Price Subsidy Schemes for Artemisinin-Based Combination Therapies (ACTs): Do They Work?

Although ACTs are recommended as first line treatment for uncomplicated malaria, actual use of ACT is very limited, partly due to its high price in pharmacies and retail stores. The Affordable Medicines Facility-malaria (AMFm), a donor-funded global price subsidy, has been proposed as a strategy to increase ACT use in malaria-endemic countries. Given that donor-supported ACT subsidy schemes are costly, it is crucial to ensure that they have their intended impact. In this Policy Brief, E2Pi reviews the available literature evaluating whether previous private sector ACT subsidy schemes have worked or not. The brief also discusses the implications of these schemes for the initial two-year AMFm pilot phase (Phase 1).

BACKGROUND

The WHO recommends that uncomplicated *P. falciparum* malaria should be treated with artemisinin-based combination therapies (ACTs) rather than older anti-malarial drugs, which are now largely ineffective due to parasite resistance.[1,2] Even though most endemic countries have adopted a policy of ACTs as first-line treatment, use of these drugs in practice remains very limited. Data from the World Malaria Report 2009 show that, on average, less than 15% of children with fever in sub-Saharan Africa received an ACT between 2007 and 2008 (the range was 3%–25%).[3] A key reason for this low usage rate is that about half of all patients in Africa with suspected malaria, and about three quarters in South East Asia, seek care in the private sector, where retail ACT prices are extremely high.[3] A course of ACT typically costs $6–8, around 10 to 20 times as much as older drugs, such as chloroquine (CQ) or sulfadoxine-pyrimethamine (SP).

The Affordable Medicines Facility-malaria (AMFm), a donor-funded global price subsidy managed by The Global Fund to Fight AIDS, Tuberculosis and Malaria (GF), has been proposed as a strategy to increase ACT use in the private and public sectors by subsidizing ACT prices in malaria-endemic countries.[4] The AMFm, which is currently being piloted in eight countries (see box to right), lowers the cost of ACTs purchased by eligible first-line buyers. Proponents of the AMFm argue that the subsidy will in turn be passed along the supply chain to the consumer, leading to reduced consumer prices for ACTs, which in turn should increase usage rates.[5] In the AMFm, the subsidy is combined with "supportive interventions" (SIs), such as public awareness campaigns and training for ACT providers, which are also aimed at boosting ACT usage.[6]

The initial costs of the AMFm pilot are estimated at US$ 343 million—$US 216 million for the subsidy and $US 127 million for the SIs.[6] Given these costs, policymakers will wish to see evidence that such schemes work, i.e., that they can: (a) reduce the price of ACTs, (b) increase ACT availability, (c) increase ACT use, and (d) crowd out less effective drugs, including artemisinin mono-therapy (such mono-therapy increases the risk of artemisinin resistance). The GF Board has stated that the GF will only expand from the AMFm pilot phase to a global scale-up on the basis of evidence gathered during the pilot that it can achieve these outcomes.[7]

AMFm PILOT COUNTRIES

Cambodia
Ghana
Kenya
Madagascar
Niger
Nigeria
Tanzania (mainland and Zanzibar)
Uganda

As of March 22, 2011, the GF website reported that subsidized ACTs had arrived in six out of these eight countries—they had not yet arrived in Uganda or Cambodia. An update of the status of the pilots is at theglobalfund.org/programs/amfm/report.aspx

The GF has commissioned an independent evaluation of the AMFm pilot, which will assess changes in three of these parameters (ACT price, availability, and market share) in all eight pilot countries.[8] The fourth parameter (ACT use) will only be assessed in a small number of the fastest-moving pilot countries (probably one or two).[9] It will also be important to know how price subsidy schemes compare with initiatives aimed at increasing ACT usage predominantly in the public sector, such as those funded by the GF or the US President's Malaria Initiative. Indeed, the GF Board has requested a study of "the comparative effectiveness and cost-effectiveness of the AMFm in relation to other financing mechanisms with similar objectives and similar duration of implementation."[10]

E2Pi recently examined the available literature evaluating whether previous private sector ACT subsidy schemes worked or not. This examination was one component of a project, commissioned by the GF, which involved estimating "benchmarks" of success for the AMFm pilot.[11] E2Pi is also in the process of co-authoring, with the Liverpool School of Tropical Medicine and the KEMRI-Wellcome Trust, a formal Cochrane systematic review of previous ACT subsidy trials. This Policy Brief gives an initial summary of the evidence to date about these subsidy schemes and lays out some lessons learned from this evidence for the initial two-year AMFm pilot phase (Phase 1).

THE AVAILABLE EVIDENCE

In reviewing the available evidence on ACT price subsidy schemes, we make a distinction between **sub-national pilot studies**, which are small-scale trials, conducted in just a few districts or municipalities, and **national programs**, in which subsidized ACTs were rolled out at national scale.

Evidence is available from four small, **sub-national pilot studies** of introducing subsidized ACTs into the private sector, two of which are ongoing (Table 1).[12–15] Only one of these was a randomized controlled trial[12] (one was quasi-randomized[13]), and to date only one has been published in a peer-reviewed journal.[13] A fifth pilot is underway in Tanzania, involving distribution of subsidized ACTs through Accredited Drug Dispensing Outlets, but outcomes data from this pilot are unavailable.[16]

Evidence is also available from six **national programs** to scale up subsidized ACTs (Table 2). Two of these programs—in Cameroon and Senegal—are led by the national government, while the others have been led by social marketing organizations, such as Population Services International.

Limitations of the evidence

Unfortunately, most of the evidence is weak, i.e., it suffers from major design flaws, which means that it is hard to draw any

Table 1. Sub-national pilots of subsidized ACT

	Lead Organization	Time frame	Design	Scale	Age group	Outlets
Kenya	Government, PSI, LSHTM, KEMRI	1 year (ended May 2010)	Cluster RCT	3 districts (all in 1 province); 9 clusters (3/district), 9 controls (3/district)	Children under 5 y	Retail outlets
Tanzania	Government, CHAI	1 year (ended Nov 2008)	Quasi-randomized trial	2 intervention districts, 1 control district	All age groups	Drug shops
Uganda	Government, MMV	Ongoing (began in Sept 2008); results at 12 and 20 months are available	Non-randomized, controlled	4 intervention districts, 1 control district	All age groups	Drug shops, clinics
Angola	Government, Mentor Initiative	Ongoing	Uncontrolled	2 municipalities (95 pharmacies)	Children under 5 y	Pharmacies

Abbreviations: PSI: Population Services International; LSHTM: London School of Hygiene & Tropical Medicine; RCT: randomized controlled trial; CHAI: Clinton Health Access Initiative; MMV: Medicines for Malaria Venture

Table 2. National ACT subsidy programs

Country	Lead organization	Launch year	Age group	Outlets	Coverage
Cameroon	Government	2007	All age groups	Public and private health facilities	Countrywide
Senegal	Government	2006	All age groups	Pharmacies	Countrywide
Cambodia	PSI	2002	All age groups	Pharmacies, drug shops	17 of 20 malaria endemic provinces
DRC	PSI	2006	Children under 5 y	Pharmacies	Limited to some districts
Madagascar	PSI	2003	Children under 5 y	Pharmacies, private providers, community agents	Countrywide
Rwanda	PSI	2007	Children under 5 y	Pharmacies	Countrywide

firm conclusions. While we have attempted to lay out some of the key lessons learned from our summary of the evidence, the weaknesses in the underlying data should be kept in mind:

- The Uganda trial was non-randomized, and a new intervention was introduced into the control district after the trial had started, making it hard to draw clear conclusions.
- The Tanzania trial was quasi-randomized (one of the districts was pre-specified as an intervention district; the remaining two were randomly assigned to be an intervention or control district).
- The Angola trial was uncontrolled, so it is hard to draw any causal inferences.
- None of the national programs involved comparing intervention with control districts. For five of the national programs, baseline data are unavailable (such data are only available for Rwanda's national program). These problems make it difficult to assess the impact of the national ACT subsidies over time.

DO PRICE SUBSIDIES WORK?

Summary Points

- Pilots found a rapid rise in ACT availability in private outlets (pharmacies, drug stores, and other retail outlets), as did one national program
- Subsidies were associated with reduced consumer prices (i.e., these subsidies were largely passed along the supply chain to the consumer)
- ACT market share increased rapidly in pilots, crowding out other anti-malarials (e.g., CQ, SP, artemisinin monotherapy), but market share did not increase rapidly in national programs
- Pilots found conflicting evidence on ACT use (one trial was positive, one was negative) and national programs found very little change in use
- The available evidence suggests that ACT price subsidies have less impact among poor, remote communities than among wealthier, urban communities

Pilots found a rapid rise in ACT availability, as did one national program

Pilots: In sub-national pilots in Tanzania, Uganda and Angola, the proportion of private outlets stocking ACTs in the intervention districts rose rapidly, from 0% at baseline to 69–81% at 1 year. The proportion in the control district fell from 1% at baseline to 0% at 1 year in Tanzania (no data are available for the control district in the Uganda pilot and the Angola pilot was uncontrolled).

Programs: Quantitative data are available from only three national programs. Only one of these programs (Rwanda) reported change in availability from baseline—it found that availability of child ACT increased rapidly, from 10% at baseline to 80–90% at 18 months.[17] For the other two programs (Cambodia and Senegal), since there are no baseline data, the change in availability over time is unknown; however, at one year into each program, ACT availability was still low. In Cambodia, at 1 year, only 22% of private drug stores stocked adult ACT doses and 6% child doses,[18] and in Senegal at 1 year only 11% of private outlets stocked adult ACTs, 43% child ACTs, and 29% infant ACTs.[19]

Subsidies were associated with reduced consumer prices

Pilots: All four pilots found that price subsidies were passed on to consumers. The pilots in Uganda, Tanzania, and Angola found that in the intervention districts, the observed retail prices of ACTs were comparable with, or below, the price of suboptimal anti-malarials (e.g., SP, CQ) at 1 year (Tanzania, Angola) or 20 months (Uganda). In the Kenya pilot, 95% of caregivers in the intervention arm said they bought the subsidized ACT at the recommended retail price of $0.25. No price data are available for the control arms in any of the pilots.

Programs: Data are available from two national programs. In Cambodia, subsidized ACTs were sold to private outlets at $0.42 and the mean price paid by consumers was $1.07 at 4 years into the subsidy program (i.e., the price mark-up was about 150%). Consumers paid a much higher price for subsidized ACTs than for CQ, which cost $0.20. In Senegal, subsidized ACTs were sold to private outlets at $0.99 and the mean price paid by consumers was $1.34 at 1 year (i.e., the price mark-up was about 35%). However, consumers paid less for subsidized ACTs than for SP, which cost $2.00.

ACT market share increased rapidly in pilots but not in national programs

Pilots: ACT market share increased from 0–1% at baseline to 38–51% at 1 year in the intervention districts in three pilots (Tanzania, Uganda, Angola). Control data are only available for the Tanzania pilot: ACT market share increased from 0% to just 6% at 1 year in children under 5 years in the control district. In the Uganda pilot, ACT market share was lower among lower socioeconomic status groups.

Programs: Data are available from only one national program: in Cambodia, ACT accounted for only 28% of all anti-malarial sales in private outlets at 6 years into the program; mono-therapies still accounted for 50% of all sales. Baseline data are unavailable, but even if ACT market share was as low as 0% at baseline, this would represent a rise of just 28% in ACT market share over 6 years.

Pilots found conflicting evidence on use, and programs found very little change in use

Pilots: There are few data on ACT use (the proportion of children under 5 years who receive an ACT within 48 hours of fever onset), and the results are conflicting. One controlled, non-randomized trial was negative (i.e., the control group did better).[14] A second trial, which was randomized, was positive: at 1 year, use increased from baseline by 40.2 percentage points in the intervention arm and by only 14.6 percentage points in the control arm.[12]

Programs: Data on use, from UNICEF and ACTWatch, are available from three countries at a range of time points after the subsidy programs were launched.[20,21] In the Democratic Republic of Congo, ACT use was 1% at about 1 year after the subsidy began, in Senegal it was 4% at about 2–3 years, and in Madagascar it was 2.4% at about 5 years. Baseline data are unavailable, but even if ACT use at baseline was as low as 0%, these results would represent only very small changes in use.

ACT price subsidies in pilot countries have less impact among poor, remote communities

Pilots: A secondary analysis of the data from the Tanzania pilot found that ACT availability in the intervention districts was lower in more remote outlets.[22] In the Uganda pilot, ACT market share was lower among lower socioeconomic status groups.[14]

Programs: Data are unavailable on the impact of price subsidies across different geographic locations or socioeconomic groups.

WHAT ARE THE LESSONS FOR THE AMFm?

Modest changes in ACT price, market share and availability can be expected

There is "proof of principle" that a private sector ACT subsidy tested at *small scale* (i.e., at sub-national level) can rapidly reduce the retail price of ACT and increase its availability and market share. However, with the exception of the "before and after" data from Rwanda, there is little evidence from national programs to show that a subsidy can have a large and rapid impact on these three outcomes when tested at national scale. Based on the very limited evidence to date, we believe that over the initial two-year pilot phase of the AMFm, it seems likely that there will be only modest changes at national scale in ACT price, availability, and market share in the private sector. There are insufficient data to be able to project changes over the long term.

It is unclear whether the subsidy will increase ACT use, particularly in the start-up phase

The evidence on whether a price subsidy increases ACT use is unclear from the two pilots reporting usage data. In previous subsidy programs rolled out at national scale, ACT use remained *extremely low* (1–4% at 1–5 years after the national subsidy began). Thus it seems unlikely that the AMFm will cause a rapid rise in usage at national level. Increasing ACT usage has been a major challenge for other types of national ACT scale-up initiatives, particularly during their initial rollout. For example, an external evaluation of the first five years of operation of the GF found "little or no evidence" that GF support had led to an increase in childhood usage of ACTs to treat fever in the public sector, even though there was evidence showing countries had purchased large amounts of ACTs.[23] There are probably several reasons for this gap between purchase and use, including ACT stock-outs and inadequate training of providers in prescribing ACTs.[24]

Other countries may have trouble replicating Rwanda's success

The impressive outcomes in Rwanda's national subsidy program may be difficult for other countries to replicate. Malaria control experts working in endemic countries argue that the success of Rwanda's national program may be related to the small size of the country, the highly engaged government, the strong drug distribution systems, and the national ban on mono-therapies.[11] These experts also argue that AMFm Phase 1 countries that are geographically large and have weak distribution systems may find it difficult to replicate Rwanda's experience.[11]

Reaching poor, rural communities is likely to be challenging

A longstanding challenge for all malaria programs has been to reach the most disadvantaged communities, including those living in poverty and/or in remote, rural regions. This challenge was acknowledged by Kenneth Arrow and colleagues, the original proponents of a global ACT price subsidy, who recognized that "even chloroquine is still out of economic reach for many people, both because even the lowest price is unaffordable, but also because price competition does not function everywhere."[25]

Nevertheless, one of the chief concerns about the AMFm is whether it will be able to increase private sector ACT coverage among "the poorest of the poor."[26] Our review of the evidence, which is limited to only two pilots, suggests that ACT availability and market share in the AMFm pilot may indeed be lower in remote areas and among the poorest communities than in more urban settings and among higher income communities. A number of strategies have been proposed to overcome this problem, such as intensive and repeated (rather than one-off) advertising and education campaigns in remote areas, aimed at store owners and the general public, to raise awareness of how subsidized ACTs can save lives.[22]

Care should be taken in extrapolating results from previous subsidies to the AMFm

Although we have laid out a series of potential lessons for the AMFm rollout based on past subsidy schemes, we also recognize the need for caution in such extrapolation. In particular, extrapolating directly from the pilots is problematic, as the pilots included four features, discussed below, that could help explain their impressive results. These features will not be included in the AMFm.

First, the pilots are very small scale, whereas the AMFm is national in scale. Second, three pilots (Uganda, Angola, Kenya) extended the drug supply chain by *adding* a direct distribution mechanism, whereas the AMFm will only use *existing* distribution mechanisms. Third, in Angola, the Mentor Initiative, which co-directs the pilot, monitors ACT prices and informs pharmacies in cases of detected price violations, making clear that such violations are intolerable.[15] It is unlikely that such tight monitoring will occur nationally in the AMFm Phase 1 pilot countries. Fourth, all four pilots included extensive public communication campaigns and training sessions for drug sellers in the intervention districts. While the AMFm Phase 1 countries must implement a set of similar SIs aimed at increasing ACT access,[4] it is unlikely that the highly intensive interventions implemented under small-scale trial conditions could be replicated at national scale.

Expectations should not be set too high

Based on our review of previous ACT subsidy schemes, we recommend that expectations should not be set too high for the AMFm Phase 1.[11] In particular, as discussed above, we believe that it is unlikely that the very impressive results of the small sub-national pilots will be replicated at national scale in the eight AMFm Phase 1 countries.

AUTHORS

This policy brief was written by Gavin Yamey and Marco Schäferhoff.

COMPETING INTERESTS

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