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The Impact of Improved Detection Technology on Drug Quality: A Case Study of Lagos, Nigeria

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Abstract

Nigeria is one of the few countries seriously affected by counterfeit drugs to have actively combated them. As part of this effort its regulatory agency, NAFDAC, has deployed handheld spectrometers to identify fake drugs in the market. In this Outlook, we analyze anti-malarial drug samples procured randomly from pharmacies in the largest city in Nigeria, the port of Lagos prior to and after the spectrometers were deployed. There is a statistically significant drop in the number of drugs failing quality control tests after the spectrometers were introduced, and a noticeable disparity in price between those passing and those failing tests as well. While it is not likely that the deployment of the spectrometers is the only reason for the improvement in drug quality, and the segmentation of the market, it is surely a major factor.

Lorraine Mooney, assisted with the experiments; Karen Porter and Philip Coticelli helped with compilation and presentation of the original data; Robert Brush helped with the spectrometry assessments; Thompson Ayodele, Franklin Cudjoe, William Awagu and two anonymous covert shoppers helped with product sampling from Nigerian pharmacies; Matthew Jensen provided excellent research assistance for this article. The Legatum Institute funded all of the research.

1. Introduction

A. The dangers of substandard and counterfeit drugs

The counterfeiting and adulteration of medicines is a global public health crisis. Recent estimates indicate that outside of advanced nations, perhaps 15% of the global medicine supply is counterfeit (Cockburn, et al. 2005). In the poorest parts of Africa, Asia and Latin America over 40% of the medicines on sale may be counterfeit, failing basic quality tests (World Health Organization 2010). Even medicines sold for notoriously deadly diseases such as malaria are faked and poorly manufactured. In some countries, what evidence there is, suggests that half of anti-malarial treatments sold are counterfeits (Dondorp, et al. 2004). Poor quality drugs, whether counterfeits or simply substandard, can be lethal. Diseases like malaria kill rapidly, and without effective drugs, death can come quickly. In addition to this problem, the Plasmodium parasite which causes malaria, adapts over time, becoming resistant to previously effective drugs. This adaptation is accelerated if the treatments are sub-strength – either low active ingredient, or low availability of active ingredient due to poor formulation or product degradation. It is crucial, therefore, that patients complete the treatment course and that their drugs are properly formulated. Sadly, in some areas where malaria is highly prevalent, treatments such as chloroquine, a cheap and safe drug, now fail to cure because parasites have developed resistance to it. Fake and substandard drugs that are under-dosed promote resistance. Combating such drugs is therefore important to ensure the continued survival of drugs to fight malaria.

In this paper, we focus on the problem of poor quality (either substandard or counterfeit) anti-malarial drugs and the impact of new drug testing technologies on the average quality of these drugs in Lagos, Nigeria. We find that the deployment of modern technologies such as handheld spectrometers may have gone a long way towards reducing the availability of low quality drugs. We also find tentative evidence of a rise in the price gap between poor and high quality drugs over time. This could be a consequence of high quality producers being better able to signal quality and differentiate their products through higher prices. Lagos can thus serve as a case study for other countries combating similar issues in their domestic markets.

B. Nigeria combats its fake drug problem

Since 2002, when nearly 41% of the drugs in the Nigerian market were estimated to be fake, Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC) has made significant efforts in combating fake drugs (Ebeleke 2010). NAFDAC has improved screening of drugs in the field; it has undertaken forensic analysis of low quality drugs and pursued those selling and marketing them. Screening has improved with the deployment from 2008 of several small portable laboratories, known as Global Pharma Health Fund e.V. Minilabs® for rapid product screening where formal laboratory facilities are sparse. From 2002, drug failures fell to roughly 16% in 2006 and are now down to about 10%, according to the director-general of NAFDAC, Dr. Paul Orhii. Dr. Orhii is pushing further by making NAFDAC the first anti-counterfeit department anywhere in the world to deploy six hand-held laser (Raman) spectrometers, which can provide immediate authentication of drugs. According to NAFDAC's Elizabeth Awagu, this deployment is helping to close down more of those locations still selling fake products. According to a NAFDAC report, the Ports Inspectorate Directorate says that the deployment of the Truscan spectrometer occurred during 2009. In personal communication, Ahura Scientific informed us that the Truscans were not deployed fully until the very end of 2009, a point repeated by Dr Orhii.[1] Thus hand held spectrometers were first widely used at the end of 2009 in Lagos and elsewhere in Nigeria, and with our data we are able to compare drug quality before and after the deployment of the spectrometers to see if the use of this technology had any impact on the availability of poor quality drugs. Spectrometry testing is increasingly used all over the world as the quickest method of product authentication. Hand held spectrometers are a convenient device allowing inspections to take place at the point of sale, unlike with Minilab testing which, as the name suggests, requires drugs to be carried over to laboratories for testing.

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[1] In NAFDAC's Our Score Card, January – December 2009, Volume 1, Taking NAFDAC to Greater Heights, page 35, Ports Inspectorate Directorate, says that the deployment of the Truscan spectrometer occurred during the period covered by the report. Ahura Scientific told us that the Truscans were not deployed fully until the very end of 2009, a point repeated by Dr Orhii. In NAFDAC's A Compendium of Press Reports on NAFDAC Activities January 2009 – December 2009, many of the articles towards the end of 2009, discussed the impending deployment of the Truscan spectrometers. Some news reports over emphasized how useful and how widespread its use would be, giving the impression – including to counterfeiters – that fake drugs were far more likely to be intercepted and their purveyors caught, at least in key locations of deployment, such as Lagos, the site of our drug sample analysis. (copy on the above document is on file with authors, it is not available online)

II. Data

Sampling methods deployed in the drug collections were developed in line with similar studies.[2] Anti-malarial drugs were obtained by local nationals from randomly selected private pharmacies in Lagos. Study agents posed as customers and were instructed to stay within a single neighbourhood and to select pharmacies at first sight on a random walk, and were blind as to the purpose for which they were collecting samples. They purchased a sample lot of anti-malarial tablet formulations, namely: sulphadoxine–pyrimethamine (SP), artemisinin monotherapies (artmono) and artemisinin combination therapies (ACTs). All drugs in all pharmacies were available without a prescription. Between mid-2007 and mid-2010, study agents conducted four samplings of pharmacies in Lagos (October 2007, December 2008/January 2009, February 2010 and August 2010). A total of 251 samples were collected and tested using the Minilab, the same spectrometer (TruScan) deployed by the Nigerian Government, and for which price information was available.

III. Types of Tests

All samples and packaging were visually inspected for obvious flaws in line with the protocol established by the Global Pharma Health Fund e.V. Minilab®. The Minilab was then used to run semi-quantitative thin-layer chromatography (TLC) and disintegration tests on each sample, within 60 days of collection, to determine the presence and relative concentration of active ingredients. Each test was run in duplicate, 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 and SP, a "pass" was awarded only if both active ingredients met this standard.

Samples were also tested using a portable Raman spectrometer (TruScan; Ahura Scientific, Inc., Wilmington, MA). Spectrometers "fingerprint" materials without using external substances. Unlike the Minilab assays which focus on specific attributes of the medicines, the spectra generated by the spectrometer reflect all contents of the sample:

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[2] (Bate, et al. 2008), (Bate, Tren, et al. 2009), (Bate, Tren, Hess, Attaran. 2009), and (Bate and Hess 2010)

active pharmaceutical ingredients, excipients, fillers, dyes, and coatings. The spectra will change when any of these contents is changed or is inherently different due to different manufacturers producing drugs with different concentrations of excipients, and perhaps entirely different excipients. Furthermore, temperature degradation or moisture degradation of a sample will affect the spectra, which is critical when assessing the viability of compounds, such as artemisinin, whose effectiveness is lowered by moisture. Methods were established for the Raman spectrometer for each brand studied, and testing was carried out in the same location as the Minilab analysis. Unlike the Minilab tests, a failure by spectrometry may indicate an intellectual property violation of a brand, rather than a product which is a risk to public health.

IV. Results

The sampled drugs comprised of Artmono, ACTs and SPs. More specifically, as Table 1 shows, our overall sample had approximately 48 percent Artmonos, 14 percent ACTs and 38 percent SPs. Of these, 84 percent passed all three tests. The highest pass rates were found for the visual appearance test, followed by the Minilab and finally the spectrometry testing. While clearly our sample size is too small to conduct any rigorous regression analysis, the aim of this exercise is merely to study trends in drug quality over time as testing for quality became more rigorous in Nigeria. The Nigerian Government introduced the use of spectrometers at the end of 2009 to attack the spread of counterfeit drugs. This provides us a clear cutoff date in our sample period to study any changes in trend that may have occurred in the sale and use of "counterfeit" medicines. Our hypothesis is that the introduction of spectrometers had a noticeable impact on drug quality and sales of poor quality drugs since the probability of being caught rose after their introduction, and as importantly the perception to counterfeiters was that it would increase markedly. Our sample allows us to compare drug quality before and after this intervention since our data samples were collected in 2007, 2009 and 2010. Of course, given the small size of the data, especially within each drug type, our results are merely suggestive rather than conclusive.

Table 2 presents averages for each of the variables in our data collection, both prior to 2010 and in 2010. Note that our 2009 sample is included in the pre-spectrometry testing period since these data were collected prior to the introduction of spectrometers. In the pre-spectrometry testing period, relatively lower percentages of

drugs cleared any of the three tests. Approximately 81 percent cleared the minilab test and 78 percent cleared the spectrometry test. In 2010, these numbers changed significantly with 89 percent of drugs clearing the minilab test and 88 percent clearing the spectrometry test. Hence there was a 10 percentage point increase in the number of drugs clearing the spectrometry test. This difference is statistically significant in the data. This provides suggestive evidence that there has been a trend shift in drug quality over time in Lagos, Nigeria, which may partly be ascribed to the introduction of spectrometers by NAFDAC.

Table 3 disaggregates the test results by drug and year. For each drug, it is clearly the case that over time a higher percentage of the sample passed each test. For instance, in 2007, only 57 percent of the artmono sample passed the spectrometry test. In 2010, 88 percent did. Within the ACT sample, approximately 96 percent of the sample passed the spectrometry test in 2010 as opposed to 86 percent in 2007. Within the SP sample, the success rate climbed from 50 percent to 85 percent.

Another interesting result that emerges from this data analysis is the effect on drug prices of this change in quality. Table 2 shows that the average price of all drugs was $2.8 in the period before 2010, and it increased to $3.75 in 2010. This overall change can be decomposed into a change in drug prices for drugs that passed the test versus those that failed any of the tests. Before 2010, for drugs that passed all the tests, the average price was just above $3. For drugs that failed any of the tests, the average price was approximately $2, leading to a net difference of $1 in the prices of "good" versus "counterfeit or substandard" drugs. In 2010, this price gap increased by 85 percent, with nearly a $1.85 difference in the prices of these drugs. Whether changes in drug quality caused the price changes is difficult to say without using more sophisticated regression techniques. However, results from another paper (forthcoming) suggest that changes in drug quality are a significant predictor of drug prices. Using data from a much larger sample of countries, years and drugs, that paper establishes that in markets with both counterfeit and genuine drugs, prices may act as a signal of quality with higher quality drugs being priced systematically higher than poorer quality drugs.

Using the Nigerian data, we graph kernel density plots of drug prices for drugs that passed all tests ("genuine") and drugs that failed any of the tests ("counterfeit"). Figure 1 shows that the two distributions are significantly different from each other. This plot uses data for all three years and all drugs. The mode of the distribution for

counterfeit drugs is clearly to the left of that for genuine drugs, and these distributions are statistically significantly different from each other.

Figure 2 plots the two distributions for the *before* period, while Figure 3 plots the distributions for the *after* period. The striking thing about the distribution for 2010 is that the mean price level for counterfeits is significantly lower than for the earlier periods. Further, for genuine drugs the mode of the distribution is further to the right relative to the earlier period.

V. Discussion

The result demonstrated in Figures 2 and 3, suggests that as counterfeits became easier to detect, price differences between genuine and counterfeit drugs became starker and prices became a better signal of quality. A possible reason for this is a reduction in the number of brands on the market as some counterfeit and substandard products exit the market, because their traders fear that their products will be intercepted and they will be arrested. The result is that the average price for the remaining products has increased as more good and more expensive products dominate the market. The remaining substandard and counterfeit products on the market are being sold at cheaper price by manufacturers to intermediaries and final purchasers to encourage their greater risk of complicity in the counterfeit drug trade. Another possible cause is that high quality producers had more of an incentive to invest in drug quality to ensure that their drugs would always pass spectrometry tests, while the low quality producers who were left in the market did not have the resources to make these investments, leading to a sharper divide between the two types.

VI. Conclusion

Our analysis of an admittedly limited data sample for Lagos, Nigeria suggests that there has been a trend towards improving the quality of drugs since the well publicized introduction of spectrometers at the end of 2009. This is reflected partly in sharper price differences between drugs that passed all the tests and drugs that failed any of the tests in the period before and after this government initiative. This corroborates the hypothesis in an earlier paper that changes in drug quality are a good predictor of changes in drug prices. Prices in markets with sales of both good quality and substandard or counterfeit drugs are shown to act as a signal of quality, with high quality producers pricing drugs at significantly higher levels than low quality

producers. In future work, we hope that with a bigger sample size and more periods of data, in more cities and rural areas, we will be able to prove these results for the Nigerian data more conclusively.

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Table 1: Descriptive Statistics

Variable	*Observations*	*Mean*	*Std.Dev.*
Registration Status	251	0.84	0.36
Minilab Result	251	0.85	0.36
Drug Price ($US)	251	3.32	2.67
Visual Appearance Test	251	0.96	0.20
Spectrometer Result	251	0.84	0.37
GDP per capita (US$)	251	1,268.13	113.38
Passed All	251	0.84	0.37
Any Fail	251	0.16	0.37
Artmono	251	0.48	0.50
ACT	251	0.14	0.35
SP	251	0.38	0.49

Table 2: Variable Averages Prior and Post Introduction of Spectrometers

	Prior-			*Post-*		
	Obs.	*Mean*	*Std.Dev.*	*Obs.*	*Mean*	*Std.Dev.*
Registration Status	114	0.80	0.40	137	0.88	0.32
Minilab Result	114	0.81	0.39	137	0.89	0.31
Drug Price ($US) Passed All Failed Any	114 89 25	2.80 3.02 2.03	1.98 2.08 1.36	137 121 16	3.75 3.97 2.13	2.57 2.61 1.52
Visual Appearance Test	114	0.96	0.21	137	0.96	0.18
Spectrometer Result	114	0.78	0.42	137	0.88	0.32
GDP per capita (US$)	114	1144.13	4.55	137	1371.31	0
Passed All	114	0.78	0.42	137	0.88	0.32
Any Fail	114	0.22	0.42	137	0.12	0.32
Artmono	114	0.47	0.50	137	0.48	0.50
ACT	114	0.11	0.31	137	0.18	0.38
SP	114	0.42	0.50	137	0.34	0.48

Table 3: Results of Different Tests, by Drug Type and Year

	Artmono			*ACT*			*SP*		
	Visual	*Minilab*	*Spectrometer*	*Visual*	*Minilab*	*Spectrometer*	*Visual*	*Minilab*	*Spectrometer*
2007	0.86	0.57	0.57	0.86	0.86	0.86	0.88	0.63	0.50
2009	0.98	0.83	0.81	1.00	0.80	0.80	0.98	0.85	0.83
2010	0.97	0.88	0.88	1.00	0.96	0.96	0.94	0.87	0.85

Figure 1: Kernel Density of Drug Prices for Drugs that Passed All Versus Drugs that Failed Any Test

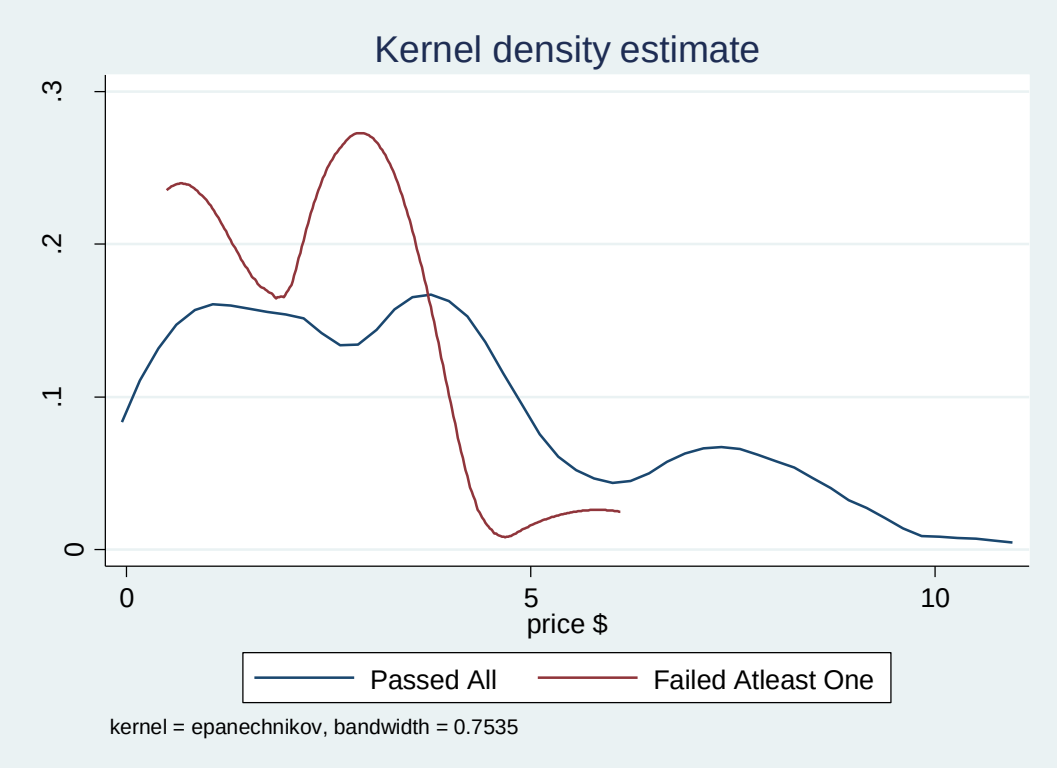

Figure 2: Kernel Density of Drug Prices for Drugs that Passed All Versus Drugs that Failed Any Test Prior to Introduction of Spectrometers

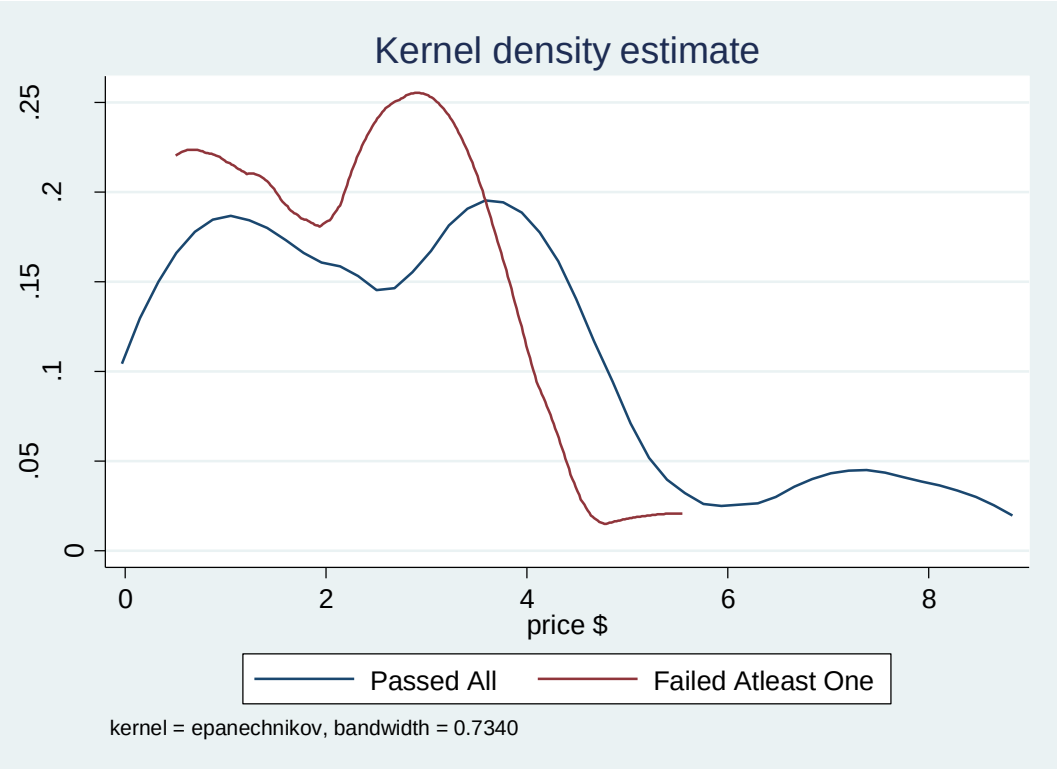

Figure 3: Kernel Density of Drug Prices for Drugs that Passed All Versus Drugs that Failed Any Test Post Introduction of Spectrometers