CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
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Issue Brief

THE FUTURE OF THE AFFORDABLE MEDICINES FACILITY-MALARIA: WILL AMFm PLAY ON?

Malaria. It's been the front-and-center disease of global poverty for the last decade and the massive control efforts have paid off. Annual deaths from malaria have fallen from one million to 650,000, and the global "malaria map" is shrinking. The principal agents of change? Millions upon millions of insecticide-treated bednets, targeted insecticide spraying in houses where mosquitoes bite and artemisinin combination treatments (ACTs). ACTs are highly-effective drugs replacing prior mainstays, such as chloroquine, that are no longer effective because of widespread drug resistance by *Plasmodium falciparum*, the deadliest malarial parasite affecting humans.

Enter AMFm (the letters stand for Affordable Medicines Facility-malaria)—a bold financing strategy first outlined in a 2004 Institute of Medicine (IOM) report entitled *Saving Lives, Buying Time.* A two-year pilot phase of AMFm is nearing completion. The twin objectives of the AMFm concept are:

> 1) to massively increase access to ACTs, especially in the private sector pharmacies and shops where many people in malaria's farthest reaches go for treatment when the illness strikes; and
>
> 2) to protect artemisinins and their partner drugs (which together form ACTs) from premature loss due to drug resistance.

At the heart of AMFm are two elements: a subsidy high in the supply chain—in fact, virtually at the factory gate—and negotiations with manufacturers of approved, high-quality ACTs yielding ACT prices well below previous wholesale levels. Together, these measures translate to a natural flow of drugs through existing channels of distribution and a purchase price-to-consumer sufficiently low that the average malaria sufferer in rural Africa can afford to buy an ACT at his or her local shop. Rounding out AMFm's pilot were in-country information campaigns and training programs to steer people to AMFm-subsidized ACTs.

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Since 2008, The Global Fund to Fight AIDS, Tuberculosis and Malaria has housed AMFm. In late 2010, the first ACTs "co-paid" through AMFm were delivered. By mid-2011, nationwide pilots had been launched in Ghana, Kenya, Madagascar, Niger, Nigeria, Tanzania (mainland and Zanzibar) and Uganda. The pilot experience has been extensively studied by an independent research team at ICF International and the London School of Hygiene and Tropical Medicine at a cost of roughly $10 million—perhaps the most exhaustive evaluation of any global financing program.

After reviewing the evaluators' preliminary report, the Global Fund's Expert Advisory Group on AMFm noted: **"the major benchmarks for success for…availability, price and market share of quality-assured ACTs have been met or exceeded in 6 of 8 pilot[s]."** In both urban and rural areas, **"pre-existing public and private channels deliver[ed] high quality malaria treatment… without excessive mark-ups by for-profit providers."**

But, of course, the future is not entirely favorable with regard to malaria control—or AMFm. Funding is leveling or declining, and at the same time, artemisinin resistance has indeed emerged in Southeast Asia (where AMFm does not currently operate); soon, artemisinin resistance may also threaten Africa. Could the money needed to continue AMFm in its current sites and/or expand the program be better spent? How should AMFm adapt to new challenges (for example, partnering ACTs with rapid diagnostic tests for malaria)? What is the long-term commitment of drug manufacturers and other funders to this groundbreaking initiative?

Based on answers to these and other questions, in November 2012, the Global Fund Board will determine whether AMFm continues as is, expands, is modified in some fashion or—quite frankly—is abandoned.

Complicating the Global Fund's decision is the fact that the U.S. government has not yet endorsed or supported AMFm. The official U.S. position on the pilot phase is captured in this excerpt from the 2008 Public Law (110-293) reauthorizing U.S. involvement with the Global Fund: "the Global Fund should not support activities involving the 'Affordable Medicines Facility-malaria' or similar entities pending compelling evidence of success from pilot programs as evaluated by the Coordinator of United States Government Activities to Combat Malaria Globally."

In short, the Global Fund independently hosted AMFm's pilot phase, without which "compelling evidence" could not have been obtained. Whether it will continue to host a possible AMFm "Phase 2" minus U.S. support is unknown.

In anticipation of the decisions ahead, on September 17-18, 2012, the Institute of Medicine and the Center for Disease Dynamics, Economics & Policy are co-hosting a meeting to review AMFm's independent evaluation and analytical work to-date.

Nobel-Prize winning economist Kenneth Arrow, the chair of the original *Saving Lives, Buying Time* report, will open the meeting. Representatives from AMFm Phase 1 countries, funders, and other experts and participants in AMFm's development and evaluation will join the pivotal discussion. The meeting agenda is attached.

MORE…

DID AMFm SUCCEED? THE BIG PICTURE TO DATE

The preliminary report of July 18, 2012 of the independent AMFm evaluation mandated by the Global Fund Board describes the success of the program in all Phase 1 pilot sites: Ghana, Kenya, Madagascar, Niger, Nigeria, Tanzania (mainland and Zanzibar) and Uganda. The evaluation was conducted by ICF International in collaboration with the London School of Hygiene and Tropical Medicine. ICF and LSHTM analysts examined measures of availability and affordability before and after AMFm launched.

In essence, proof of concept was achieved: AMFm increased availability and kept prices low, meeting its initial, ambitious benchmarks in most, but not all, settings.

Key findings follow:

- According to the evaluation, AMFm proved a "game changer" in private sector pharmacies and shops in all countries except Niger and Madagascar. Overall, it led to better availability, lowered price and increased market-share of quality-assured ACTs. These changes occurred within months, demonstrating, in the evaluators' words, **"the power of tapping into the distributional capacity of the private sector.**" Furthermore, the longer AMFm operated in most sites, the better it performed.

- With respect to specific prices and mark-ups, AMFm was also deemed a success. ACT prices in the private, for-profit sector ranged from $0.51 in Madagascar to $1.96 in Uganda. Mark-ups were less than 70% in all test locales except Uganda (133%) and Zanzibar (100%).

- In many pilot countries, the public sector supply of ACTs **"continued to be hindered by problems with procurement and grant requirements, leading to substantial delays in ordering**" although total public-sector supplies did increase in four pilot countries (Ghana, Nigeria, Uganda and Zanzibar).

- As it unfolded, artemisinin monotherapies did not need "crowding out" because so few of them were sold in the pre-AMFm period (probably because of price). In any event, the market-share of artemisinin monotherapies did not

increase with the initiation of AMFm. On the other hand, ineffective drugs such as chloroquine and sulfadoxine-pyrimethamine remained widely available in nearly every site.

- The evaluation reinforced the importance of private, for-profit outlets in the seven pilot countries: both at baseline and at the end of the pilot phase, private vendors supplied anywhere from 40% to nearly 100% of all antimalarials obtained by consumers.

- Finally, relatively few private sector outlets offered malaria diagnostic tests. Only in Kenya, Uganda and Zanzibar were such tests routinely available in private shops and clinics. Public sector clinics in pilot countries were more likely to perform malaria diagnostics; nonetheless, at the time of the final survey, public sector diagnostic performance still ranged from a low of 29% in Nigeria to a high of 98% in Zanzibar.

UNDERLYING PROS AND CONS OF AMFm

AMFm began with an audacious idea first proposed in a 2004 Institute of Medicine report: namely, to subsidize the world's most effective antimalarial drugs at the top of the supply chain, then let the drugs flow directly to patients in the same way older, now-ineffective agents once did—and still do.

The IOM committee that envisioned AMFm understood the need for a high-level subsidy because of several facts:

1. ACTs were much more costly than their widely-available but ineffectual competitors.
2. Parents of sick, febrile children in malaria-endemic regions were far more likely to purchase antimalarial remedies from private vendors than to seek treatment at public clinics.
3. Given their general unaffordability, minus a subsidy, many shopkeepers would never even stock ACTs.

The ability to distribute good-quality drugs and diminish counterfeits are added benefits of the AMFm approach. AMFm distributes only ACTs that meet quality standards and combine artemisinins with other effective antimalarials, a

pharmacologic approach fundamental to preserving long-term efficacy of the artemisinin class.

On the other hand, what some consider AMFm's major strength—the ability to harness the existing private sector—is also a major source of criticism. By making high-quality ACTs available over-the-counter at pharmacies and drug shops, AMFm does nothing to promote the formal healthcare system. It can also be argued that it perpetuates the overuse of ACTs by people who do not have malaria.

Unfortunately, at this time, formal healthcare is often lacking when and where malaria sufferers need it most. Especially in rural areas, clinics are far-flung and all too frequently have no ACTs on their shelves. The tension between strengthening health systems in the long run and offering what some deem a short-term "band-aid" solution is not likely to resolve in the next few years.

AMFm AT THE GLOBAL FUND

The IOM committee that produced the *Saving Lives, Buying Time* report was chaired by economist Professor Kenneth Arrow, a passionate proponent of the report's recommendations. Between the publication of *Saving Lives, Buying Time* and the arrival of the first subsidized drugs in Ghana were six years of development, argument, persuasion and compromise.

In 2008, the Global Fund to Fight AIDS, Tuberculosis and Malaria assumed responsibility for AMFm as a program financially and administratively separate from the Fund's grant-making activities. The high-level subsidy envisioned by the IOM committee plus vigorous ACT price negotiation conducted by the Clinton Health Access Initiative (CHAI) were centerpieces of the new enterprise.

Scaling back from the proposed "global" subsidy to a pilot phase involving seven countries was a significant departure from the original IOM plan. Nonetheless, following the development of rules of engagement and the selection of countries, AMFm's objectives remained in keeping with its founders' vision, namely to:

1. increase affordability of ACTs
2. increase availability of ACTs
3. increase use of ACTs, especially by vulnerable sub-groups; and
4. "crowd out" oral artemisinin monotherapies, chloroquine and sulfadoxine-pyrimethamine by increasing ACT market share.

AMFm was supported by the Roll Back Malaria Partnership, the World Bank, and others, including lead funders of the pilot, the U.K. Department for International Development, UNITAID, and the Bill & Melinda Gates Foundation. The Canadian International Development Agency also contributed. Pilot funding exceeded $300 million.

THE CHANGING MALARIA LANDSCAPE

Clearly, the global malaria situation has changed over the past decade. While AMFm evolved from an idea to Phase 1 implementation, deaths declined and new tools became available. In some places—most notably Phase 1 participant Zanzibar—malaria is nearly eliminated thanks to insecticide-treated bednets and ACTs. On the other hand, in most *P. falciparum*-endemic countries, the disease remains a major killer of children and long-term, sustained success is far from assured.

Rapid diagnostic tests are new tools that must now be factored into any major malaria treatment strategy. In 2010, the World Health Organization recommended that no patient receive antimalarial treatment unless he or she tests positive for the infection, either by a rapid diagnostic test or microscopic identification of blood parasites. The challenge? With a price tag roughly equal to that of a full course of ACTs, rapid diagnostic tests are still too expensive for many malaria sufferers, especially in rural Africa.

Another major challenge facing malaria control is future funding. Following an 11-year meteoric rise in all-source global funding (from less than $100 million in 2000 to $2 billion in 2011), total malaria control investments in 2015 are currently projected at roughly $1.5 billion.[1]

Partial artemisinin resistance by *P. falciparum* parasites—now confirmed in several parts of southeast Asia—is the final biologic event to be weighed. In a sense, this development could constitute the most compelling argument for AMFm's strategy of "crowding out" artemisinin monotherapy (common in Asia as opposed to Africa), a known predictor of drug resistance. Unless contained, artemisinin-resistant parasites will inevitably spread to Africa and elsewhere. No equally effective replacement drug is yet on the horizon.

[1] WHO, *World Malaria Report 2011* (Geneva: 2011).

AMFm, PHASE 2?

In November, the Global Fund Board will determine the future of AMFm. In preparation, the independent evaluation reviewed the Phase 1 AMFm experience and the Bill & Melinda Gates Foundation commissioned a series of prospective analyses. The following questions, among others, must now be discussed:

- Will AMFm continue to operate in its seven phase 1 countries—or reduce or expand in scope?

- Will AMFm integrate more fully into the Global Fund, both operationally and financially?

- Should the most vulnerable group of malaria sufferers, namely children, be the principal target of the next round of the AMFm subsidy?

- How can a subsidy for rapid diagnostic tests be incorporated into AMFm to ensure diagnosis before treatment?

THE SEPTEMBER 17-18, 2012, IOM/CDDEP MEETING

Day one will focus on the independent evaluation of AMFm and the analytical work projecting possible Phase 2 scenarios. Speakers will include malaria control and AMFm managers from several Phase 1 countries. Other invitees include senior representatives of major funders and the U.S. Government. Professor Arrow will open the meeting by reviewing *Saving Lives, Buying Time*'s original recommendations, then compare them with AMFm implementation to-date.

Day two of the meeting will move beyond malaria and pneumonia to a broader focus on "febrile illness" in resource-poor settings. The challenge is to develop strategies to diagnose and treat patients whose fevers are not due to malaria. Speakers will discuss both the funding and technology needed to achieve this goal.