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UNVEILING THE MYSTERY OF ONLINE PHARMACIES: AN AUDIT STUDY

Roger Bate Ginger Zhe Jin Aparna Mathur

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ABSTRACT

This study assesses the trade-off between drug safety and price savings in online drug purchases. Focusing on five brand-name prescription drugs, we acquire 370 drug samples from 41 online pharmacies and test their authenticity. Of the 41 websites, 8 are clearly US-based and verified by the National Association of Boards of Pharmacy (NABP) or LegitScript.com. We refer to them as tier 1. Another 23 websites – referred to as tier 2 – are not verified by NABP or LegitScript but verified by PharmacyChecker.com or the Canadian International Pharmacy Association (CIPA). The remaining 10 websites are not verified by any of the four verification agencies and therefore classified as tier 3. Most tier 2 and tier 3 websites are foreign.

We have two main findings. First, according to our Raman spectrometry test, no failure of authenticity is found in drugs that came from verified websites, the only failures are Viagra from non-verified websites in tier 3. Second, within verified websites, tier 1 websites on average charge 52.5% more than tier 2 websites in final price (including shipping and handling) for the same drug and dosage except for Viagra. On Viagra, tier 1 and tier 2 websites are both safer and cheaper than non-verified websites in tier 3. These findings confirm the FDA warning against rogue websites but suggest that a blanket warning against any foreign website may deny consumers substantial price savings from verified tier 2 websites.

Roger Bate American Enterprise Institute 1150 Seventeenth Street, NW Washington DC 20036 rbate@aei.org

Ginger Zhe Jin University of Maryland Department of Economics 3105 Tydings Hall College Park, MD 20742-7211 and NBER jin@econ.umd.edu Aparna Mathur American Enterprise Institute 1150 Seventeenth Street, N.W. Washington, DC 20036 amathur@aei.org

I. Introduction

Online retailing is growing rapidly. At first glance, prescription medication seems a perfect fit for e-commerce: millions of Americans are eager to find affordable medication and every prescription drug has a searchable standard trade name and dosage. The reality is rather different – prescription medication has been slow in picking up e-commerce despite its enormous market size and long history of mail order.

One obvious reason for the slow development of the online drug market is demographic: most prescription drug takers are seniors and have less ability to navigate the Internet. In addition, both immediate access to medication for acute conditions and lack of insurance reimbursement for purchases from foreign websites probably contribute to the slow growth. But for chronic conditions and for those able and willing to search on the Internet, demand has grown. One major concern remaining for these potential buyers is safety. Numerous law enforcement cases demonstrate the danger of counterfeit and substandard drugs from rogue websites. Consequently, the Food and Drug Administration (FDA) advises consumers to avoid foreign websites and only purchase drugs from websites that are located in the US and have been accredited by the National Association of Boards of Pharmacy (NABP). Another potential obstacle to online drug purchase is the difficulty in finding correct and timely information about price savings and any possible association with drug safety. To our best knowledge, no academic research has quantitatively documented the safety-price trade-off for online pharmacies, although many news reports and political statements have cited data for drug safety and price savings separately.

The goal of our study is to provide a better understanding of drug safety and price savings for online pharmacies. By online pharmacies, we mean website-based entities that sell the same types of pharmaceutical products one historically has only been able to purchase from bricks and mortar pharmacies. In particular, we conduct an audit study of five best-selling brand-name prescription drugs in 41 online pharmacies. Not only do we attempt to distinguish US and foreign websites according to the FDA guidelines, we emphasize the role of website verification. In particular, we group the 41 sampled pharmacies into three groups: 8 US websites approved by the NABP and/or LegitScript.com (tier 1); 23 websites verified by PharmacyChecker.com and/or the Canadian International Pharmacy Association (CIPA) but not approved by the NABP and LegitScript.com (tier 2); and 10 websites that are not verified by any of the above four verification agencies (tier 3). Most websites in tiers 2 and 3 operate in a non-US country.¹ After acquiring drug samples from these online pharmacies, we compare their chemical contents against the authentic version of the drug via a Raman spectrometry test.

We have two main findings: first, no failure of authenticity is found in drugs from verified websites (tier 1 and tier 2), the only failures are Viagra from some of the non-verified websites (tier 3); second, conditional on same drug brand and dosage, tier 1 websites on average charge 52.5% more in final price (including shipping and handling) than tier 2 websites for all the tested drugs other than Viagra. On Viagra, tier 1 and tier 2 websites show no difference in drug safety and price, but if one aims to get authentic Viagra, verified websites are both safer and cheaper than non-verified tier 3 websites. These findings confirm the FDA warning against rogue websites but suggest that a blanket warning against any foreign website may deny consumers substantial price savings from verified tier 2 websites.

The rest of the paper is organized as follows: Section 2 describes the background, Section 3 reviews related literature, Section 4 describes our sample and methodology, and Section 5 presents the main data analysis. Discussion and conclusion are offered in Section 6.

II. Background

Prescription medication has an enormous market in the US. According to IMS health, overall sales of prescription medication in the US have grown from \$135 billion in 2001 to \$307 billion in 2010.² Of this, prescriptions serviced through mail, the closest proxy to online sale, have accounted for approximately 6.6 percent of sales in 2010.

Despite its large market size, prescription medication is a late-comer in e-commerce. A report issued by Forrester Research in 2007 shows that only six percent of prescription drug

1 As detailed below, two tier 2 and one tier 3 websites display a US mailing address on the web page but some of their deliveries are manufactured or packaged in foreign countries.

2 IMS Institute, April 2011. "The Use of Medicines in the United States: Review of 2010. Accessed at http://www.imshealth.com/deployedfiles/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_UseOfMed_report1_.pdf on March 20, 2012.

consumers purchased prescription drugs on the Internet in the past year.³ Asking a similar question in 2008, Deloitte Center for Health Solutions finds that 21 percent of prescription drug users reported buying drugs online or through the mail in the previous 12 months and this number increased to 30 percent in 2009.⁴

From the consumers' point of view, one potential benefit of online purchase is cost savings. GAO (2011) shows that retail price of 100 commonly used prescription medications⁵ increased at an average annual rate of 6.6 percent from 2006 to 2010. The annual price rise is particularly high in brand-name drugs (8.3%) as compared to generic drugs (-2.6%). The pain of high prices is real and substantial: according to the Commonwealth Fund, 48 million Americans did not fill a prescription due to cost in 2010, up 66% since 2001.⁶

What cost savings are available on the Internet? Within the US, GAO (2001) collected cash-paying price of 17 prescription drugs across 5 internet pharmacies, 5 large discount card stores, and bricks and mortar pharmacies through 5 areas. Their data suggest that internet pharmacies offer on average 15% discount from bricks and mortar retail stores, but these internet prices are 9.7% higher than the discount card programs that are typically run by large pharmacy benefit management (PBM) companies and only available to their members. If we restrict the sample to brand name drugs only, the price of online pharmacies is very similar to that of discount card programs, both approximately 12.5% lower than the average bricks and mortar price.⁷

There are no solid data on the potential savings from foreign online pharmacies, although politicians have claimed that US drug prices are 30 percent higher than in other industrial nations.⁸ The potential larger savings from foreign sources have motivated consumers to cross

7 These numbers are computed by the authors based on tables presented in GAO (2001).

³ Forrester Research report "Who Buys Drugs Online? Most Consumers Still Buy Offline And Ignore Drug Advertisements" by Carlton A. Doty, Carrie Johnson, Jacqueline Lyons and Brendan McGowan, June 12, 2007, <u>http://www.forrester.com/rb/Research/who_buys_drugs_online/q/id/41582/t/2</u>.

⁴ Deloitte Center for Health Solutions (2009) 2009 Survey of Health Care Consumers: Key Findings, Strategic Implications. Accessed at <u>http://www</u>. deloitte.com/assets/Dcom-

UnitedStates/Local%20Assets/Documents/us_chs_2009SurveyHealthConsumers_March2009.pdf on March 20, 2012.

⁵ In GAO(2011), retail price – also referred to as the usual and customary price – is defined as the price an individual without prescription drug coverage would pay at a retail pharmacy.

 $^{6\} http://www.commonwealthfund.org/Surveys/2011/Mar/2010-Biennial-Health-Insurance-Survey.aspx$

⁸ US News & World Report, July 28, 2011, "How to Cut Your Drug Costs" accessed at <u>http://money.usnews.com/money/blogs/the-best-life/2011/07/28/how-to-cut-your-drug-costs</u> on February 28, 2012.

the US-Canada border for prescription drugs, and more recently, order prescription drugs directly from online pharmacies allegedly based in Canada. By 2003, anecdotal evidence suggested that about one million Americans were purchasing medication online annually.⁹

One danger of online purchase is drug safety. To attract consumers that seek cost savings, privacy and convenience on the Internet, rogue websites peddle fake or real medication without requiring a prescription. These websites often ask patients to fill out a brief medical questionnaire and then an "online physician" will review the information and ship the drug directly to the "patient's" home. The lack of physician-patient contact can be dangerous because the "online physician" cannot examine the patient physically or ask probing questions to determine patient need of medication. Some rogue websites also aim to steal consumer credit card information for identity theft.

In numerous actions, the FDA has confiscated parcels at Customs and discovered various problems with foreign online pharmacies: first, drugs that are claimed to be of Canadian origin could come from 27 different countries¹⁰; second, some parcels have counterfeit or substandard drugs which contain no active ingredients, or the wrong active ingredients or incorrect amounts of the active ingredients and could generate serious health problems if consumed by human beings¹¹; third, even if the drugs are authentic, they may not be adequately labeled in English to help assure safe and effective use. Even the belief of cost savings can be misleading: FDA's examination of foreign mail shipments finds that about 45 percent of imported products are already available in the US as an FDA-approved generic drug and about half of the these generic drugs can be obtained from national pharmacy chains at the relatively low cost of \$4 each.¹²

The drug safety problem is not limited to shady operations outside the US. On August 21, 2005, the US Attorney's Office for the Western District of Missouri indicted three businesses and eleven individuals for their involvement in a \$42 million conspiracy to purchase and sell

⁹ Orlando Sentinel, May 2, 2012. "It's Illegal, but desperate Americans are buying drugs online from Canada" Accessed at: <u>http://articles.orlandosentinel.com/2010-05-02/news/os-drugs-canada-online-20100502_1_doughnut-hole-canadian-online-pharmacy-drugs on March 20</u>, 2012.

^{10 &}quot;FDA Operation Reveals Many Drugs Promoted as "Canadian" Products Really Originate From Other Countries", December 16, 2005, accessed at

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2005/ucm108534.htm on February 29, 2012. 11 "The Possible Dangers of Buying Medicines over the Internet", updated January 26, 2011, accessed at http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048396.htm on February 29, 2012.

¹² FDA announcement "FDA Finds Consumers Continue to Buy Potentially Risky Drugs Over the Internet", July 2, 2007, accessed at <u>http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108946.htm</u> on February 29, 2012.

counterfeit, misbranded and illegally imported Lipitor and other drugs. Similar arrest and conviction were extended to individuals in the state of Washington, Texas, Florida, and California, involving counterfeit Lipitor, Viagra, Cialis, and other blockbuster drugs¹³.

To be clear, the safety problem of online pharmacies is not driven by *lack* of regulation. Rather, Clifton (2003) argues that online pharmacies are subject to "an inefficient patchwork of state and federal regulations that are unable to offer uniform and adequate consumer protection." At the local level, state governments have the authority to license and regulate online pharmacies, but laws vary greatly from one state to another regarding online dispensing and prescribing. At the federal level, regulation of online pharmacies could involve the FDA, the Federal Trade Commission, the Department of Justice, the Drug Enforcement Agency, and the Federal Bureau of Investigation.

To overcome differential regulations across states, the NABP, a national organization that represents all the states' boards of pharmacy, initiated the Verified Internet Pharmacy Practice Sites (VIPPS) in 1999. The VIPPS program accredits US-based online pharmacies that comply with laws in both the state of their business operation and the states that they ship medications to. As of February 29, 2012, VIPPS has accredited 30 online pharmacies. Twelve of them are run by large PBM companies and open to members only. The other open-to-all VIPPS-accredited pharmacies include national chain pharmacies (such as cvs.com and walgreens.com) and large online-only pharmacies (such as drugstore.com).

Another private verification agency is LegitScript.com, founded by John Horton who was a White House aide on drug policy issues from 2002 to 2007. Like the NABP's VIPPS program, LegitScript only approves US-based websites for online drug sales. As of March 5, 2012, the home page of LegitScript announces that they monitor 228,419 Internet pharmacies among which 40,233 are active. Within active websites, LegitScript finds 221 legitimate (0.5%), 1,082 potentially legitimate (2.7%) and 38,929 not legitimate (96.8%). Their certification criteria includes valid license with local US jurisdictions, valid registration with the US Drug Enforcement Administration (DEA) if dispensing controlled substance, valid contract

^{13 &}quot;Counterfeit Drugs: Statement of Randall W. Lutter, Acting Associate Commissioner for Policy and Planning, FDA, before the Subcommittee on Criminal Justice, Drug Policy and Human Resources, House Committee on Government Reform", November 1, 2005, accessed at <u>http://www.fda.gov/newsevents/testimony/ucm112670.htm</u> on February 29, 2012.

information, valid domain name registration, requiring valid prescription, only dispensing FDA approved drugs, and protecting user privacy according to the HIPAA Privacy Rule (45 CRF 164),

By definition, both NABP and LegitScript.com do not approve non-US pharmacies, on the grounds that importing prescription drugs is technically illegal. However, personal importation is almost always overlooked by the FDA if the amount is small (no more than 90 days supply) and the medication is not a controlled substance.¹⁴ The FDA also advises consumers to avoid foreign websites and only buy prescription medication from the NABPapproved US websites that require prescription from a licensed health care professional.

This FDA guideline intends to protect American consumers from the risk of unsafe drugs on foreign websites; it also helps define consumer attitudes to foreign websites. If some foreign websites sell safe prescription drugs with substantial price discount but American consumers are guided to buy from US websites only, the FDA could potentially discourage price competition between US and foreign pharmacies and therefore reduce drug affordability within the US.

The danger of reducing price competition depends on whether consumers can distinguish trustworthy websites from the vast pool of foreign websites. Like all markets where consumers desire information on unobservable product quality, consumer demand fosters private verification services. For example, the Canadian International Pharmacy Association (CIPA), a trade association of Canadian pharmacies, has provided a list of verified Canadian websites that comply with Canadian laws. From American consumers' point of view, one shortcoming of CIPA is that it only verifies websites that are officially registered in Canada.

Another private verification agency, PharmacyChecker.com, casts a wider net over US, Canada, UK, Israel, and other countries. Started in 2003, PharmacyChecker verifies that any approved website has a valid pharmacy license from its local pharmacy board, requires a prescription for US purchase if the FDA requires prescription on the medication, protects consumer information, encrypts financial and personal information, and presents valid mailing address and phone number for contact information. As of March 9, 2012, PharmacyChecker has approved 73 foreign websites and 51 US websites.¹⁵

¹⁴ FDA "Travelers Alert" updated on June 30, 2012, accessed at

http://www.fda.gov/ForIndustry/ImportProgram/ucm173743.htm on February 29, 2012.

¹⁵ Note that the websites listed on PharmacyChecker's Pharmacy Ratings page is only a selected list of PharmacyChecker-approved websites. To appear on this list, the website does not only need the PharmacyChecker approval but also chooses to pay for the appearance on PharmacyChecker.com.

To summarize, there are at least four private verification agencies that verify the credentials and business practices of online pharmacies, mostly upon voluntary application (with fees) from online pharmacies. By definition, NABP and LegitScript.com only approve US websites, CIPA only approves Canada-based websites, and PharmacyChecker.com covers websites operating in US, Canada and other countries. By this design, it is not surprising that the lists of verified US websites overlap between NABP and LegitScript, and the lists of verified foreign websites overlap between CIPA and PharmacyChecker.¹⁶ In the audit study, we will group websites into tiers according to their verification status.

III. Literature Review

The goal of our study is to assess the safety and price differences across verified and non-verified websites. According to economic theory (Milgrom 1981, Grossman 1981, Jovanovic 1982), voluntary certification could work as well as mandatory certification if disclosure cost is zero, the independent verification agency always reveals the true product quality of the applicant, and most importantly, consumers are homogenous and rationally interpret the meaning of being verified or non-verified. These classical theories predict that drugs from verified online pharmacies represent higher drug safety and therefore should be sold at higher prices than drugs from non-verified websites.¹⁷

This prediction can be violated if some consumers are unaware of quality verification or have difficulty interpreting the meaning of non-verified products. In that case, fly-by-night sellers may take advantage of uninformed or misinformed consumers by pretending to be high quality. To the extent that some gullible consumers associate higher price with better quality, non-verified sellers could even charge higher price than verified sellers and flee after the transaction.

Another set of economic theories investigates the relationship between search cost and price dispersion. Stigler (1961) argues that reduction of search cost may encourage consumers to

¹⁶ Both PharmacyChecker and LegitScript only provide a selected list of approved websites on the web, so we cannot precisely quantify the degree of overlap across the four verification services.

¹⁷ See Dranove and Jin (2010) for a review of economic literature on quality disclosure and certification, including empirical evidence on the price difference between certified and non-certified products in industries other than prescription drugs.

search more intensively for lower price thus reducing both the mean and dispersion of transaction price. Follow-up theories show that this prediction is not always true: price dispersion may increase or decrease with search cost depending on specific model assumptions (Baye, Morgan and Scholten 2006).

Empirical evidence is mixed as well: on the one hand, Sorensen (2000) shows that retail price of prescription drugs is less dispersed for chronic conditions than for acute conditions because chronic patients have more time and incentives to search for lower prices. On the other hand, a number of products, including books, electronics, and CDs, demonstrate substantial price dispersion on the Internet, although price search platforms arguably reduce consumer search cost dramatically. Researchers try to explain online price dispersion by more diverse demand on the internet, more differentiated supply, heterogeneity in consumer awareness and retailer trust (Brynjolfsson and Smith 2000), seller engagement in obfuscation strategies to frustrate consumer search (Ellison and Ellison 2009), and an equilibrium model of clearinghouse (Baye, Morgan and Scholten, 2004).

The above literature on search cost and price dispersion can be applied to the distinction of verified and non-verified drug websites, depending on whether verification services reduce consumer search cost on online pharmacies. By definition, a list of approved websites is likely to reduce consumer search cost for at least drug safety information across websites. However, not all verification services provide a complete list of their approved websites on the Internet (some requires extra fees to list an approved website explicitly on the main page of the verification agency). Approval across different verification services also overlaps incompletely. These information frictions could frustrate consumer search. On the price side, only one of the four verification agencies – PharmacyChecker – provides a head-to-head price comparison across approved online pharmacies. This practice is similar to that of price search platforms studied by Brynjolfsson and Smith (2000), Ellison and Ellison (2009), and Baye, Morgan and Scholten (2004), and should facilitate price search.

In the context of prescription drugs, we need to consider one more factor contributing to price dispersion on foreign websites: different countries may have different price regulations on prescription drugs, which could affect both the wholesale cost of acquiring prescription drugs and the retail price of selling the drugs. One may argue that foreign websites could specify

different prices for US and local customers, hence their US price need not be subject to local demand or local regulations. Unfortunately, we do not have any first-hand experience on this, but some websites do post price online for all potential consumers around the world and this could limit their ability to price discriminate against US customers.

Above all, theory is ambiguous on whether average price and price dispersion should be lower or higher in verified websites. If all consumers are aware of verified websites and believe verified websites provide greater drug safety, drugs from verified websites should be priced higher. However, consumer unawareness, wrong belief, and regulatory heterogeneity across countries could all result in lower price in verified and/or foreign websites. Similarly, to the extent that verification services reduce consumer search cost for quality and price information, it could lead to lower price dispersion across verified websites. But other factors such as heterogeneous consumer belief, seller obfuscation, and price regulations could result in higher price dispersion across verified and/or foreign websites. One contribution of our audit study is to resolve these theoretical ambiguities in price and price dispersion, and confirm that verification agencies do provide useful information about drug safety.

While no academic study has evaluated price and price dispersion by the verification status of online pharmacies, our study builds on a small literature of drug safety. For example, public health researchers, as well as the World Health Organization (WHO), have examined the extent of counterfeit and substandard drugs, mostly in less developed countries, on drugs targeting infectious diseases such as malaria, and focusing on drug safety only (WHO 2011, USP and USAID 2009, Bate et al. 2009, Bate et al. 2008). Bate and Hess (2010) tabulate drug safety and price data based on a fraction of the sample used in this paper, but their sample is too small to warrant rigorous statistical tests of price and price dispersion by types of websites. In another study conducted by us (Bate, Jin and Mathur 2011), we demonstrate that the probability of counterfeit and substandard drugs varies by drug safety regulations in the country of purchase but neither retail price nor the subjective assessment of the quality of the pharmacy store constitutes a clear signal of actual drug quality. That study focuses on bricks and mortar pharmacies only in 17 mid-income and developing countries.

Focusing on prescribing safety instead of drug safety, Munger et al. (2008) compare 500 internet prescribing records from a Utah-based online pharmacy (KwikMed.com¹⁸) with another 500 records from a traditional multi-disciplinary primary care system in the Salt Lake City, UT. Across the two samples, they find no significant difference in the number of inappropriate prescriptions for PDE-5 Inhibitor (a drug for erectile dysfunction), after controlling for disease and medication covariates. This suggests that remote prescription on the internet can be safe if done appropriately. This finding also highlights the importance of distinguishing rogue pharmacies from the pharmacies that offer effective internet prescribing and safe drugs on the internet, a task that verification agencies should help to achieve.

IV. Data and Methodology

Our data collection consists of three steps: first, we purchased five best-selling prescription drugs from three types of online pharmacies; second, we compared the purchased sample to the authentic version of the drug via a Raman spectrometry test; third, we analyze test result and transaction price across pharmacy type.

To identify drugs that American consumers are most likely to purchase on the Internet, we consulted several sources including lists of the most-popular online drug searches from licit website pharmacies and IMS's list of the top 10 products "most often prescribed" in the United States in 2007.¹⁹ The five drugs selected for purchase were (in order of selection priority):

- Lipitor[®] 10mg (atorvastatin calcium) a synthetic lipid-lowering agent to reduce cholesterol, manufactured by Pfizer;
- Viagra® 100mg (sildenafil citrate) an oral therapy for erectile dysfunction, manufactured by Pfizer;
- Celebrex® 200mg (celecoxib) a nonsteroidal anti-inflammatory drug for treatment of arthritis, manufactured by Pfizer;

¹⁸ Kwikmed.com is approved by PharmacyChecker.com but not approved by the NABP or LegitScript. 19 The Wall Street Journal Online/Harris Interactive Health-Care Poll (2004) Six Million People Have Bought Prescription Drugs Online; Most Are satisfied. The Wall Street Journal Online 3(6).

- Nexium® 40mg (esomeprazole magnesium) a proton pump inhibitor for treatment of Gastroesophageal Reflux Disease, manufactured by AstraZeneca Pharmaceuticals LP; and
- Zoloft® 100mg (sertraline HCl) a selective serotonin reuptake inhibitor for treatment of depression, manufactured by Pfizer.

The dosages chosen were the most popular among identified websites and after consultation with Joseph Moody, MD, the physician advising this study. With the approval of his state health board, Dr. Moody provided prescriptions for the drugs. During the procurement process, we always instructed website pharmacies to provide brand-name drugs, and did not procure from websites where only generic versions were available. Once the most popular dosages were identified, reference standards were established for the chosen handheld Raman spectrometer. The spectrometer created a detailed spectral "fingerprint" for each reference standard, which was then compared against spectral readings from drugs procured over the Internet.

To create the reference standards, genuine samples provided via prescription by a national pharmacy chain (West Lafayette, Indiana, US) were analyzed using the Raman spectrometer and cross-checked against a second lot from a separate national pharmacy chain store to verify consistency and determine method robustness. In cases where it appeared slight lot-to-lot variation was present (as in the case for Lipitor coating thickness), a reference spectrum from both lots was included in the Raman spectroscopic method. In all cases, the two lots of drugs matched well and it was deemed that they were representative samples of authentic products.

Drugs were ordered in two rounds, first in January and February 2009, and then in November 2011. We identified online pharmacies using Google and Yahoo! search criteria and the list of approved and not recommended websites provided by verification agencies, as well as examination of spam emails sent to the authors and those caught in the spam filters of their organizations. While every reasonable effort was made to procure drugs from each website, this was not always possible. The lead author attempted to procure drugs from websites experiencing problems three times before moving on to the next website.

In total, we ordered from 41 pharmacies, 8 of which are US-based and verified by NABP and/or LegitScript. We refer to them as tier 1. Another 23 websites are not approved by NABP

and LegitScript, but verified by either PharmacyChecker or CIPA. We refer to them as tier 2. The remaining 10 websites are not approved by any of the four verification agencies thus grouped as tier 3.

Most websites in tiers 2 and 3 are straightforwardly foreign. The only exceptions are two tier 2 websites and one tier 3 website, who leave a US mail address in their "contact us" web page. However, the country of operation as said on the web page is not necessarily consistent with the country of drug manufacturing, repackaging or delivery. Such inconsistency is prevalent in many tier 2 and tier 3 websites. Even one tier 1 website, which is also a well-known retail chain with outlets in both US and Canada, delivered us drugs that appear to be manufactured or repackaged in non-US countries. For this reason, most of our empirical analysis focuses on the tier distinction by verification status rather than differences in the country of website operation, drug manufacturing, drug packaging, and mail delivery. At the end of Section 5, we examine whether the country of drug source as shown on the delivered drug package helps to explain price variations in our sample²⁰.

To obtain a better understanding of these websites, our research assistant went through each website in February 2012 to collect information on whether each website remains valid in February 2012, whether a prescription is required, method to check prescription (mail, email, fax or doctor contact), whether an online questionnaire is required, standard shipping cost (single package with smallest weight), the average delivery time of standard shipping, and whether discreet delivery is available. In discreet delivery, there is no identifiable packaging to show what the product is or where it has been bought from.

Condition on being able to make an order online, some orders did not lead to a successful delivery of the ordered drug. In round 1, two tier 1 pharmacies returned prescriptions; three tier 3 websites would not accept payment; and in another two cases ordered drugs were not delivered (both from tier 3 websites). In round 2, fewer problems occurred, with one tier 3 website refusing payment and two tier 3 websites not delivering products after taking payment.

²⁰ The internal AEI ethical review conducted for the early part of this project in 2009 concluded that no websites would be named.

We assessed drug quality using Raman spectrometry.²¹ Numerous studies have demonstrated that Raman spectrometry is a quick, reliable and cost-effective way for non-specialists to differentiate between genuine and counterfeit drugs (de Veij et al. 2007; Witkowski 2005; Gryniewicz et al. 2007; Bugay and Brush 2010). To ascertain the nature, and not just the spectra, of all compounds in a given drug, including impurities and degradation products as well as active ingredients, high-performance liquid chromatography (HPLC), considered the current gold standard analytical method in drug analysis, would be required. HPLC requires sophisticated sample preparation that is expensive and time consuming and requires trained chemists for analysis and interpretation of results. Given that the aim of this study was to authenticate a finished product (rather than its individual components), comparison with a known HPLC standard was unnecessary.

We used a handheld Raman spectrometer, the TruScan by Thermofisher (formerly Ahura Scientific of Wilmington, MA), on loan for the duration of the study. One necessity, and potential limitation, of spectrometers is that they require exact reference standards, obtained by scanning each separate brand with the same formulation for calibration. This means that a drug substituted for the branded version would record likely as a failure (since the excipients - binding agents - could be different, yielding different spectra, between two equally effective drugs). For this reason, generic substitutes were not sought from websites for this study. While a pass identifies a good quality drug, a "failure" does not mean that a given drug is necessarily of low quality. The spectrometer recorded a "failure" if a sampled drug was spectroscopically inconsistent with the reference standard; under this metric, both copy versions, FDA-approved bioequivalent generics of the chosen drugs, and different types of formulations sometimes found in different markets but made by innovator companies Pfizer and Astra Zeneca, may fail, because while they must contain the same quantities of active ingredient, they often contain different excipients in different concentrations. The spectrum created by the spectrometer is for the total sample formulation, not only the active ingredient.

In order to compare prices of drugs with the same formulations, purchased in the same quantities, the authors identified prices posted on the website or quoted by a pharmacy

²¹ The lead author did the testing after being trained by a spectroscopist from the company that owns the spectrometer platform. In addition to the company's assistance, all testing was completed in the observation of a professional outside our research team.

representative over the phone. If the formulation was not available in the same quantity, the authors selected the closest quantity available. Prices were calculated as "stand-alone" orders; that is, shipping expenses were not amortized across the entire five-drug order. Prices of tier 1 online pharmacies were compared with five bricks and mortar US-based pharmacies but there was no significant difference in price – not surprising since some of these pharmacies have bricks and mortar operations.

All prices are presented as price per pill including shipping and handling. Prices from the first round are kept nominal, while prices from the second round are deflated to February 2009 according to the Consumer Price Index for all urban consumers published by the US Department of Labor.²²

V. Data Analysis and Results

Table 1 summarizes pharmacy characteristics (as of February 2012) by tier. Not surprisingly, all tier 1 websites – by definition US-based and verified by either NABP or LegitScript – remain valid in February 2012, all requiring and checking prescription, all denying discreet shipping, with an average \$0.625 shipping cost per standard package (most with free shipping) and 10.625 days in shipping time. About half of them require an online questionnaire. Half of tier 1 pharmacies are national chains in the US with bricks and mortar retail stores throughout the country, one of them even has retail stores in Canada.

In contrast, 7 of the 10 tier 3 websites – by definition non-verified and mostly foreign – do not exist any more as of February 2012, and all three remaining ones require an online questionnaire. Two of the three remaining tier 3 websites offer "discreet shipping", and one of them does not require prescription. While the count of tier 3 websites is very small, it confirms the casual impression that non-verified foreign websites are likely fly-by-night sellers, trying to lure customers by privacy and often without requiring a prescription.

Tier 2 websites are somewhere in between. Three of the 23 tier 2 websites became invalid in February 2012. Among the remaining 20 websites, 70% of them require an online questionnaire and only two (10%) offer discreet shipping. Eighteen (or 90%) of them have clear

²² Historical CPI table for all urban consumers as of February 17, 2012 accessed at <u>ftp://ftp.bls.gov/pub/special.requests/cpi/cpiai.txt</u> on March 13, 2012.

prescription requirement (and check methods) on the web page, the other two (both US-based) offer internet prescribing of specific medications using an online (and free) diagnostic consultation and claim this practice is licensed by the local licensing authority.²³ On average, tier 2 and tier 3 websites charge higher shipping cost, not surprising given that most of them ship from foreign countries.

Table 2 lists the number of samples obtained by drug type and pharmacy tier. We have 105 samples for Viagra and between 62 and 71 samples for each other drug. Viagra is a lifestyle drug and is offered in more tier 3 websites, which is consistent with the fact that Tier 3 websites are more likely to offer discreet shipping without prescription. Of the total 370 drug samples, 219 are from round 1 and 151 are from round 2.

A. Summary of Drug Quality and Testing

A limited number of the drug samples were not testable because although innovator products were ordered, some innovator formulations, sold outside of US were different from those sold in US. Additionally some generics were substituted for innovator products and given the method of authentication chosen, these also could not be tested. As shown in the bottom of Table 1, all of the Celebrex and Lipitor samples were testable, but 14 Nexium samples (some Nexium sold outside US is in tablet form whereas it is capsule form in US), 12 Viagra (all generic substitutes) and 14 Zoloft (6 were generic substitutes, 8 were Zoloft in different formulations) were not testable. Conditional on being testable, Celebrex, Lipitor, Nexium and Zoloft all had a 100 percent success rate: there were no detectable failures, and the spectrometry test revealed the spectra to be identical to that of the reference drugs. In the case of Viagra, 8 out of a total of 94 testable samples were recorded as failures.

Dividing up the results by tier, we see that tier 1 websites are most likely to deliver testable samples (97.44%), followed by tier 2 (89.10%) and tier 3 (79.01%). All the 8 failures for Viagra came essentially from tier 3 pharmacies but only one of these failures can be linked to a particular website because the other seven are all discreet delivery with no website information on the mail package. However, we are sure that these failures are from tier 3 websites because all the tier 1 and tier 2 orders are accounted for. Within the eight failures for Viagra, all of them have

²³ When we purchased from tier 2 websites, every one of them required prescription.

China as the source of drug packaging but it is not always clear where the drug was manufactured and where it was shipped from. In one case, the drug was undoubtedly mailed from China (the bank account for this rogue site was in Panama); in another two samples the postal marks were from Austria and India. This is consistent with the FDA finding that orders on online foreign pharmacies could come from many countries even if they appear Canada-based.²⁴

B. Summary of Drug price

In this section, we summarize the distribution of drug price by drug type, pharmacy tier and drug authenticity conditional on testable samples.

As shown in Table 3, Celebrex, Lipitor and Zoloft are similar in several aspects: (1) on average, tier 1 is the most expensive, tier 2 is in the middle, and tier 3 is the cheapest, although some of the mean price differences are not statistically significant due to small samples; (2) even the minimum price from tier 1 is higher than the average price of tier 2 and tier 3; (3) there are wide price variations within the same drug same tier, and the biggest difference between minimum and maximum price appears in tier 2. The price pattern of Nexium is similar to Celebrex, Lipitor and Zoloft except that its average price in tier 3 is higher than tier 2.

It is worth noting that Lipitor started to face generic competition on November 30, 2011, which is right after our second round purchase. While Pfizer has engaged in aggressive pricing after November 2011²⁵, the price slash does not appear in our data. In fact, the average price of our Lipitor purchases is slight higher in the second round (\$2.139 per pill) than the first round (\$2.017) in real terms.

The pricing pattern of Viagra is different from the other four drugs. Unlike the other drugs, tier 2 Viagra is slightly more expensive than tier 1 on average (\$16.765 vs. \$16.465) and the average price of tier 3 Viagra is much higher than the other two tiers if the sample is authentic (\$19.931) but much cheaper than the other two tiers if the sample if not authentic (\$12.773). While these numbers are based on very small samples, they could be explained by

^{24&}quot;FDA Operation Reveals Many Drugs Promoted as 'Canadian' Products Really Originate From Other Countries' accessed at <u>http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2005/ucm108534.htm</u> on February 29, 2012.

²⁵ See more on Pfizer's pricing strategy at a 12/1/2012 Times article "Lipitor Already Cheaper after Patent Expiration" by Josh Sanburn accessed at <u>http://moneyland.time.com/2011/12/01/lipitor-patient-expiration-wont-mean-cheaper-generics-yet/</u> accessed on March 14, 2012.

Viagra's reputation as a lifestyle drug (Keith 2000, Catalano 2008). Potential users of Viagra may place value on privacy, non-prescription requirement, and discreet shipping, all of which are more prevalent among tier 3 websites. For the privacy reason, Viagra users may also rely more on private internet search and have less reliable information on drug price and quality across various websites. There is also an active black market for Viagra (without prescription), which could motivate middlemen to arbitrage more on price across websites in different tiers.

C. Regression results on testability and price

The above summary statistics are based on detailed and sometimes very small subsamples by drug type and pharmacy tier. To ensure statistical rigor, we regress the key outcomes (sample test-ability and price) on the dummies of tier 1 and tier 3 (tier 2 is the default), after controlling for a full set of drug type fixed effects (α_d) and a dummy of purchase round one. In particular, the specification is:

$$Y = \alpha_d + \beta_1 \cdot \mathbf{1}_{tier1} + \beta_2 \cdot \mathbf{1}_{tier3} + \gamma \cdot \mathbf{1}_{round1} + \varepsilon.$$

When Y is the dummy of whether a drug sample is testable, we run the specification by probit. We cannot run a probit estimation of whether a drug sample is authentic conditional on being testable because all the non-authentic drugs are Viagra. For price, we define Y as log of price (because of its skewed distribution) and run the specification by linear OLS (for inference on average price) as well as quantile regressions at 25, 50, and 75 percentile (for inference on price dispersion). In probit and OLS, we cluster errors by drug type and allow them to be robust.²⁶ Quantile regressions do not allow robust error or error clustering.

Table 4 report regression results for the full sample, the sample of all drugs except Viagra, and the sample of Viagra only. Within three samples, we also report a price regression conditional on authentic drug samples only. Overall, regression results confirm the summary statistics presented above: except for Viagra, tier 1 websites are more likely to deliver testable drugs and conditional on being testable, drugs from tier 1 websites are more expensive than both

²⁶ Robust and clustered errors are not possible in the sample of Viagra only.

tier 2 and tier 3 drugs.²⁷ Compared to tier 2, the average price hike of tier 1 is 41% higher in the full sample and 52.5% higher if we exclude Viagra. While substantial price differences exist at different percentiles of the price distribution, it is more so at the low end (25th and 50th percentiles) than at the high end (75th percentile). Surprisingly, in the full sample tier 2 are priced similarly to tier 3, and tier 2 price is even lower than tier 3 at the 75th percentile. This is partially driven by Viagra: when Viagra is excluded from the analysis sample, tier 2 price is 10.68-12.37% higher than tier 3 at the median and 75th percentile. Like the full sample, the price hike in tier 1 is greater at the 25th and 50th percentiles than at the 75th percentile, suggesting that tier 1 has less price dispersion than the other two tiers.

Because authenticity test does not fail except for Viagra, the comparison of full and authentic-only samples is most meaningful when we focus on Viagra only: the full testable sample shows no price difference across all three tiers, but conditional on authentic samples, prices from verified websites (both tier 1 and tier 2) are 17% lower than tier 3 on average. This suggests that it is *safer and cheaper* to buy Viagra from verified websites if one has a prescription.

Above all, regression results suggest that purchasing from verified tier 2 websites could lead to substantial savings from verified US websites (tier 1) without compromise in drug safety. In fact, tier 2 websites demonstrate large price dispersion, if consumers are willing to search within verified tier 2 websites, the price savings can be even higher than what has been shown on average (52.5%) or in median (49.3%). For Viagra, there is no statistical difference between tier 1 and tier 2 websites, both are better in safety and price than non-verified tier 3 websites.

One possible explanation for the lower price of tier 2 products as compared with tier 1 is because PharmacyChecker.com is the only verification agency that presents head-to-head price comparisons, in addition to pharmacy verification. While our sample is too small to confirm this as the major cause, it is consistent with the intuition of Stigler (1961) that reduction in search cost could lead to reduction in average price. Lower price dispersion in tier 1 on non-Viagra drugs (relative to tier 2) does not confirm Stigler's predicted effect on price dispersion. This could be due to variations in demand, regulation and supply across different foreign countries.

²⁷ Column 1 of table 4 includes 297 observations rather than 370 since it drops certain observations that perfectly predict the outcome variable.

D. Drug source

A remaining question is why tier 2 websites are on average substantially cheaper than tier 1 websites on non-Viagra drugs. One potential explanation is that most tier 2 websites have their drugs sourced from non-US countries and these countries have better price due to more consumer friendly price regulation, more price sensitive demand in their own domestic market, or more competition in price. We cannot distinguish these specific explanations, but we can correlate drug source with price. By drug source, we mean the country source of drug manufacturing or packaging as indicated on the delivered drug package. If the drug labels manufacturing and packaging countries differently, we define drug source as manufacturing country. To be consistent with above analysis, we will focus on testable drug samples only.

Table 5 displays count of testable samples by drug source and pharmacy tier. Of the total 328 samples, 68 are sourced from US, 116 from Canada, 90 from Europe (Italy/Turkey/UK/Germany), and 37 from Asia and Pan-pacific regions (China/India/Israel/Australia). Probably because of discreet shipping, 17 drug samples do not provide clear label of drug source. Cross tiers, all but eight tier 1 samples are from US and all the ones with missing drug source are from tier 3.

Conditional on testable samples, we add drug source dummies (Europe, Asia/Pacific, Canada, missing) to the OLS regression of log price. We omit US and missing drug source because all US sourced drugs are in tier 1 and all drugs with missing source are in tier 3.²⁸ To account for the fact that four of our tier 1 pharmacies have retail outlets and may price differently because of this, we also include a dummy of having retail stores in the regression.

Table 6 reports the regression results for all testable drugs, all testable and authentic drugs, all testable (and authentic) drugs without Viagra, and authentic Viagra only. To our surprise, on top of the significant effect of tier 1 on price, there are no price differences across Asia/pacific, Europe and Canada as compared to the default of US. This is partly driven by Viagra: when we exclude Viagra, Europe is the only drug source category that correlates with significantly lower price. For Viagra only, the R-square of the price regression drops dramatically (to less than 1%), and no drug source categories indicate higher or lower price once we condition

²⁸ Recall that not all tier 1 websites have drug source from US, this allows us to identify tier dummies separately from drug source dummies.

on authentic Viagra. This supports our conjecture that there is relatively complete price arbitrage on Viagra due to its popularity as a lifestyle drug. We also try the sample regression including both authentic and non-authentic Viagra: it does return several significant coefficients, but they are all driven by the 8 non-authentic Viagra samples of which one is from China and the other have missing drug source. We believe this result is not reliable thus do not report it in Table 6.

Above all, data suggest that price variations in our sample are mostly driven by tiers instead of country of drug source. The only exception is relatively lower price from Europe for non-Viagra drugs. This is somewhat surprising, but likely driven by the small size of our sample. In particular, countries with potentially lower manufacturing cost – for example China and India – have very few observations in our sample and therefore we cannot distinguish them from other Asia/pacific countries statistically. A more definite answer on the role of drug source in drug price and safety calls for future research.

VI. Conclusion

This paper uses a sample of 370 self-collected drugs from a stratified list of US and foreign online pharmacies to assess drug price and quality. After classifying pharmacies into three tiers by verification status, we have a few key findings: first, while verified US websites in tier 1 are more likely to deliver testable drugs (this is primarily because a few foreign sites mailed slightly different brand formulations made by innovators in those foreign markets), we find no failure of authenticity among testable drugs except for 8 Viagra samples from non-verified tier 3 websites. Second, conditional on verified websites, tier 1 and tier 2 websites show no difference in drug safety – all 100% authentic according to our Raman spectrometry test – but tier 1 websites (US-based) are on average 52.5% more expensive than tier 2 websites (US and foreign) for all the tested drug types except for Viagra. On Viagra, there is no price and safety difference between tier1 and tier 2 websites, but both tiers are safer and cheaper than tier 3 if one aims for authentic Viagra. Following Stigler (1961), since PharmacyChecker is the only verification entity which allows for head to head price comparisons, this may encourage lower search costs and hence lower prices among tier 2 (PharmacyChecker verified) web pharmacies.

These findings suggest that the FDA guideline against any foreign website is most likely based on FDA lack of jurisdiction, and inability to oversee quality, outside of US, rather than a careful assessment between drug safety and price savings. In the US, tens of millions of Americans go without prescribed medication due to cost each year. For most uninsured Americans, lower priced drugs from foreign online pharmacies are an attractive option and for many a necessary one. Clearly there is a greater danger when ordering from non-credentialed a program that educates consumers about buying drugs online from sites and could domestic and foreign sources reduce the likelihood of consumers purchasing non-authentic products.

The current illegal-but-no-enforcement approach on personal importation of prescription drugs does not stop consumers from buying drugs on foreign websites, but it does leave consumers in the gray area of searching for unofficial information on their own. Admittedly, our sample is probably too small and of only five products to justify the overall drug safety on all verified tier 2 websites. However, our small sample suggests that verification agencies deliver useful information for both domestic and foreign websites. In light of this, we wonder whether a blanket warning against foreign websites has limited price competition between US and foreign websites, and whether a more open and educational policy could make better use of the existing verification services for consumer savings in authentic drugs.

References:

- Bate, Roger; Peter Coticelli; Richard Tren; and Amir Attaran (2008) "Antimalarial Drug Quality in the Most Severely Malarious Parts of Africa – A Six Country Study. *Public Library of Science One* 3(5).
- Bate, Roger; Richard Tren; Lorraine Mooney; Kimberly Hess; Barun Mitra; Bibek Debroy; and Amir Attaran (2009) "Pilot Study of Essential Drug Quality in Two Major Cities in India" *Public Library of Science One* 4(6).
- Bate, Roger and Kimberly Hess, (2010) "Assessing Website Pharmacy Drug Quality: Safer Than You Think?" *Public Library of Science One* 5(8).
- Bate, Roger; Ginger Zhe Jin; and Aparna Mathur (2011) "Does Price Reveal Poor-Quality Drugs? Evidence from 17 Countries" *Journal of Health Economics* 30(6): 1150-1163.

- Baye, Michael R.; John Morgan and Patrick Scholten (2004) "Price Dispersion in the Small and in the Large: Evidence from an Internet Price Comparison Site" *Journal of Industrial Economics*, LII(4): 463-496.
- Baye, Michael R.; John Morgan; and Patrick Scholten (2006) "Information, Search and Price Dispersion," Chapter 6 in *Handbook in Economics and Information Systems* Volume (T. Hendershott, Ed.), Amsterdam, Elsevier, 2006.
- Brynjolfsson, Erik and Michael D. Smith (2000) "Frictionless Commerce? A Comparison of Internet and Conventional Retailers" *Management Science* 46(4): 563-585.
- Bugay D. and R. Brush (2010) "Chemical Identity Testing by Remote-Based Dispersive Raman Spectroscopy" *Applied Spectroscopy* 64(5): 467–475.
- Clifton, Ludmila Bussiki Silva (2003): "Internet Drug Sales: Is it Time to Welcome "Big Brother" into Your Medicine Cabinet?" Journal of Contemporary Health Law and Policy 20: 541-570.
- Catalano, Charles Stephen (2008) "The Viagra Juggernaut: An Analysis of the "Rock Star" of the Prescription Drug World's Direct-to-Consumer (DTC) Advertising, Mega-brand Status, and Cultural Iconicity", Purdue University Dissertation.
- Dranove, David and Ginger Zhe Jin (2010) "Quality Disclosure and Certification: Theory and Practice" *Journal of Economic Literature*, 48(4): 935-63.
- Ellison, Glenn and Sara Fisher Ellison (2009) "Search, Obfuscation, and Price Elasticities on the Internet" *Econometrica*, 77(2): 427-452.
- US Government Accountability Office (GAO): "Prescription Drugs: Trends in Usual and Customary Prices for Commonly Used Drugs," published February 2011, GAO-11-306R.
- US Government Accountability Office (GAO): "Prescription Drugs: Prices Available Through Discount Cards and From Other Sources," published December 2001, GAO-02-280R.
- Grossman, S. (1981), "The Informational Role of Warranties and Private Disclosure about Product Quality," *Journal of Law and Economics*, 24: 461-489.
- Gryniewicz C, Spencer J, Hankins M, Kauffman J (2007) "Spectroscopic Methods for Rapid Determination of Diethylene Glycol in Glycerin." *American Pharmaceutical Review* 10(7): 24–30.

- Jovanovic, B. (1982), "Truthful Disclosure of Information," *Bell Journal of Economics*, 13:36-44.
- Milgrom, P. (1981), "Good News and Bad News: Representation Theorems and Applications," *The Bell Journal of Economics*, 12: 380-391.
- Munger, Mark A.; Gregory J. Stoddard; Allen R. Wenner; John W. Bachman; John H. Jurige; Laura Poe and Diana B. Baker (2008) "Safety of Prescribing PDE-5 Inhibitors via e-Medicine vs Traditional Medicine" *Mayo Clinic Proceedings* 83(8): 890-896.
- Keith, A. (2000) "The Economics of Viagra" Health Affairs, 19, no.2 (2000):147-157.
- Sorensen, Alan (2000) "Equilibrium Price Dispersion in Retail Markets for Prescription Drugs," *Journal of Political Economy*, v. 108 n. 4.
- Stigler, George (1961) "The Economics of Information," *Journal of Political Economy*, 69(3), pp. 213-225.
- United States Pharmacopeia and USAID (2009) "Survey of the Quality of Selected Antimalarial Medicines Circulating in Madagascar, Senegal, and Uganda" *US Pharmacopeia*. Available:

http://www.usaid.gov/our_work/global_health/hs/publications/qamsa_report_1109.pdf. Accessed March 20, 2012.

- de Veij M, Vandenabeele P, Alter Hall K, Fernandez F, Green M, et al. (2007) "Fast detection and identification of counterfeit antimalarial tablets by Raman spectroscopy" *Journal of Raman Spectroscopy* 38: 181–7.
- Witkowski M (2005) "The Use of Raman Spectroscopy in the Detection of Counterfeit and Adulterated Pharmaceutical Products" *American Pharmaceutical Review*.
 Available:http://www.horiba.com/fileadmin/uploads/Scientific/Documents/Raman/aprra man.pdf. Accessed April 16, 2009.
- World Health Organization (2011) "Survey of the quality of selected antimalarial medicines circulating in six countries of Sub-Saharan Africa" World Health Organization. Available: http://www.who.int/medicines/publications/WHO_QAMSA_report.pdf. Accessed March 20, 2012.

	Tier 1	Tier 2	Tier 3	Total
Total Count	8	23	10	41
Verified by	NABP or LegitScript.com	PharmacyChecker.com or CIPA, not by NABP nor by LegitScript.com	None	
Valid in February 2012?	1	86.96%	30%	75.61%
Conditional on valid on February 2012				
Country of operation (as indicated on the web page)	US only	2 US, others Foreign	1 US, others Foreign	
Has retail store under the same pharmacy naeme	50%	0%	0%	9.76%
Require and check RX by email/mail/fax/doctor contact?	1	90% (the other 10% offers internet prescribing based on online consultation according to local licensing requirement)	66.67%	90.32%
Require online questionnaire?	50%	70%	100%	67.74%
Shipping and handling cost per standard package	\$0.625	\$9.525	\$7.667	\$7.048
Average shipping time per standard package (days)	10.625	15.15	10.5	13.53

Table 1: Pharmacy characteristics as of February 2012

	Celebrex	Lipitor	Nexium	Viagra	Zoloft	Total	
Count of all							
Total	71	70	62	105	62	370	
Tier 1	16	16	16	16	14	78	
Tier 2	46	46	36	46	37	211	
Tier 3	9	8	10	43	11	81	
Round 1	37	37	38	68	39	219	
Round 2	34	33	24	37	23	151	
Count of testable	samples						
Tier 1	16	16	16	16	12	76	
	100%	100%	100%	100%	85.71%	97.44%	
Tier 2	46	46	22	46	28	188	
	100%	100%	61.11%	100%	75.68%	89.10%	
Tier 3	9	8	7	32	8	64	
	100%	100%	70%	74.42%	72.73%	79.01%	
Total testable	71	70	45	94	48	328	
	100%	100%	72.58%	89.52%	77.42%	88.65%	
Count of authenti	Count of authentic samples condition on being testable						
Tier 1	16	16	16	16	12	76	
	100%	100%	100%	100%	100%	100%	
Tier 2	46	46	22	46	28	188	
	100%	100%	100%	100%	100%	100%	
Tier 3	9	8	7	24	8	56	
	100%	100%	100%	75%	100%	87.5%	
Total authentic	71	70	45	86	48	320	
	100%	100%	100%	91.49%	100%	97.56%	

Table 2: Summary of drug samples by drug type and pharmacy tier

Drug	Statistic	Tier 1, all authentic	Tier 2, all authentic	Tier 3, authentic	Tier 3, non-authentic only
Celebrex	Mean (SD)	3.682 (0.487)	2.249 (0.532)	1.631 (0.201)	-
	Min.	2.579	1.247	1.482	-
	Max.	4.577	3.602	2.139	-
	Ν	16	46	9	
Lipitor	Mean (SD)	2.826 (0.266)	1.891 (0.477)	1.625 (0.160)	-
	Min.	2.289	0.938	1.482	-
	Max.	3.283	2.701	1.970	-
	Ν	16	46	8	-
Nexium	Mean (SD)	5.711 (0.687)	2.980 (1.181)	4.888 (1.110)	-
	Min.	4.662	1.341	3329	-
	Max.	6.763	5.271	6.594	-
	Ν	16	22	7	-
Viagra	Mean (SD)	16.465 (2.639)	16.765 (4.653)	19.931 (5.821)	12.773 (2.819)
	Min.	12.953	11.612	12.381	9.895
	Max.	20.748	33.766	32.810	16.986
	Ν	16	46	24	8
Zoloft	Mean (SD)	3.647 (0.538)	2.245 (0.554)	2.203 (0.666)	-
	Min.	2.926	0.985	1.501	-
	Max.	4.605	3.311	3.555	-
	Ν	12	28	8	

Table 3: Summary of price by drug type, pharmacy tier and sample authenticity

conditional on testable samples only

	All	Conditional on being testable				
	(1)	(2)	(3)	(4)	(5)	(6)
	Testable?	ln(price)	ln(price)	ln(price)	ln(price)	ln(price)
		· · ·	25th	50th	75th	(authentic
			percentile	percentile	percentile	only)
Madal	Probit		Owertile	Owertile	Owertile	OI S
Model	Marginal effect	OLS	Quantile	Quantile	Quantile	OLS
Full sample						
Tion 1	0.0052	0.4100**	0.4277***	0.4553***	0.3446***	0.4108**
Tier I	(0.0025)	(0.1200)	(0.0455)	(0.0489)	(0.0454)	(0.1197)
T'	-0.0072	0.048	-0.073	0.033	0.0860*	0.0816
Tier 3	(0.0086)	(0.0993)	(0.0501)	(0.0549)	(0.0488)	(0.1208)
D 1 1	-0.0120***	-0.0161	-0.0155	-0.0211	-0.0087	-0.0234
Round I	(0.0029)	(0.0197)	(0.0371)	(0.0409)	(0.0372)	(0.0132)
Drug type FE	Yes	Yes	Yes	Yes	Yes	Yes
N	297	328	328	328	328	320
R2	0.285	0.9125	0.6406	0.7246	0.7688	0.9127
All drugs except	t Viagra					
T ' 1	0.0020*	0.5249**	0.5913***	0.4930***	0.3780***	0.5249**
lier l	(0.0007)	(0.0542)	(0.0503)	(0.0389)	(0.0393)	(0.0542)
Tier 3	0.0002	-0.0059	-0.0642	-0.1237**	-0.1068**	-0.0059
	(0.0004)	(0.1690)	(0.0615)	(0.0493)	(0.0502)	(0.1690)
D	-0.0044***	-0.0372*	-0.0745*	-0.0802**	-0.0334	-0.0372*
Round I	(0.0011)	(0.0120)	(0.0415)	(0.0333)	(0.0343)	(0.0120)
Drug type FE	Yes	Yes	Yes	Yes	Yes	Yes
N	192	234	234	234	234	234
R2	0.309	0.6057	0.3445	0.4222	0.4803	0.6057
Viagra only						
T ' 1		-0.0011	-0.0224	0.0992	0.0762	-0.0011
Tier 1	-	(0.0533)	(0.0645)	(0.0751)	(0.1450)	(0.0529)
Tier 3		0.0493	-0.0526	0.1028	0.1562	0.1706**
	-	(0.0722)	(0.0549)	(0.0621)	(0.1246)	(0.0714)
Round 1		0.0273	0.0232	0.0198	0.0222	-0.0155
	-	(0.0592)	(0.0521)	(0.0657)	(0.1128)	(0.0550)
Drug type FE	-	No	No	No	No	No
N	-	94	94	94	94	86
R2	-	0.0144	0.0091	0.0395	0.0394	0.0956

Table 4: Regression Results on test-ability and price

Note: Number of observations in probit regressions is smaller because some variables predict whether a drug is testable perfectly and these observations are dropped out of the probit sample. For the probit result of testability on Viagra only, all the key variables (tier 1, tier 2 and round 1) are dropped out of the specification and only the constant is estimated. That's why we do not report the probit result for Viagra only. Standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Probit and OLS have robust errors clustered by drug type for full sample and the sample without Viagra. For the sample without Viagra, because all testable drugs are authentic, Column (6) is the same as Column (2).

Drug Source	Tier 1	Tier 2	Tier 3	Total
Missing	0	0	17	17
Australia	0	22	10	32
Canada	2	95	19	116
China	0	0	1	1
Germany	0	6	0	6
India	0	0	1	1
Israel	0	3	0	3
Italy	0	16	8	24
Turkey	4	29	7	40
UK	2	17	1	20
USA	68	0	0	68
Total	76	188	64	328

Table 5: Summary of drug source by pharmacy tier, testable drug samples only

Table 6: Regression Results of Drug Price with Drug Source

	Ln(drug price)				
	All testable	All testable	All testable	All testable	
		and authentic	non-Viagra	and	
			(all authentic)	authentic	
				Viagra	
Tier 1	0.4143***	0.2994*	0.3633*	0.1076	
	(0.1117)	(0.1194)	(0.1224)	(0.1063)	
Tier 3	0.0330	0.0513	-0.0195	0.2037**	
	(0.1219)	(0.1276)	(0.1678)	(0.0908)	
Round 1	-0.0112	-0.0217*	-0.0313	-0.0066	
	(0.0190)	(0.0101)	(0.0082)	(0.0557)	
Drug source: Asia/pacific	0.0825	-0.0385	-0.0768	0.1555	
	(0.1129)	(0.0889)	(0.0697)	(0.1078)	
Drug source: Europe	-0.0905	-0.2029*	-0.2619***	0.0204	
	(0.1166)	(0.0870)	(0.0372)	(0.1032)	
Drug source: Canada	0.0110	-0.1049	-0.1571	0.1392	
	(0.1379)	(0.1140)	(0.0880)	(0.1004)	
Has retail stores in US	-0.0259	-0.0020	0.0052	-0.0425	
	(0.0315)	(0.0268)	(0.0283)	(0.0869)	
Drug type fixed effects	Yes	Yes	Yes	No	
N	328	320	234	86	
R-squared	0.9159	0.9169	0.6298	0.0098	

Note: Standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Errors are robust and clustered by drug type for all testable, all testable and authentic, and all testable non-Viagra samples.