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Corruption and Medicine Quality in Latin America: A Pilot Study

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Abstract

Fake and substandard medicines are a significant problem in developing nations, and a growing problem in developed ones too. There have been assessments of basic medicine quality from many countries and regions across the world but almost none in Central and South America. Over the past decade, as part of our research, we have collected over ten thousand samples of medicines from 22 cities in emerging markets, but the only one from the Latin region was Sao Paulo in Brazil. We have now rectified this gap, at least for one critical medicine, the broad spectrum antibiotic ciprofloxacin. Using original, self-collected data from ten countries in Latin America, we test whether the samples of 687 Ciprofloxacin drugs pass the Global Pharma Health Fund e.V. Minilab® protocol to identify substandard or counterfeit medicines. In terms of quality, 93 percent of drugs were good quality. Within the drugs that failed the quality test, the majority were substandard rather than fake. About 26.4% of the poor quality drugs were fake i.e had zero active pharmaceutical ingredient (API), while the rest were substandard i.e. they had less than 80% API. In line with results from our earlier studies, we find that products that were locally registered, as well as those with SRA or WHO pre-qualification, were more likely to pass the test. A new finding in this paper is the role of corruption in influencing the quality of drugs. As highlighted in the literature, corruption can play a large, negative role in the healthcare system, particularly adversely impacting those with very low incomes. Bribery of regulators and public officials can affect the procurement process for drugs and allow counterfeit producers to supply low quality drugs without facing the consequences. Our study finds that corruption is strongly correlated with poor quality drugs. Less corrupt countries on the other hand, had higher levels of passing drugs.

1. Introduction

Fake and substandard medicines are a significant problem in developing nations, and a growing problem in developed ones too. There have been assessments of basic medicine quality from many countries and regions across the world (Institute of Medicine 2013), but almost none in Central and South America. Over the past decade, as part of our research, we have collected over ten thousand samples of medicines from 22 cities in emerging markets, but the only one from the Latin region was Sao Paolo in Brazil. We have now rectified this gap, at least for one critical medicine, the broad spectrum antibiotic ciprofloxacin. We have undertaken considerable research on Cipro before (Bate, Jin & Mathur 2015; Bate, Jin, Mathur & Attaran 2016), and it is the one drug we have found in every city and most pharmacies within each city. We therefore expected to be able to find it in each of the nine Latin cities (in addition to Sao Paolo) we sampled, which include Asuncion, Buenos Aires, Caracas, Guatemala City, Guayaquil, La Paz, Lima, Montevideo, Sao Paolo and Tegucigalpa.

A study by the Pharmaceutical Security Institute ranked Latin America second (Mackey, Liang, York & Kubic 2015), after Asia, as the region with the highest level of pharmaceutical counterfeiting and theft.¹ The likely reasons include decades of political unrest that have resulted in economic depression and the import and export of fake products, lack of judicial action against counterfeiters due to corruption and bribery of officials and weak laws, and finally poverty itself, which has led to people demanding cheaper, poorer quality products in place of genuine, expensive ones.² Of course, it is also true that people who buy these drugs don't have perfect information

¹ In 2004, in Argentina, several women died after receiving a fake iron-based medicine to treat anemia. In 2009, Pfizer seized 8.5 million fake pills bound for Latin America. In Venezuela, Primaquine tablets were found to contain low levels of Primaquine, and one patient developed Plasmodium Vivax malaria after taking Primaquine containing 46% of the active ingredient.

² <http://www.grr.com/download/dmmasintellectualpropertymagazine2010.pdf>. Statements made by Katharine Murphy of the Patients Association and Julian Harris of the International Policy Network suggest that consumers often purchase fake drugs because they are cheaper and more conveniently available. However, people are also

about quality. Therefore, it is hard to tease out whether it is poverty or lack of information that is fueling demand for these drugs.³ According to another study, Mexico is a major global source of fake medicines with a sales value of \$650 million per year, about 10 percent of total drug sales in the country (Morris & Stevens 2006). Furthermore, Brazil is one of the most developed nations in South America, and is widely seen as having the best medicine regulator, yet it still has significant flaws in medicine oversight (Pugatch, Tortensson & Laufer 2015).

Our study uses a sample of 687 Ciprofloxacin treatments from ten Latin American cities (including Sao Paolo). Using the Global Pharma Health Fund e.V. Minilab protocol®, we test for drug quality, and link drug quality to local indicators of drug regulation, demographics, distribution channels and price. At the same time, other studies have highlighted factors such as the degree of corruption in procurement and enforcement systems, lack of training and professionalism and pressure to buy from local suppliers rather than procuring drugs from good quality supply chains (Tortensson & Pugatch 2010). Therefore, the contribution of this paper is that it is the first to systematically study fake and substandard drugs in Latin America, but also one of the first to specifically study the role of corruption in influencing drug quality in Latin America. Corruption in healthcare systems is of particular concern in developing economies where public resources are scarce and health service provision is compromised, particularly negatively affecting low-income individuals (Vian 2002). This can lead to poor quality treatments and care and also an increase in the cost of care. Moreover, corruption in healthcare is likely reflective of the tolerance of corruption in other aspects of the economy. Dora Akunyili, the former head of Nigeria's

unaware of the risks of consuming these drugs and think of counterfeiting as a “victimless crime”. In his book, *Phake*, Roger Bate presents several pieces of anecdotal evidence that people will often buy what they can even if they suspect the products won't work as well (Bate 2012).

³ As per a Gallup survey, 10% of Americans thought corrupt police were a major reason behind the increase in counterfeiting and 30% blamed the high prices of genuine drugs for counterfeiting practices.

National Agency for Drug and Food Administration and Control and winner of Transparency International's 2003 integrity award, says in the Global Corruption Report 2006 produced by Transparency International "Drug counterfeiting, facilitated by corruption, kills en masse and anybody can be a victim" (Akunyili 2006). The authority she then ran found cases of water being substituted for adrenaline and of active ingredients being diluted by counterfeiters. Rose-Ackerman (2015) highlights the role of corruption in the Chinese healthcare system which affects the procurement of drugs, the regulation of drug safety and monitoring processes and bribe-taking by doctors and healthcare providers. A study by the International Monetary Fund (Davoodi, Gupta & Tiongson 2000) shows that higher levels of corruption are associated with higher rates of infant and child mortality. Hunt (2007) finds evidence of bribery in healthcare in Peru and Uganda.

Since information on corruption in health care systems is usually highly specific and not comparable across countries, we use a general corruption perception index indicator (CPI) developed by Transparency International to proxy for this. Corruption in health systems in Latin American countries affect the procurement of drugs, their delivery, regulations relating to drugs, and accountability of public health officials. By some estimates, about \$28 billion are stolen or diverted from health systems per year in Latin America (Savedoff 2007). One prominent reason for this is hypothesized to be the bribes paid to government officials to prevent or avoid regulations, leading to an increase in fake drugs both in Latin America as well as around the world. For instance, a recent paper on the Colombian health system found that bribe taking by government officials had resulted in widespread problems in the health system and prices of pharmaceutical products being so high that it resulted in a major public health crisis (Webster 2012). Another report highlights several instances of abuse by public officials (Global Health Intelligence 2016). In Honduras, the vice-president was charged with having links to a company that embezzled the

state by selling poor quality medicines at inflated prices. In Guatemala, political corruption in the health system leads to a loss of life for at least five patients with kidney failure. The general link between corruption and health is also established in a few papers (see Afzar & Gurgur 2008, Rose 2006). A study by the IMF showed that countries with a higher incidence of corruption have higher rates of infant mortality.⁴

In an earlier paper (Bate, Jin & Mathur 2012), we differentiated fake and substandard drugs as follows. We classify drugs with zero active ingredient as “counterfeits⁵” while those with some but less than 80% active ingredient as “substandard”. All other drugs are considered to be “passing” i.e. they pass the quality test. This definition focuses on the amount of active ingredient because it is much more likely that a drug with zero active ingredients has worse health outcomes than a drug with lower amounts of the active ingredient⁶. Also, in our earlier work (Bate et al. 2015), we find that pricing of counterfeits and substandards varies significantly. On average, substandard drugs are priced lower than comparable generics in the same city, while there is no significant difference between the price of counterfeits and the genuine targeted drugs. Finally, targeting counterfeit and substandard drugs requires different strategies. Substandard drugs arise from the poor production techniques by legitimate manufacturers and therefore can be addressed through better regulations and manufacturing standards (Caudron et al. 2008). In contrast, counterfeit drugs with zero active ingredient requires arresting criminal activity through better law enforcement and prosecution (Cockburn et al. 2005). Our definition is different from that of World

⁴ <https://www.imf.org/external/pubs/ft/wp/2000/wp00116.pdf>

⁵ We use the word counterfeit in this paper since it is the most familiar to economists, but the term of art preferred today in medical circles is “falsified”, which denotes a product that is misidentified, whereas counterfeit remains the term of art for intellectual property violations (IOM 2013). The two perfectly overlap in our sample because all falsified medicines also had fake identifiers on the packaging, however, some were not passing themselves off as a particular generic or branded medicine, so in some instances no specific IP holder was harmed.

⁶ However, substandard medicines with some but not enough active ingredient may actually drive resistance to even the best quality medicines by “selecting” the most robust and dangerous pathogens.

Health Organization (WHO) which defines counterfeit medicines as “medicines that are deliberately and fraudulently mislabeled with respect to identity and/or source”. This definition emphasizes the intent to deceive as the primary characteristic of a counterfeit drug, which as an empirical matter is hard to prove. However, it is extremely rare for counterfeit medicines to contain the correct active ingredients, so our definition is a reasonable proxy (Bate 2012).

II. Methodology

We instructed covert shoppers from the region to randomly walk into pharmacies and claim that a family member needed ciprofloxacin. To mimic real patients as much as possible, the covert shoppers did not present a doctor’s prescription and always purchased the pharmacist-suggested brand. Shoppers moved from pharmacy to pharmacy until the allocated budget was used up. In most cities every pharmacy stocked Cipro, but in Caracas six did not.

Informal drug vendors (bus vendors, mobile carts, etc.) occur in some locations, but to be able to compare across all locations, our shoppers only visited pharmacies with a regular storefront. As a result, our samples are likely to understate the problem of poor-quality drugs, given the expectation and existing evidence that informal vendors sell worse drugs (Institute of Medicine 2013).

All medicines were assessed following the Global Pharma Health Fund (GPHF) e.V. Minilab® protocol to identify substandard or falsified medicines (Jähnke et al. 2001). The key test for our sample is the semi-quantitative thin-layer chromatography (TLC), which assesses the presence and concentration of active ingredient in a test sample as compared to the reference standard. A sample is referred to as falsified if it contains zero correct API, and referred to as substandard if it contains some correct API but the amount of API is under-dosed (below 80%).

This technique has been used for the past decade by our team in every sampling. All tests were conducted within 60 days after purchase, following the classification in Bate et al. (2015).

It is important to note that medicines can be substandard and still pass TLC, since they may not be soluble or be poorly formulated in other ways. As a result our assessments are likely to underestimate the number of poor quality medicines⁷.

As acknowledged in other studies (Attaran et al. 2012), the legal distinction between falsified and substandard products is one of intention: both sorts of compromised medicines are not as labeled and violate the relevant technical standards, but substandard medicines are compromised accidentally or negligently, while falsified medicines are compromised intentionally, with this difference not always being apparent from the content of the medicine. In other words, legally speaking, falsified products are the product of organized criminal intent, but substandard medicines are wrongfully produced by otherwise legitimate, law-abiding manufacturers. However, this legal distinction breaks down when a legitimate manufacturer cuts corners and produces poorly formulated medicines, or if it buys cheaper ingredients that may not be robust. And it may even intentionally cheat, knowing it is buying inferior ingredients, or skipping key production processes, which make a known substandard product. In light of the difficulty to detect the intent of manufacture, this paper distinguishes substandard and falsified drugs by API only.

To assess the quality of Ciprofloxacin drugs in Latin America, we bought a total of 687 drugs across the cities of Asuncion, Buenos Aires, Caracas, Guatemala, Guayaquil, La Paz, Lima, Montevideo, Sao Paulo and Tegucigalpa. Table 1 presents the summary statistics. In terms of

⁷ In ongoing investigations 27 treatments were tested with more sophisticated techniques, and three medicines which passed TLC failed these tests and were substandard, so our data almost certainly underestimates the rate of substandard medicines in the market.

quality, 93 percent of drugs were good quality. Within the drugs that failed the quality test, the majority were substandard rather than fake. About 26.5% of the poor quality drugs were fake (i.e. had zero active ingredient), while the rest were substandard (i.e. they had less than 80% API). The cities that we cover in our sample are generally high income with an average adult literacy rate of 93%. Most of our sample comes from large chain pharmacies (79.3%), 86.5% of drugs are locally registered while 5.2% are innovator brands.

Table 2 shows the distribution of the sample across different cities. Nearly 23 percent of the sample came from Sao Paolo, and none of these drugs were counterfeits. Only 3.8% were substandard. Another 16 percent came from Asuncion. 65 percent were bought in 2016, 25 percent were bought in January 2017, and the rest represent samples from earlier years. The failure rate of drugs was relatively high in Asuncion and Caracas, and among failing drugs there were more substandards in Caracas and equal numbers of failing and substandard drugs in Asuncion. Buenos Aires had the highest rate of passing drugs.

Table 3 shows where the drugs came from or were made based on what was listed on the packaging. Overall, a large share of poor quality drugs listed that they were made in India (44%), followed by China (22.9%) and Brazil (20.8%). Within these drugs that failed the test, 35.7% of the counterfeits were labeled as made in Brazil. Within substandard drugs, 52.9% of drugs were reportedly manufactured in India.

In line with our earlier study, we find that all products in our sample registered by western regulators or the World Health Organization pass, except for two. For locally registered products, the failure rate was 3.5%.

An area of interest for our study was to explore the link between price and quality of drugs. In our earlier paper (Bate et al. 2015), we found significant price differences across passing and

failing drugs. Within failing drugs, counterfeit drugs were more likely to mimic prices of genuine drugs while the price of substandards was significantly lower than the price of comparable generics. These findings hold in this sample as well. Table 4 shows that the price of counterfeits is identical to that of the genuine drug that they are trying to mimic. The price of substandards relative to the generics in the same city-year varies a lot, but is in all cases significantly lower than for the passing generic.

Table 5 reports the correlation between the corruption perception index (CPI), the logistics performance index (LPI) and the quality of drugs. Data on CPI are obtained from Transparency International. The CPI ranks countries on a scale from 0 to 100, where 0 implies most corrupt and 100 refers to least corrupt. The index is constructed through expert assessments and opinion surveys that reflect opinions about the public sector in each country (Transparency International 2015). We use this as a proxy for corruption in the delivery of healthcare as well as healthcare systems.

The first row shows that the average CPI in countries (cities) with passing drugs was relatively higher than for those with substandard drugs. However, the CPI for countries with substandard drugs was relatively higher than for those with counterfeit drugs. Therefore, on average, low levels of corruption correlate with better quality drugs.

Another variable that we use is the LPI. In our sample, drugs were listed as being manufactured not just locally within the city or country of purchase but were listed as being manufactured in UK, USA, Europe, India and China. Therefore, to see if the quality of imported drugs was affected by any type of border enforcement mechanism, we use two sub-measures from the LPI index. The LPI is an index produced by the World Bank (World Bank 2016). It is based on an assessment of professionals working inside the country and it provides two useful measures

that might influence or directly reflect the quality of drugs coming into the country. The first is the percent of shipments receiving physical inspection and the second is the shipments meeting quality criteria. The former may impact the ease with which poor quality drugs can be brought into the country and is therefore likely a good predictor of the supply of counterfeit drugs in each country. The latter is more likely to be correlated with the supply of counterfeits in the country. In other words, if a higher percentage of shipments meets the quality criteria, it is less likely that poor quality drugs are coming into the country. Unfortunately, neither of these measures is available for Paraguay and Venezuela. The table shows a negative correlation between drug quality and these two measures. In general, for countries with high levels of counterfeit drugs (or worse quality drugs), the physical inspections of shipments are higher and the quality of shipments is lower. In general, countries with low levels of corruption (high CPI) also tend to have fewer physical inspections of shipments (correlation = -0.48) and higher quality of shipments (correlation = 0.38).

III. Regression Analysis

To see whether drug quality is a function of price and non-price factors, we regressed drug quality on variables such as the city GDP, as a proxy for average incomes, adult literacy rates, the maximum penalty for drug counterfeiting expenses (in months), whether the country has price regulations and indicators for corruption and border enforcement.

Our variables can be separated into city-specific and drug-specific. The drug-specific variables were collected for each drug sample tested. We use several indicators, including for whether the drug has been registered with the stringent regulatory authority (*sra_whopq*); whether the drug being tested is an innovator brand or a generic brand (*innovator*); whether the drug has been registered with the local regulatory authority (*prodregis*); As shown in Oxfam (2011) and

Bate, Putze, Naoshy, McPherson & Mooney (2010), local drug registration is a relatively basic regulation on legitimate drugs but its availability and implementation vary greatly across countries. Using drug registration data collected in Bate et al. (2010) and Bate, Mooney & Hess (2010), we created a dummy variable equal to one if a drug has been registered in the purchase country at the purchase time.

International authorities also take actions to address drug quality. For example, if a manufacturer in Brazil or India wishes to sell products in Nigeria or China, buyers in these latter countries may want proof of quality that the products achieve high standards, and may not accept registration in India and Brazil as proof. The company can choose to register these products in a western country with a stringent drug regulatory authority to establish quality, but this is expensive, time consuming, and rarely done if the company does not intend on selling in western nations.⁸ To assist such producers, as well as donors that might wish to buy quality generics, the WHO established a prequalification program, where generics producers could at a much lower cost establish higher levels of quality control than regulatory authorities in emerging countries could achieve.

It is commonly believed that approval by a western country with stringent standard (referred to as SRA approved) and WHO prequalification, is more stringent than registering locally in a low-to-middle-income purchase country.

We recorded the original transaction price in local currency, and then translated it into US dollars by exchange rate at the time of purchase. These nominal prices were then deflated using US CPI data. In the tables, all prices are real price in US dollars as of January 2016.⁹ We choose

⁸ In our data, registration with a stringent regulatory authority in a western country is perfectly collinear with whether the drug sample carries an innovator brand.

⁹ Deflated according to the US Census Consumer Price Index for all urban consumers.

to standardize price by exchange rate instead of PPP because PPP is not available for the largest round of sample collection (2016).

We also collected city-specific data. *América Economía*, the first Latin American business magazine, conducts research and rankings on major topics relevant to business and economics in Latin American countries (Echeverría 2016); we use their data on city GDP per capita in Latin America (*gdp_city*). The year- and city-specific GDP per capita data are denominated in US\$ of purchasing power parity (PPP). We also used the adult literacy rate from UNESCO (*literacy*); the percent of shipments receiving physical inspection (*phys_inspect*) and meeting local quality criteria (*q_criteria*) from the World Bank's Logistics Performance Index; the Corruption Perception Index for 2015 from Transparency International (*cpi*).

We also hand-collected information on whether a country has drug price regulations (*pricereg*). Drug regulations focus on issues other than drug safety, for example the purchase country could issue price ceilings, mandatory retail price, and price guidance. We hand collected these regulations from each country's most recent government documents. Given the wide variety of price regulations, we define a binary variable equal to one if a country has adopted any price regulation on pharmaceuticals in the data collection year and zero otherwise.

Another variable we use is the maximum penalty in months for producing or selling counterfeit medicine (*max_penalty*). We proxy it by the number of months a person will be sentenced in prison if he is found guilty for counterfeiting drugs. We hand collected minimum and maximum penalty from the latest legal documents we can find in each country.

Finally, we also have information on whether the drugs were purchased from a large chain pharmacy, and how our shoppers ranked these pharmacies based on their general appearance and location.

All medicines were assessed following the Global Pharma Health Fund e.V. Minilab® protocol to identify substandard or counterfeit medicines. The first test is a visual inspection of packaging and pills for correctness. Depending on the drug being analyzed this can be followed by dye tests for presence of active ingredient and a disintegration test for basic solubility, but by far the most important test, and the key test for our sample, is the semi-quantitative thin-layer chromatography (TLC) for assessing the presence and relative concentration of active ingredient. All the tests were conducted with the Africa Fighting Malaria Minilab in the United Kingdom within 60 days of purchase.

Minilab tests were run in duplicate, with the generous assumption that the result more consistent with the reference standard Cipro (provided by GPHF) was recorded. Quality control of the Minilab was performed daily prior to testing and consisted of performing TLC on Minilab-reference samples for the medicine classes being analyzed. In addition, Minilab reagents were quality control tested using reference samples when a new lot was introduced. The Minilab protocol awards medicines a “pass” for active ingredient (by TLC) if they have 80% or more of the labeled active ingredient(s).

Table 6 presents probit regressions of quality. In column (1), we include all the explanatory variables aside from price that are specific to the city in which the drugs are bought as well as characteristics relating to the drug as well. Our results show that countries with low levels of corruption are more likely to have higher quality drugs. Drugs that are locally registered and countries with more regulated prices are significantly more likely to have higher quality drugs. Further, when pharmacies are assessed to be good quality by our covert shoppers, this also implies better quality drugs. These results generally hold across different specifications. In an earlier paper we found that large chain pharmacies were more likely to stock good quality, locally registered

products. In column (2), (3) and (4), we include an indicator for whether the drug was purchased from a large chain pharmacy. However, while the effect is positive, it is not statistically significant suggesting that either chain pharmacies don't matter or that since chain pharmacies typically store locally, registered products, the effects are not significant controlling for registration. In regressions not shown here, we do find that if we drop product registration variables, then large chain pharmacies are associated with a marginally higher likelihood of passing drugs. In Column (3), we include one of our LPI indicators, the percentage of shipments that undergo physical inspection. In Column (4), we include an indicator for the share of shipments that meet the quality criteria. Neither of these is significant, even though we exclude CPI from these regressions. In Column (5), we include variables that are drug-specific but not city specific. We then add country dummy variables to account for the other city-specific variables. We continue to find that low levels of corruption, product registration and the assessment of the pharmacy by covert shoppers all correlate with a higher likelihood of passing drugs.

Another finding that stands out in these regressions is that the quality of drugs is better when the drug labels show that the drugs are coming from China and India. This may seem surprising given that both these countries are large producers of generics but that they are also known to supply drugs of poor quality. This result may largely be driven by the fact that the omitted category for this variable is drugs made in Latin America. In our sample, all the drugs that were labeled as having been manufactured in UK, USA or Europe, proved to be passing drugs. Therefore, when we tried to control for this variable in the regression, observations relating to drugs manufactured in these countries were being dropped from the regression since they predicted success perfectly. Therefore, the only omitted category is drugs made in Latin America. Hence the correct interpretation of our results is that relative to drugs manufactured in Latin America, the

drugs coming from India and China were more likely to be passing drugs, controlling for other factors.

Table 7 regresses drug price on drug quality, drug-specific variables and other local variables. Column (1) reproduces results from our earlier papers, that higher drug quality is associated with higher drug prices. Also, product certification (SRA) and local product registration, large chain pharmacies and GDP are associated with better quality products. Higher levels of corruption (higher CPI) and higher literacy rates lead to lower prices. These results hold generally across all columns. In column (5), we exclude city-specific variables and put in city fixed effects. Our results are robust to this specification. In addition, when we include an indicator variable for whether the drug was listed as manufactured in India or China, we find that these drugs tend to be priced substantially lower relative to drugs manufactured in our omitted category Latin America. Again, this could signal that better quality drugs coming from these countries tend to be priced lower overall than poorer quality drugs coming from within Latin America.

Some discussion of the effect of corruption on drug prices is warranted here. Corruption in the healthcare system can lead to the proliferation of counterfeit producers who are not regulated and who pay bribes to government officials to avoid discovery and prosecution. They bypass regulations (like product registration), avoid penalties if caught and avoid other types of price controls as well. This increases the supply of fake drugs¹⁰ which as we saw earlier may lead to high prices because counterfeiters are more likely to price their products almost exactly identical to the high quality generics in the local market. At the same time, if regulators receive kickbacks to procure poor quality drugs from the counterfeiters, this might reduce the supply of good quality drugs in the local market which may in turn drive up prices even more. As noted in a 2007 World

¹⁰ It may also increase the supply of substandard drugs if local producers pay bribes and cut corners in production to avoid oversight.

Bank article, procurement is one area that is most prone to corruption (Cohen 2005).¹¹ That's because regulators have to make many subjective decisions regarding the volume of drugs to be purchased, the monitoring of drug quality and the prices at which the drugs can be purchased. Hence our results suggest that corruption leads to higher prices of drugs possibly because of one or more of these factors. These high prices unfortunately further encourage the entry of more counterfeiters into these markets.

IV. Discussion

The United States Trade Representative publishes special 301 reports on intellectual property violations. Nations of highest concern are placed on its priority watch list. Of the dozen nations on the most recent watch list two, Argentina and Venezuela, are covered by our research. While this is a general listing not specific to medicines, it is an important indication of counterfeiting problems in the region (U.S. Trade Representative 2016). Furthermore, Paraguay is one of the world centers for counterfeiting consumer products, most of which do not find their way into US markets and hence are less of concern to USTR. Organized criminals in Paraguay are increasingly faking pharmaceuticals causing significant problems including recent deaths (Wells 2013).

This also helps explain why many of the fake products are allegedly made by Brazilian manufacturers. Brazil is the largest market in South America and its locally produced medicines have a good reputation, so passing ones products off as Brazilian is rational for counterfeiters. Furthermore, while Brazil has a good drug regulator it shares large and fairly porous borders with key counterfeiting nations (Paraguay and Argentina). Notably on the Paraguayan side of border is

¹¹ Also see Kohler et al. (2015) and Rose-Ackerman (2015)

Ciudad Del Este, which is a large city and border zone, and a key transit point for counterfeit products in the whole of South America. Ongoing research in Paraguay found that two of the fake treatments in our sample, bought in Asuncion, were passed off as Brazilian made products were in fact made locally, probably in Ciudad Del Este. According to experts one of us (Bate) spoke with in the region, these same criminal producers of fake medicine are also implicated in wider counterfeiting, and possibly finance terror activities. It is not surprising that so many fake products proliferate in Paraguay when companies formerly run by the President, Horacio Cartes, are implicated in smuggling and illicit trade (Martin and Spinetto 2016). It is extremely likely that other fakes we found in other nations were made there too, but the opaque nature of the trade mean that even local experts and US Government officials are unsure of where many of the Paraguayan fakes end up.

Brazilian authorities cannot do anything about products made in Ciudad del Este until they enter Brazil, and since its own law enforcement efforts are sometimes compromised by corruption, faked products passed off as Brazilian are trade widely within Brazil. Nevertheless, Sao Paolo does not have as bad a problem with poor quality medicines as other nations, partly because other Latin American enforcement is far worse than Brazil. When it comes to substandard medicines, Brazil is also well off, since its drug regulator compares favorably with other mid-income countries (Bate, Mooney & Hess 2010).

India is most implicated in the production of substandard medicines, partly because of poor quality ingredients (Pugatch et al. 2015). India is one of the largest producers of cheap generics across the world and these generics are in demand everywhere. So it is no surprise that they are the single largest source of generics in our sample, 222 of 687 (32%) treatments. But 53% (18 of

34) of substandard medicines were made in India. This is in keeping with our other research where India was the largest source of medicines and an even larger source of substandards.

So how should countries proceed with tackling the issue of corruption in healthcare? Several initiatives around the world seem relevant. As detailed in a recent paper by Vian (2007), the first step is to introduce more transparency, since without transparency it is difficult to know which policy changes are required and when implemented which are working. Transparency policies may include government-mandated disclosure of information. Strategies to increase transparency include public service 'report cards', price monitoring and release of government documents or decisions through web sites, public databases, public meetings and the media (World Bank 2003). An example can be found in Argentina. The Ministry of Health in Argentina created a price monitoring system that tracked prices paid by 33 public hospitals for common drugs. The effect of the transparency policy was that purchase prices fell immediately by an average of 12%, and stayed below the baseline for over a year (Schargrotsky, Mera & Weinschelbaum 2001). A second step might be better detection and enforcement. Detection and enforcement includes steps taken to collect evidence that corruption has occurred, and to punish those who engage in corruption. Mechanisms of enforcement can function within the bureaucracy or externally through policing and the criminal justice system. Enforcement includes such activities as surveillance, internal security, fraud control, investigation (including investigative journalism), and punishment. Such disciplinary systems can potentially increase accountability and deter corruption.

V. Conclusion

Using original, self-collected data from nine countries in Latin America, we test whether the samples of 687 Ciprofloxacin drugs pass the Minilab Test, or fail. If they fail, we classify them

into counterfeit or substandard contingent upon the amount of active ingredient. In terms of quality, 93 percent of drugs were good quality. Within the drugs that failed the quality test, the majority were substandard rather than fake. About 26.5% of the poor quality drugs were fake i.e. had zero active ingredient, while the rest were substandard i.e. they had less than 80% API. In line with results from our earlier studies, we find that products that were locally registered, as well as those with SRA or WHO pre-qualification, were more likely to pass the test. A new finding in this paper is the role of corruption in influencing the quality of drugs. As highlighted in the literature, corruption can play a large, negative role in the healthcare system, particularly adversely impacting those with very low incomes. Bribery of regulators and public officials can affect the procurement process for drugs and allow counterfeit producers to supply low quality drugs without facing the consequences. Our study finds that corruption is strongly correlated with poor quality drugs. Less corrupt countries on the other hand, had higher levels of passing drugs.

While drugs may be locally manufactured, our sample suggests that a large share of drugs are imported from places like UK, USA, India, China and several countries in Europe. We find that all the drugs that were listed as being manufactured in UK, USA and Europe were good quality. Further, the quality of drugs manufactured in India and China were on average better than those manufactured within Latin America. To see if this was linked to effective customs practices, another variable that we tested was the percent of shipments that were inspected at the border. In general, we find that countries with higher levels of poor quality drugs also had higher levels of shipment inspections and lower percentages of good quality shipments.

While our sample size is currently inadequate to allow large scale generalizations about the role of corruption in driving the quality of drugs in these countries, it does suggest that this is an avenue for further research and exploration.

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Table 1: Summary Statistics

Variable name	Description	(1) N	(2) mean	(3) Sd	(4) min	(5) Max
large_chain	Large Chain	687	0.783	0.412	0	1
pharmassess	Pharmacy Assessment	687	0.859	0.348	0	1
sra_whopq	SRA/WHO Registration	687	0.195	0.397	0	1
Innovator	Innovator Brand	687	0.045	0.208	0	1
	Drug Price (Nominal \$)	687	31.99	20.01	9.20	104.40
	Drug Price (Real \$)	687	32.13	20.22	9.20	107.82
Quality	Passes Quality test	687	0.930	0.255	0	1
Prodregis	Local Registration	687	0.840	0.367	0	1
known_fake	Known Fake	687	0.020	0.141	0	1
known_sub	Known Substandard	687	0.049	0.217	0	1
gdp_city	City GDP per capita	687	12808	5536	3627	20981
literacy	Adult literacy rate	687	93.62	4.84	79.31	98.43
max_penalty	Maximum penalty	687	101.9	60.4	30	180
pricereg	Price Regulation	687	0.518	0.500	0	1
cpi	Corruption Perception Index	687	36.60	14.36	17	74
before2016	Collected pre-2016	687	0.102	0.303	0	1
phys_inspect	Pct. Physical inspection	540	14.90	14.11	1.58	35.57
q_criteria	Pct. Meeting local criteria	540	81.19	14.65	40.00	92.13

Table 2: Quality Test Results

City of Purchase	N	Passing	Counterfeit	Substandard
Asuncion	111	0.874	0.063	0.063
Buenos Aires	75	0.973	0	0.027
Caracas	36	0.833	0.056	0.111
Guatemala	52	0.923	0.019	0.058
Guayaquil	43	0.953	0	0.047
La Paz	34	0.912	0	0.088
Lima	56	0.929	0.018	0.054
Montevideo	78	0.949	0.026	0.026
Sao Paolo	157	0.962	0	0.038
Tegucigalpa	45	0.933	0.022	0.044
Total	687	639	14	34

Table 3: Poor Quality Drugs by City of Purchase and Country of Manufacture

A. All Poor Quality Drugs

City of Purchase	Listed Country of Manufacture						Total
	Argentina	Brazil	China	Ecuador	India	Mexico	
Asuncion	1	3	3	0	7	0	14
Buenos Aires	0	0	2	0	0	0	2
Caracas	1	1	0	0	3	1	6
Guatemala	0	0	1	0	2	1	4
Guayaquil	0	0	0	1	1	0	2
La Paz	0	0	1	0	2	0	3
Lima	0	2	1	0	1	0	4
Montevideo	0	0	2	0	2	0	4
Sao Paolo	0	4	0	0	2	0	6
Tegucigalpa	1	0	1	0	1	0	3
Total	3	10	11	1	21	2	48

B. All Counterfeit Drugs

City of Purchase	Listed Country of Manufacture					Total
	Argentina	Brazil	China	India	Mexico	
Asuncion	0	3	1	3	0	7
Caracas	1	1	0	0	0	2
Guatemala	0	0	0	0	1	1
Lima	0	1	0	0	0	1
Montevideo	0	0	2	0	0	2
Tegucigalpa	1	0	0	0	0	1
Total	2	5	3	3	1	14

C. All Substandard Drugs

City of Purchase	Listed Country of Manufacture						Total
	Argentina	Brazil	China	Ecuador	India	Mexico	
Asuncion	1	0	2	0	4	0	7
Buenos Aires	0	0	2	0	0	0	2
Caracas	0	0	0	0	3	1	4
Guatemala	0	0	1	0	2	0	3
Guayaquil	0	0	0	1	1	0	2
La Paz	0	0	1	0	2	0	3
Lima	0	1	1	0	1	0	3
Montevideo	0	0	0	0	2	0	2
Sao Paolo	0	4	0	0	2	0	6
Tegucigalpa	0	0	1	0	1	0	2
Total	1	5	8	1	18	1	34

Table 4: Drug Prices, by Quality of Drug Across Cities

City of Purchase	Passing Drugs (2016 \$US)	Substandard Drugs (2016 \$US)	Counterfeit (2016 \$US)	Comparator Price of Drug
Asuncion	24.75	17.1	19.6	19.68
Buenos Aires	32.38	-	-	-
Caracas	52.28	19.07	33.2	33.2
Guatemala	27.93	12.66	22.3	22.3
Guayaquil	24.97	16.2	-	-
La Paz	18.86	10.16	-	-
Lima	27.39	24.83	28.8	28.8
Montevideo	31.51	13.2	-	-
Sao Paolo	40.64	19.55	-	-
Tegucigalpa	26.65	15.15	28.2	-

Table 5: Corruption Perception Index, Logistics Performance Index and Drug Quality

	Passing Drugs	Substandard Drugs	Counterfeit Drugs
Corruption Perception Index	36.87	32.85	33.29
Pct. of shipments receiving physical inspection	14.78	16.69	19.36
Pct. of shipments meeting local quality criteria	81.41	76.72	79.17

Table 6: Regression of Drug Quality on Regulatory Factors and Demographics

Method	(1)	(2)	(3)	(4)	(5)
VARIABLES	Probit quality	Probit quality	Probit quality	Probit quality	Probit quality
cpi	0.0171*** (0.0027)	0.0154*** (0.0031)			
sra_whopq	0.3592 (0.3606)	0.3048 (0.3406)	0.0673 (0.3034)	0.0856 (0.3038)	
prodregis	0.9894*** (0.3374)	0.9625*** (0.3471)	1.0420*** (0.3210)	1.0199*** (0.3151)	
max_penalty	-0.0013 (0.0013)	-0.0013 (0.0012)	-0.0038*** (0.0011)	-0.0043*** (0.0017)	
pricereg	0.2912** (0.1272)	0.2495* (0.1344)	-0.0524 (0.0604)	0.0032 (0.0626)	
literacy	-0.0171* (0.0089)	-0.0153 (0.0010)	-0.0203** (0.0093)	-0.0155** (0.0062)	
log(gdp_city)	-0.0317 (0.1421)	-0.0444 (0.1400)	0.3089*** (0.0656)	0.3087*** (0.1117)	
madeinasia	0.4233 (0.3059)	0.4048 (0.2965)	0.1519 (0.3377)	0.1429 (0.3341)	-0.0275 (0.1546)
before2016	-0.2232* (0.1217)	-0.1668 (0.1588)	-0.2268 (0.1702)	-0.1081 (0.0996)	-0.2846*** (0.0469)
pharmassess	1.0487*** (0.2019)	0.8987*** (0.2408)	0.8712** (0.4283)	0.8341** (0.4099)	1.2803*** (0.2010)
large_chain		0.3495 (0.2701)	0.0442 (0.3831)	0.0745 (0.3679)	
phys_inspect			-0.0071 (0.0046)		
q_criteria				0.0008 (0.0036)	
Constant	1.0450 (1.1141)	0.9928 (1.0730)	-0.3031 (0.7381)	-0.8970 (0.8378)	0.2804 (0.1812)
City fixed effects	No	No	No	No	Yes
Observations	687	687	540	540	687

Robust clustered standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Table 7: Regression of Drug Price on Regulatory Factors and Demographics

VARIABLES	(1) log(price)	(2) log(price)	(3) log(price)	(4) log(price)
quality	0.1611** (0.0634)	0.1530** (0.0645)	0.1888** (0.0780)	0.1610** (0.0680)
cpi	-0.0006 (0.0014)		0.0034 (0.0036)	
known_fake	0.1117 (0.0846)	0.1408 (0.0891)	0.2363* (0.1002)	0.1185*** (0.0809)
prodregis	0.0377 (0.0734)	0.0256 (0.0683)	0.0489 (0.1037)	0.0482 (0.0744)
sra_whopq	0.5869*** (0.0504)	0.5698*** (0.0550)	0.5425*** (0.0387)	0.5408 (0.0446)
pharmassess	0.0234 (0.0300)	-0.0341 (0.0257)	-0.0522 (0.0296)	-0.0394 (0.0256)
large_chain		0.1244** (0.0467)	0.1388** (0.0567)	0.1216** (0.0467)
madeinasia	-0.5756 (0.0424)	-0.5790*** (0.0413)	-0.5957*** (0.0443)	-0.5949*** (0.0376)
before2016	0.1402** (0.0526)	0.1441** (0.0500)	0.0906*** (0.0165)	0.0994*** (0.0073)
max_penalty	-0.0006 (0.0004)	-0.0005 (0.0003)	0.0006 (0.0006)	
pricereg	-0.0051 (0.0273)	-0.0061 (0.0345)	0.021 (0.0613)	
literacy	-0.0219*** (0.0032)	-0.0214*** (0.0032)	-0.0213*** (0.0026)	
log(gdp_city)	0.4357*** (0.0497)	0.4185*** (0.0342)	0.3270*** (0.0575)	
phys_inspect			-0.0015 (0.0021)	
Constant	1.3039** (0.4805)	1.3660*** (0.3662)	1.9090*** (1.9085)	3.2160*** (0.1210)
City fixed effect	No	No	No	Yes
Observations	687	687	540	687
R-squared	0.825	0.831	0.833	0.736

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1