 F CFA ($0.65) for child and infant doses. To supplement treatment access in the public sector, the government launched the distribution of subsidized AS+AQ through private pharmacies in September 2006. AS+AQ was assigned a suggested retail price (SRP) to match that of the public sector.

Methodology

Data presented in this report were gathered one year after distribution of subsidized ACT began in the private sector. The Institute for Research and Development led the design and implementation of this evaluation, which centered on four primary methods: a pricing survey based on the Health Action International-WHO methodology, mystery shoppers, GPS mapping, and qualitative interviews with key institutions (the National Program to Fight Malaria, Ministry of Health, PNA, and private wholesalers) (World Health Organization/Health Action International 2008). The research was developed to answer key questions about the availability and pricing of ACT in the public, nongovernment, and private sector.

The HAI-WHO pricing survey covered a sample of public, nongovernment, and private sector outlets from both urban and rural areas of Senegal. Survey areas were selected based on population density and proximity to national borders. Outlets were identified by purposively selecting public health facilities and searching for all other outlets in the surrounding area. In the urban Dakar region and Mbour city (located 80 km south of Dakar), six public, five NGO, and 28 private outlets were identified from ten areas. In the rural areas of Takhoum (near an urban center), Niakhar and Ndangalma (removed from any major towns or roads), and Nioro (on a border), 12 public, three NGO, and 13 private outlets were identified. Because of the distances between outlets, the rural survey limited itself to private outlets located within a 10 km radius of an identified public health center.

Mystery shoppers visited stores in private pharmacies, 40 in urban areas and 110 in rural settings. On visiting a store, the mystery shopper presented a prescription for either an adult dose (44 percent) or child dose (56 percent). If the outlet did not stock AS+AQ, the shopper purchased the recommended alternative. In Senegal, an agreement between private pharmacies and wholesalers allows unsold medication with more than six months to expiration to be returned to the wholesaler for a refund. The ACT used for private sector distribution had a sell-by date of November 2007. As a result, June and July 2007 orders for ACTs were low. Because the data

presented here were collected in August 2007, it is possible that stocking of ACT was unnaturally low because the product was soon to expire.

Results

Availability

The HAI-WHO survey found that overall stocking of AS+AQ in urban areas was higher in the public than in the private sector. Among public and NGO facilities, 83 percent (nine of 11) stocked all three doses. Among private outlets, only 7 percent (two of 28) did so. Stocking adult ACT was particularly high in public and NGO facilities (91 percent) and the child dose higher in private facilities (43 percent). By comparison, 96 percent of private shops stocked SP and 79 percent stocked chloroquine+proguanil. Stocking in rural areas followed a similar pattern, with all three doses more available at public and NGO facilities (67 percent) than at private shops (8 percent).

Stocking Level

Stocking levels of AS+AQ in urban areas were substantially higher in public facilities than in private shops, with an average of 85 doses for children under five per public facility, versus only 4 doses per private outlet. In addition, stocking at outlets in urban settings was higher than in rural ones: only 52 doses for children under five were found per public facility in rural areas.

Pricing

In urban areas, the outlet pricing survey found adult doses of AS+AQ on sale at private shops at an average of 621.32 F CFA ($1.34), which was similar to the observed public sector price of 606.22 F CFA ($1.31). The private and public sector selling prices for child and infant doses are also comparable, at 322 F CFA ($0.69) in the public and at 304.16 F CFA ($0.66) in the private sector. Prices reported from mystery shoppers at private shops are consistent with these findings. Shoppers paid on average 627.5 F CFA ($1.25) for the adult doses and 332 F CFA ($0.72) for the child and infant doses. Prices in rural areas followed these trends at an average of 615 F CFA ($1.33) for adult doses and 320 F CFA ($0.69) for child and infant doses in private shops.

As shown in table 6, the recommended price structure indicates that outlets should sell AS+AQ at a 30 percent mark up. Although mark-ups in the private sector appear to follow this

policy, the purchase price for the private sector has been assumed to reflect government policy and was not verified.

Discussion

The relationship between the public and private sectors in Senegal differs substantially from many countries. Unlike in much of East Africa, an established system of the government medical stores distributes products to private for-profit outlets as well to public facilities. The distribution of ACTs through this system thus provides a unique opportunity to examine the experience of subsidy schemes. However, although ACTs have been distributed through private shops for roughly two years, no evaluation was built into the project and the exercise later conducted focused only on pricing and availability. The evidence gathered to date does not answer questions related to uptake of and access to subsidized ACTs. Moreover, the survey was conducted on a relatively small number of outlets over a short period. Despite limited data, useful lessons can be derived from this experience.

The most notable finding was the comparable pricing of AS+AQ in the public and private sectors. Because of the cost recovery system, public facilities receive AS+AQ from the central medical stores at a rate only modestly below the market price and in turn apply a small mark-up. Although private shops apply higher mark-ups to include profit margins, they buy ACTs at a lower price (though still modestly subsidized compared with other countries), which enables them to sell to consumers at the same level as the public sector. It is therefore interesting that stocking AS+AQ was considerably lower in private shops. It is impossible to determine without further data, but the dramatically higher rates of stocking of SP and other products by private shops suggests the continued high price of AS+AQ compared to these alternatives limited consumer demand. Private businesses appeared to consistently apply reasonable mark-ups on the subsidized ACTs. Consumers paid only 4 percent more than the RRP for the adult dose of AS+AQ on average, and the highest price observed was only 4 percent above that average.

Lessons Learned

The case studies examined here provide an initial picture of the impact and challenges that can be expected as the global malaria community devotes increased attention and resources to delivering ACTs through the private sector. Although the limited data prevent broad conclusions, the experiences of these countries can provide valuable lessons to guide policymaking. Indeed, a number of important themes emerge from analysis across the countries.

Subsidies and the Private Sector

The Kenya and Tanzania studies indicate that subsidy programs can lead to more rapid uptake of ACTs among individuals seeking treatment at private outlets. In Tanzania, the proportion of consumers purchasing ACTs rose more than forty-fold after five months. The lack of change in ACT purchasing in the control district during the same period confirms the role of the subsidy intervention in this increase. There was a similar change in Kenya. The increased uptake of ACTs led to a corresponding decrease in the use of other therapies such as SP and amodiaquine. Although neither study found substantial sales of artemisinin monotherapies at baseline, it can be inferred that these treatments would have similarly been crowded out by increased sales of ACTs, as has been assumed in the studies underpinning the AMFm (Laxminarayan et al. 2006).

The Cambodia experience presents an important exception to this trend. After five years of implementation, the most commonly purchased antimalarials at private shops were tetracycline and an artemisinin monotherapy, with use of ACTs appearing to rise only marginally. Although the available data are suboptimal and may underrepresent the uptake of ACTs at certain times during the project, evidence suggests that subsidized ACTs have not gained traction with consumers in Cambodia.

There are many possible reasons for the low uptake in Cambodia compared to the other countries, some of which are examined in greater detail below and in a forthcoming publication. The antimalarial environment is fundamentally different in Cambodia than in sub-Saharan Africa. Artemisinin monotherapies have been widely available for many years and consumers appear to perceive them to be safe and effective. There was thus little incentive for consumers to switch to the co-blistered A+M, as mefloquine is associated with unpleasant side effects. Unfortunately it is difficult to draw conclusions about price sensitivity from the available data. By comparison, consumers in East Africa were typically using SP and amodiaquine for which significant resistance has developed (Schonfeld et al. 2007). However, anecdotal evidence indicates that some patients prefer SP to ACTs because of its simpler dosing schedule, suggesting that the pricing and promotion of ACTs in those countries contributed to the more rapid uptake.

Outlets and Access

Another possible driver of the difference in uptake between the case study areas is the type of outlet. Here, the difference is most notable between Kenya and Tanzania. In Kenya, a limited number of franchised shops hired registered nurses and were upgraded to clinics to

dispense ACTs and RDTs. By comparison, the *duka la dawa baridi* that distributed ACTs in Tanzania were often staffed by individuals with no formal medical education and only a two-day training on malaria and ACTs before the subsidy. Thus only nine shops across three districts distributed ACTs in Kenya, compared to 146 shops in two districts in Tanzania. This in turn led to radically different provision: shops in Kenya distributed 2,086 ACTs over nine months (232 doses per month on average) whereas those in Tanzania dispensed 8,932 doses in a single month. Subsidized ACTs in Cambodia are intended to flow through a range of private outlets approved to sell medicines, but because data are not linked to the types of outlets similar comparisons are difficult.

The principal reason for limiting the private outlets that can supply drugs is concern about quality of care provided and overtreatment with antimalarials. These studies provide limited but useful insight. In Kenya, the CFW clinics almost always dispensed the correct dose and followed treatment guidelines such as weighing children and observing the first dose more frequently than in public facilities in the area. Although these metrics were not captured in Tanzania, it is reasonable to assume that few shops engaged in these practices because they were not trained as comprehensively and the relevant equipment (e.g., scales) was typically not available. Shops in Tanzania did, however, dispense the correct ACT dose (according to age) almost as frequently as those in Kenya and there was little evidence of packages being split or opened. This finding is in line with other studies (Goodman 2004). Nevertheless, it appears that the clinics in Kenya consistently provide better care than the more informal shops in Tanzania. Less information was available on the appropriateness of ACT prescriptions and the role of diagnostics, including the impact of RDT use in Cambodia and Kenya. This is a critical topic for further research, particularly if ACT subsidies are to be introduced in areas with low or moderate malaria transmission.

These studies thus highlight the fundamental tension between access and quality in private sector ACT distribution that policymakers must grapple with as large-scale interventions are increasingly rolled out (Goodman et al. 2007). Many sub-Saharan countries take an approach similar to Kenya's, allowing ACTs to be distributed only through a limited number of outlets (e.g., pharmacies). At the same time, most other antimalarials are available over the counter from a wide range of outlets, including general stores. It is doubtful that introducing AMFm or any other large-scale subsidy intervention into a narrower private sector will have a dramatic impact on ACT access or use of monotherapies. Although some subsidized ACTs will undoubtedly be distributed illegally to other outlets, regulatory authorities will likely apply greater scrutiny to publicly financed subsidy interventions, dissuading wholesalers from distributing to smaller,

unapproved outlets. This experience suggests that prescription-only ACTs and associated restrictions on outlets must be at the center of discussions on the AMFm, both within countries and across the global community.

Markups and Limiting Prices

The markups placed on subsidized ACTs as they flow through the private supply chain have substantial impact on eventual uptake by consumers and are a considerable source of concern for policymakers. The evidence provided by the Senegal and Tanzania studies is generally optimistic in this regard. In Tanzania, consumers paid, on average, the same or less for subsidized ACTs as for the most common alternative antimalarials. In both Tanzania and Senegal markups on average were reasonable and the data indicate no instances of price gouging. Both studies found no correlation between the location of the shop and the price paid by consumers.

In contrast, in Cambodia, the average retail price for adult doses was 70 percent above the RRP and in specific cases, as much as six times higher. RDTs were similarly marked up above the RRP. As with ACT uptake, the reason for the difference between Cambodia and the other countries is unclear. All of the factors discussed, including consistent supply shortage and the initial introduction of the product at a considerably higher RRP, likely had an influence. In addition, the differences in subsidy level and recommended price certainly played a role. The RRP in Tanzania was roughly 225 percent higher than the subsidized price at which the wholesaler reported selling ACTs to retailers. This difference provided consumers with a retail price equivalent to other antimalarials and the retailers with substantial revenue. By comparison, the RRP in Cambodia was roughly 15 percent higher than the recommended price, which may have generated inadequate revenue for businesses, creating incentives for them to raise prices and promote other more lucrative products. This issue reinforces the importance of global institutions and countries determining the optimal subsidy level and, if relevant, recommended retail prices.

The Senegal experience also illustrates an important reality of many countries. Discussion of strategies to increase ACT access often centers on a dichotomy of free public sector distribution versus charges in the private sector. The Senegal study, however, found that patients paid equivalent amounts for ACT treatment in the public and private sectors. Although this finding is particularly relevant in West African countries implementing the Bamako Initiative, charges at public facilities are common in many other malaria-endemic countries (Uzochukwu et al. 2004; Mubyazi et al. 2006; Hetzel et al. 2008). A recent study in Tanzania, for

example, found that patients spent equally for malaria treatment from public and private sources (Hetzel et al. 2008).

Strategies and Settings

Ultimately, the most important question of any subsidy intervention is whether it increases overall coverage among patients. These case studies are not capable of robustly answering that question about ACTs and malaria. The data from Kenya and Tanzania provide rough initial indications, however. In Tanzania, the total number of ACTs dispensed by the public and private sectors in the study areas rose substantially between the data collection periods, with subsidized ACTs accounting for nearly half of that increase. The increase in Kenya was similar. That increase, however, was driven predominantly by increased distribution from public sector facilities, with the private sector accounting for a small minority. Although this may be in part because of the relatively few private shops dispensing ACTs in the study area, it highlights the considerable role that improvement of supply and promotion in the public sector can have on access. Consequently, though private sector interventions will be imperative to increasing access in some countries, in others, with limited resources and different epidemiology and patient behavior, impact may be greater through investment in improving public sector distribution.

These experiences suggest that private sector subsidies can play an important role in efforts to increase ACT coverage in many malaria-endemic areas, though additional operational research is needed to robustly discern impact and guide the development of optimal approaches. After only five months, two-thirds of consumers buying antimalarials for children under five in Tanzania are buying ACTs rather amodiaquine and other therapies, and businesses in both Tanzania and Senegal are applying reasonable markups. Above all, however, these studies emphasize the need for ACT distribution strategies to be carefully tailored to each country. Malaria affects many countries, each with largely unique epidemiology, demographics, health systems, and resources. In addition, potential private sector treatment interventions must take into account broad differences in treatment seeking behavior, private outlets, regulatory frameworks, and consumer preferences. Each country must engage in an independent process to decide if and how to pursue increased ACT access in the private sector, including through the AMFm.

References

Amin, A., and R. Snow. 2005. Brands, Costs, and Registration Status of Antimalarial Drugs in the Kenyan Retail Sector. *Malaria Journal* 4: 36.

Amin, A.A., D. Zurovac, B.B. Kangwana, J. Greenfield, D.N. Otieno, W.S. Akhwale, and R.W. Snow. 2007. The Challenges of Changing National Malaria Drug Policy to Artemisinin-Based Combinations in Kenya. *Malaria Journal* 6: 72.

Brugha, R., and A. Zwi. 1998. Improving the Quality of Private Sector Delivery of Public Health Services: Challenges and Strategies. *Health Policy and Planning* 13: 107-120.

Cambodia National Malaria program/Cambodia Ministry of Health (2003). Community Drug Use Practices in Malaria in Cambodia: A Cross-Sectional Survey:Draft. Phnom Penh, Cambodia.

Cambodia National Malaria program/Cambodia Ministry of Health/and partners (2008). Annual Progress Report. Phnom Penh, Cambodia.

Dondorp, A.M., P.N. Newton, M. Mayxay, W. Van Damme, F.M. Smithuis, S. Yeung, A. Petit, et al. 2004. Fake Antimalarials in Southeast Asia Are a Major Impediment to Malaria Control: Multinational Cross-Sectional Survey on the Prevalence of Fake Antimalarials. *Tropica Medicine and International Health* 9(12): 1241-6.

East African Network for Monitoring Antimalarial Treatment. 2003. The Efficacy of Antimalarial Monotherapies, Sulphadoxine-Pyrimethamine and Amodiaquine in East Africa: Implications for Sub-Regional Policy. *Tropical Medicine and International Health* 10: 860-867.

Farooq, U., and R. Mahajan. 2004. Drug Resistance in Malaria. *Journal of Vector Borne Diseases* 41(3-4): 45-53.

Foster, S. 1995. Treatment of Malaria Outside of the Formal Health Services. *American Journal of Tropical Medicine and Hygiene* 98(29-34).

Global Fund To Fight AIDS, T., and Malaria, (2008). Report of the Policy and Strategy Committee to the Seventeenth Board Meeting. Geneva.

Goodman, C. (2004). An Economic Analysis of the Retail Market for Fever and Malaria Treatment in Rural Tanzania. Department of Public Health and Policy. London, London School of Hygiene and Tropical Medicine, University of London. PhD Thesis.

Goodman, C., S. Kachur, S. Abdulla, P. Bloland, and A. Mills. 2007. Drug Shop Regulation and
    Malaria Treatment in Tanzania - Why Do Shops Break the Rules, and Does It Matter?
    Health Policy and Planning 22(6): 393-403.

Hamer, D.H., M. Ndhlovu, D. Zurovac, M. Fox, K. Yeboah-Antwi, P. Chanda, N. Sipilinyambe,
    J.L. Simon, and R.W. Snow. 2007. Improved Diagnostic Testing and Malaria Treatment
    Practices in Zambia. *Journal of the American Medical Association* 297(20): 2227-31.

Hetzel, M., B. Obrist, and C. Lengeler. 2008. Obstacles to Prompt and Effective Malaria
    Treatment Lead to Low Community-Coverage in Two Rural Districts of Tanzania. *BMC
    Public Health* 8(1): 317.

Institute of Medicine. 2004. *Saving Lives, Buying Time*. Washington, D.C: National Academies
    Press.

Kachur, S., C. Black, S. Abdulla, and C. Goodman. 2006. Putting the Genie Back in the Bottle?
    Availability and Presentation of Oral Artemisinin Compounds at Retail Pharmacies in
    Urban Dar-Es-Salaam. *Malaria Journal* 5: 25.

Laxminarayan R, Over M, and S. D. 2006. Will a Global Subsidy of New Antimalarials Delay
    the Emergenece of Resistance and Save Lives? *Health Affairs* 25(2): 325-326.

Laxminarayan, R., Over M, and S. D. 2006. Will a Global Subsidy of New Antimalarials Delay
    the Emergenece of Resistance and Save Lives? *Health Affairs* 25(2): 325-326.

Mbogoro, D. 2002. Population and Housing Census Results Republic of Tanzania. Dar es
    Salaam: Tanzania Ministry of Health.

McCombie, S. 1996. Treatment Seeking for Malaria: A Review of Recent Research. *Social
    Science & Medicine* 43(6): 933-945.

Mubyazi, G., J. Massaga, M. Kamugisha, J.N. Mubyazi, G.C. Magogo, K.Y. Mdira, S. Gesase,
    and T. Sukwa. 2006. User Charges in Public Health Facilities in Tanzania: Effect on
    Revenues, Quality of Services and People's Health-Seeking Behaviour for Malaria
    Illnesses in Korogwe District. *Health Services Management Research* 19(1): 23-35.

National Bureau of Statistics, ORC Macro. 2005. Tanzania Demographic and Health Survey
    2004-05. Dar es Salaam, Tanzania.

National Institute for Public Health (2005). Report of the Cambodia National Malaria Baseline
    Survey 2004. Phnom Penh, Cambodia.

Newton, P.N., A. Dondorp, M. Green, M. Mayxay, and N.J. White. 2003. Counterfeit Artesunate Antimalarials in Southeast Asia. *Lancet* 362(9378): 169.

Noor, A. 2008. Personal Communication.

Population Services International (2006). Cambodia (2006): Malaria Trac Survey among Populations Living in Malaria Endemic Areas, Cambodia. First Round. Social Marketing Research Series.

Population Services International (2008). Cambodia (2007): MAP Study Evaluating the Coverage and Quality of Coverage of Malaria Prevention and Treatment Products in Endemic Areas. Social Marketing Research Series.

President's Malaria Initiative (2008). Senegal Malaria Operational Plan. Washington, DC.

Republic of Senegal (2007). Senegal Global Fund Round 7 Proposal

Resistance to Artemisinin Derivatives Along the Thai-Cambodian Border. 2007. *Weekly Epidemiological Record* 82(41): 360.

Reyburn, H., H. Mbakilwa, R. Mwangi, O. Mwerinde, R. Olomi, C. Drakeley, and C.J. Whitty. 2007. Rapid Diagnostic Tests Compared with Malaria Microscopy for Guiding Outpatient Treatment of Febrile Illness in Tanzania: Randomised Trial. *British Medical Journal* 334(7590): 403.

Roll Back Malaria Partnership (2007). Technical Design of the Affordable Medicines Facility - Malaria. Geneva.

Roll Back Malaria/Malaria Case Management Working Group (2005). Roll Back Malaria Consultative Meeting on the Role of Medicine Sellers in the Management of Malaria: What's Worked and Where Do We Go from Here? Accra, Ghana.

Rozendaal, J. 2001. Fake Antimalaria Drugs in Cambodia. *Lancet* 357: 890.

Schonfeld, M., I. Barreto Miranda, M. Schunk, I. Maduhu, L. Maboko, M. Hoelscher, N. Berens-Riha, A. Kitua, and T. Loscher. 2007. Molecular Surveillance of Drug-Resistance Associated Mutations of Plasmodium Falciparum in South-West Tanzania. *Malaria Journal* 6: 2.

Senegal National Malaria Control Program (2006). Senegal National Malaria Control Program Activity Report. Dakar, Senegal.

Tanzania Food and Drug Authority. 2007.

Tanzania National Malaria Control Programme (2007). Mid-Term Strategic Plan 2008-2012 (Draft).

Thior, M. (2008). Experience of Senegal in Act Implementation. <u>Medicines for Malaria Venture Access Symposium.</u> Accra, Ghana.

UNICEF/Roll Back Malaria Partnership (2007). Malaria and Children: Progress in Intervention Coverage New York.

Uzochukwu, B., O. Onwujekwe, and B. Eriksson. 2004. Inequity in the Bamako Initiative Programme--Implications for the Treatment of Malaria in South-East Nigeria. *International Journal of Health Planning and Management* 19 Suppl 1: S107-16.

World Health Organization (2002). Achieving Impact: Roll Back Malaria in the Next Phase." Report of the External Evaluation of Roll Back Malaria: Draft. Geneva, WHO.

World Health Organization (2004). Equitable Access to Essential Medicines: A Framework for Collective Action. Geneva, WHO.

World Health Organization/Health Action International (2008). Measuring Medicines Prices, Availability, Affordability and Price Components. Geneva, WHO.

World Health Organization/UNICEF (2003). The Africa Malaria Report 2003 Geneva, WHO.

Yeung, S., W. Van Damme, D. Socheat, N.J. White, and A. Mills. 2008. Access to Artemisinin Combination Therapy for Malaria in Remote Areas of Cambodia. *Malaria Journal* 7: 96.

Yeung, S., and N. White. 2005. How Do Patients Use Anti-Malarial Drugs: A Review of the Evidence. *Tropical Medicine and International Health* 10(2): 121-138.

Tables

Table 1. Current Distribution of ACTs through Private Sector

Country	Lead	Type of ACT	Project Launch	Age group	Coverage	Outlet	Supporting interventions	M&E
Cambodia	PSI	AS+MQ	2002	all	17 provinces	pharmacies, drug shops	training, IEC, SRP, packaging	see table 4
Kenya	SHEF/ WHO-TDR	AL	Dec. 2006	all	3 districts	franchised clinics	outlet upgrade, regulatory supervision, diagnosis	baseline Dec. 2006; 1-year study in Mar. 2008
Senegal	government	AS-AQ	Sept. 2006	all	national	private sector pharmacies	SRP	Nov. 2007
Tanzania	government/ CHAI	AL	Oct. 2007	all	2 districts	drug shops	training, IEC, packaging, SRP	baseline Aug. 2007. Quarterly for 1 year
Madagascar	PSI	AS-AQ	2003	< five	national	pharmacies, private providers, community agents	training, IEC, packaging, SRP	late 2008
Nigeria	government/ PSI-SFH	AL	2006	< five	targeted districts	pharmacies, drug shops, and PPMVs	training, IEC, packaging	May 2008
Rwanda	PSI	AL	2007	< five	~22 districts	pharmacies	training, IEC, packaging	outlet survey Feb. 2008; HH survey May 2008
Myanmar	PSI	AL	June 2003	all	ended 2005	clinic franchises	training, IEC, packaging, with rapid diagnostic test	HH and outlet surveys 2008
Uganda	government/ MMV	AL	Sept. 2008	all	6 districts	drug shops, clinics	training, IEC, OTC rescheduling, packaging, SRP, upgrading outlets, pharmacovigilance	supply and HH surveys Aug 07; baseline: Sept 2008; quarterly for 1 year
Kenya	government/ PSI	AL	Oct. 2008	< five	3 districts (selected locations)	drug shops and general stores	training, IEC, packaging	cluster randomized study; baseline mid 2008, evaluation at one year
Tanzania	PMI-MSH	AL	Nov. 2007	all	2 regions	accredited drug dispensing outlets	training, outlet upgrade, packaging, SRP	no specific evaluation
DRC	PSI	AS-AQ	TBD	< five	limited	pharmacies	TBD	TBD
Angola	government/ PMI	AL	TBD	< five	pilot study	private clinics, pharmacies, community agents	training, IEC	TBD
Source: To come.								

Table 2. Number of Shops in Competition Index Categories

Competition Index (CI)	Number of shops (November 2007)	Number of shops (March 2008)
0	45	38
1	28	47
2-3	58	39
4	13	41
5+	66	51

Table 3. Consumers Purchasing Antimalarials in Maswa and Kongwa Districts

		Baseline (August 2007)	Month One (November 2007)	Month Five (March 2008)
Total exit interviews		n = 417	N = 297	n = 290
Adults (ages 16+)	**Product selection (Maswa/ Kongwa)**			
	Any antimalarial	281/ 42	164/ 64	130/ 62
	AL	0 (0%)/ 0 (0%)	40 (24%) / 19 (30%)	44 (34%)/ 22 (35%)
	SP	187 (67%)/ 26 (62%)	89 (52%)/ 37 (58%)	50 (38%)/ 32 (52%)
	AQ	71 (25%)/ 10 (24%)	23 (14%) / 5 (8%)	22 (17%)/ 6 (10%)
	Art monotherapy	1 (0%)/ 0 (0%)	3 (2%)/ 0 (0%)	0 (0%)/ 2 (3%)
	Price (median – Maswa/ Kongwa)			
	AL	N/A	$0.47/ $1.00	$0.42/ $1.00
	SP	$0.67/ $0.50	$0.42/ $0.50	$0.42/ $0.50
	AQ	$0.33/ $0.33	$0.33/ $0.35	$0.33/ $0.33
Children Under Five	**Product selection (Maswa/ Kongwa)**			
	Any antimalarial	38/ 6	44/ 14	47/ 34
	AL	0 (0%)/ 0 (0%)	13 (30%)/ 10 (71%)	24 (51%)/ 26 (76%)
	SP	1 (3%)/ 2 (33%)	5 (11%)/ 1 (7%)	3 (6%)/ 2 (6%)
	AQ	35 (92%)/ 4 (67%)	24 (55%)/ 3 (21%)	13 (28%)/ 6 (18%)
	Art monotherapy	0 (0%)/ 0 (0%)	0 (0%)/ 0 (0%)	0 (0%) / 0 (0%)
	Price (median – Maswa/ Kongwa)			
	AL	N/A	$0.17/ $0.25	$0.38/ $0.25
	SP	$0.25/ $0.33	$0.42/ $1.00	$0.42/ $0.46
	AQ	$0.83/ $1.25	$0.67/ $0.83	$0.83/ $1.04

Table 4. Coverage of AL in Intervention Districts in Kenya

	Baseline (December 2006)	Evaluation (March 2008)
Surveyed patients receiving any antimalarial	414	1105
Patients receiving AL	64 (15%, 95% CI 12–19%)	457 (42%, 95% CI 39–45%)
From public facilities	41 (64%, 95% CI 52–76%)	393 (86%, 95% CI 83–89%)
From CFW clinics	0	42 (9%)
From other sources	23 (36%, 95% CI 24–48%)	23 (5%, 95% CI 3–7%)
Source: To come		

Table 5. Major Surveys on ACT Distribution in Cambodia

Survey	Implementer	Study content	Data collection and sampling	Coverage	Dates
Access to ACTs in remote areas of Cambodia	MORU and CNM	Treatment seeking behavior and antimalarial usage with and without supporting interventions	HH survey, purposive sampling of areas and random sampling of villages	Thai-Cambodia border	July-September 2002
Cambodia Drug Usage Survey (CDUS)	CNM and partners	Overall antimalarial usage	HH and drug outlet survey, stratified multi-stage sampling design	Thai-Cambodia border	October 2002
Cambodia Malaria Baseline Survey (CMBS)	CNM and partners	Baseline malaria indicator survey including prevalence	HH and drug outlet surveys, stratified multistage sampling design and opportunistic selection of drug outlets	All malaria endemic provinces	November-December 2004
Cambodia: Malaria Tracking Results Continuously (TRaC) Survey	PSI	Behaviors related to use of ITNs and diagnostic blood tests for malaria	HH survey and stratified multistage sampling	17 malaria endemic provinces targeted by PSI's malaria program	June-July 2006
Cambodia (2007): Measuring Access and Performance (MAP)	PSI	Coverage, market penetration and quality of coverage of PSI's malaria products	Drug outlet survey, LQAS technique to draw 19 communes from three strata (high, medium, low endemic areas)	17 provinces targeted by PSI's malaria program	September 2007
Source: To come					

Table 6. Public and Private Sector AS+AQ Prices During HAI-WHO Survey

		RRP	Actual public (n = 18)	Actual private (n = 31)
Selling price	Adult	$ 1.29	$ 1.30	$ 1.34
	Child	$ 0.65	$ 0.65	$ 0.69
Purchase price	Adult	$ 0.99*	$ 1.26	$ 0.99*
	Child	$ 0.50*	$ 0.61	$ 0.50*
Mark up ($US)	Adult	$ 0.30	$ 0.04	$ 0.35
	Child	$ 0.15	$ 0.04	$ 0.19
Mark up (%)	Adult	30%	3%	35%
	Child	30%	6%	40%
*Purchase prices for private pharmacies from wholesalers have been set by the government. Prices indicated are assumed to follow government policy but were not confirmed and in practice may vary. Source: To come				