Markups and Fixed Costs in Generic and Off-Patent Pharmaceutical Markets*

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August 2021

Abstract

There is wide dispersion in pharmaceutical prices across countries with comparable quality standards. Under monopoly, off-patent and generic drug prices are at least four times higher in the United States than in comparable English-speaking high income countries. With five or more competitors, off-patent drug prices are similar or lower. Our analysis shows that differential US markups are largely driven by the market power of drug suppliers and not due to wholesale intermediaries or pharmacies. Furthermore, we show that the traditional mechanism of reducing market power – free entry – is limited because implied entry costs are substantially higher in the US.

JEL Codes: I11, F14, L44

*Thanks to Joe Shapiro, Chris Snyder, Steve Berry, Fiona Scott Morton, Jason Abaluck, Jon Skinner, Leila Agha, John Rust, Nina Pavcnik, Stuart Craig, Samuel Moy and seminar participants. Thanks to Serena Sampler and Ray McCormick for excellent research assistance. Part of this research was conducted while Ganapati was a Fellow at Dartmouth College and at Ludwig-Maximilians-Universität Munich. All errors are our own.
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1 Introduction

Would increasing competition reduce the prices of off-patent pharmaceuticals in the United States? The US largely relies on competitive forces to set the price of pharmaceuticals that are no longer protected from competition by patents (primarily, but not exclusively, generic drugs). It is assumed that once patents expire, firms that produce generic versions of the drugs will enter the market and drive prices down to competitive levels. In contrast, many countries with comparable safety standards use a combination of competition and government purchasing power to attain low generic drug prices. We document that prices of generic and off-patent drugs in markets with few competitors are higher in the US than in these comparable countries. We then investigate these price differences to understand the relative roles of (1) competition between pharmaceutical suppliers (which includes both manufacturers and firms approved to import pharmaceuticals into the US) that face barriers to market entry and (2) markups along the value chain.

In the US, generic drugs account for 90% of prescriptions and 23.2% of expenditures in the $324 billion prescription drug market (IQVIA, 2018). Empirical evidence indicates that off-patent drugs are not sold in perfectly competitive marketplaces at marginal cost. For example, the price of pyrimethamine, an anti-parasitic developed in the 1950's, increased overnight from $13 to $750 per dose (Pollack, 2015).[1] Although no longer patent protected, many markets may not be large enough to attract the number of competitors needed to achieve marginal cost pricing – Berndt et al. (2017) and Dave et al. (2017) show that 50% of US markets are monopolies or duopolies. Generic drug markets may also be amenable to collusive behavior (Rowland, 2018).

Motivated by these observations, we compute a price differential for the US by comparing US prices to the those of four countries with comparable safety standards: Australia, Canada, New Zealand, and England.[2] We find that the final (retail) price of off-patent drugs in the

[1] Since 2010, 20% of US generic molecules have temporarily doubled in price (GAO, 2016).

[2] We focus on Ontario and British Columbia.

US relative to each of these countries declines as more suppliers enter the market.[3] With one American supplier, the price is at least four times higher. However, when there are five or more suppliers, retail prices are either similar or lower. We focus on prices paid by the US Medicaid program, however, results for Medicare Part D and private insurance are broadly similar.

Additionally, we compute the price differential using prices that approximately capture relationships at earlier points in the supply chain: specifically the price paid to suppliers and the acquisition cost for pharmacies. This suggests that the price differential that we observe is driven by suppliers rather than intermediary pharmacies, wholesalers, or benefit managers, and that the current price mechanism used by Medicaid programs is not an effective tool in small markets. Our results suggest that while competition is an effective mechanism for lowering prices in markets with many suppliers and manufacturers, which tend to be large markets with many patients, smaller markets have high fixed costs preventing entry and competition. We find that fixed costs must be four times higher in the US than Australia. If implicit fixed costs cannot be lowered, some form of second best price intervention such as bargaining could be necessary.

We build on Berndt et al. (2017), who described the landscape of generic drug markets in the US and noted the potential absence of competition, and an empirical literature that makes cross-country comparisons of drug prices (Danzon and Furukawa, 2003, 2011; Kanavos et al., 2013; Wagner and McCarthy, 2004; Danzon and Chao, 2000a). We build a uniquely detailed dataset using publicly available prices to first examine whether competition is indeed failing in some markets in the US, and then investigate where along the supply chain this occurs. Previous cross-country drug comparisons have focused primarily on determining which country (or system) produces the lowest prices. Danzon and Chao (2000b) broadly consider if one system of regulation has systematically lower or higher prices (using data from the 1990s), we seek to understand the the current situation the US, which has changed

[3]While the US has higher prices for drugs with limited competition, it often has the lowest prices for the most widely disseminated drugs.

considerable in the past thirty years (Berndt et al., 2017), and how it varies in different segments of the market - as well as up and down the value chain. This paper also contributes to the broader literature on generic drugs, which has primarily focused on the effect of exogenous entry on list prices (Reiffen and Ward, 2005; Berndt et al., 2017; Grabowski and Vernon, 1992), or how competition-based policies could increase competition and hence lower prices (Scott Morton, 1999; Berndt et al., 2017; Gupta et al., 2018; Bollyky and Kesselheim, 2017; Berndt et al., 2018).

2 Institutional Background

Competition in off-patent drug markets is shaped by manufacturing supplier approvals, insurance systems, and pharmacy regulation. We briefly describe how these elements affect prices at each stage of the supply chain in each country as it applies to generic and off-patent patient-administered drugs purchased in pharmacies. At a high level, supply chains share many similarities. In the countries we study, suppliers obtain approval from a regulatory body to market their products, the suppliers sell to wholesalers, who sell to pharmacies, who retail the products to consumers. The retail price paid depends on the consumer's health insurance policy. However, the US differs in an important way - there are many insurers (or their subcontracted pharmacy benefit managers) who arrange their own price agreements with pharmacies and suppliers (with potential consumer cost-sharing). In contrast, other countries have one predominant price setter - the government, which enables them to offer a set price schedule for generic drugs.

2.1 Entry Regulations

Manufacturing and entry regulations are nearly identical across our sample countries. Before a drug can be sold, suppliers must apply for local regulatory authorization. Regulators monitor the drug's safety, efficacy, and manufacturing quality. Approval requirements differ depending on whether the drug is innovative or a generic. Innovative drugs require extensive

(and costly) clinical trials to demonstrate their safety and efficacy profile. Generic drug approval requires evidence that the generic is bioequivalent to an already approved innovative drug. Assessing bioequivalence typically requires a study that shows the generic delivers the same amount of the active ingredients in the same amount of time as the original drug. The generic must be identical in terms of dosage form, strength, route of administration, and intended use. All five countries follow the International Conference on Harmonization (ICH) guidelines in assessing bioequivalence. In addition to demonstrating bioequivalence, suppliers must also demonstrate compliance with production quality standards. All five countries have Good Manufacturing Practice guidelines that comply with the ICH. These regulations ensure that products are properly produced, packaged, and safe (FDA, 2018).

2.2 Insurance & Pricing

Final prices are determined by the relationships between suppliers, wholesalers, pharmacies, and insurers. The US has three major insurance regimes covering prescription drugs sold in pharmacies: private insurance, Medicare Part D, and Medicaid. In 2016, private insurance accounted for 41% of retail prescription drug spending, Medicare accounted for 30% and Medicaid accounted for 11% (out of pocket payments (15%) and other government programs (4%) make up the rest) (CMS, 2018). However, within these three groups there are numerous independent insurers – Medicaid is a separate program in each state, and each state may be have a component that is outsourced to private managed care plans.

All three types of insurers frequently outsource the management of their prescription drug plans to pharmacy benefit managers (PBMs). The market for PBMs is concentrated, with three companies controlling 66% of the market (Sood et al., 2017). PBMs act as intermediaries between health plans, pharmacies, and suppliers. They also set the formularies and network of covered pharmacies. For drugs with a single supplier, PBMs negotiate directly with suppliers for favorable placement on formularies (when there are drugs in the same therapeutic class that are close substitutes) in return for rebates, some or all of which they

keep as profit. When there are multiple suppliers, PBMs provide a Maximum Allowable Cost (MAC) list to pharmacies, which states how much they will pay for the drugs. While MAC lists for private insurers and Medicare Part D are decided between the insurer and the PBM, Medicaid reimbursement rates are subject to statutory rules. These statutory rules vary by state, but broadly, they compute potential prices using four different methods and set the reimbursement at the lowest one. In addition, a federally mandated manufacturer rebate is set by statute.[4]

In contrast with the US, Australia, England, and New Zealand have government-operated universal health insurance plans while Canada has a mixed public/private system.[5] In these countries, the government uses its purchasing power to obtain lower prices for drugs. For on-patent drugs, governments directly bargain with suppliers. In the case of generics, each country stipulates how much it will pay and the suppliers can take it or leave it. The method used for setting prices for generic drugs differs across countries. Australia and England both use a reference price system, based on reported supplier prices. Suppliers report their sales prices and the health plan reimburses based on the average price. In Australia, prices are not revised upwards without approval, whereas in England, the price fluctuates with the market. Australia also has a mandatory price reduction of 16% when the first generic enters the market. New Zealand uses a competitive tendering system to lower the price of generic drugs. The winning supplier has their product exclusively eligible for reimbursement by the national health plan. All Canadian provinces except Quebec set the price of generics entering the market from 2014 onwards using a tiered pricing system.[6]

There are two further intermediaries between the consumer and the manufacturer: wholesalers and pharmacies. The wholesale market is very concentrated in all five countries

[4]During our study period this rebate was a 13% for generic drugs.

[5]Workers may have private insurance and each province has its own public drug plan, which cover disadvantaged segments of the population. We focus on the two largest English-speaking provinces: Ontario and British Columbia.

[6]The reimbursement rate is set at 85% of the price of the branded drug when there is one generic, 50% with two generics and 25% when there are three or more generics. For generics introduced before 2014 the provincial reimbursement rates are used. Ontario sets the reimbursement rate at 25% while British Columbia sets it at 20%.

— Australia, the US, England, and Canada have three dominant wholesalers, while New Zealand has just two wholesalers. The pharmacy landscape varies by country. Large retail chains dominate the US, Canadian and English markets.[7] Regulations around pharmacy ownership in Australia and New Zealand make them more difficult to compare.[8]

3 Framework

Our empirical analysis can be understood within the framework of a static entry model (akin to Bresnahan and Reiss (1991) and Scott Morton (1999)), which are the appropriate choice for stable markets for long off-patent molecules. Generic suppliers s enter the foreign location (country/province) f and provide drug product d if the profit of doing so ($\pi_{f,d}$) is greater than the fixed cost of entry F_f. We assume that there is a fixed cost of entry into each foreign location (F_f) that is foreign location specific and independent across foreign locations.[9] A marginal supplier s enters a foreign location$f$ if and only if:

$$\pi_{f,d}(s;S) = [\mu_{f,d}(s;S) - 1] \times c_{f,d} \times q_{f,d}(s;S) > F_f.$$

The profitability ($\pi_{f,d}$) of the marginal s^{th} supplier over the set of S suppliers of entering each market is the product of a foreign location specific mark-up ($\mu_{f,d}$) over marginal cost ($c_{f,d}$), multiplied by the quantity sold ($q_{f,d}$).

We assume that the marginal cost within a market in a foreign location is constant across suppliers ($c_{f,d,s} = c_{f,d}$), as approval requires the same raw materials.

[7]The largest five US pharmacies account for approximately 64% of the market (Drug Channels Institute, 2019), in England they hold 80% (Sukkar, 2016) and in Canada they are 60% (Yeates and Hernandez, 2019).

[8]In Australia no entity can own more than five pharmacies (Hattingh, 2011), but four corporations control 63% of the market through franchising (Medicine.com.au, 2019). In New Zealand, a pharmacy must be owned by a pharmacist. However, 45% of pharmacies have some affiliation with a single corporation (Pharmaceutical Society of New Zealand Incorporated, 2017)

[9]The second part of this assumption is less restrictive than it initially seems. We consider marginal generic entrants - as opposed to the original innovator. Many of the implied fixed costs are country-specific, such as the regulations, lobbying, bilateral payments, and/or campaign contributions. Physical manufacturers are often "contract" manufacturers, which are separate from the official government-approved supplier. Contract manufacturers receive a specification and produce final packaged products for the government-approved supplier and simply have to pass safety related inspection measures and are not responsible for the vast majority of entry costs, which are borne by the government approved supplier (Miller, 2017). Lastly, a survey of foreign factories for a sample of drugs shows that there are a large mass of potential suppliers that do not appear in our sample. See the appendix for further analysis.

Next we consider the price. As described in Section 2, there are many actors involved in setting the price of a product along the supply chain. These actors include wholesalers, PBMs, pharmacies, consumers, insurers and governments. We focus on the retail price of each market (molecule-dose-route) in each foreign location averaged across products ($p_{f,d}$). The retail price p of a product comprises an amount paid by consumers (a copay δ_{copay}) and the amount the government contributes (δ_{gov}); $p = \delta_{gov} + \delta_{copay}$. The retail price $p_{s,f,d}$ of a supplier s, of product d in foreign location f can be represented as a series of mark-ups ($\mu_{s,f,d}$) over the common marginal cost of producing the product:

$$p_{s,f,d} = \mu_{s,f,d}^{pharmacy} \times \mu_{s,f,d}^{PBM} \times \mu_{s,f,d}^{wholesaler} \times \mu_{s,f,d}^{supplier} \times c_{f,d}.$$

We choose to use the entire retail price rather than just the government contribution as the government may subsidize markets for redistribution purposes. Therefore, the entire retail price is the welfare relevant price. We take the average of the retail price of a product across pharmacies because we view changes in the average price best capture what is ultimately paid. Retail prices differ across pharmacies as individual consumers select the pharmacy to fill their prescription. There is generally no restriction on pharmacy choice in the non-US countries, but limited restrictions apply in the US. We then compute the average price of a drug d in foreign location f as the market-share weighted average across suppliers of the drug.

The price we measure is:

$$p_{f,d} = \sum_{s \in S} share\,(s) \times p_{s,f,d}.$$

This market share weighted average allows for differential pricing (and markup) between different suppliers. In some markets, there is substantially different pricing and market shares between the original branded entrant and other generic entrants (Kanavos et al., 2008). We account for this when we consider the bound for a fixed cost to enter a market and gain distribution:

$$\frac{\sum_{s \in S} \mu_{s,f,d} q_{s,f,d} \mathbb{I}_{s \neq Branded}}{\sum_{s \in S} \mathbb{I}_{s \neq Branded}} \geq F_f,$$

where we simply focus on marginal entrants, as opposed to the original branded entrant

(e.g., generic atorvastatin versus Pfizer's Lipitor).

4 Data

We compare prices, competition structure, and market size across countries for off-patent patient administered drugs.[10] This requires data on the prices, quantities of prescriptions, and the number of suppliers of each drug for all five countries. We define a drug market as all products with the same molecule-dose-route.[11] This follows the definition used by the US Food and Drug Administration (FDA) in determining generic entry eligibility. We allow for imperfect substitutability between branded and unbranded generics, which has been shown in the literature to be an important distinction (summarized in Kanavos et al., 2008).

Data on molecule-dose-routes in the US are obtained from the drugs@FDA database. We include molecules administered as "capsule" or "tablet". We only include markets where the original product is off-patent and hence generics can enter (regardless of whether they have). A molecule-dose-route is classified as off-patent if an Abbreviated New Drug Application (ANDA) has been approved or if there are no patents or exclusivities listed in the FDA orange book. As it takes time for the first generic to be reviewed and the first approved generic receives 180 days of exclusivity against additional generic entry, we exclude markets with the first FDA approval within 20 years of the analysis period.[12] The number of suppliers supplying each US market reflects the number of approved ANDAs. Data on drugs for corresponding foreign markets are obtained from the relevant regulatory authorities. We merge each of these data sets together and keep the subset of drugs that are available in both the US and the other country. Further details are provided in Appendix A.

[10] We mix the usage of the term generic and off-patent, even though not all off-patent drugs are generic copies.

[11] For robustness, we also conduct the analysis with markets defined at the molecule level. We also examine the potential role of therapeutic substitutes as defined by the Anatomical Therapeutic Chemical (ATC) codes.

[12] The US Hatch-Waxman Act effectively allows for five years of exclusivity after the patent expiry, allowing for 25 total years of near exclusivity (similar but not identical to patent protection). However, this period starts at discovery, before clinical trials and FDA approval, a process that can take upwards of 10 years. Excluding drugs with an initial approval in the 20 years preceding the analysis period should be sufficient to cover the period during which the original molecule is protected from competition.

The retail price and quantity prescribed in each off-patent market in the US is obtained from the Medicaid State Utilization data, which we aggregate across states. We compute per-unit prices net of dispensing fees and manufacturer rebates. We focus the analysis on Medicaid because it is the only publicly available source of prices that can be adjusted for manufacturer rebates and pharmacy dispensing fees, which is needed in order to make the US data directly comparable with international data.[13] As Medicaid only accounts for about 10% of US prescription drug spending, we include data from Medicare Part D and private insurance (through the National Average Drug Acquisition Cost dataset), as a robustness check. These extensions are described in the appendix.

Data on retail drug prices and ex-manufacturer prices in Australia, Canada (Ontario, British Columbia), England, and New Zealand are obtained from the national health plan administrative statistics. These prices need to made comparable with the US prices. We convert all prices into US dollars using the average annual exchange rate for each calendar year. We then recover the per-unit price of a drug, net of a fixed per-prescription pharmacy dispensing charge. For Australia, we use the price paid by Pharmaceutical Benefits Scheme (PBS) to the pharmacy, available from the Schedule of Benefits for 2009-2017. This price excludes the dispensing fee and the allowed pharmacy mark-up.[14] For Ontario, we use the Ministry of Health and Long-Term Care's drug benefit prices for 2017. This price omits the fixed dispensing fee and variable patient copayment, which can only offset the dispensing fee. Data on British Columbia is obtained from British Columbia PharmaCare for 2014-2017. We

[13]Drug prices in the US are typically difficult to measure. There are many different types of drug prices available, many of which are not true prices but rather list prices and because of rebates paid from suppliers to insurers, which are secret, it is very difficult to obtain true measures of price. However, in the case of Medicaid the rebates are fixed using a published formula, which means we can compute the rebate and adjust the Medicaid prices to account for them. During our study period the rebate is set at 13% of the Average Manufacturer Price (AMP). The AMP is not available for some drugs in the sample because the AMP is not published in cases where there has never been a generic entrant and the only product available is the original innovator product , for those missing data points, we substitute 13% of the final retail Medicare price as an upper bound. We show that excluding these drugs yields broadly similar result in the online appendix.

[14]Patient copays in Australia are variable and are capped at AU$30.70-AU$38.80 during this period. Generic drugs often have patient copays below the cap, as maximum co-pays are capped at the combined cost of the pharmaceutical, dispensing, and preparation fees. Reported prices are inclusive of this variable patient copay.

use the maximum allowable price, the maximum amount the drug benefit will reimburse, net of dispensing fees.[15] Any difference between the retail price and this price is paid by the patient. For New Zealand, we obtain data on retail prices from PHARMAC. Since this price excludes the patient copay, we add it back in. Prices for England are obtained from the NHS England Drug Tariff. These prices are the amount of the NHS subsidy. It does not include professional fees paid to pharmacists for dispensing the products.

Table 1 shows the number of observations for each country and the years included in the analysis. Prices for all non-US markets are net of average fixed per-prescription pharmacy dispensing fees. The key variable of interest is the relative price of each drug in the US compared with the same drug in each of the other countries. The mean and standard deviation of the US price ratio, with respect to each base country are shown in Panel A of Table 1. On average US prices are only slightly higher than foreign prices (zero would mean they were the same).

Panel B of Table 1 highlights the variation in suppliers in the US for our sample. While drugs with just one supplier account for 1% of doses, they make up 10% of off-patent Medicaid spending. Drugs with five or fewer suppliers account 25% of doses, but for 50% of total spending. While the majority of doses sold are in competitive markets, likely priced near marginal cost, many drugs have a limited number of suppliers.

5 Analysis

We compare the retail price of off-patent drugs across the foreign locations and show that *in markets with few domestic suppliers, Medicaid pays substantially higher prices than foreign governments*. We then show evidence that suggests the price differential is due to suppliers, as opposed to pharmacy or wholesaler markups, which dissipate as the number of domestic suppliers increases.

[15] Which are currently capped at C$10.

5.1 Prices are higher in markets with low competition

We compute the relative price differential between the US Medicaid price and a foreign price as:

$$\text{premium}_{fdy} = \frac{\text{price}_{(f=US)dy}}{\text{price}_{fdy}}, \tag{1}$$

in drug d, in year y, and in comparison to foreign location f. The price differential allows for the differencing out of multiplicative market-level fixed effects between country pairs, netting out the common cost of manufacturing. We recover the relationship between the price differential and the number of suppliers participating in the US marketplace with US FDA regulatory approvals to distribute drugs:

$$\ln\left(\text{premium}_{fdy}\right) = \sum \beta_s \mathbb{I}_S\left(S_{f=US,dy}\right) + \delta_{fy} + \epsilon_{fdy}. \tag{2}$$

$\mathbb{I}_S$ is an indicator function for the number of US approved suppliers in year y for drug d: $S_{f=US,dy}$. The β_s are a vector of prices differences, δ_{fy} are year-foreign-location fixed effects, and ϵ_{fdy} represents measurement error.

Figure 1 shows the estimated β_s from Equation 2 of the price differential paid by Medicaid relative to each foreign country by the number of US suppliers in 2017.[16] As the number of suppliers increases, the price differential declines. With a single supplier in the US, the price is at least 400% higher than in comparison foreign locations. The price differential declines as there are more suppliers in the US market. US drugs are cheaper if there are 5 or more US suppliers. This pattern holds across all foreign location comparisons and for all various types of US insurance (see Appendix B for results using data from private insurance and Medicare).

These results are formalized by estimating regressions of the price differential between US Medicaid and another country on the of the number of US suppliers. Yearly fixed effects

[16] 2017 is the only year with data for all comparisons. Pooling data across years, and estimating the coefficients relative to the 7+ category yields a similar pattern. Similar results hold for NADAC and Medicare Part D data. See Appendix B.

capture exchange rate fluctuations.

$$\ln\left(\text{premium}_{fdy}\right) = \beta \ln\left(S_{f=US,dy}\right) + \delta_{fy} + \epsilon_{fdy}. \tag{3}$$

As is standard in demand estimation, we assume prices are more flexible than market entry and have no dynamic effects. If ϵ represents a mean zero shock after supplier entry, we can interpret β as a causal relationship between the number of suppliers and the pricing differences (but not absolute price levels). Panel A Table 2 presents the results. A one percent increase in the number of suppliers in the US is correlated with a decrease in the price differential between US Medicaid and Australia of 1.2%, British Columbia by 1.2%; New Zealand by 0.8%; Ontario by 1.0%, and England by 0.9%.

There are a few clear threats to identification, from both the supply side and the demand side. On the supply side, ϵ may allow for differences in marginal cost between markets. Marginal costs may be systematically related to the number of suppliers. However, we directly control for the marginal cost of production by considering the relative prices between two foreign locations and absorb differences in distribution costs and exchange rates using the foreign-location-year fixed effect δ_{fy}.

On the demand side, there may be differences in substitutability between markets. For example, there may be many cardiovascular over-the-counter alternatives, but very few such anti-epileptic alternatives. However, our relative price differences are robust, controlling for a drug's age, the number of similar drugs, Anatomical Therapeutic Chemical (ATC) code-year controls, on-patent competitors, the number of dosage forms, and the lagged number of suppliers to control for sticky prices. These relationships have been stable since 2010, with limited observable changes in the relationship between suppliers and the price differential.

We now take a look at competition in foreign locations. It is possible that the price differential can be explained by differences in the market size across foreign locations, due to differences in preferences for new versus generic drugs or differences in the prevalence of diseases. We examine this issue by estimating Equation 4, which controls for the number of suppliers in the comparison foreign location. Assuming marginal cost are the same across

foreign locations:

$$\ln\left(\text{premium}_{fdy}\right) = \beta_{US}\ln\left(S_{f=US,dy}\right) + \beta_F \ln\left(S_{fdy}\right) + \delta_{fy} + \epsilon_{fdy}. \tag{4}$$

If the price differential can be explained by the foreign location markets having more suppliers than the US market, then controlling for the number of foreign suppliers should explain the price differential. If not, (and β_F is insignificant) this suggests a larger role for differences in market structure and markup determinations. Panel B in Table 2 shows results with both the number of US and comparison country suppliers. Foreign suppliers are insignificant for three comparisons (Ontario, New Zealand, and England). A change in the number of competitors in a foreign market is not correlated with either higher or lower prices (relative to the US). One possible reason is that governments in foreign countries set strict price controls. This means that regulations may limit producer surplus, irrespective of the number of suppliers. The coefficients are negative for Australia and British Columbia, but have little impact on the estimated impact of the number of US suppliers on the price differential.

5.2 Markups Along the Value Chain

We investigate potential reasons for this price differential. Accurate pricing data at different points along the supply chain is notoriously difficult to obtain. However, we have three prices that can be used provide deeper insight into the mechanism driving the observed price differential. The first is the Average Manufacturer Price (AMP), the average price received by US suppliers: $p_{d,s}^{AMP} = \mu_{d,s}^{supplier} \times c_d$. The second price is the National Average Drug Acquisition Cost (NADAC) , which captures the average price paid by pharmacies: $p_{d,s}^{NADAC} = \mu_{d,s}^{Wholesaler} \times \mu_{d,s}^{Supplier} \times c_d$. The third price is that received by the pharmacy – the Medicaid price before rebates, but including dispensing fees (rebates are paid directly to

Medicaid).[17] We compute the following markups:

$$\mu_{d,s}^{pharmacy} \times \mu_{d,s}^{PBM} = \frac{p_{d,s}^{medicaid}}{p_{d,s}^{NADAC}}$$

$$\mu_{d,s}^{Wholesaler} = \frac{p_{d,s}^{NADAC}}{p_{d,s}^{AMP}}$$

$$\frac{\mu_{d,s}^{supplier}}{\mu_{d,s}^{foreign}} = \frac{p_{d,s}^{AMP}}{p_{d,s}^{foreign}}.$$

We normalize the supplier/manufacturer price using foreign prices to net out manufacturing cost $c_{d,m}$, but introduce foreign markups as the denominator. As AMP prices are only available with more than one manufacturer, we normalize all markups relative to two manufacturers.

Figure 2 shows each of these three relative markups with respect to the average foreign price. Pharmacy and PBM markups are increasing as the number of suppliers increases. This is mechanical, as dispensing fees are rebated as a function of the number of prescriptions, regardless of the price of the underlying pharmaceutical or number of suppliers.[18] Wholesale and pharmaceutical supplier markups are both decreasing in the number of suppliers, with the magnitude more than twice as large the supplier markup. Thus supplier and wholesaler markups are largest in the most concentrated markets. With this we turn to measuring the fixed costs necessary to rationalize concentration and market entry.

6 Bounding the Fixed Cost

The traditional cure for market power is free entry. US markets are highly concentrated suggesting that entry is costly. What costs do such new entrants face, if they already have manufacturing abilities?[19] As the conceptual framework allows us to understand relative

[17] We use the price inclusive of the dispensing fees here to understand markups for pharmacies and PBMs.

[18] The relative Medicaid to NADAC price is often denoted as "the spread" captured by middlemen. An alternative explanation is that PBMs and pharmacies are able to capture greater profit when there is more upstream competition. However, this has a limited effect as the overall markup is relatively low when there are many US suppliers (as shown in Figure 1).

[19] There is a large number of Chinese, Indian, and other Asian manufacturers. On TradeIndia.com and Alibaba, we collect the number of possible suppliers. The number of suppliers dwarfs the actual number of entrants to all of our markets. See Appendix D.

markups, we can measure relative fixed costs. If all non-branded generic competitors have common costs, the lower bound for relative fixed entry costs between markets can be rewritten as:[20]

$$F_{US}/F_{foreign} = \frac{q_{US}^{generic} \times p_{US}^{generic}}{S_{US}^{generic}} / \frac{q_{foreign}^{generic} \times p_{foreign}^{generic}}{S_{foreign}^{generic}} \tag{5}$$

As our data is limited, we adjust the US quantity by the aggregate market size of the Medicaid market (11%). We only use Australia as a comparison. New Zealand quantity data is publicly unavailable and for England, British Columbia, and Ontario drug approvals may occur at the European Union or Canadian levels. We also aggregate all dosages, as US FDA applications allow for a single generic (ANDA) approval application. Figure 3 shows that median US fixed costs are least four times larger than Australian fixed costs, though individual markets exhibit a log-normal dispersion.[21]

Our fixed cost estimates recover the effective market value of entry. This incorporates a range of factors including regulatory costs, capacity constraints, and access to the distribution network. In our framework, it is not possible to fully decompose the fixed cost. Understanding what drives it is an important area for future research, particular in terms of policy: is this a regulatory barrier that can be addressed directly by the FDA or is this a result of the complex downstream bargaining between PBMs, suppliers, and pharmacies? Our hypothesis is the latter, primarily because the regulatory process is similar across countries but the downstream pricing mechanism is much more complex in the US compared with all the other comparison countries. We explore this further in Appendix E.3 by examining the drivers of the numerator and denominator of Equation 5. The results show that for non-US markets, prices are invariant to both market size and entry. In the US, prices are inversely related to both market size and entry. This suggests price controls play a role in lowering the relative implied entry costs in the comparison countries. However, we are unable to rule

[20] Relative fixed costs are: $\frac{\pi_1}{\pi_2} = \frac{q_1\left(\frac{p_1}{p_2}\mu_2 - 1\right)/S_1}{q_2(\mu_2-1)/S_2}$. However we only know relative markups; so we take the limit μ_2 to ∞. While this may seem extreme, a large Australian markup of 1.5, implies that US fixed costs are eight times higher.

[21] We show in Appendix E.3 that this is not driven mechanically by the US having larger markets but not a comparably larger numbers of entrants.

out other factors and there is a potential role for more than one mechanism.

7 Conclusion

Our analysis indicates the US Medicaid pays more for off-patent drugs in small markets than other government insurance programs. Current US policy focuses on encouraging more generic entry. For example, the US FDA 2019 Drug Competition Action Plan proposes that the FDA work with its international counterparts to harmonize the generic approval process (Gottlieb, 2018). This would allow suppliers to gain approval to sell in multiple countries essentially using one application process, thereby reducing a fixed cost of entry. Such policies are also advocated by the European Union in preliminary negotiations for the Transatlantic Trade and Investment Partnership (TTIP), seeking the harmonization of procedures to "entail significant cost savings" (European Commission, 2014). While this is a sensible policy direction, our results indicates that facilitating competition may not be enough to lower generic drug prices to marginal cost. Perhaps, greater attention should be given to price interventions.

Table 1: Summary Statistics

Panel A: Cross-Country Data Comparison with US Medicaid

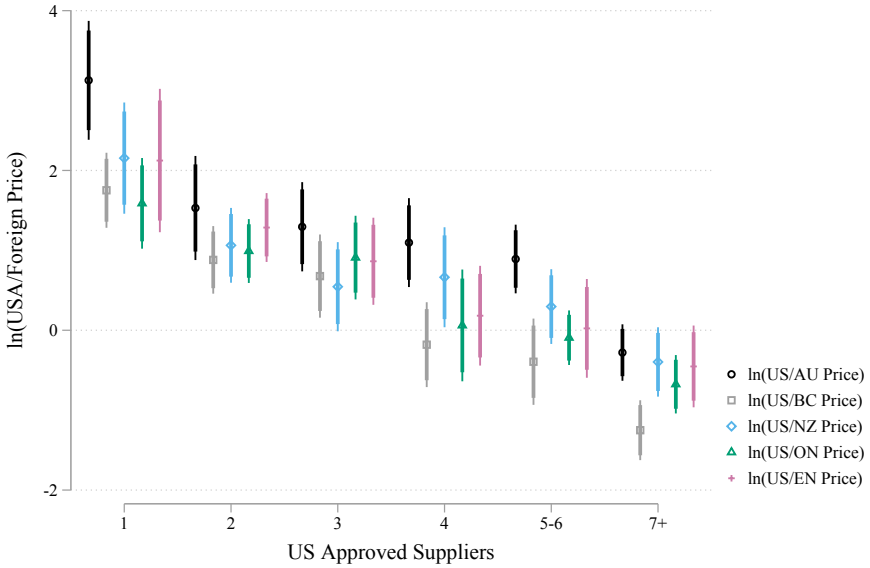
Comparison	Obs	First Year	Last Year	$\log(P_{US}/P_{Dest})$ Mean	$\log(P_{US}/P_{Dest})$ Std. dev.	Mean First US Approval	Mean # US Sellers
Australia (AU)	1,694	2009	2017	0.55	1.67	1980	4.5
British Columbia (BC)	926	2015	2017	0.23	1.81	1983	4.4
New Zealand (NZ)	1,599	2009	2017	0.35	1.52	1981	4.4
Ontario (ON)	371	2017	2017	0.27	1.64	1984	5.0
England (EN)	1,752	2010	2017	0.22	1.83	1981	4.3

Panel B: 2017 US Medicaid Spending

US Approved Suppliers	Doses Sold	Share	Value ($)	Share
1 Supplier	274,956,936	1.6%	925,299,971	11.6%
2 Suppliers	289,929,208	1.7%	325,655,963	4.1%
3 Suppliers	563,073,887	3.4%	1,029,792,909	12.9%
4 Suppliers	1,213,034,299	7.2%	1,144,322,237	14.4%
5 Suppliers	2,015,934,718	12.0%	901,022,647	11.3%
6-10 Suppliers	8,644,976,343	51.6%	2,583,099,832	32.5%
11+ Suppliers	3,761,466,615	22.4%	1,043,415,082	13.1%
Total	16,763,372,006		7,952,608,641	

Notes: Based on authors' calculations of public expenditure, price, and seller data. Prices reflect rebates and accounting for dispensing fees. The AMP data do not provide rebate data where there is only one US supplier, we conservatively use a rebate off 13% off the Medicaid list price as a lower bound on the US markup. See text for further details.

Figure 1: Role of Competition - Price Difference and Competition



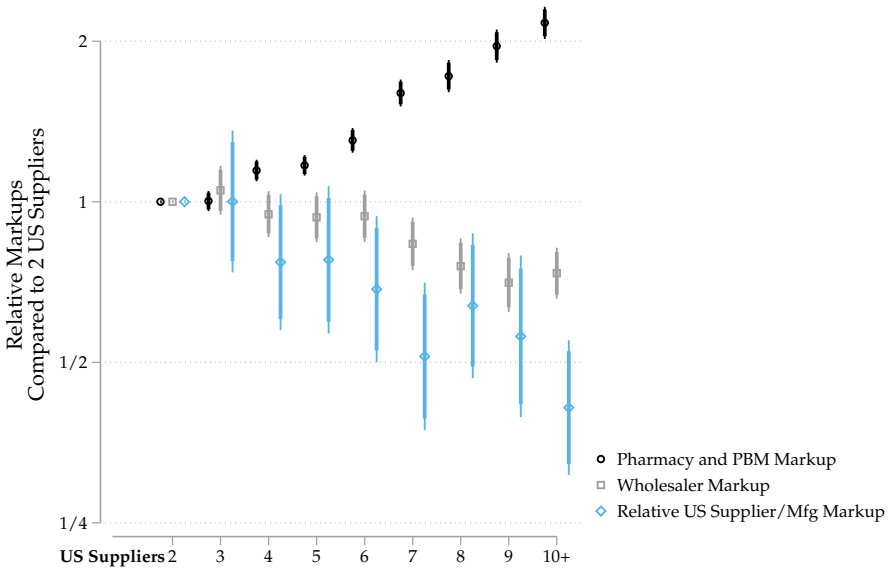
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Each comparison is estimated separately for 2017. 95% and 90% confidence intervals displayed. Results generated by pooling all years and including year fixed effects with the 7+ supplier category omitted produce similar results. The AMP data do not provide rebate data where there is only one US supplier, we conservatively use a rebate off 13% off the Medicaid list price as a lower bound on the US markup. If Medicare pays more than wholesalers, this will be a lower bound on US markups. See text for data sources and details.

Table 2: Relationship between Price Differentials and Number of US Suppliers

Panel A: US Suppliers Only					
	(1)	(2)	(3)	(4)	(5)
	$ln(p_{US}/p_{AU})$	$ln(p_{US}/p_{BC})$	$ln(p_{US}/p_{NZ})$	$ln(p_{US}/p_{ON})$	$ln(p_{US}/p_{EN})$
ln(US Suppliers)	-1.171	-1.208	-0.778	-1.019	-0.925
	(0.105)	(0.0878)	(0.0920)	(0.101)	(0.118)
Constant	1.985	1.680	1.303	1.670	1.355
	(0.157)	(0.130)	(0.150)	(0.156)	(0.186)
Adj. R-Square	0.325	0.268	0.170	0.199	0.136
Observations	1694	926	1599	371	1752
Fixed Effects	Year	Year	Year	Year	Year
Panel B: US and Foreign Suppliers					
	(1)	(2)	(3)	(4)	(5)
	$ln(p_{US}/p_{AU})$	$ln(p_{US}/p_{BC})$	$ln(p_{US}/p_{NZ})$	$ln(p_{US}/p_{ON})$	$ln(p_{US}/p_{EN})$
ln(US Suppliers)	-0.958	-1.059	-0.773	-0.983	-1.233
	(0.120)	(0.104)	(0.109)	(0.124)	(0.280)
ln(Foreign Suppliers)	-0.348	-0.300	0.00367	-0.0791	0.179
	(0.0841)	(0.0904)	(0.104)	(0.103)	(0.172)
Constant	1.992	1.917	1.281	1.709	1.819
	(0.157)	(0.163)	(0.155)	(0.168)	(0.355)
Adj. R-Square	0.348	0.288	0.161	0.207	0.127
Observations	1694	824	1537	362	214
Fixed Effects	Year	Year	Year	Year	Year

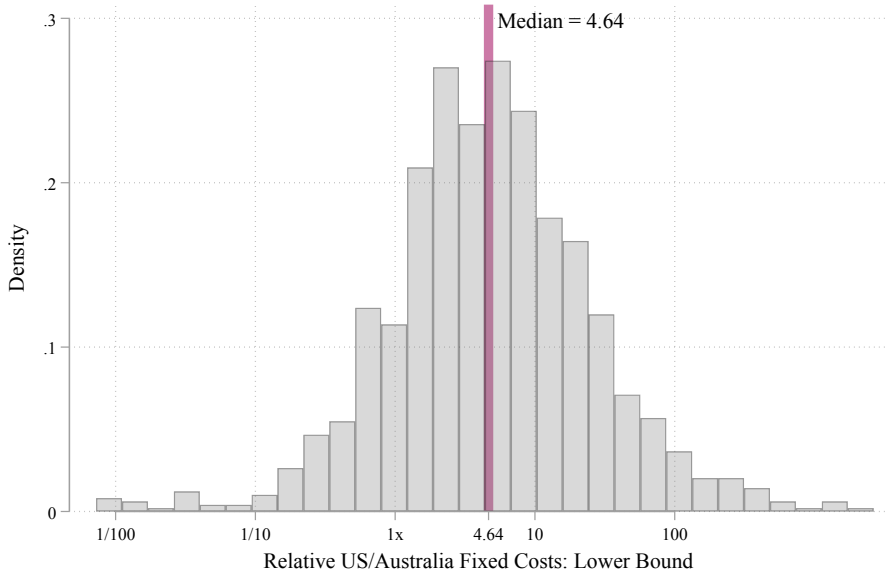
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route). Regression specification from Equation 4 with standard errors clustered at the molecule level. See text for data sources and details. The AMP data do not provide rebate data where there is only one US supplier, we conservatively use a rebate off 13% off the Medicaid list price as a lower bound on the US markup. Data for Panel B is more limited than Panel A, due to missing data for the number of suppliers for some foreign markets.

Figure 2: Value Chain Markups Breakdowns



Notes: All markups relative to those for two or more suppliers. Pharmacy and PBM markups computed using relative absolute Medicaid and NADAC prices. Wholesaler markups computed using NADAC and AMP prices. Relative US Supplier markups computed using AMP and an unweighted average of foreign prices. 95% and 90% confidence intervals displayed. See text for data sources and details.

Figure 3: Relative Entry Cost Estimates



Notes: Relative entry cost estimates computed under the assumption of minimal marginal manufacturing costs in all foreign locations. Computed as the relative ratio of US and Australian revenues for generic (unbranded) suppliers. See text for data sources and details.

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Online Appendix

A Data Construction

A.1 United States Data

Each market contains a set of similar pharmaceuticals with an associated NDC code. The manufacturer can be identified from the first 5 digits of the NDC code. A list of approved molecules are obtained from the drugs@FDA database. We include molecules for which the form of administration is listed as "capsule" or "tablet". The application numbers are matched with the 2009 FDA Orange Book. The orange book lists all unexpired patents and exclusivities. A molecule is classified as off-patent if there are no exclusivities listed in the Orange Book or if there is ANDA approval. There are several potential sources of price data. For the primary analysis we use data from Medicaid, however, our results are robust to data from Medicare Part D and private insurance data. The data on reimbursement and quantities comes from the State Utilization Data.

A.1.1 FDA Approvals and Drug Codes

Historical National Drug Code (NDC) and approval data is acquired from the National Bureau of Economic Research (NBER). Each drug for sale package includes data on the manufacturer, active ingredients, dosage, form, and packaging details. This data additionally includes details regarding the firm that applied for approval, the date of approval, and the current status of the drug. We stack this data across time to merge to the Medicare, Medicaid, and NADAC data. We retain data on all approved drugs that appear in either tablet or capsule form. We additionally make use of the NBER's NDC crosswalk that concords two different version of drug codes. An NDC is a composite of three variables: the drug code, the manufacturer, and the package's details. One version reports all three variables separately and another concatenates the variables in a semi-arbitrary fashion. We convert all data to the former form.

A.1.2 State Medicaid Data

State-level Medicaid data is sourced from the Centers for Medicaid and Medicare Services (CMS) and is published at the monthly level.[22] This dataset provides the total amount paid out by Medicaid for each 11-digit NDC, as well as the total number of units dispensed through Medicaid FFS. To compute the price we divide the total payments by the units dispensed, this provides an average price actually paid for each product (in contrast reported prices. We collapse the data by year, molecule, dose and form, harmonizing names across years.
We make several adjustments to the price to ensure the Medicaid data is comparable with the international data. Firstly, the Medicaid payment data is net of discounts (notably 340B)

[22] We leave the separate state-by-state analysis to further work and consolidate the data to the national level.

with the exception of the statutory rebate, which is a payment made from manufacturers back to state Medicaid programs. During our time period, the statutory reimbursement rate is 13% of the average manufacturers price (AMP) for multiple source drugs. For single-source, non-innovator drugs, the statutory reimbursement rate is calculated with a similar formula based on the average manufacturer price. We adjust our compute price for the statutory rebate using publicly available data on the AMP.[23] The AMP is not reported in situations where there is just one innovator drug and no generic products. In these cases we compute the rebate using 13% of the final retail Medicare price, which is likely to overestimate the rebate and hence lower our price, working against our findings.

Second, the CMS reports that "This amount represents both federal and state reimbursement and is inclusive of dispensing fees." As all other countries separately report dispensing fees, we further account for this. In 2007, the median dispensing fee was approximately $5 and in 2017 the median dispensing fee was approximately $10. We code this in.

Finally, as part of the Affordable Care Act (ACA), US states instituted Federal Upper Limits (FUL), the maximum allowable price. We consider any prices above these FUL in ACA years to be computed in error and thus exclude them from our analysis.

A.1.3 Federal Medicare Part D Data

Medicare Part D plans are regulated prescription drug plans that cover 75% of the United States Medicare population (Cubanski et al., 2018). We use national-level aggregates from the Centers for Medicaid and Medicare Services (CMS) that are constructed from the complete universe of Part D patients. CMS maintains a Chronic Condition Data Warehouse (CCW), "a database with 100% of Medicare enrollment and final-action Part D prescription drug event (PDE) data." Publicly available information does not report on individual dose sizes and forms. Rather, this data is reported at only the molecule level. We aggregate this data by year in order to perform analysis. In addition, there are two further caveats: the molecule level data is inclusive of manufacturer rebates and dispensing fees. This makes it harder to align with foreign data, leaving this as a robustness check with our mainline results.

A.1.4 National Average Drug Acquisition Cost (NADAC) Data

For a subset of drugs, we additionally append price data with National Average Drug Acquisition Cost (NADAC) data. This data is collected by the CMS to help aid states in setting Medicaid reimbursement costs. The NADAC reflects the average drug acquisition costs for retail, consumer-facing pharmacies from a nationally representative sample. While sampling variation is not revealed by the CMS, they reveal that the NADAC sampling average margin of error is below 2.5%.

This data is collected by a federal subcontractor and reflects the price paid by the retailer to the pharmaceutical distributor. This data does not include the dispensing fee, any upstream rebates, nor the retailer markup. It includes all transactions paid using cash, private insurance (including Medicare Part D plans), and public insurance.[24] Data is released at

[23] Source: XXXXXX, last accessed June 30 2021.

[24] Patients on 340b plans are excluded.

the National Drug Code level. We aggregate this data to a year-molecule-dose-form using national Medicare market shares for all prescription pharmaceuticals that appear in either a tablet or capsule form.

A.2 Canadian Data

A.2.1 Canadian Manufactures Data

Data on approved Canadian pharmaceutical providers is obtained from Health Canada, which maintains their Drug Product Database (DPD). This database includes all "human, veterinary, disinfectant, and radiopharmaceutical products approved for use by Health Canada". The database includes all approved, marketed, cancelled, and dormant products. We consider all pharmaceutical products that are produced in a tablet or capsule form. Then we consider the start year of Canadian availability, i.e. the year the drug was first approved or marketed. The last day of Canadian availability is the first year when a drug is flagged as "cancelled" or made "dormant". Since active ingredients in the DPD have slight variations with corresponding US and provincial drug names, we perform manual cleaning to align drug names. We create a manufacturing database with the (1) list of active ingredients, (2) year, and (3) number of approved companies.

A.2.2 British Columbia Price Data

Data on British Columbia pharmaceutical prices is obtained from PharmaCare, which has eight plans that cover all patients under the Medical Services Plan of B.C. (MSP), the statewide sing-payer health insurance plan for all province residents that are either Canadian citizens or legal permanent residents. This plan is targeted to achieve universal health care. PharmaCare covers both pharmacy dispensing fees as well the maximum price it will recognize for each drug in the British Columbia PharmaCare formulary. The PharmaCare plan operates on a income-based subsidy scheme, where lower income participants are reimbursed for a proportion of all pharmaceutical costs. The provincial government maintains an online database for the last three years of prices, including data on discontinued drugs. We consider only the unsubsidized price, which is the maximum that can be charged. Any subsidy simply offsets this cost.[25]

For drugs in this formulary, we consider all doses markets as either a tablet or capsule. For each active ingredient we extract out the dosage of each active ingredient. As active ingredients in PharmaCare have slight variations with corresponding US and other provincial drug names, we perform manual cleaning to align drug names. We create a provincial database with the (1) list of active ingredients, (2) form, (3) dosages, (4) year, and (5) average price. We additionally create a second database that averages drug prices across forms and dosages for comparability to US Medicare Part D data. Data is converted from Canadian Dollars to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

[25] As with all non-US sources, the final dispensing fees are not included.

A.2.3 Ontario Price Data

Data on Ontario pharmaceutical prices is obtained from the six main Ontario Public Drug Programs that cover 43% of all provincial spending on prescription drugs. This plan has coverage primarily targeted at the poor, disabled, and elderly. This is roughly comparable to the population coved by the US Medicaid and Medicare programs. These plans cover the cost of drugs in monthly published formularies.

We use the 42nd Edition edition formulary for 2017, considering all drugs classified as either a tablet or capsule. We then extract out both the active ingredients and respective dosages. As active ingredients in Ontario's Public Drug Formulary have slight variations with corresponding US and other provincial drug names, we perform manual cleaning to align drug names. We create a provincial database with the (1) list of active ingredients, (2) form, (3) dosages, (4) year, and (5) average price. We additionally create a second database that averages drug prices across forms and dosages for comparability to US Medicare Part D data. Data is converted from Canadian Dollars to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

A.3 Australian Data

A.3.1 Australian Price and Manufacturer Data

Australian data comes from the Australian Government's Department of Health, which runs the national and universal Pharmaceutical Benefits Scheme (PBS). It maintains a monthly database of drug prices both inclusive and exclusive of the government subsidy. We take this data for January of each year and concord molecule names, routes, and dosages across time. These prices include both the price to the manufacturer and the price to the pharmacy.[26] In contrast to databases maintained by some other nations, this data also includes names on all of the approved manufacturers.

For drugs in this formulary, we consider all doses markets classified as either a tablet or capsule. We then extract out the dosage of each active ingredient. As active ingredients in the PBS have slight variations with corresponding US drug names, we perform manual cleaning to align drug names. We create a database with the (1) list of active ingredients, (2) form, (3) dosages, (4) year, (5) average price across packages. We additionally create a second database that averages drug prices across forms and dosages for comparability to US Medicare Part D data. Data is converted from Australian Dollars to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

A.3.2 Australian Prescribed Doses Data

Until 2015, the Drug Utilisation Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee published an annual report on all prescription drugs by dose, form and molecule. This annual database, the Australian Statistics on Medicines (ASM), is sourced from all the underlying reimbursed dosages from the PBS. This includes both the number

[26] As with all non-US sources, the final dispensing fees are not included.

of prescriptions written and the total expenditure at a molecule, dose, and route level. The ASM data is currently available through 2015. For data on 2016 and 2017, we turn to a slightly different database, the Section 85 PBS, RPBS Section 85 Date-of-Processing and Date-of-Supply data. This data is updated monthly and includes the number of prescriptions written and the total expenditure at a molecule, dose, and route level.

A.4 United Kingdom

A.4.1 Manufacturer Data

We obtain manufacturer data for the entirety of the United Kingdom from the electronic Medicines Compendium (eMC). This resource is run by the non-profit Datapharm, which coordinates data between the UK Medicines and Healthcare products Regulatory Agency (MHRA) or the European Medicines Agency (EMA), and drug companies. Since this data is not available for bulk download, we web scraped the website in 2017 for data on nearly 2,000 active molecules available for sale. We create a database that includes all products that are available in either tablet of capsule form. As we do not have time variation, we use this database for all years of United Kingdom Data.

A.4.2 National Health Service

English National Health Service price data is not directly available online from NHS Business Services Authority (NHSBSA). We repurpose data acquired from a freedom of information request from the Centre for Evidence-Based Medicine (EBM Datalab) within the Nuffield Department of Primary Care Health Sciences at University of Oxford. EBM Datalab cleaned the messy and inconsistent data into a usable format. As active ingredients in the NHS data have slight variations with corresponding US and other provincial drug names, we perform manual cleaning to align drug names. We collapse the data down to year-molecule-dose-form with average prices.[27] We create a similar, second database with data collapsed to the year-molecule form. Data is converted from British Pounds to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

A.4.3 UK Prescribed Doses Data

While the formulary data from the UK does not include the number of prescribed doses, a separate database is maintained by the NHS Business Services Authority for England. This data is classified as the Prescription Cost Analysis (PCA) data and collected monthly. We collect all data and collapse by year to get the total number of prescribed doses by "Pharmacy & Appliance Contractor", which refer to local pharmacies. Data is converted from British Pounds to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

[27] As with all non-US sources, the final dispensing fees are not included.

A.5 New Zealand

A.5.1 Manufacturers

New Zealand manufacturer data for 2006-2018 is obtained from Medicines and Medical Devices Safety Authority, which operates under the auspices of the Ministry of Health. From their online product search, we obtain a list of all pharmaceutical products, with data on the active ingredient, manufacturer, status, approval date, and notification date (for drugs with lapsed or not available approvals). We use a web-scraping program to download the relevant data. We first download a list of all drugs by their first letter and then iterate through all the listed molecules.

A.5.2 Prices

Prices for consumers in New Zealand are obtained from the Pharmaceutical Management Agency, a government agency referred to as Pharmac. It maintains a monthly database of drug prices both inclusive and exclusive of the government subsidy. We take this data for January of each year and concord molecule names, routes, and dosages across time. In New Zealand, consumers are also required to pay a $5 per prescription co-pay. We add this price back into the cost of the drug.[28][29]

For drugs in this formulary, we consider all doses sold as either a tablet or capsule. We then extract out the dosage of each active ingredient. As active ingredients in Pharmac have slight variations with corresponding US drug names, we perform manual cleaning to align drug names. We create a database with the (1) list of active ingredients, (2) form, (3) dosages, (4) year, and (5) average price across packages. We create a second database that averages drug prices across forms and dosages for comparability to US Medicare Part D data. Data is converted from New Zealand Dollars to United States Dollars using exchange rate data from the Board of Governors of the Federal Reserve System access through the FRED database.

A.6 Pharmaceutical Tariffs

One possible source of pricing difference would be differential tariff regimes. In our sample tariffs are zero or negligible. As of 2017, Australia, Canada, the European Union, New Zealand, and the United States all apply zero or near zero tariff rates for all pharmaceutical imports. In particular the European Union does not apply any tariffs whatsoever on all pharmaceutical supplies. Canada, New Zealand, and the United States apply small tariffs on surgical and medical devices, which are not included in our sample. Australia places a 2.5% tariff on all immunological products. These products are primarily vaccines that are largely injected, which we do not include in our study. (UNCTAD, 2018; WTO, 2018)

[28] This fee is subsidized by the government for special categorizes of patients, such as those under the age of 13, and those with over 20 prescriptions.

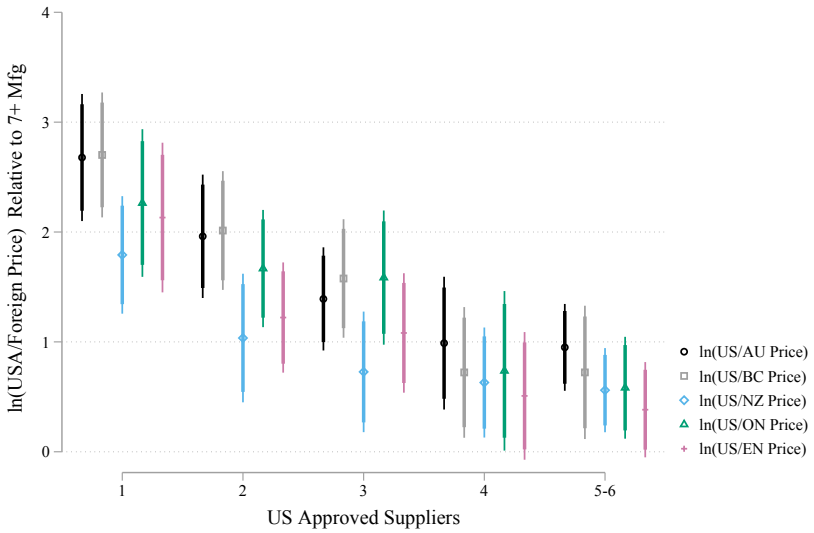
[29] As with all non-US sources, the final dispensing fees are not included.

Table A1: Summary of Data Sources

Data Type	**Data Type**	**Observation Level**
US FDA Manufacturer Data (via National Bureau of Economic Research)	Manufacturers	Molecule-Dose-Form and Molecule
US Medicaid Data (Centers for Medicaid and Medicare Services)	Prices, Quantities	Molecule-Dose-Form and Molecule
US Medicare Part D (Centers for Medicaid and Medicare Services)	Prices, Quantities	Molecule
US National Average Drug Acquisition Cost (NADAC) Data	Prices	Molecule-Dose-Form and Molecule
British Columbia PharmaCare formulary	Prices	Molecule-Dose-Form and Molecule
Ontario Public Drug Programs	Prices	Molecule-Dose-Form and Molecule
Health Canada Drug Product Database (DPD)	Manufacturers	Molecule-Dose-Form and Molecule
UK National Health Service (England) - Centre for Evidence-Based Medicine Datalab (via Oxford)	Prices	Molecule-Dose-Form and Molecule
UK National Health Service (England) - Prescription Cost Analysis	Prices, Quantities	Molecule-Dose-Form and Molecule
UK Datapharm	Manufacturers	Molecule-Dose-Form and Molecule
Australia Pharmaceutical Benefits Scheme	Prices, Manufacturers	Molecule-Dose-Form and Molecule
Australia Australian Statistics on Medicines/Section 85	Quantity	Molecule-Dose-Form and Molecule
New Zealand Pharmac	Prices	Molecule-Dose-Form and Molecule
New Zealand Medicines and Medical Devices Safety Authority	Manufacturers	Molecule
US Federal Reserve	Exchange Rates	

Notes: See text for full details.

Figure A1: Price Difference and competition with all pooled data



Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

B Alternative Specifications

Replication with Pooled Data Figure A1 replicates 1, using all the data in the sample and normalizing against markets with 7+ suppliers.

Pooled Replication without Manufacturer Rebates or Dispensing Fees Figure A2 replicates A1, without normalizing for rebates or dispensing fees.

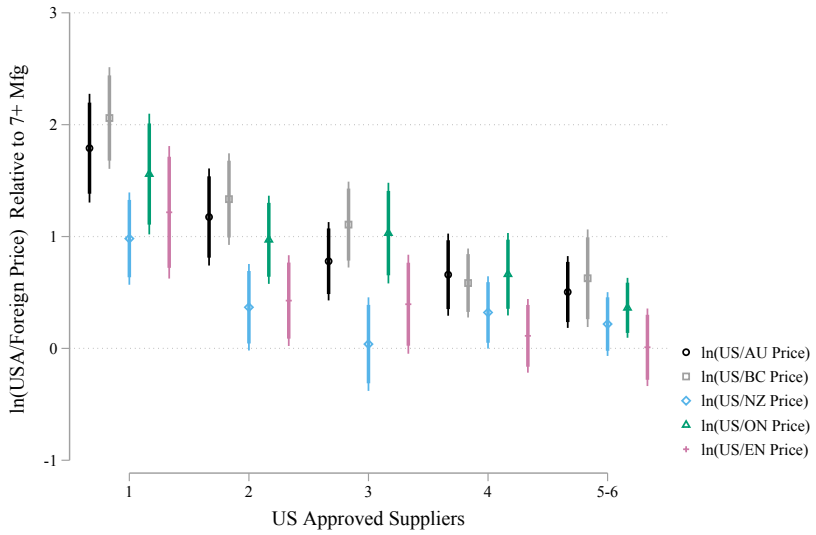
Pooled Replication with Only Generic Data Figure A3 replicates A1, dropping all markets with suppliers that also control the original branded entrant.

Pooled Replication with Medicare Part D Data Figure A4 replicates A1, using Medicare Part D data at the molecule level (data is unavailable at the route-dose level).

Pooled Replication with NADAC Data Figure A5 replicates A1, using US NADAC data reflects the overall US market, minus retail and PBM markups.

Pooled Replication with ATC 3-digit-year Fixed Effects Figure A6 replicates A1, controlling for ATC 3-digit-year fixed effects to control for changes in market definitions.

Figure A2: Price Differences and competition without manufacturer rebates or dispensing fee adjustments



Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Pooled Replication Controlling for On-Patent alternatives Figure A7 replicates A1, with fixed effects for the number of on-patent drugs with a ATC 3-digit group to control for substitution patterns to newer drugs.

Pooled Replication Controlling for On-Patent alternatives Figure A8 replicates A1, with fixed effects for the the number of alternative dosages and routes.

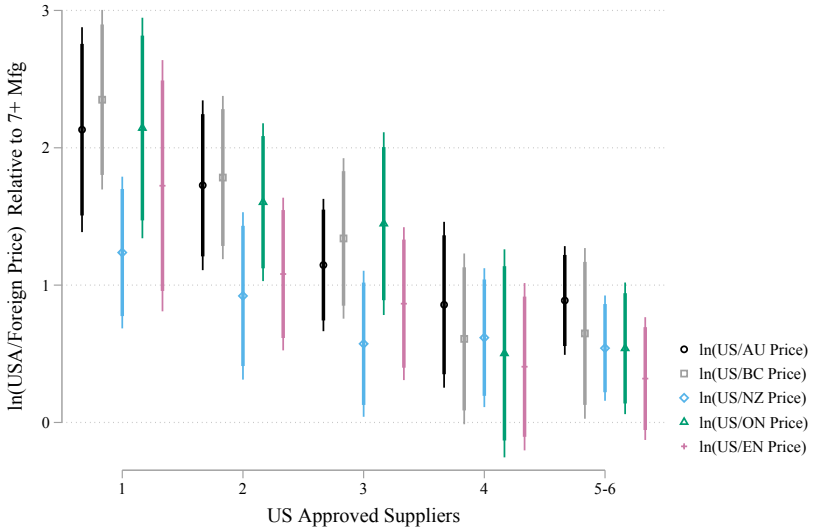
Pooled Replication Controlling for Age Figure A9 replicates A1, with fixed effects for the number of years since the initial FDA approval of the branded variant.

Pooled Replication Used Lagged Number of Manufacturers Figure A9 replicates A1, but uses the lagged number of FDA approved suppliers that currently participate in the market to account for potential anticipation effects.

Non-parametric regression results Our main result (Figure 1) is estimated using Equation 2 using a single year of data (2017). Table A2 the non-parametric analog of the results show in Table 2 (pooling all years of data and including year fixed effects).

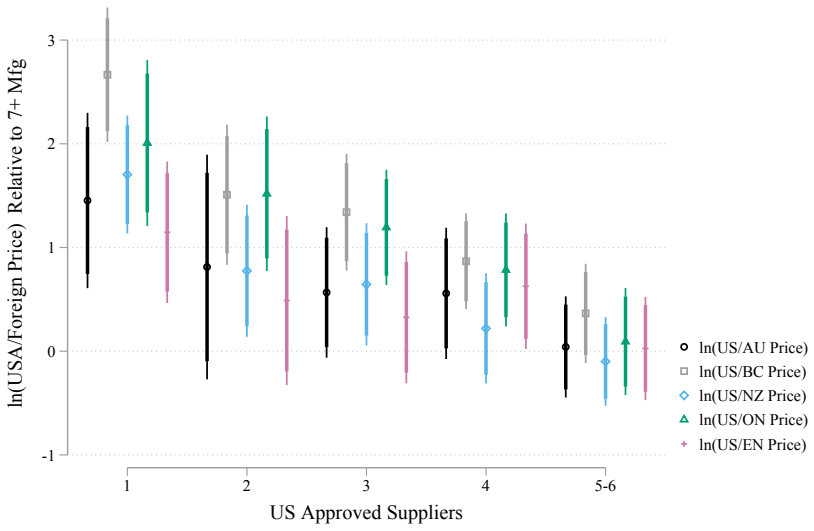
Markups accounting for Dispensing Fees Figure A11 replicates the Pharmacy/PBM markups with and without dispensing fees included.

Figure A3: Price differences and competition for molecules without branded competition



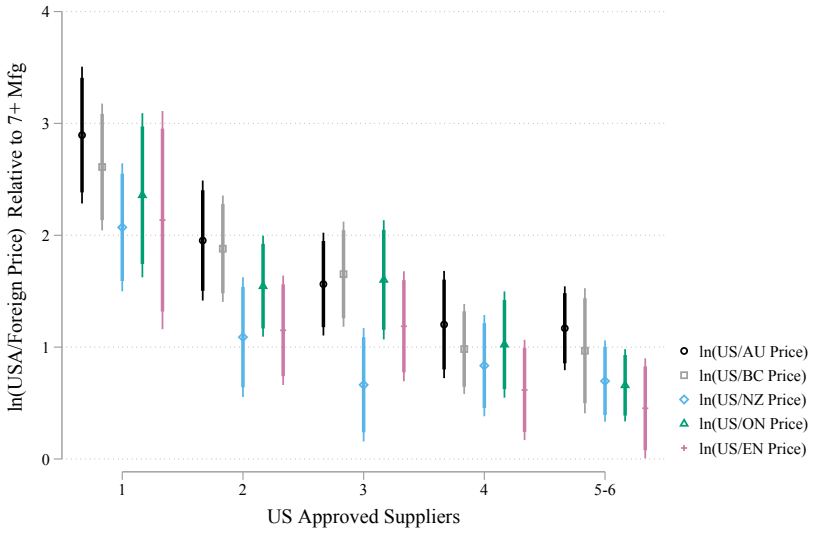
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier.

Figure A4: Price differences and competition with Medicare Part D data (at the molecule level)



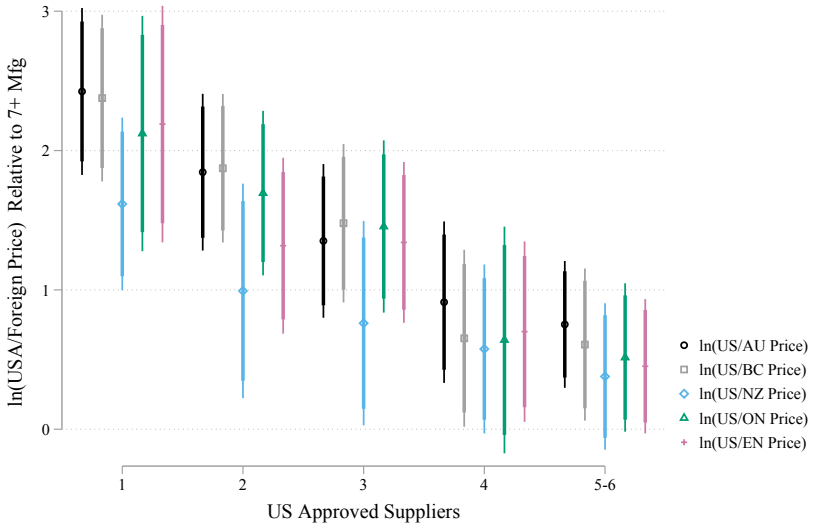
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A5: Price differences and competition with NADAC Data



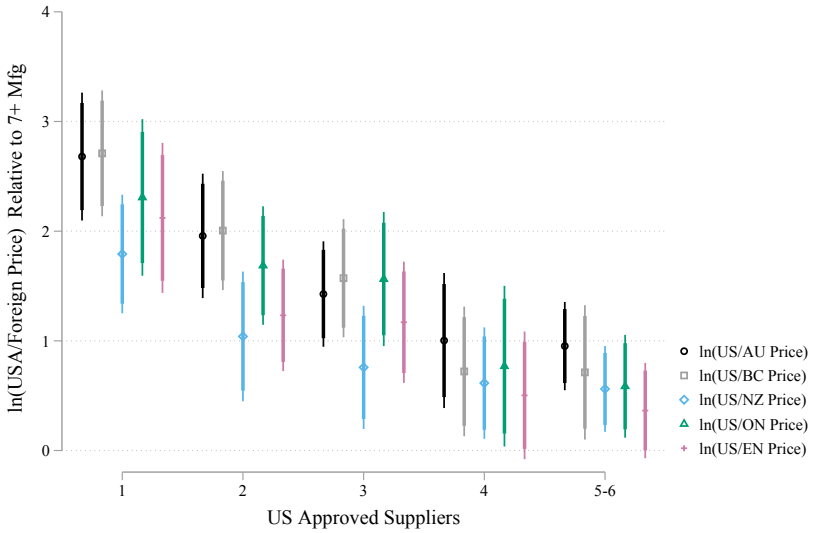
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A6: Price Differences and competition with ATC 3-digit fixed effects



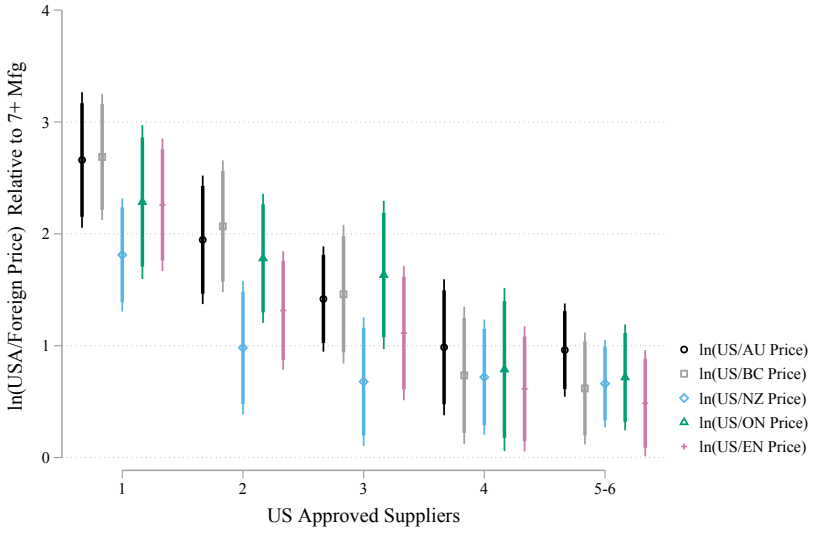
Notes: Average price difference between the two countries taken across drugs (molecule-dose) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A7: Price Differences and competition with controls for number of on-patent drugs within the ATC 3-digit category



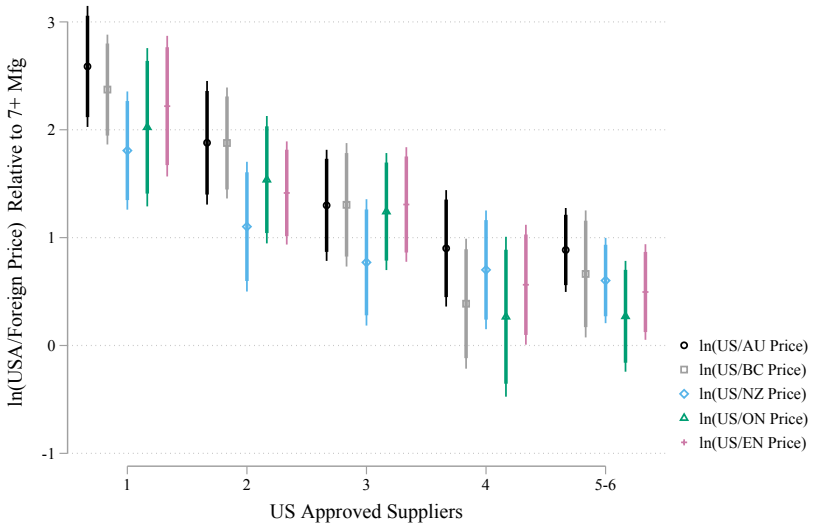
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A8: Price differences and competition with controls for number of formulations (dosage types)



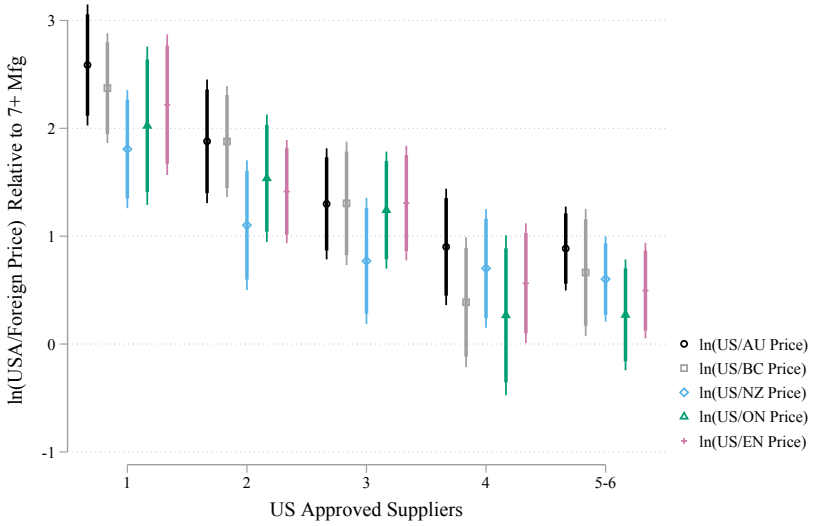
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A9: Price differences and competition with controls the age of drug



Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Figure A10: Price differences and competition with the lagged number of US approved suppliers



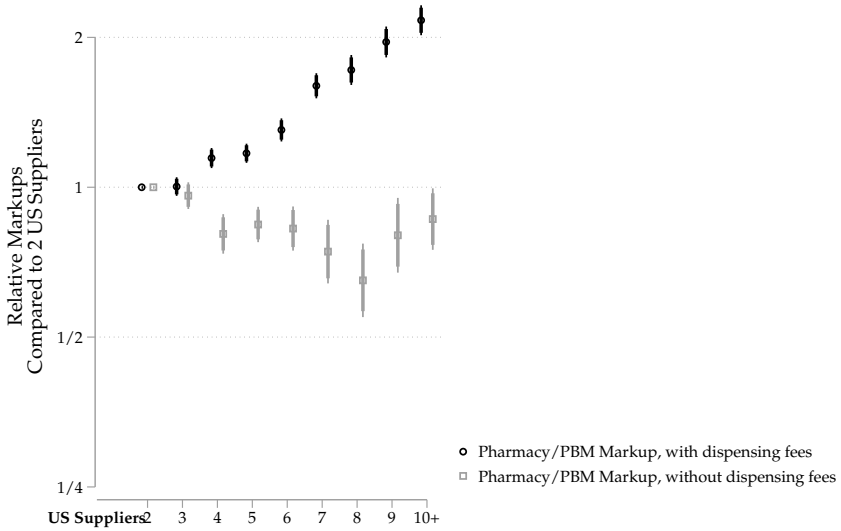
Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) compared with the number of FDA approved competitors of the US. Regression specification from Equation 2 with standard errors clustered at the molecule level. Results generated by pooling all years and including year fixed effects with the 7+ supplier. 95% and 90% confidence intervals displayed.

Table A2: Relationship between Price Differentials and the Number of US Suppliers

	(1) $ln(p_{US}/p_{AU})$	(2) $ln(p_{US}/p_{BC})$	(3) $ln(p_{US}/p_{NZ})$	(4) $ln(p_{US}/p_{ON})$	(5) $ln(p_{US}/p_{EN})$
US Suppliers=1	0	0	0	0	0
	(.)	(.)	(.)	(.)	(.)
US Suppliers=2	-0.716	-0.687	-0.754	-0.596	-0.910
	(0.219)	(0.231)	(0.246)	(0.278)	(0.286)
US Suppliers=3	-1.288	-1.123	-1.066	-0.679	-1.050
	(0.231)	(0.237)	(0.264)	(0.294)	(0.323)
US Suppliers=4	-1.691	-1.980	-1.161	-1.528	-1.623
	(0.268)	(0.259)	(0.239)	(0.367)	(0.315)
US Suppliers=5	-1.628	-1.562	-1.129	-1.555	-1.619
	(0.236)	(0.240)	(0.237)	(0.308)	(0.320)
US Suppliers=6	-1.841	-2.545	-1.363	-1.821	-1.875
	(0.246)	(0.277)	(0.280)	(0.293)	(0.345)
US Suppliers=7	-2.269	-2.771	-1.255	-2.216	-2.338
	(0.295)	(0.304)	(0.280)	(0.384)	(0.339)
US Suppliers=8	-2.558	-2.776	-1.815	-2.446	-2.417
	(0.278)	(0.262)	(0.266)	(0.340)	(0.385)
US Suppliers=9	-2.931	-2.962	-1.766	-3.095	-1.939
	(0.305)	(0.433)	(0.275)	(0.680)	(0.343)
US Suppliers=10	-3.234	-2.861	-1.908	-1.983	-1.852
	(0.298)	(0.279)	(0.293)	(0.324)	(0.367)
US Suppliers=11	-3.168	-2.768	-2.389	-2.374	-2.053
	(0.382)	(0.251)	(0.338)	(0.314)	(0.366)
US Suppliers=12	-3.235	-2.496	-2.617	-1.918	-1.616
	(0.330)	(0.449)	(0.274)	(0.348)	(0.400)
US Suppliers=13	-2.742	-2.621	-2.112	-2.458	-1.848
	(0.499)	(0.386)	(0.657)	(0.553)	(0.511)
US Suppliers=14	-2.982	-2.552	-2.729	-2.299	-3.107
	(0.453)	(0.487)	(0.583)	(0.621)	(0.697)
US Suppliers=15	-2.345	-2.061	-3.565	-0.892	-2.369
	(0.689)	(0.402)	(0.560)	(0.396)	(1.433)
US Suppliers=16	-2.434	-1.305	-2.075	-0.655	-0.968
	(0.447)	(0.163)	(0.272)	(0.216)	(0.634)
US Suppliers=17	-1.197	-1.085	-1.847		-1.113
	(0.761)	(0.280)	(0.374)		(0.780)
US Suppliers=18	-1.613	-1.414	-1.604	0.479	-1.253
	(0.928)	(0.834)	(0.212)	(0.216)	(1.180)
Constant	1.950	1.658	1.378	1.588	1.512
	(0.193)	(0.162)	(0.185)	(0.216)	(0.256)
Adj. R-Square	0.339	0.290	0.175	0.220	0.146
Observations	1694	926	1599	371	1752
Fixed Effects	Year	Year	Year	Year	Year

Notes: Regression specification from Equation 2 with standard errors clustered at the molecule level. See text for data sources and details.

Figure A11: Value Chain Markups Breakdowns



Notes: All markups relative to those for two or more suppliers. Pharmacy and PBM markups computed using relative absolute Medicaid. 95% and 90% confidence intervals displayed. See text for data sources and details.

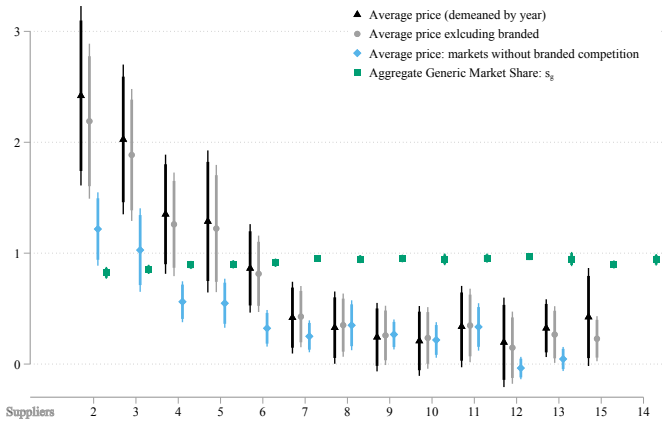
C Robustness Check: The Role of Brands

A large literature finds that branded molecules command a higher price than chemically identical generic competitors, as consumers do not consider generics as perfect substitutes (for a summary see Kanavos et al., 2008). Our main empirical result averages the price of all molecules in the market regardless of brand status. These results may be driven by cross-country differences in the price differential and market share for the branded version of the molecule. If this mechanically generates our results, the branded molecules in the US will have higher price differentials and or market shares than in the foreign locations. We directly disentangle the effects of branded molecules from the US data in two ways.[30] First, we show that the influence of branded drugs on the calculated US price is small. Second, we limit the sample to markets without an original branded entrant.

The triangles in Figure A12 depict the average per-dose US price (with yearly fixed effects removed) from in the main results. The circles show this same price computed without including the original branded molecules. The branded drugs do command a premium, but play a small role in the average price. This is due in part to the small market share of branded drugs. In markets with fewer suppliers, branded drugs have a larger market share, however, even in markets with only two suppliers branded drugs account for fewer than 20% of the market (the average aggregate generic market share is depicted using squares in Figure A12). In the second exercise, we limit the analysis to markets where there the original branded drug is no longer in the market. Just under half of the US markets in our sample (48%) have no original branded product. Appendix FigureA12) shows these results

[30] Our data does not allow us to remove the effect of branded molecules in the foreign locations.

Figure A12: Branded vs Generic Prices using US Medicaid



Notes: The x-axis depicts the number of suppliers in markets with both branded and generic competitors. The triangle, circle and diamond are in $USD, demeaned with yearly fixed effects. The squares are interpreted as a proportion, the share of units sold that are sourced from generic suppliers. Robust standard errors with 95% CI.

are broadly similar.

D Asian Manufacturer Data

In interpreting our fixed cost estimates we assume that there are unlimited fringe of marginal suppliers that could contract with a US distribution outlet - if they could receive US FDA approval (or similar approval in Australia). To confirm this, we scraped data on possible suppliers from Alibaba.com and TradeIndia.com. The sheer number of suppliers and brands is staggering. See Table A3 for statistics. We were able to match 395 molecules to data. As shown in our sample, there are over 25 potential global suppliers per US approved supplier and 4 Indian suppliers per US approved suppler. Breaking data down by the number of US approved suppliers, we find similar statistics.

E Role of Market Size

This section presents several empirical exercises with a view to understand the potential for competition policy to be an effective tool at lowering prices in these markets through additional entry. We show several facts that suggest a link between fixed costs, market entry, and competition and propose an explanation for our finding that fixed costs are higher in the US.

E.1 US Prices are relatively higher in markets with few patients

A natural policy response to insufficient competition would be to allow more entrants. In Figure A13 as market size increases, the US price differential decreases. This combined

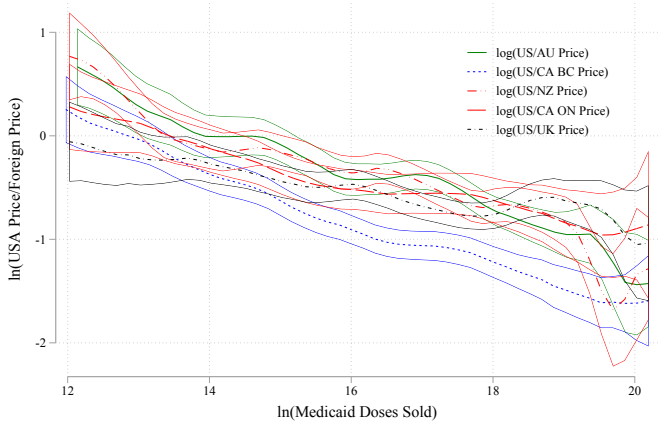
Table A3: Foreign Supplier Data

US Suppliers (2017)	Alibaba Suppliers (Median)	TradeIndia Suppliers (Median)	Molecules (number)
Panel A: Median Across Molecules			
4	126	15	395
Panel B: By Number of US Suppliers			
1	80	5	80
2	80	9	56
3	115.5	12	48
4	79.5	11	39
5	166	19	28
6	190	11.5	35
7	337	23.5	18
8	168.5	20	22
9	221	21	19
10 or more	263	50	50

Notes: Data scraped from supply websites over December 2017-March 2018. Data collected at the molecule level (not molecule-dose-route level).

with the earlier finding that that drugs with few suppliers have large US price differentials indicates that the number of entrants is limited by the underlying demand for a particular molecule from patients and doctors.

Figure A13: Role of Market Size

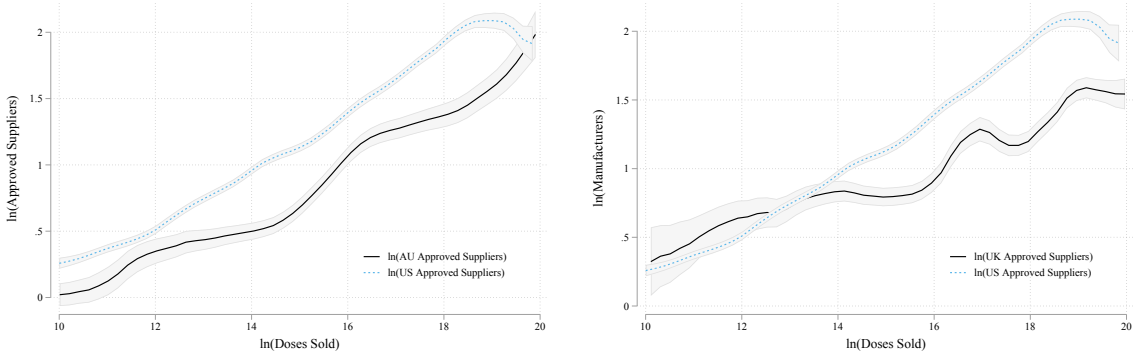


Notes: Average price difference between the two countries taken across drugs (molecule-dose-route) within the market size of the US with sales of over 150,000 doses per year.

E.2 Market size is highly correlated with the number of competitors

Here we examine the incentives of a generic pharmaceutical supplier to enter a marketplace. If there are few treatable patients requiring a small number of doses, there may be a smaller incentive for a supplier to enter the marketplace. We directly consider the relationship of suppliers to market size in Figure A14. This comparison in only done between Australia, the United States (under Medicaid), and England as these systems make publicly available the total number of capsules/tablets sold.

Figure A14: Relationship between Suppliers and Market Size



(a) Australia-US Medicaid

(b) England-US Medicaid

As shown in Figure A14, an increase in the number of prescribed doses is correlated with an increase in the number of suppliers. Across all three countries a doubling in the number of patients is correlated with an approximately 20-30% increase in the number of pharmaceutical suppliers. This means that the marginal benefit of entry in terms of capturing profit from quantity (market size) is approximately the same across countries. This is in contrast to the results of Section 5.1, which showed that marginal benefit to entry to capture profit from higher prices is larger in the United States, than in either Australia or the United Kingdom. One possible rationalization is that the US has higher entry costs (or barriers to entry), preventing supplier entry and lower prices.

E.3 Underlying Fixed Cost Mechanisms

Our results in Section 6 indicate that US fixed costs are typically at least four times higher than Australian fixed costs. Is this simply because the typical markets in the US are eight times larger than Australian markets, but do not have eight times more entrants? In this section we provide several additional empirical facts that suggest that the story is more complex and that the following explains the difference in fixed costs.

Our hypothesis is that (1) In all non-US markets, prices are effectively set by a government-mandated mechanism, such that manufacturers price slightly above marginal cost regardless of market size. This means that in these markets, there is a little surplus to pay for fixed costs and market entry mechanically has no effect on prices. Entry is thus mostly a function of market size. (2) For the US, prices are set though a competitive mechanism, which means more entry for larger markets. For small US markets (few patients), with few entrants - there are very high prices (as shown in 1), this mechanically generates 'high relative fixed costs', even when very few doses are sold. Here, the high US fixed costs appear to be driven by both high prices and low entry. In large US markets (in terms of doses), there is more entry and very low prices - the large US market still generates high fixed costs. But critically, entry in the US seems to have an effect on prices; more entry means lower prices, reducing entry incentives. Here, high US fixed costs appear to be driven by large markets having relatively lower entry - as prices are either similar or even lower than other markets.

We form this hypothesis by combing our empirical facts in the context of the computation

of fixed costs. Recall that mechanically our fixed cost bounds are computed as:

$$F_{US}/F_{foreign} = \frac{q_{US}^{generic} \times p_{US}^{generic}}{S_{US}^{generic}} / \frac{q_{foreign}^{generic} \times p_{foregin}^{generic}}{S_{foreign}^{generic}} \tag{6}$$

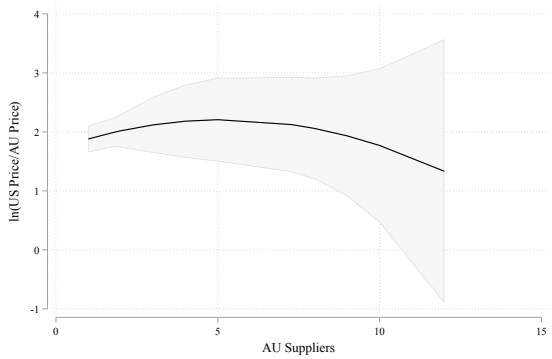
For the numerator, we know from our main analysis that in the US, large markets have high q, low p, and moderate S (as additionally entrants drive prices down). In the US, small markets have low q, high p, and low S - due to the small number of doses sold. Our estimates of the bounds shows that in both cases, this leads to relatively large relative fixed costs in the US.

We supplement our previous analysis with two additional data exercises. Firstly, we look at markets with just one US entrant and ask "What happens to the price differentials, when there are different numbers of foreign suppliers?". Second, we do the reverse and look at what happens to the price differential in markets where there is just one foreign location supplier as more US suppliers are present in the market. Due to data limitations, discussed previously, we will use the Australia as the foreign location for this exercise.

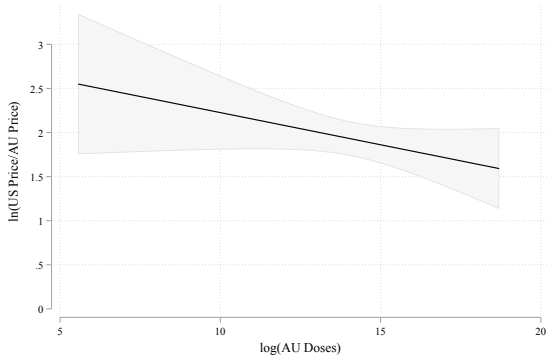
Figure A15(a) shows the price differential relative to the number of Australian suppliers for drugs that have one US supplier. The relative prices between the US and Australia are invariant, even as the number of Australian suppliers increases. When Australian markets have one supplier and US markets have one supplier; US prices are 200 log points higher than Australian prices. When Australian markets have ten suppliers and US market have one suppler; US prices are still higher by the same amount, when compared to Australian prices. Figure A15(b) shows the same exercise for the market size (raw number of prescribed doses). Holding US entrants fixed, in larger Australian markets there is very little difference in the price difference between the US and Australia. This lends evidence (short of a formal structural model), that prices in Australia (relative to the US), have little to do with market forces, either in terms of competition or in terms of market size.

Figure A15: Price Differences - Fixing One US supplier

(a) Number of AU entrants (Polynomial Fit)



(b) Number of AU doses (Polynomial Fit)

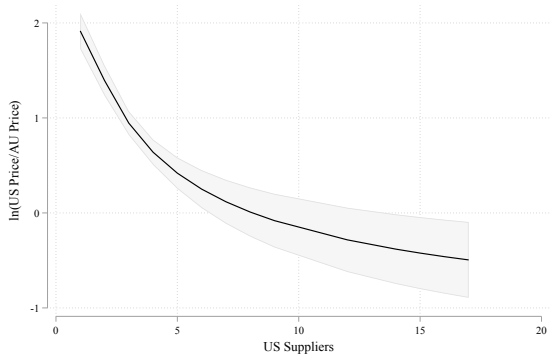


When we conduct this same exercise in reverse (i.e markets with only 1 Australian supplier) we see that increasing the number of US suppliers dramatically lowers the price differential (Figure A16(a)). While in Australia competition doesn't seem important - it does seem very important in the United States. We repeat this using the number of doses (Figure

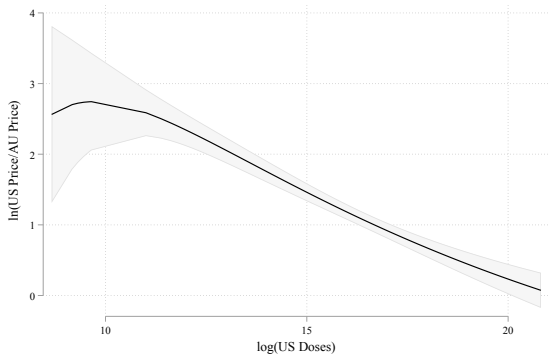
A16((b)).

Figure A16: Price Differences - Fixing One AU supplier

(a) Number of US entrants (Polynomial Fit)



(b) Number of US doses (Polynomial Fit)



Ruling out a pure market size effect

While the median market in the US has 8 times more doses sold than than in Australia (in line with a 12x difference in overall populations), if the fixed costs estimates were purely due to the US having 8 times the market size but not 8 times the entrants we would expect to see that the relative fixed costs between the US and the foreign country varies with the relative number of manufacturers. In particular, we expect to see the relative fixed costs rising as the relative entrants increase (if the reason for the high fixed cost estimate is that it is not necessary to have additional entrants after a certain level of entry). Figure A17 suggests that this is not the case.

Figure A17: Relative Fixed Costs and Entrants