

## The changing market and quality of antimalarials in key African cities

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In 2007 my research team undertook its first assessment of medicine quality by procuring antimalarials in the largest cities of six key West and East African nations. We found that about a third of the antimalarials we bought and tested failed very basic quality control.<sup>1</sup> Over the next few years we sampled again from many of the same cities and found greater availability of the best standard of care, the artemisinin combination therapies (ACTs).

In 2018 we revisited two of those cities (Lagos and Accra) to see how the market and product quality had changed. We followed the same protocol as in 2007, although we only procured ACTs. Today many of the older products are still on sale, even though products like chloroquine and sulfadoxine pyrimethamine have been only partially effective for decades. Additionally monotherapy artemisinin products were also available in some locations. Monotherapies have been banned in most locations in order to limit the chance of resistance development to artemisinin, which is the single best antimalarial product (and hence should only be sold in combination with older but still effective therapies, such as amodiaquine or lumefantrine).

In 2007 only one ACT was prevalent on the market, artemether lumefantrine (Coartem™), and the vast majority of the product sold was made by Novartis, a large Swiss drugmaker. This drug had penetrated many of the pharmacies in the cities but were far more expensive than older products and not as ubiquitous as they are today. During our first sampling, the only failing ACTs were fakes, made to look like Novartis' Coartem. Over subsequent samplings we encountered fakes, but also substandard products made by legal manufacturers as well. Over time fewer fakes were found and more substandards, but as can be seen from the chart below, overall product quality improved. By 2014, only about 7% of samples failed quality control. Today we encountered four different products, made by eleven different manufacturers, the vast majority produced in India and China.

Surveillance programs were established to monitor drug quality, funded by the private sector and by donors who procure a lot of medicine. The Global Fund to Fight AIDS TB and Malaria (GFATM) and the Presidents Malaria Initiative (PMI) notably either undertook surveillance themselves or contracted it out to organizations like US Pharmacopeia. In addition projects like the AMFm<sup>2</sup> – now a part of the Global Fund – attempted and partially succeeded in flooding the market with cheaper legitimate (and for the most part good quality) ACTs.

The efforts worked as access to quality ACTs improved. This assessment in two cities is to see if quality was sustained.

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<sup>1</sup> Bate, R., Coticelli, P., Tren, R., & Attaran, A. (2008). Antimalarial drug quality in the most severely malarious parts of Africa—a six country study. *PLoS One*, 3(5), e2132.

<sup>2</sup> [https://en.wikipedia.org/wiki/Affordable\\_Medicines\\_Facility-malaria](https://en.wikipedia.org/wiki/Affordable_Medicines_Facility-malaria)

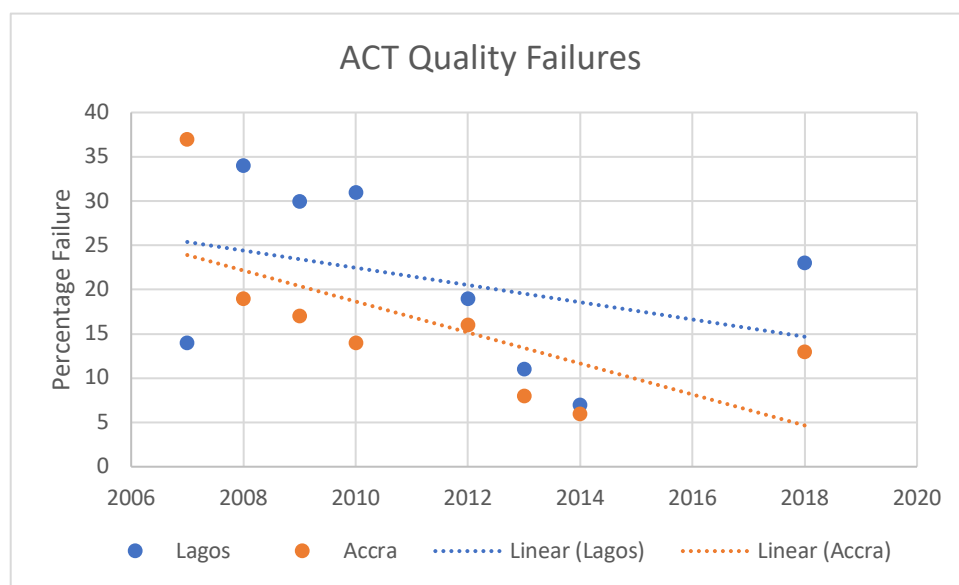
## Methods

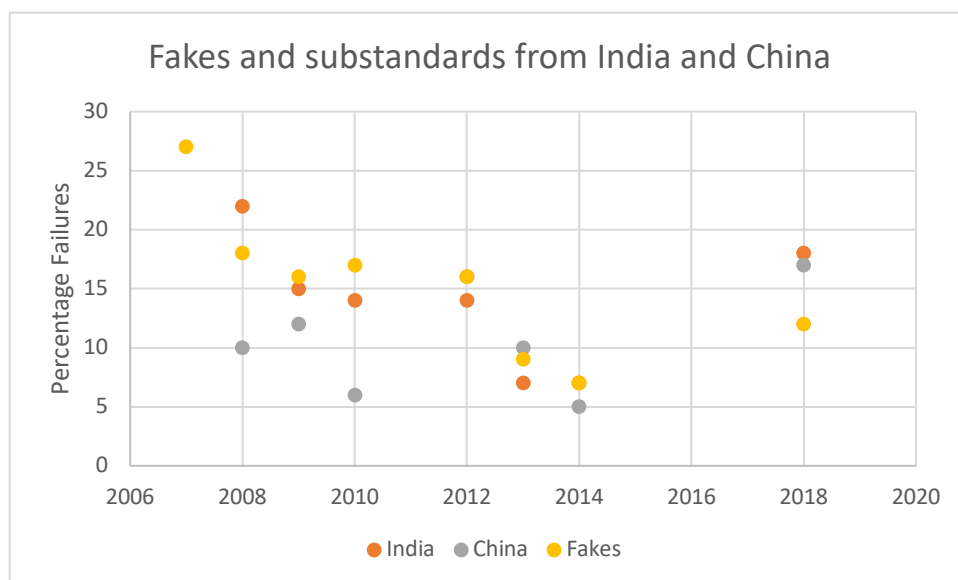
Artemisinin combination therapies (ACTs) were procured in mid-income areas of Lagos and Accra by local city residents. Samples were collected from 23 storefront pharmacies in each city. A total of 134 samples were collected, 66 from Accra and 68 from Lagos. Procurement was easily made without a prescription. Testing occurred within 40 days of sample collection.

The Global Pharma Health Fund e.V. Minilab® was used to run semi-quantitative thin-layer chromatography (TLC) on each sample to determine the presence and relative concentration of active ingredients. Tests were repeated twice with the generous assumption that the result more consistent with the reference was recorded. The Minilab® protocols award products a “pass” if they have 80% or more of the labeled active ingredient(s) (note there is no upper-bound limit). For fixed-dose combinations, “pass” was awarded only if both active ingredients met this standard.

## Results

15 (23%) samples failed in Lagos and 9 (13%) in Accra. Of products procured there were two obvious fakes in each city, meaning the majority of failures (20/24 - 84%) were due to substandard production (or storage post=production or in transit – pharmacy storage is unlikely the problem as problems did not occur with all brands).





By definition one doesn't know the source of a fake medicine unless a thorough investigation is undertaken. But medicines that are legal but fail quality control are made by producers, often well known ones. None of the products made by European producers failed in any of the samplings (including the most recent one). Disregarding the fake medicines, all other failures were made in India and China. In the chart immediately above one notices a decline in substandards over time until the most recent sampling where poor quality medicines made in India and China increase. Fakes also increased in the recent past.

### Discussion

Using all the samples collected over time one sees a downward trend line for both cities (top chart above), but a much stronger decline in Accra than Lagos. It should be noted that the 2007 sampling was very small for ACTs, with only 15 samples (8 Accra and 7 Lagos), later samplings are probably more representative. In both cities there is a significant increase in this latest sampling. One off samplings prove nothing. It is quite possible these data are an outlier from a generally improved situation. Yet, anecdotally, antimalarial products were found to be available in markets and other locations like kiosks and buses, where they are not supposed to be, which although not the focus of this study, does suggest that there is leakage of product from the legitimate market. Indeed, one of the unintended downsides of the AMFm approach of flooding the market with ACTs was that it encouraged non-legitimate untrained distribution chain actors (like travelling salesmen or roadside kiosk owners) to take part in malaria drug sales. Additionally, and while further investigation is needed, the lack of enforcement of prescription rules and greater access at unauthorized retailers suggests that quality has deteriorated.

### *Causes of inferior quality medicine*

Counterfeiters and producers of substandard medicines can switch production fairly quickly. Between 2007 and 2014 production of inferior drugs shifted away from antimalarials to other product categories (analgesics or antibiotics). The most likely reason for this is such products had weaker oversight. One could put it like this – make a bad antimalarial and you might end up in jail, make a bad antibiotic or pain killer and no one will do anything.

Up to 2015, regular assessments and reports of drug quality were filed by donor-funded security experts, national government health ministries were informed, and although not happy with the findings and publicity, they allowed programs to continue. But in the past three years there seems to have been little attention. February 2015 marks the last time World Health Organization (WHO) issued a rapid alert over artemether lumefantrine, the most important antimalarial medicine.<sup>3</sup> The WHO claims to maintain a “full” list of medical product alert, but a cursory review shows it to be woefully inadequate.<sup>4</sup> In light of our recent findings as well as prior conversations with an investigator who noted several example of falsified antimalarials in the past three years that are nowhere to be seen in the reports, it is clear that the present day surveillance is inadequate.

At its core, the lack of oversight stems from a lack of political will and accountability. No one in power really wants these data published or examined. The people who are affected by these substandard medications are patients and physicians in emerging markets lacking political sway. For everyone else the inferior antimalarial drugs is an embarrassment. Furthermore, acknowledging the failure would demand a concrete response. Not until newsworthy deaths occur will this change.

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<sup>3</sup> World Health Organization. Falsified anti-malarial medicine circulating in West Africa. UPDATE. (February 2015). <http://www.who.int/medicines/publications/drugalerts/Artemether-LumefantrineENversion.pdf>.

<sup>4</sup> <http://www.who.int/medicines/publications/drugalerts/en/>