Pharmaceutical Followers*

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Abstract

We estimate a model of drug demand and supply that incorporates insurance, advertising, and competition between branded and generic drugs within and across therapeutic classes. We use data on antiulcer drugs from 1991 to 2010. Our simulations show generics and "me-too" drugs each increased consumer welfare more than $100 million in 2010, holding insurance premiums constant. However, insurance payments in 2010 fell by nearly $1 billion due to generics and rose by over $7 billion due to me-too antiulcer drugs.

JEL: I11, L13, L65

1 Introduction

Prescription drug spending as a share of U.S. national income more than tripled between 1984 and 2010.[1] This occurred despite the generic share of prescriptions quadrupling over the same period.[2] The increased use of generic drugs was facilitated by the U.S. Drug Price Competition and Patent Term Restoration Act of 1984 (also known as the Hatch-Waxman Act) which exempted generic manufacturers from costly clinical trials. However, some branded manufacturers responded by launching "me-too" drugs, meaning patented drugs that require clinical testing for regulatory approval, but are little differentiated from drugs already on the market. The quintessential me-too drug is Nexium (esomeprazole) which became one of the highest-selling drugs of all time, despite being the fifth branded drug in its class and facing competition from generic versions of other drugs in its class. We formulate a demand and supply model to examine how pharmaceutical followers – both generic and me-too drugs – affect competition and welfare.

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[1]Prescription drug expenditures as a share of national income rose from 0.5% in 1984 to 1.7% in 2010, according to National Health Expenditure data.

[2]The generic share of prescriptions rose from 19% in 1984 to 78% in 2010 (Berndt and Aitken, 2011).

Some contend me-too drugs waste resources, perceiving that the gains in therapeutic value are small given that their molecular structure is similar to existing drugs and, unlike generics, me-too drugs require costly clinical trials to gain approval. In 2000, the editor of the *New England Journal of Medicine* recommended that regulators reject drugs that are too similar to existing options: "requiring manufacturers to demonstrate that a new drug is substantially better than anything available would help to stem the rising tide of me-too drugs" (Angell, 2000). Me-too drugs may also drain regulatory resources, because they require approval by the U.S. Food and Drug Administration (FDA), which has a backlog of drugs to review.[3]

A key challenge in quantifying the impact of new product entries in the U.S. drug market is the pervasive role of health insurance.[4] Insured patients only pay a fraction (copayment) of the full price of pharmaceutical products, so the relevant price that the decision-maker faces is typically much lower than the posted price recorded in national datasets. Moreover, insurers often receive substantial rebates from manufacturers, creating an additional disconnect between the price observed in the data and the actual payoff to the producer. Accounting for both distortions is critical to performing meaningful counterfactuals: ignoring the first risks incorrectly concluding that patients are insensitive to price, while ignoring the second distorts the implied costs faced by suppliers.

Ours is the first study to tackle the distortions from both insurance copayments and rebates. To account for copayments, we estimate the relationship between price and copayment using insurance plan data, imputing copayments at the national level. The copayment-price relationship is then used to link the supply-side modeling of pricing decisions to copayments. To account for rebates paid by manufacturers to insurers, we exploit a government policy that constrains optimal rebates prior to generic entry. For rebates after generic entry, we identify implied rebate levels from changes in estimated marginal costs over time under the assumption that rebates are constrained prior to generic entry. After generic entry, fixed-rebate marginal costs jump, indicating a change in rebates consistent with the aforementioned cost distortion. We exploit this discrete jump to estimate the new rebate level.

Our demand model also allows for rich substitution patterns among drugs, which is important for obtaining accurate counterfactual predictions. To do so, we extend the work of Ellison et al. (1997), Stern (1996), Branstetter et al. (2011), and Bokhari and Fournier (2013) by modeling pharmaceutical demand using a discrete choice framework developed by Bresnahan et al. (1997). The framework allows for correlations across multiple nests, or clusters, of products. In particular, we allow for preferences to be correlated among products of the same class, same brand status

[3]While faster review for potential blockbuster drugs can be worth hundreds of millions of dollars to some manufacturers (Ridley et al., 2006), faster review for other drugs might be inefficient. For example, the fifth branded drug in a class might not provide much variety or competition. Likewise, the same might be true for the fifth generic version of the same drug.

[4]While insurance is an important feature of health care markets in developed countries, in developing countries like India there is little health insurance, so estimation of pharmaceutical demand does not need to account for the role of insurance. See, for example, Chaudhuri et al. (2006).

(branded or generic), same form (tablet or capsule), and same molecule. Our framework allows the data to inform whether (and quantify the extent to which) drugs that vary across one or more of these dimensions are substitutes. Alternatively, drugs that vary across a dimension could be treated as perfect substitutes, or as non-substitutes that exist in separate markets altogether. On the supply side, we follow Bresnahan (1987) and others in modeling firms as playing a static pricing game. Incorporating the supply side allows us to recover marginal costs as well as simulate how prices would change under counterfactual scenarios.

We use monthly U.S. pharmaceutical price, advertising, and utilization data from 1991 to 2010. We focus on classes of drugs that contain quintessential me-too drugs: the H2 antagonists (H2s) and proton pump inhibitors (PPIs), including the aforementioned Nexium (esomeprazole), which treat ulcers and reflux. Our data include generic entry for every H2 and PPI molecule that has a generic version as of 2010.[5]

We estimate own-price (copayment) elasticities for branded drugs in the range of -1.5 to -5.1, with higher magnitudes corresponding to branded drugs that face generic competition. As expected, we find higher cross-price elasticities associated with the same classes, brand/generic statuses, forms, and molecules. Cross-price elasticities are also higher when a drug faces more competition from other sources. For example, an increase in the price of Nexium (esomeprazole), the market leader from 2005 to 2010, has a much larger effect on other PPIs that face generic competition than those that do not. This occurs because the primary market for PPIs faces generic competition from those who have preferences for branded drugs. Hence, these drugs are particularly sensitive to price movements by branded competitors.

Using our estimates of the supply-side and demand-side parameters, we perform two sets of counterfactuals. The first considers removing the pharmaceutical followers currently on the market. Removing me-too drugs (i.e. only keeping the first molecule in each class) or removing all generics leads to substantial drops in utilization which correspond to drops in consumer welfare of more than $100 million per year, holding insurance premiums fixed. However, the removal of these two groups has starkly different effects on insurance payments and manufacturer profits, effects that dwarf the consumer surplus changes. When generics are removed, profits gross of fixed costs rise by over $1 billion as the market becomes less competitive. Insurance payments rise nearly $1 billion. When me-too drugs are removed, insurance payments plummet, falling by over $7 billion annually, with manufacturer profits also falling by more than $4 billion.

Our second set of counterfactuals examines the effects of generic competition for the blockbuster me-too Nexium (esomeprazole). In the short run (a few months after generic entry) with one generic manufacturer, the branded drug reduces its price and competes, so consumer welfare rises. Adding additional generic competitors beyond the first has little effect on welfare because there is already significant price competition between the branded and generic manufacturers. However, adding

[5]The number of generic manufacturers that enter to compete with the branded manufacturer depends on market size (Reiffen and Ward, 2005; Grabowski et al., 2007), advertising by the branded manufacturer (Scott Morton, 2000), and the manufacturer's previous experience (Scott Morton, 1999; Gallant et al., 2011).

generics does shift sales from the branded drug to the generics, effectively shutting the branded drug out of the market.

If only one generic version of Nexium (esomeprazole) were available, we find that consumer welfare would actually be higher in the short run than in the long run. In the long run, generic quality is sufficiently high and marginal costs sufficiently low that the branded manufacturer would raise its prices to compete only for consumers with strong preferences for branded drugs. This phenomenon – the branded manufacturer raising its price in the face of generic competition – is known as the "generic paradox" (Scherer, 1993).[6] When the branded manufacturer raises price, it is not only bad for consumers of the branded drug, but also for consumers of the generic drug, because the generic drug manufacturer can raise its price as well. In this example, there is only one generic manufacturer. However, in markets with high demand, many generic manufacturers enter. With a second generic manufacturer, prices fall and consumer welfare rises. We estimate that with two or more generic manufacturers of Nexium (esomeprazole), consumer welfare will rise by about $200 million per year.

Dubois and Lasio (2013) also examine pharmaceutical demand in the antiulcer market. However, in contrast to our study of the U.S. market, they consider the impact of price regulation, a key institutional feature of most high-income markets, excluding the U.S. Exploiting cross-sectional variation in the degree or existence of price regulation, they are able to identify the impact of regulation in the settings in which it binds. Using their demand and supply estimates, they then identify the impact of regulation and examine counterfactuals in which regulation is eliminated.

While several studies have examined the welfare implications of pharmaceutical competition (Chaudhuri et al., 2006; Granlund, 2010; Branstetter et al., 2011; Dutta, 2011; Bokhari and Fournier, 2013), our paper is alone in tackling the intervening role of insurance, a key institutional feature of the U.S. market.[7] Pharmaceutical studies using U.S. data frequently recover price elasticities that are inconsistent with profit maximization under standard models of supply, making it difficult if not impossible to solve for equilibrium prices in counterfactual simulations, thereby sharply limiting the scope of analysis.[8] Further, consumer welfare calculations hinge on the magni-

[6]When faced with generic competition, the price of the branded drug sometimes remains relatively high or even increases. This might be explained by a perception among consumers that the branded drug is higher quality (Frank and Salkever, 1997; Grabowski and Vernon, 1992; Regan, 2008). Alternatively, the branded manufacturer's optimal price path might be increasing, with entry by a generic causing a fall relative to trend but not relative to previous prices (Bhattacharya and Vogt, 2003). Finally, branded drug prices might increase slowly after generic entry due to consumer heterogeneity in price sensitivity and the resolution of consumer uncertainty about generic quality (Ching, 2010a).

[7]Bokhari and Fournier (2013) also solve for counterfactual prices using U.S. data, but their study differs from ours in two important ways. First, they use an Almost Ideal Demand System instead of a discrete choice framework. Second, like the aforementioned studies, they lack copayment data and must use price.

[8]Pharmaceutical studies using U.S. data frequently estimate price elasticities in the inelastic portion of the demand curve. For example, in a meta-analysis by Gemmill et al. (2007), mean demand elasticity for pharmaceuticals was -0.2 (and mean standard error was 0.026). There are two concerns with estimates of demand that are inelastic. First, the inelastic demand estimates typically apply only to cases where copayments or prices move in unison. Previous studies focused on copayments moving together due to a paucity of data. For example, Leibowitz et al. (1985), one of the drug demand elasticity studies surveyed by Gemmill et al. (2007), wrote that they could not estimate cross-copayment

tude of the price coefficient in the estimated indirect utility function, highlighting the importance of having correct pricing data.[9] We show that our linking of prices and copayments yields economically reasonable elasticity estimates, making it possible to obtain both counterfactual equilibrium prices as well as conduct welfare analysis.

The rest of the paper proceeds as follows. Section 2 provides background on the antiulcer market and shows how it has evolved over time. Section 3 describes the demand model, including a discussion of copayments and the evolution of the outside good. Section 4 explains the model of supply and the role of rebates. Section 5 gives the estimates of both the demand and supply models as well as showing their implications for elasticities and the evolution of rebates. Section 6 shows the counterfactuals, including the removal of generic or me-too drugs and the introduction of generic Nexium (esomeprazole). Section 7 concludes.

2 Background and Data

Our focus is on the "antiulcer" market, which includes not only drugs that treat ulcers but also reflux ("heartburn").[10] The prevalence of reflux in the population is between 10% and 20% (Fedorak et al., 2010) and the prevalence of ulcers is approximately 1% (Kurata and Haile, 1984). The earliest entrants into the antiulcer market were H2 antagonists (H2s), followed by proton pump inhibitors (PPIs). H2s inhibit peptic acid by blocking histamine receptors on acid-secreting cells in the stomach lining. PPIs work more directly than H2s by inhibiting the proton acid pump in the lining of the stomach.[11]

The H2s and PPIs include quintessential me-too drugs. For example, Zantac (ranitidine) was the second drug in the H2 class, and became one of the top-selling drugs in the world in the 1990s. Nexium (esomeprazole) was the fifth drug in the PPI class, and became one of the top-selling drugs in the world in the 2000s.

The scientific community, including the FDA, regards the antiulcer drugs as close substitutes. Only the first H2 and the first PPI were granted priority review at FDA. However, manufacturers

elasticity because coinsurance was the same across products. Second, the inelastic demand estimates make it hard to construct a model of profit maximization and thus estimate counterfactuals. After all, if firms price in the inelastic portion of the demand curve, then raising price would increase profit. In contrast to the previous literature, our study uses variation in copayments and prices across drugs within a given year to estimate cross-copayment elasticity. One exception is Ridley (2014) who used data that is similar to ours and found demand to be considerably more elastic than in previous research, but in a reduced-form analysis.

[9] See Brand et al. (2012) for a discussion of the importance of using copayments rather than price when analyzing health care markets in the United States. They treat hospital copayments as resulting from a bargaining game between hospitals and insurance companies.

[10] We use the term "antiulcer" to be consistent with previous economic research (Berndt et al., 1995, 2003).

[11] The antiulcer drugs are indicated for short-term treatment, but can be used considerably longer. For example, Nexium's FDA-approved label says that it is indicated for short-term treatment (4 to 8 weeks) in the healing and relief of symptoms associated with erosive esophagitis. However, the label also says that Nexium may be used for additional weeks if the patient has not yet been healed. Furthermore, the label says that the use of Nexium may be continued to maintain the healing. Finally, Nexium is indicated for treatment of heartburn and other symptoms associated with GERD.

of these me-too drugs assert that their drugs are superior, or at least different. For example, the manufacturer of Zantac (the second H2) claims at least five advantages over the first mover, including lower relapse rates, fewer side effects, and more indications (Berndt et al., 1995). Likewise, Nexium (the fifth PPI) is advertised as the "healing purple pill". The FDA-approved label reads: "Nexium 40mg demonstrates higher healing rates in erosive esophagitis than Prilosec 20mg (the approved dose for this indication)". Hence, while the FDA regards the drugs as close substitutes, the manufacturers claim otherwise. Ultimately, the question is whether doctors and patients see the drugs as close substitutes. Using a revealed preference approach, we investigate whether demand is sensitive to price differences across the drugs, and whether the availability of new drugs in the class increases welfare.

The two most popular forms of H2s and PPIs are capsules and tablets. As shown in Table 1, tablets dominate the H2 market and capsules dominate the PPI market. However, there is some crossover: nizatidine (an H2) competes as a capsule, while pantoprazole and rabeprazole (PPIs) compete as tablets.

The first H2s came off patent early in our sample period, while the three most recent PPIs remain on patent at the end. As shown in Table 1, branded H2s entered from 1977 to 1988 and began facing generic competition in 1994. By 2001, all branded H2s faced generic competition, with cimetidine and ranitidine each having more than thirty generic manufacturers. Branded drugs in the PPI class entered between 1989 and 2009 with generic entry beginning in 2002.

We use sales and advertising data from SDI Health (later acquired by IMS Health). The sales data include units (for example, number of pills), prescriptions, and dollar value for sales of prescription drugs sold at U.S. retail pharmacies from 1991 through 2010. The advertising data include detailing at the molecule-manufacturer-month level. We show the evolution of prescriptions, prices, and advertising in sections 2.1 through 2.3.

A second data source is needed because the price the manufacturer receives from a sale is generally not the price the consumer faces due to insurance. Information on copayments (the prices consumers face) were provided by AdvancePCS, a pharmaceutical benefit plan administrator. The copayment data include copayment by molecule-insurer-month for a subset of the years. We describe the copayment data and the details of the insurance market in section 2.4.

2.1 Prescriptions

We first examine how prescription quantities vary over time. Our analysis focuses on retail sales of the most popular doses of prescription medications.[12] Figure 1 illustrates the evolution

[12]The market we examine is restricted along three dimensions. First, we focus on retail sales rather than hospital sales. From 2003 to 2010, retail sales accounted for 91% of PPI prescriptions. We were able to compare retail to hospital sales using another data set with less periodicity (annual rather than monthly) and a shorter time period (2003-2010 rather than 1991-2010). Second, we focus on the most popular dose for each drug which covers approximately 90% of all prescriptions. Third, we focus on prescription medications rather than the over-the-counter market. According to an analyst report, over-the-counter drugs accounted for 16% of the retail PPI market from February 2009 to February 2012. Section 3.3 describes how we account for over-the-counter availability in our

of the market's composition by molecule and brand/generic (B/G) status, while Table 2 provides corresponding market shares by molecule. Here, prescriptions are aggregated across all generic manufacturers of the same molecule. Prior to 1993, H2s controlled the market, with branded ranitidine (Zantac) as the market leader, accounting for over half of all prescriptions. In the mid 1990s, branded omeprazole (Prilosec, the first PPI) became the market leader. Later, branded lansoprazole (Prevacid, the second PPI) became the market leader. In the last five years of the sample, omeprazole (now available as a generic) had a quarter of the market, as did esomeprazole (available exclusively as the branded drug Nexium), with the remaining half of the market distributed across various H2s and PPIs.

Figure 1 illustrates the fic growth in the PPI market. The PPI market grew rapidly in part by stealing from the H2 market as can be seen in the decline of the H2 market. However, the total prescription anti-ulcer market was clearly expanding. New entrants to the PPI market advertised heavily. Also, new patients might have entered the market, for example seeking relief from ulcers caused by non-steroidal inflammatory drugs. Finally, generic entry increased access by dramatically reducing prices (Figure 3). With lower generic prices, branded share eroded rapidly. For example, six months after the entry of generic ranitidine, the branded share had fallen by 90%. The impact was similar for the remaining H2s and the PPIs with generic versions. Nonetheless, branded drugs maintain a small segment of the market for a few years after initial generic entry.

The overall evolution of market shares is different for PPIs and H2s, reflecting differences in both business stealing and market expansion. H2 prescriptions peaked in 1995 at just over 3.5 million, but declined steadily thereafter as more PPIs were brought to market. However, total prescriptions rose dramatically, from just over 2.25 million in 1991 to over 9 million by 2011. Both trends are illustrated in Figure 2.

Preferences for particular forms may also be important, as the side effects and release times can vary between tablets and capsules.[13] Nizatidine and famotidine have similar branded shares in the 1990s, but dissimilar generic shares in the 2000s. The difference occurs when PPIs are becoming bigger players. A possible explanation for generic famotidine outpacing generic nizatidine is that PPIs are generally of the same form (capsule) as nizatidine and are therefore better substitutes.

2.2 Prices

We next examine the evolution of prices. Our data include revenue and the number of prescriptions. We divide revenue by prescriptions to calculate an average price per prescription. We do not use list price. We have only retail sales data, but retail accounts for 90% of the market for

estimation.

[13] Breitkreutz and Boos (2011) note that oral forms (i.e. tablets and capsules) are generally preferred, but some patients might not find them easy to swallow, and also note that different patients can have different sensitivities to inactive ingredients (which can vary across forms). Jones and Francis (2000) find that, when comparing tablets to capsules, the relative ease of swallowing, perceived speeds of action, and perceived durations of action can all vary from patient-to-patient. As the authors conclude, "consumers have preferences for particular dosage forms."

Table 1: Entry by Molecule

Class	Molecule	Brand Name	Brand Entry	OTC Entry	1st Gen Entry	Gen Entrants	Top Form
H2	cimetidine	Tagamet	Aug-77	Aug-95	May-94	36	Tab
	ranitidine	Zantac	Jul-83	Apr-96	Jul-97	32	Tab
	famotidine	Pepcid	Nov-86	Jun-95	Apr-01	19	Tab
	nizatidine	Axid	May-88	Jul-96	Oct-98	9	Cap
PPI	omeprazole	Prilosec	Oct-89	Sep-03	Nov-02	12	Cap
	lansoprazole	Prevacid	May-95	Nov-09	Nov-09	4	Cap
	rabeprazole	Aciphex	Sep-99	-	-	-	Tab
	pantoprazole	Protonix	Apr-00	-	Dec-07	4	Tab
	esomeprazole	Nexium	Feb-01	-	-	-	Cap
	omeprazole $NaHCO_3$	Zegerid	Oct-04	Mar-10	Jul-10	2	Cap
	dexlansoprazole	Dexilant	Feb-09	-	-	-	Cap

Table 2: Share (%) of Prescriptions by Molecule

Class	Molecule	1991-1995	1996-2000	2001-2005	2006-2010
H2	cimetidine	14.4	7.2	1.8	0.6
	ranitidine	51.6	25.1	14.8	9.2
	famotidine	10.7	9.4	4.1	3.1
	nizatidine	8.9	5.7	1.1	0.3
PPI	omeprazole	14.2	35.7	16.6	26.5
	lansoprazole	0.2	15.5	22.7	14.9
	rabeprazole	–	1.1	8.0	5.3
	pantoprazole	–	0.3	14.1	15.0
	esomeprazole	–	–	16.8	24.2
	omeprazole $NaHCO_3$	–	–	–	0.6
	dexlansoprazole	–	–	–	0.3

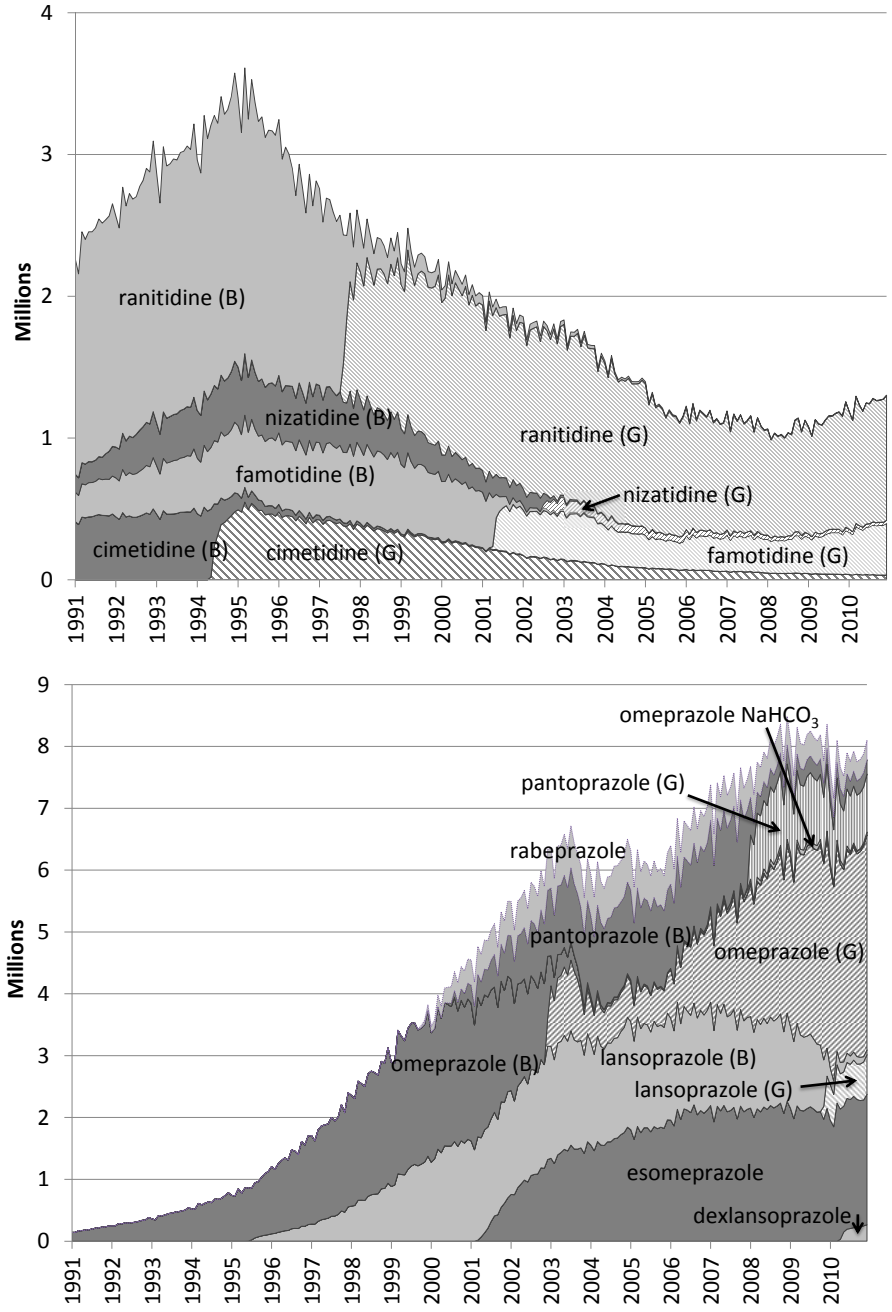


Figure 1: Monthly prescriptions for H2 antagonists (top) and PPIs (bottom). The molecules without a parenthetical have no generic version so a "(B)" is implied.

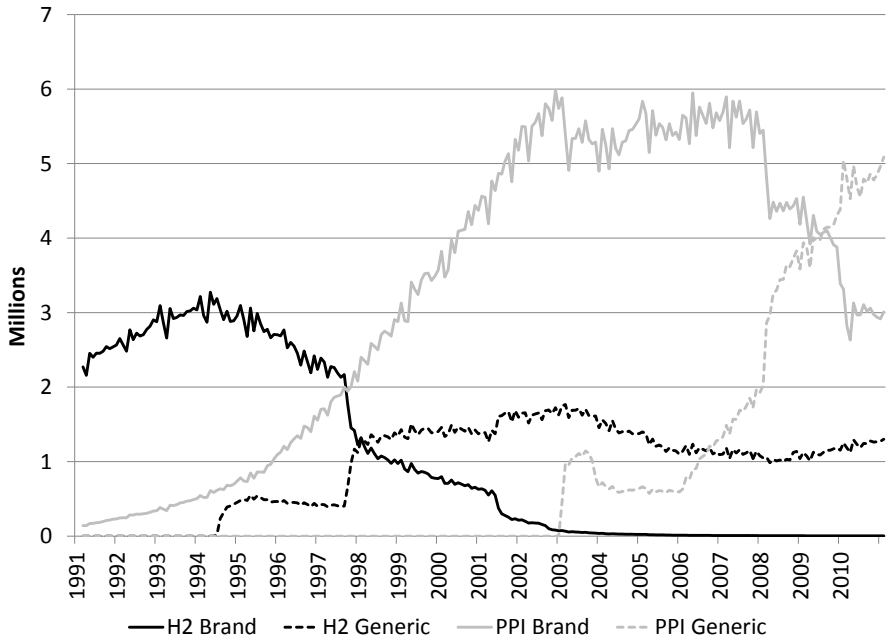


Figure 2: Prescriptions for brand and generic drugs by class.

antiulcer drugs. All prices are adjusted to January 2010 dollars.

Figure 3 shows average prices. Branded prices (solid lines) in Figure 3 are typically flat or increasing following generic entry while generic prices (dotted lines) fall over time. For example, the price of branded cimetidine was approximately $100 in 1994, while generics entered with a price near $75. Over time, the branded price climbed to nearly $150, while the generic price fell below $20. The decline in generic prices might be explained by an increase in generic competition over time, or by falling marginal costs due to learning-by-doing in production. The fact that branded prices do not fall (and often rise) despite the collapse of their market shares suggests the relevant competitive adjustment occurs along a different dimension. From Figure 1, however, the fall in H2 generic prices does not appear to be associated with increased prescriptions. This suggests the rise of PPIs — in addition to expanding the prescription market — results in fewer generic prescriptions.

2.3 Advertising

We include detailing data at the molecule-manufacturer-month level. While manufacturers also use direct-to-consumer advertising, spending on detailing to physicians is much greater.[14] Over 99%

[14]From 1996 to 2005, manufacturers spent $58 billion on detailing compared to $27 on direct-to-consumer advertising (Donohue et al., 2007). For PPIs from 2000 to 2002, manufacturers spent four times more on detailing than direct-to-consumer advertising (Ridley, 2014).

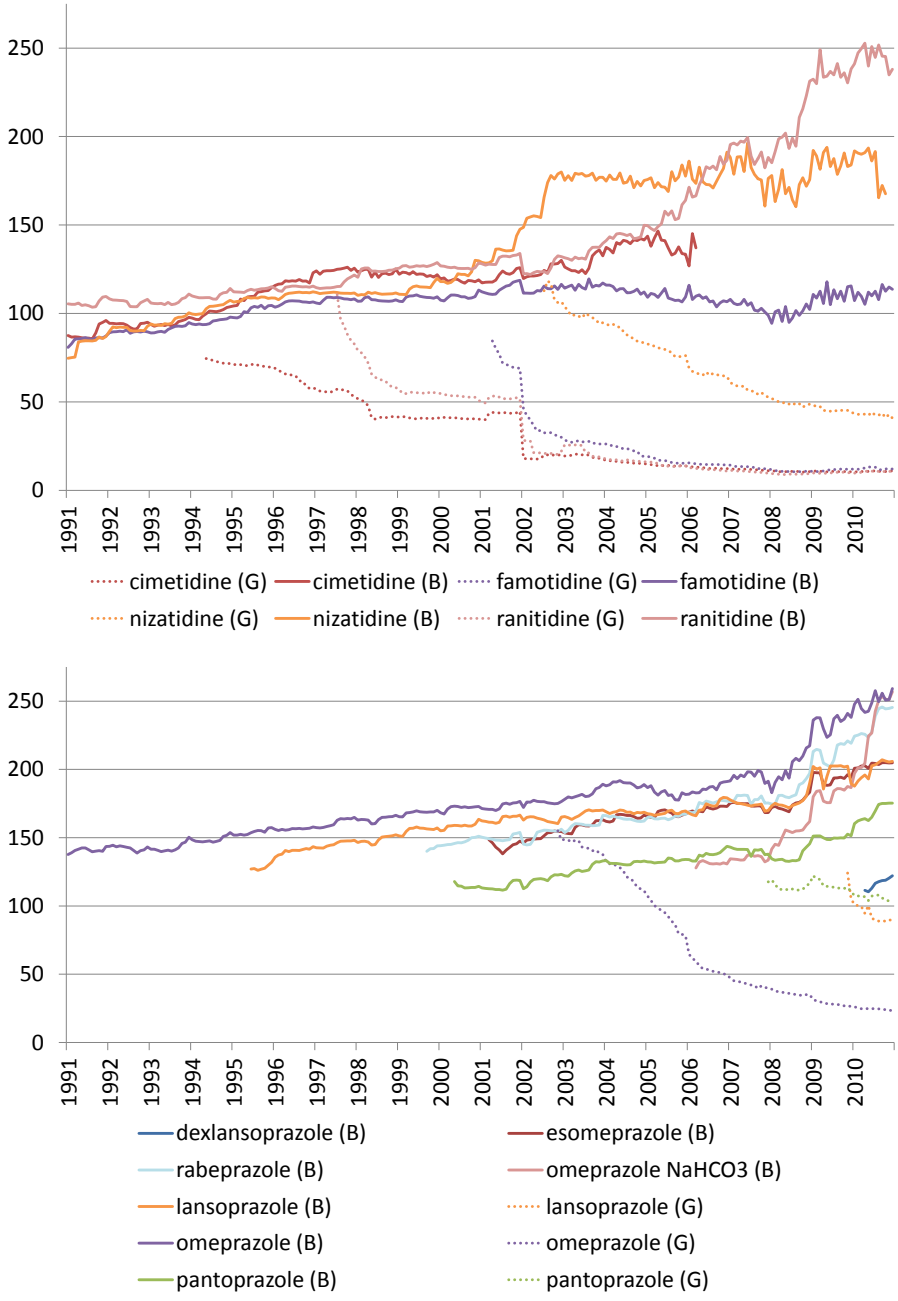


Figure 3: Prescription Prices for H2 antagonists (top) and PPIs (bottom).

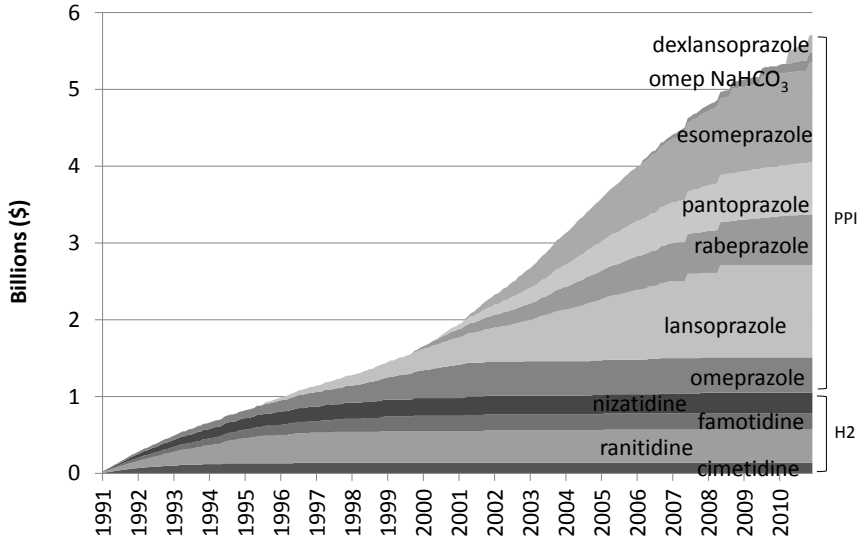


Figure 4: Cumulative advertising for H2 antagonists and PPIs.

of detailing was by branded manufacturers. Generic advertising is excluded because it is negligible and could not be attributed to a particular firm.

Figure 4 illustrates cumulative advertising expenditures. For a given molecule, branded advertising (of all types) typically ends once a generic enters.[15] Advertising substantially increased after the introduction of PPIs, particularly for lansoprazole and esomeprazole. The trends in advertising expenditures match well with changes in prescriptions, paralleling the dramatic increase in PPI prescriptions since 2000. Hence, while advertising may promote product switching, it also appears to expand the market.

2.4 Insurance

In 2010, 96% of prescriptions for H2s and PPIs were purchased with insurance. Insurance complicates the modeling of pharmaceuticals by separating the price paid by the consumer from the price received by the manufacturer. First, copayments paid by the insured are below prices received by the manufacturer. Second, branded manufacturers give substantial rebates to insurance companies. We account for both copayments and rebates.

First, we account for copayments. Because copayments are below prices, the insured have higher quantity demanded than the uninsured. This is the "moral hazard" problem.[16] We ac-

[15] One exception (from outside our market) was Pfizer which continued to advertise anti-cholesterol drug Lipitor for 6 months after patent expiration, but Pfizer's strategy was novel, and unsuccessful in retaining sales.

[16] Insurers can drive down prices using their market power and the promise of steering market share for one drug (Duggan and Scott Morton, 2010; Ridley, 2014). Hence, insurers can get lower prices than the uninsured. Nevertheless, the moral hazard problem remains because insured consumers pay copayments that are below the actual prices.

count for the relationship between price and copayment using copayment data from AdvancePCS, a pharmaceutical benefits manager. The sample includes the first four PPIs (omeprazole, lansoprazole, rabeprazole, pantoprazole), 63 insurance groups, and 25 months between 2000 and 2002.[17] Insurance groups with $0 copayments were dropped as unrepresentative.

The copayment sample is representative of the U.S. market along three dimensions. First, average copayments for the sample match average copayments nationally. Mean price was $150 and mean copayment was $18, which is consistent with national averages for the sample period. According to the Kaiser Family Foundation, in 2002 the average branded copayment for insurers with two tiers (generic, brand) was $18.[18] Second, average market shares across insurance groups in the sample match market shares nationally. Average market shares from the insurance data differ from the national data by no more than one percentage point. Third, the data vendor (AdvancePCS) reports that its own analysis shows that its data closely match United States Census Bureau estimates of the distribution of the U.S. population based on age, sex, and geographic region.

Using the copayment data, we estimate the relationship between copayment and price. We need this relationship to hold over time in order for the two-year sample to represent the full two decades of the study. As we show in Figure 3, branded prices are rising over time and generic prices are falling. Hence, in order for our method to represent the full two decades, then national branded copayments must be rising as branded prices rise, and national generic copayments must be falling as generic prices fall. In fact, this is true. Between 2002 and 2010, branded copayments rose from $18 to $28, while generic copayments changed from $9 to $10. Hence generic copayments decreased in inflation-adjusted terms.

Second, we account for rebates, although we do not directly observe rebates. Rebates are paid by the manufacturer to the insurer in return for a lower copayment tier. The rebates are not public, presumably because manufacturers will pay an insurer a greater rebate if that manufacturer's other customers are unaware of it (Kyle and Ridley, 2007).[19] While rebate data are not public, an understanding of the regulation suggests a method for inferring rebates. Under the Medicaid Drug Rebate Program, branded drug manufacturers must either give the U.S. government their best price or 15.1% off their average price.[20] During the 1990s and 2000s, if a manufacturer increased its rebate to any insurer above 15.1% of its average price, then the manufacturer had to increase its rebate to the U.S. government. Hence, manufacturers could credibly tell an insurer it was too costly to offer a rebate above 15.1% off its average price. In the antiulcer market, it is reasonable to expect high rebates. Hence, we assume a corner solution: a rebate of 15.1% prior to generic entry. Prior to generic entry, manufacturers attempt to keep rebates at 15.1% to limit the best price

[17] Note that this is a period where no generic PPI's are present.

[18] Kaiser Family Foundation, "Employer Health Benefits Survey 2013," http://ehbs.kff.org/.

[19] While rebates are not included in our data, discounts are included. For example, if the manufacturer gives the wholesaler a discount for prompt payment, such a discount is captured in the data.

[20] The 15.1% discount was established by the Omnibus Budget Reconciliation Act of 1990. See Sec. 1927(c) of the Social Security Act, available at http://www.ssa.gov/OP_Home/ssact/title19/1927.htm. The rebate was increased to 23.1% under the Patient Protection and Affordable Care Act of 2010.

obligation to Medicaid. We use this to identify the marginal costs. After patent expiration, the Medicaid penalty constraint is lifted because Medicaid switches to generics. Hence, we assume that the jump occurs at patent expiration. After generic entry, the constraint is relaxed, because sales to Medicaid become a much smaller share of business (state Medicaid programs typically don't pay for a branded drug when a generic version is available). Hence, we assume that the rebate jump occurs when generics enter. To check whether our rebate estimates are sensible, we compare data on pharmaceutical sales for a molecule in a year to annual reports from the companies regarding revenue from the molecule in the year. The results are described in section 4.1.

We assume that insurance separates the price consumers pay from the price manufacturers receive, and thus we assume that insurance is purely distortionary. We ignore an often cited benefit of health insurance: reducing the variation in health spending which increases the utility of risk-averse people. For example, a person insures against hospital costs, because hospital costs can vary dramatically for a given person across years. However, in the antiulcer market, there is much less variation in spending, so antiulcer drugs are less like hospitalization and more like gasoline, and people typically do not purchase gasoline insurance. The presence of insurance for drugs in this class might not be driven by risk aversion, but driven by direct government subsidies to constituents, such as seniors (in the form of the Medicare drug benefit), or by indirect subsidies in the form of tax breaks (U.S. health insurance is an untaxed benefit when provided by an employer). Hence, our assumption that insurance is distortionary might be appropriate in this context.

3 Demand

Our demand model allows for four types of product differentiation: (i) between classes (H2 and PPI), (ii) between brands and generics (for example, branded omeprazole and generic omeprazole), (iii) between forms (capsule and tablet), and (iv) between molecules (branded omeprazole and branded lansoprazole).

One type of switching – from brand to generic of the same molecule – is quite common. The pharmacist can freely switch a patient from branded lansoprazole to generic lansoprazole, unless expressly forbidden by the physician.[21] A second type of switching – from brand to brand of different molecules – is also common. Physicians might prescribe a different molecule based on experience (Crawford and Shum, 2005), on scientific evidence (Azoulay, 2002), or on information provided by detailing from drug sales representatives (Berndt et al., 1995; Ching and Ishihara, 2010; Ridley, 2014).[22] The third and fourth types of switching (across classes and forms) have received less attention in the literature.

[21] In most states, a pharmacist can substitute generic lansoprazole for branded lansoprazole unless the physician forbids it, for example by writing "do not substitute" (in California) or "dispense as written" (in Colorado) on the prescription.

[22] There is mixed evidence about which of the aforementioned types of switching is more important. Ellison et al. (1997) found that competition between a brand and its generic is greater than between brands. However, Lichtenberg and Philipson (2002) found the opposite.

Our model allows products with the same characteristics in any of our types of differentiation to be better substitutes than those products that are not. For example, a consumer taking branded omeprazole might consider branded lansoprazole to be a better substitute than generic omeprazole. Similarly, a consumer that prefers capsules (due to their faster release time) may let the form drive their choice of therapy.

3.1 Theory

Consumer choice is modeled using a differentiated products, discrete choice demand system. Potential buyers choose one of $J_t + 1$ treatments, with the first J_t requiring a prescription (the remaining choice being the "outside good"). Consumer i's conditional indirect utility from choosing product j in period t is given by:

$$u_{ijt} = \alpha p^c_{jt} + X_{jt}\beta + \zeta_j + \xi_{jt} + \epsilon_{ijt}, \tag{1}$$

where p^c_{jt} is the time-t copayment (consumer price) for product j (described in detail shortly), X_{jt} is a set of time-varying observed product characteristics (e.g. advertising), ζ_j is a product-specific intercept (fixed effect) that captures any product characteristics (observed or unobserved) that are fixed over time, and ξ_{jt} is a time-varying random effect that captures unobserved shocks to demand, promotional activity, or changes in brand equity. Note that the coefficient on copayment gives us the utility-to-dollars conversion. Individual preference heterogeneity enters through an idiosyncratic taste parameter ϵ_{ijt}, that is independent across buyers but may be correlated among similar products. The *mean* utility (across consumers) for product j at time t is then given by

$$\delta_{jt} = \alpha p^c_{jt} + X_{jt}\beta + \zeta_j + \xi_{jt}. \tag{2}$$

A flexible distribution for ϵ_{ijt} is essential for capturing rich substitution patterns, which play a key role in the counterfactual exercises that follow. To do so, we use the approach developed by Bresnahan et al. (1997) which extends the familiar nested logit to allow unobserved preferences to be correlated across multiple nests.[23] For example, the unobserved preference for a particular form of a branded drug will be correlated with the unobserved preferences for other drugs of the same form but will also be correlated with the unobserved preferences for other branded drugs. In particular, we assume that the unobserved preference parameters follow a generalized extreme

[23] An alternative is the random coefficients (mixed) logit framework developed by Berry et al. (1995) which does not require an ex-ante choice of nests and yields flexible substitution patterns. We believe the Principles of Differentiation Generalized Extreme Value (PDGEV) approach developed by Bresnahan et al. (1997) to be a reasonable choice in our context because 1) the set of nests (or clusters) of products is straightforward here, 2) the relevant product characteristics are almost exclusively binary, and 3) we do not have access to rich demographic or multi-market share data that are key to pinning down a more flexible distribution of random parameters (we must rely on changes over time in the set of available products and their relative prices). See Bresnahan et al. (1997) for a detailed discussion of the mechanism by which the PDGEV approach affords richer substitution patterns than the either the multinomial or nested logit.

value (GEV) distribution with multivariate cumulative distribution function $F(\epsilon_{i0t}, \ldots, \epsilon_{iJt})$. From Proposition 1 of McFadden (1978),

$$F\left(\epsilon_{i0t}, \ldots, \epsilon_{iJt}\right) = \exp[-G(e^{\epsilon_{i0t}}, \ldots, e^{\epsilon_{iJt}})] \tag{3}$$

implying that the market share for product j at time t is given by:

$$s_{jt} = \frac{e^{\delta_{jt}} G_j\left(e^{\delta_{0t}}, \ldots, e^{\delta_{Jt}}\right)}{G\left(e^{\delta_{0t}}, \ldots, e^{\delta_{Jt}}\right)} \tag{4}$$

where G_j is the partial derivative of G with respect to the j^{th} argument. Let L indicate the number of (observed) characteristics on which the unobserved preferences may be correlated and let λ_l denote the possible values of characteristic l, for $l = 1, \ldots, L$. Following Bresnahan et al. (1997), we can then specify G as:

$$G\left(e^{\delta_t}\right) = e^{\delta_{0t}} + \sum_{l=1}^{L} a_l \left[\sum_{k \in \lambda_l} \left(\sum_{j=1}^{J} I(j,k,l) e^{\frac{\delta_{jt}}{\rho_l}}\right)^{\rho_l}\right], \tag{5}$$

where $I(j,k,l)$ is an indicator variable taking on the value one if product j has the k^{th} value of the l^{th} characteristic and $\rho_l \in [0,1]$ is the nesting parameter along the l^{th} dimension. Finally, the scaling parameters a_l are defined as:

$$a_l = \frac{1 - \rho_l}{\sum_{l=1}^{L}(1 - \rho_l)},$$

which assures the a's for any product j add up to one and the properties of a multivariate GEV distribution are satisfied for $\rho \in [0,1]$.

The market share of product j at time t can then be found by differentiating the log of G with respect to its j^{th} element, and can be computed in closed form. Denoting k_{jl} as the value that product j has on the l^{th} dimension,

$$s_{jt} = \frac{1}{G(e^{\delta_t})} \sum_{l=1}^{L} a_l e^{\delta_{jt}/\rho_l} \left[\left(\sum_{j'=1}^{J} I(j', k_{jl}, l) e^{\delta_{jt}/\rho_l}\right)^{\rho_l}\right]. \tag{6}$$

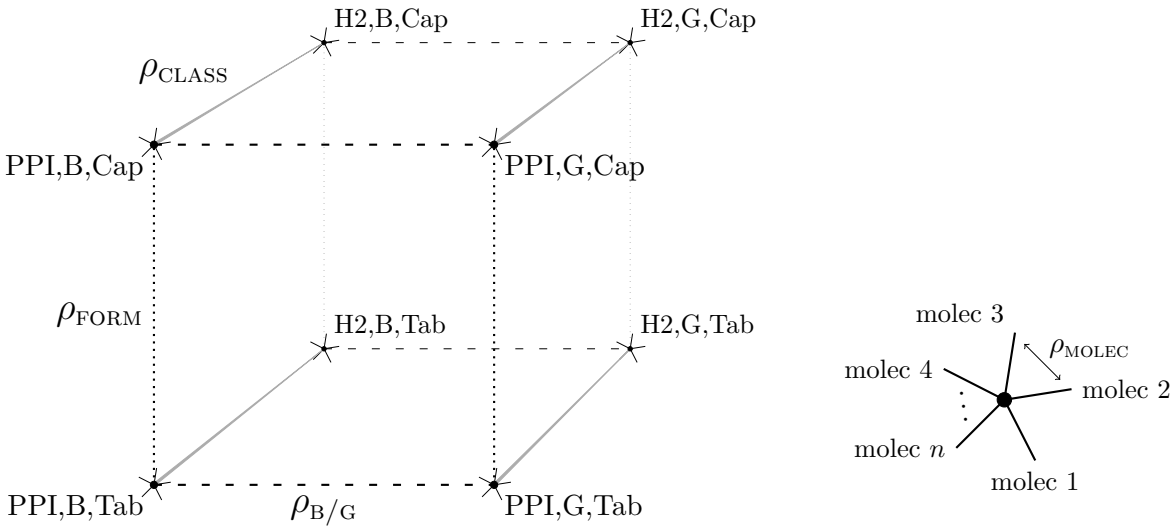
with the outside good's share given by:

$$s_{0t} = \frac{e^{\delta_{0t}}}{G\left(e^{\delta_t}\right)}. \tag{7}$$

Note that, as in Bresnahan et al. (1997), when all ρ's go to 1, we move to a multinomial logit, whereas when all ρ's but one go to 1, we move to a nested logit.

Figure 5 illustrates the nesting structure. For the cube on the left, each vertex represents a unique combination of the class, brand/generic, and form. The gray edges represent substitution

Figure 5: Nesting Structure and Substitution Parameters



across classes. The dashed edges represent substitution between branded and generic drugs. The dotted edges represent substitution across forms. At each vertex, there are a given number of molecules (generally greater than two, and varies for different class-brand/generic-forms). Each molecule is represented by a single spoke of a vertex, as shown by the close-up on the right.[24]

3.2 Copayments and Price

The price a consumer pays (p^c_{jt}) is different from the price received by the pharmaceutical manufacturer (p_{jt}) due to insurance. First, the insurer sets copayment tiers. For example, an insurer sets generic copayments at \$10, preferred branded copayments at \$30, and non-preferred branded copayments at \$50. While we do not model the optimal formulary structure for insurers, these decisions are likely independent of any one drug or class of drugs. Second, the insurer assigns drugs to tiers based on the price. For example, if the price of Nexium is high, then Nexium is assigned to the non-preferred branded tier of \$50. We model the relationship between copayment and price as a power function where the power is less than one.[25] In particular, we assume log copayments are a linear function of log price:

$$\ln\left(p^c_{jt}\right) = \phi_0 + \phi_1 \ln\left(p_{jt}\right) \tag{8}$$

[24]To be clear, molecule does not constitute a lower level nest; however, there is no molecule that exists as both an H2 and as a PPI, so there cannot be substitution across classes without substitution across molecules. Molecules are depicted differently in Figure 5 in part because at least one of the four types of differentiation could not be depicted as a spatial dimension, and also because it is the only type that is not binary, so that representing molecules along a spatial dimension would have required a substantially more complicated diagram.

[25]The power function pushes low copayments higher and high copayments lower. This matches reality, because copayments are rarely as low as the lowest price (some people have generic copayments of \$10 while Wal-Mart sells some generics for \$4) and rarely as high as the highest price (which is the nature of insurance).

We estimate the parameters of equation (8) using our SDI Health data merged with AdvancePCS copayment data.[26]

We use these estimates and our data on prices to form predicted copayments for branded drugs in all periods in which they did not face generic competition as none of the drugs in the AdvancePCS data faced generic competition. To obtain copayments for generic drugs and branded drugs with generic competitors, we assume that the curvature of the pricing relationship is the same as in (8). For generic drugs, we adjust the price level such that the average price of generics are equivalent to the average price of generics given in Kaiser Family Foundation's report "Employer Health Benefits Survey 2013."[27] For branded drugs who face generic competition, we add an indicator variable to the indirect utility function, implying that facing generic competition leads to a level change in the copayment formula.

3.3 Outside Good

Estimation of an aggregate discrete choice demand system requires the overall sales (or market shares) of the inside goods as well as the number of consumers who choose the outside good. To construct the share (and overall size) of the outside good, we assume the market for H2 antagonists and PPIs is 20% of the total U.S. population (the estimates are not particularly sensitive to this choice), which is in the range reported by Fedorak et al. (2010). Multiplying the 20% prevalence by the U.S. population gives the market size. For example, in December 2010 the U.S. population was 311 million, so the overall market size is assumed to be 62 million.

In addition to prescription drugs, there are over-the-counter drugs available without a prescription. The first over-the-counter H2 (famotidine) became available in 1995 (Ling et al., 2002), and the first over-the-counter PPI (omeprazole) became available in 2003. Over-the-counter drugs are typically available at half the prescription strength and may be viewed as competing with other over-the-counter drugs (including calcium carbonate which is sold as "Tums"). Over-the-counter H2s and PPIs are a small share of the market that changes little over time. For example, according to an analyst report, over-the-counter drugs accounted for a mean of 16% (standard deviation of 2%) of the retail PPI market from February 2009 to February 2012.[28] Nevertheless, it is important to account for over-the-counter sales.

We account for changes in the over-the-counter market in two ways. First, we include time dummies that vary by class. Hence, over-the-counter drugs can have differential effects by class. We assume that when an H2 drug goes over-the-counter, it affects all H2 prescriptions in the same way and all PPI prescriptions in the same way, but the effects may vary across classes. We are able to include time dummies by class because we have twenty years of monthly data. Second, we

[26] In subsequent estimation stages, we treat these imputed prices as given. Alternatively, the entire procedure could be bootstrapped (or the moments efficiently stacked) to improve inference.

[27] http://ehbs.kff.org/

[28] Source: BofA Merrill Lynch Global Research using IMS Health prescription data and Nielsen over-the-counter data, April 2012.

include a dummy variable for whether an over-the-counter drug of the same molecule exists and interact this variable with generic status. In this way we relax the assumption that when a PPI goes over-the-counter it affects all PPI's identically as well as allowing the competitive effects of over-the-counter drugs to vary by branded/generic status.

3.4 Time-Varying Characteristics

We allow for time-varying product characteristics, X_{jt}, to affect utility (any time-invariant characteristics will be subsumed by the product-specific fixed effects). First, as described above, we allow for time dummies that vary by class. This is important because consumer perceptions and over-the-counter offerings may change over time.

Second, we include cumulative log advertising at the molecule-manufacturer-month level. As discussed in the data section, our measure of advertising is detailing, which only occurs for branded drugs. In previous studies of the effect of detailing on demand for antiulcer drugs, the estimated depreciation rate for the (detailing) advertising stock was zero percent (Berndt et al., 1995; Ling et al., 2002; Ridley, 2014). Hence, we use the advertising stock with zero depreciation. All forms of the same molecule receive the same utility bump from advertising. Note that we treat advertising as exogenous. Advertising schedules and budgets are typically laid out far in advance, and do not react to the high-frequency (monthly) shocks to demand that constitute our econometric error (recall that we include a full set of product fixed effects, which should absorb any omitted factors that are constant over time). Moreover, the inclusion of time-since-entry dummies (discussed next) should account for any tendency to advertise more intensely during the initial introduction phase. Note that we do not attempt to solve for new advertising trajectories when performing counterfactuals.

Third, we include a set of time-since-entry dummy variables for each of the first twelve months after product entry, which may capture product availability or aspects of consumer awareness. The coefficients on the time dummies and on cumulative advertising are allowed to vary by class. Generics gain market share in the first several months after patent-expiration. These time-since-entry variables are an attempt to account for this stylized fact, which has been documented in several empirical studies.[29]

Finally, in addition to the time-varying product characteristics, we also include product-level fixed effects, where a product is defined at the manufacturer-molecule-form level.

3.5 Estimation

Our estimation procedure closely follows the algorithm proposed by Berry (1994) and further developed by Berry et al. (1995). A key econometric issue is the endogeneity of price, which will be correlated with the structural error ξ_{jt} via the strategic price-setting process employed by the firms. This endogeneity is controlled for using instrumental variables, an approach which first extracts ξ_{jt}

[29] It is possible that these time dummies are accounting for learning effects as in Ching (2010b).

from the (nonlinear) share equation (6) by inverting the shares and solving for the mean utilities (δ_{jt}'s) using a contraction mapping similar to that of Berry et al. (1995). Denote the mean utilities computed by this inversion as $\delta(s, \rho)$, a function of the observed market shares and the non-linear parameters that index the GEV distribution (the remaining linear parameters are packed within the mean utilities). We can then compute ξ_{jt} as

$$\xi_{jt} = \delta_{jt}(s_t, \rho) - \left(\alpha p^c_{jt} + X_{jt}\beta + \zeta_j\right), \tag{9}$$

Exploiting an orthogonality condition between the structural error and a vector of suitable instruments, Z_{jt}, estimation proceeds using the standard Generalized Method of Moments (GMM) criterion function given by

$$\min_{\rho,\alpha,\beta} : \xi' Z W^{-1} Z' \xi, \tag{10}$$

in which W is the appropriate weighting matrix.

Identifying suitable instruments is difficult for discrete choice demand systems as the usual supply side candidates (e.g., cost shifters) tend not to vary by product. We follow Bresnahan et al. (1997), Berry et al. (1995), and the majority of the empirical industrial organization literature in using instruments that exploit the (assumed) exogeneity of the X's and the induced variation in markups implied by each product's relative isolation in product space (often called "Bresnahan style" instruments after Bresnahan (1981, 1987)).[30] Here we use the number of competitors in particular categories to capture this source of exogenous variation. In particular, we use: the number of molecules for the same form, number of molecules of the same form in the same class, whether generics are present in the same form, whether generics are present in the same molecule, number of generics present of the same molecule, number of generics present of the same form, and number of generics present of the same form in the same class.

4 Supply

Consistent estimation of the demand system does not require a supply side, but performing counterfactuals does, because we will need to predict how prices change when products are added or deleted from the market.[31] We follow the convention of the empirical industrial organization

[30] We explored various subsets of the instruments to ensure robustness. Another approach, employed by Hausman (1996) and Nevo (2000, 2001), uses prices of the product in other (geographically separate) submarkets as instruments. Because our data are drawn from a single (national) market, we cannot use this strategy.

[31] We assume Bertrand (price) competition rather than Cournot (capacity) competition because branded manufacturers do not have binding capacity constraints. Typically branded manufacturers have excess capacity because of the high opportunity cost of lost sales. However, generic manufacturers, especially manufacturers of generic sterile injectables, do sometimes face capacity constraints. This is evident in the fact that nearly all drug shortages are for injectable generic drugs (Woodcock and Wosinska, 2012). Injectable drugs are not relevant for our analysis, because we focus on oral solid forms (tablets and capsules) that comprise the vast majority of prescriptions in the antiulcer market.

literature in assuming a static, multi-product Nash equilibrium in prices.[32] Using the first order conditions from this pricing game, we can find the implied marginal costs and associated measures of market power (for example, markups and price-cost margins). We closely follow the notation of Nevo (2000) in what follows.

Each firm f produces a subset, $\mathcal{F}_f$, of the $j = 1, \ldots, J$ different products in a specific period. The profits for firm f are then given by[33]

$$\Pi_f = \sum_{j \in \mathcal{F}} (p_j - mc_j) M s_j(p) - C_f \tag{11}$$

where $s_j(p)$ is the market share of brand j, mc_j is its marginal cost, M is the size of the market, and C_f is the fixed cost of production (both M and C_f drop out of subsequent calculations). The first-order condition determining the price of product j produced by firm f is then given by

$$s_j(p) + \sum_{k \in \mathcal{F}_f} (p_k - mc_k) \cdot \frac{\partial s_k(p)}{\partial p_j} = 0. \tag{12}$$

To solve for the implied marginal costs, first define $S_{jk} = -\frac{\partial s_k(p)}{\partial p_j}, j, k = 1, \ldots, J$ and

$$\Omega_{jk} = \begin{cases} S_{jk}, & \text{if } \exists f : \{j, k\} \subset \mathcal{F}_f \\ 0, & \text{otherwise,} \end{cases} \tag{13}$$

where Ω is a $J \times J$ matrix. In vector notation, the first order conditions can be written as

$$s(p) - \Omega \cdot (p - mc) = 0 \tag{14}$$

Assuming Ω is non-singular, marginal costs are then given by

$$mc = p - \Omega^{-1} s(p). \tag{15}$$

Implied markups and price-cost margins follow directly. The recovered marginal costs can be projected onto additional covariates to model their evolution over time and across products, but

[32] We follow the majority of the empirical IO literature in treating the supply side as a static, Nash-in-prices, stage game. This approach facilitates the computation of counterfactuals and mirrors a large empirical literature on differentiated products, but does ignore some potentially important dynamics that could arise from consumer switching costs or strong brand loyalty. If firms are able to influence these costs or exploit this loyalty through their pricing decisions, a static supply side would ignore these incentives. In fact, there is evidence that pharmaceutical firms will sometimes price a new product quite low (leaving the price of the old version high) in combination with a strong advertising campaign to direct patients to the new product (e.g. AstraZenaca's marketing of Nexium). Note that this would not impact our demand side estimates, so long as consumers remain myopic, but could impact the results of our counterfactuals.

[33] Note that the firm chooses price which then gets translated into copayment according to $p_j^c = \exp(\phi_0) p_j^{\phi_1}$ (see equation (8)). While it is the copayment that is relevant for calculating consumer demand, *revenues* are given by *price* (rather than copayment) times the quantity demanded.

we must first address the role of manufacturer rebates.

4.1 Rebates

Another complication that arises in the context of pharmaceutical competition is the extensive use of rebates paid by the manufacturer to the insurer. As noted earlier, we have a good measure of rebate levels prior to generic entry but do not observe them thereafter. We now propose a simple model to estimate rebate levels after generic entry, which again exploits our assumed model of conduct and the first order conditions that determine optimal prices.

Consider a single product branded firm producing product j. With the firm choosing p_{jt} at time t, its profit maximization problem reduces to:

$$\max_{p_{jt}}(p_{jt} - mc_{jt})s_{jt}(p) \tag{16}$$

where p includes j's price as well as competitor prices.

To incorporate rebates, let r_{jt} denote the time-t rebate's proportion of the price, the firm's problem changes to:

$$\max_{p_{jt}}((1 - r_{jt})p_{jt} - mc_{jt})s_{jt}(p) \tag{17}$$

with first order condition given by:

$$0 = (1 - r_{jt})s_{jt}(p) + ((1 - r_{jt})p_{jt} - mc_{jt})\frac{\partial s_{jt}(p)}{\partial p_{jt}} \tag{18}$$

Let τ_{jt} be time since entry and let g and h be flexible functions of time and time since entry, respectively. We specify marginal costs as:

$$mc_{jt} = \gamma_j + g(t) + h(\tau_{jt}) + \varepsilon_{jt}, \tag{19}$$

where γ_j is a product fixed effect and ε_{jt} is white noise. The flexible function of time, $g(t)$, captures differences in input prices that affect everyone. The flexible function of time since entry, $h(\tau_{jt})$, allows for learning by doing.[34] In practice, we use monthly indicator variables for time and time since entry, stopping the latter after 36 months.

We assume that all firms charge the same rebate prior to generic entry (assumed to equal 15.1%), and adjust immediately to a new common rebate upon generic entry. Denote the firm's rebate level before generic entry by r_{PRE}. We want to obtain r_{POST}. For periods before generic entry, we can express known variables (p_{jt}, $s_{jt}(p)$, $\partial s_{jt}(p)/\partial p_{jt}$, r_{PRE}) as a function of marginal costs:

$$(1 - r_{PRE})\left(p_{jt} + \left(\frac{\partial s_{jt}(p)}{\partial p_{jt}}\right)^{-1} s_{jt}(p)\right) = \gamma_j + g(t) + h(\tau_{jt}) + \varepsilon_{jt} \tag{20}$$

[34] See Scott Morton (1999) and Gallant et al. (2011) for the importance of experience in the pharmaceutical market.

Table 3: Regression results. Dependent variable is Ln(copayment).

	Coefficient	Standard Error
Constant	2.558	(0.279)
Ln(price)	0.113	(0.056)

N=100. Observations are at the insurance group-molecule-month level.

Table 4: Nesting Parameters

	Coefficient	Standard Error
Class	0.628	(0.330)
Brand	0.722	(0.389)
Form	0.538	(0.276)
Molecule	0.050	

N=8169. The molecule parameter converged to the lower bound of 0.05

Let I_{POSTt} be an indicator for periods post generic entry. We can express the relationship above for all periods as:

$$(1 - r_{PRE}) \left(p_{jt} + \left(\frac{\partial s_{jt}(p)}{\partial p_{jt}} \right)^{-1} s_{jt}(p) \right) = (1 + \pi I_{POSTt})(\gamma_j + g(t) + h(\tau_{jt}) + \varepsilon_{jt}) \tag{21}$$

Estimating π using data on multiple products over time allows us to back out r_{POST} via:

$$1 - r_{POST} = \frac{1 - r_{PRE}}{1 + \pi} \tag{22}$$

where we expect $\pi > 0$, implying rebates are bigger in the post-period.[35]

5 Results

Key demand-side parameter estimates are presented in Tables 3, 4, and 5. Table 3 contains the parameter estimates that link copayment to price. The coefficients show copayment increases with price, but at a diminishing rate. We then use these parameters to form copayments for all periods in the data, taking into account the adjustments outlined in section 3.2.

The non-linear, or nesting, parameters, which drive cross-product substitution, are presented in Table 4. The molecule nesting parameter converged to the set lower limit of 0.05, while the

[35]Some pharmaceutical manufacturers increase rebates to slow falling sales from generic competition. For example, "In the face of sudden generic discounts, Pfizer seems to have given a lot of rebates to keep Lipitor on insurance company formularies," according to Matthew Herper writing in *Forbes* in May 2012.

Table 5: Linear Parameters

			Interaction with PPI	
	Coefficient	Standard Error	Coefficient	Standard Error
Copay	−0.545	(0.070)		
Brand x generic competition	−0.063	(0.115)		
Own-Molecule OTC	−0.484	(0.113)		
Brand x Own-Molecule OTC	0.492	(0.112)		
Ln Cumulative Advertising	2.196	(0.247)	−0.440	(0.205)
1 month on market	−1.389	(0.091)	−0.292	(0.174)
2 month	−0.617	(0.091)	−0.090	(0.183)
3 month	−0.486	(0.092)	0.003	(0.182)
4 month	−0.392	(0.091)	0.082	(0.184)
5 month	−0.319	(0.092)	0.052	(0.187)
6 month	−0.234	(0.093)	−0.060	(0.183)
7 month	−0.258	(0.088)	0.097	(0.198)
8 month	−0.208	(0.09)	−0.012	(0.192)
9 month	−0.202	(0.089)	0.040	(0.194)
10 month	−0.189	(0.088)	0.116	(0.198)
11 month	−0.144	(0.088)	0.140	(0.198)
12 month	−0.122	(0.088)	0.102	(0.198)

N=8169. Estimated jointly with nesting parameters. Also includes manufacturer-molecule-form fixed effects, month dummies, and month dummies cross PPI. There are 614 linear parameters.

other nesting parameters did not. This indicates that drugs of the same molecule are very good substitutes, i.e. consumers are particularly resistant to switch from their preferred molecule. For example, if generic omeprazole capsules are removed from the market, a consumer who buys generic omeprazole capsules is more inclined to switch to the branded or tablet versions of their preferred drug than to generic capsules of a different molecule. The other nesting parameters range from 0.54 to 0.72, reflecting a correlation across products with similar characteristics that is strongest along the form dimension and weakest along the brand/generic dimension, which indicates that consumers are more particular with regards to their preferred form than with regards to a drug's class or brand/generic status. The fact that most of our estimated substitution parameters do not converge to a boundary helps justify our flexible framework because imposing either of the possible extreme assumptions (i.e. perfect substitutes or non-substitutes) would have prevented us from explaining regularities in the data.

Table 5 presents selected linear parameters. The price and advertising coefficients indicate – not surprisingly – that consumers buy products with low prices and heavy advertising, all else equal. Advertising has slightly less impact for PPIs, perhaps because H2 advertising has already made consumers aware of the availability of antiulcer drugs. The time-since-entry coefficients suggest new products can take a year to gain traction. PPIs are particularly slow in the first month, but are much like H2s later. Finally, generic drugs facing over-the-counter competition in the same molecule see lower demand. This is not true for branded drugs indicating that over-the-counter drugs are seen as better substitutes for generics.

5.1 Elasticities

A strength of the Bresnahan et al. (1997) estimation approach is it accommodates flexible substitution patterns. Tables 6 and 7 present own and cross-price elasticities. Table 6 is for the last period in our data (December, 2010) and Table 7 is for an earlier period (December, 2005). The columns associated with each drug report how its market share responds to price changes by each alternative. We report results for all branded drugs, as well as for the most popular generic version of each molecule. Consistent with economic theory, all own-price elasticities are less than negative one.[36] Own-price elasticities are also substantially higher for generics, reflecting the more competitive nature of the generic portion of the market.

The most interesting patterns are revealed by the set of cross-price elasticities. In particular, the cross-substitution effects are strongest for alternative drug therapies that share class, brand/generic status, form, or molecule; they are also stronger from products with high shares. Consider lansoprazole, which has two branded forms (capsule and tablet) as well as a generic option. The two branded forms have limited effects on each other, primarily because they are small players. Changes in the price of generic pantoprazole, which is a tablet, has a substantial effect on branded

[36] In contrast, before correcting prices for the role of copayments, we found that the majority of firms were pricing on the inelastic portion of the demand curve.

lansoprazole tablets, with a cross-price elasticity of 0.69, while the cross-price elasticity for branded lansoprazole capsules is only 0.10. Generic lansoprazole (a capsule) likewise has asymmetric effects on the two forms of branded lansoprazole. If we consider the earlier period in Table 7, generic lansoprazole is not present and branded lansoprazole capsules has a much larger share of the market than in Table 6. Consequently, changing prices for branded lansoprazole capsules results in much larger cross-price elasticities in Table 7 than in Table 6.

Pantoprazole is the only PPI with relatively large shares of tablets. This combined with the presence of few generic pantoprazole manufacturers results in an enormous impact of price changes by the leading generic pantoprazole manufacturer on the market share of branded pantoprazole. The effects are again not symmetric, as branded pantoprazole has significantly fewer sales than its generic counterpart. Further illustrating the importance of the size among similar drugs, price changes by esomeprazole (the leading branded drug), have large effects on the shares of other branded molecules. This effect is particularly strong for those molecules with a generic competitor, in which case branded manufacturers compete almost exclusively for patients who strongly prefer branded drugs.

Table 6: Elasticity and Cross Price Elasticity Estimates for December 2010

			H2 Brand		H2 Generic				PPI Brand							PPI Generic		
		Share	*famotidine*	*ranitidine*	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*dexlansoprazole*	*esomeprazole*	*lanso. (cap)*	*lanso. (tab)*	*omeprazole*	*pantoprazole*	*rabeprazole*	*lansoprazole*	*omeprazole*	*pantoprazole*
H2 B	famotidine	0 %	-2.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0 %	0.01	-2.26	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.00
H2 G	cimetidine	0.03 %	0.01	0.01	-7.61	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	famotidine	0.34 %	0.19	0.21	0.04	-3.73	0.03	0.14	0.00	0.00	0.00	0.08	0.00	0.10	0.03	0.01	0.01	0.05
	nizatidine	0.02 %	0.00	0.00	0.00	0.00	-10.21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.53 %	0.47	0.51	0.10	0.21	0.07	-6.12	0.01	0.01	0.01	0.22	0.01	0.27	0.07	0.02	0.02	0.13
PPI B	dexlansoprazole	0.43 %	0.15	0.13	0.01	0.01	0.01	0.01	-1.52	0.07	0.18	0.15	0.20	0.10	0.04	0.02	0.03	0.01
	esomeprazole	3.39 %	1.75	1.59	0.05	0.05	0.07	0.05	0.58	-1.71	2.62	1.87	2.72	1.33	0.46	0.38	0.73	0.17
	lanso. (cap)	0.08 %	0.14	0.13	0.00	0.00	0.00	0.00	0.04	0.06	-2.25	0.14	0.20	0.10	0.03	0.03	0.03	0.01
	lanso. (tab)	0.04 %	0.08	0.08	0.00	0.01	0.00	0.02	0.02	0.02	0.07	-2.27	0.08	0.10	0.03	0.00	0.01	0.03
	omeprazole	0.01 %	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.02	-2.23	0.01	0.00	0.00	0.00	0.00
	pantoprazole	0.37 %	0.56	0.57	0.05	0.14	0.01	0.26	0.09	0.14	0.44	0.89	0.51	-5.05	0.24	0.03	0.04	8.88
	rabeprazole	0.5 %	0.24	0.24	0.02	0.05	0.01	0.10	0.05	0.07	0.20	0.36	0.24	0.34	-1.70	0.02	0.02	0.11
PPI G	lansoprazole	0.52 %	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.05	0.19	0.04	0.07	0.04	0.02	-6.36	0.08	0.03
	omeprazole	2.27 %	0.03	0.03	0.06	0.07	0.07	0.09	0.15	0.38	0.63	0.24	0.47	0.22	0.08	0.30	-5.08	0.16
	pantoprazole	1.11 %	0.23	0.28	0.08	0.20	0.03	0.35	0.03	0.05	0.10	0.69	0.09	25.08	0.22	0.07	0.09	-2.53

Rows correspond to price changes and columns correspond to quantity changes. For example, if the price of branded esomeprazole falls 1% then demand for generic omeprazole falls by 0.73%. Shares for generics correspond to the top-selling generic of that molecule.

Table 7: Elasticity and Cross Price Elasticity Estimates for December 2005

			H2 Brand				H2 Generic				PPI Brand						PPI Generic
		Share	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*cimetidine*	*famotidine*	*nizatidine*	*ranitidine*	*esomeprazole*	*lanso. (cap)*	*lanso. (tab)*	*omeprazole*	*pantoprazole*	*rabeprazole*	*omeprazole*
H2 B	cimetidine	0 %	-2.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	famotidine	0 %	0.02	-2.09	0.02	0.02	0.00	0.00	0.00	0.01	0.00	0.00	0.01	0.00	0.00	0.00	0.00
	nizatidine	0 %	0.01	0.01	-2.35	0.01	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.01 %	0.05	0.05	0.05	-2.21	0.01	0.01	0.01	0.02	0.00	0.00	0.02	0.01	0.01	0.01	0.00
H2 G	cimetidine	0.05 %	0.02	0.03	0.02	0.03	-7.44	0.01	0.01	0.02	0.00	0.00	0.01	0.00	0.00	0.00	0.01
	famotidine	0.17 %	0.10	0.12	0.10	0.12	0.04	-5.86	0.03	0.07	0.00	0.00	0.04	0.00	0.02	0.02	0.02
	nizatidine	0.02 %	0.01	0.01	0.63	0.01	0.00	0.01	-12.23	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	ranitidine	0.49 %	0.40	0.48	0.41	0.52	0.14	0.19	0.12	-5.33	0.01	0.01	0.19	0.01	0.11	0.08	0.07
PPI B	esomeprazole	3.3 %	0.96	0.76	1.34	0.68	0.05	0.05	0.16	0.05	-1.67	1.46	1.35	2.75	0.52	0.44	0.93
	lanso. (cap)	2.8 %	0.81	0.64	1.10	0.57	0.04	0.04	0.13	0.04	1.24	-1.69	1.12	2.24	0.43	0.37	0.74
	lanso. (tab)	0.1 %	0.12	0.13	0.07	0.14	0.02	0.03	0.00	0.05	0.04	0.04	-2.16	0.12	0.12	0.09	0.02
	omeprazole	0.04 %	0.04	0.03	0.04	0.03	0.00	0.00	0.00	0.00	0.03	0.03	0.04	-2.23	0.02	0.01	0.02
	pantoprazole	2.25 %	1.05	1.30	0.50	1.45	0.23	0.39	0.03	0.68	0.34	0.33	2.70	0.92	-1.63	1.02	0.20
	rabeprazole	1.01 %	0.39	0.46	0.21	0.50	0.08	0.13	0.01	0.22	0.14	0.13	0.91	0.37	0.47	-1.69	0.08
PPI G	omeprazole	0.36 %	0.00	0.00	0.04	0.00	0.04	0.05	0.06	0.06	0.09	0.09	0.07	0.15	0.03	0.03	-9.15

Rows correspond to price changes and columns correspond to quantity changes. Shares for generics correspond to the top-selling generic of that molecule.

Relative to 2010 (Table 6), there are more branded H2 antagonists and fewer generic PPIs available in 2005.

5.2 Marginal Costs and Rebates

Having estimated our model of consumer behavior, we can now use our model of price-setting to recover marginal costs. Recall branded drug manufacturers provide rebates to insurance companies that may change once a generic of the same molecule enters the market. Illustrating how ignoring rebates leads to implausible marginal cost implications, Figure 6 plots implied marginal costs for pantoprazole as a function of months since generic entry. There is little reason to expect the sharp jump in production costs (shown by the vertical segment of the graph) once the first generic enters the market. Examining other molecules reveals similar patterns.

The jumps are driven by the relatively muted price response of branded drugs to generic competition. Recall how quickly branded firms lost share to generic producers upon generic entry. Once generic competition is present, we would have expected branded drug prices to drop, all else equal. But branded prices show little response to generic competition. Hence, absent rebate adjustments, the model "rationalizes" the lack of a price response by a substantial increase in marginal costs.

As described in section 4.1, our model of rebate adjustment allows firms to respond to the increase in competition through this channel as well. In practice, we estimate equation (21) using data from single product branded firms where we see a generic entrant and generic firms producing those same molecules. The set of molecules satisfying these restrictions are cimetidine, famotidine, nizatidine, and pantoprazole. In effect, we are exploiting an assumed common temporal pattern in the adjustment of marginal costs across branded and generic manufacturers to pin down the more discrete adjustment in the rebate level implied by optimal pricing behavior.

Table 8 presents supply-side results. Relative to cimetidine, famotidine has lower marginal costs while nizatidine and pantoprazole have higher marginal costs. The marginal cost for nizatidine is particularly high, reflecting its status as the only capsule among the four molecules. Branded molecules have significantly higher marginal costs. The (market-share-weighted) average marginal cost for generic molecules in the last period of the data was \$28.25. Hence, the \$23.65 additional cost for branded drugs is a substantial premium. For the counterfactual policy simulations, the key parameter is the post-generic rebate. Our estimates suggest average branded drug rebates increase from 15.1% to 48.3% once a generic version enters the market.

Are our post-generic rebate estimates reasonable? While rebates are not publicly available, we can do a "back-of-the-envelope" estimate of rebates and compare it to our results. Companies publish revenue net of rebates in their annual reports. Some companies even break out the net revenue by company and drug. In those cases, we can compare the net revenue to sales data. However, our sales data include only retail sales and omit hospital sales. Hence, we obtained another data set that includes annual data on both hospital and retail sales, albeit for fewer years. By subtracting a company's reported net revenue from total sales, we can estimate rebates. We were able to find net revenue in company annual reports for two of the three PPIs in our sample facing generic competition.[37]

[37] We did not find data for lansoprazole which was sold by a Japanese firm in an alliance with a U.S. firm.

Table 8: Marginal Cost and Rebate Parameters

	Coefficient	Standard Error
Post-generic rebate	0.483	(0.002)
Branded	23.652	(0.044)
Famotidine	−10.732	(0.041)
Nizatidine	10.367	(0.045)
Pantoprazole	9.549	(0.056)
3 months since entry	11.978	(0.196)
6 months	10.391	(0.194)
1 year	7.610	(0.200)
3 years	2.037	(0.189)

N=2142. Additional controls included month dummies and month since entry up to 36 months. Reference molecule is cimetidine.

Omeprazole faced generic competition beginning in November 2002. In 2002, the difference between our sales data and the company reported net revenue for omeprazole sales in the U.S. was 18%. In 2003, the difference rose to 44%. This increase is consistent with an increase in rebates following generic entry. Likewise, pantoprazole faced generic competition beginning in December 2007. In 2007, the difference between our sales data and the company reported net revenue was 22%. In 2008, the difference rose to 36%. Similarly, this increase is also consistent with an increase in rebates following generic entry.

The estimates also suggest significant learning by doing or economies of scale/scope. Marginal costs fall substantially over three years. Indeed, generic and branded manufacturers actually have similar marginal costs for the first few months after generic entry. The cost advantage of generics comes later. These results were forecast in Figure 3, which reveals that generic prices continue to drop over time. While this could have been caused by increased generic competition, our results indicate a significant portion of the drop is due to falling marginal costs. While it is not possible to identify the source of these economies, they could reflect either learning by doing or scale/scope economies on the part of the generic producers. In particular, as the generic market for a particular molecule expands, the generic producer might switch production from an older, higher cost, production facility to a newer one. Alternatively, they might instead reflect increasing access to efficient distribution channels (e.g. high volume pharmacies) that take time to establish. Khanna et al. (2010) note that "Teva reported unit-cost reductions of 30% in 2001-2005 due primarily to scale effects". As their relationships with large chain pharmacies have expanded, Teva has invested in advanced information systems and automated distribution, streamlining operations and driving down their cost per pill (Singer, 2010).

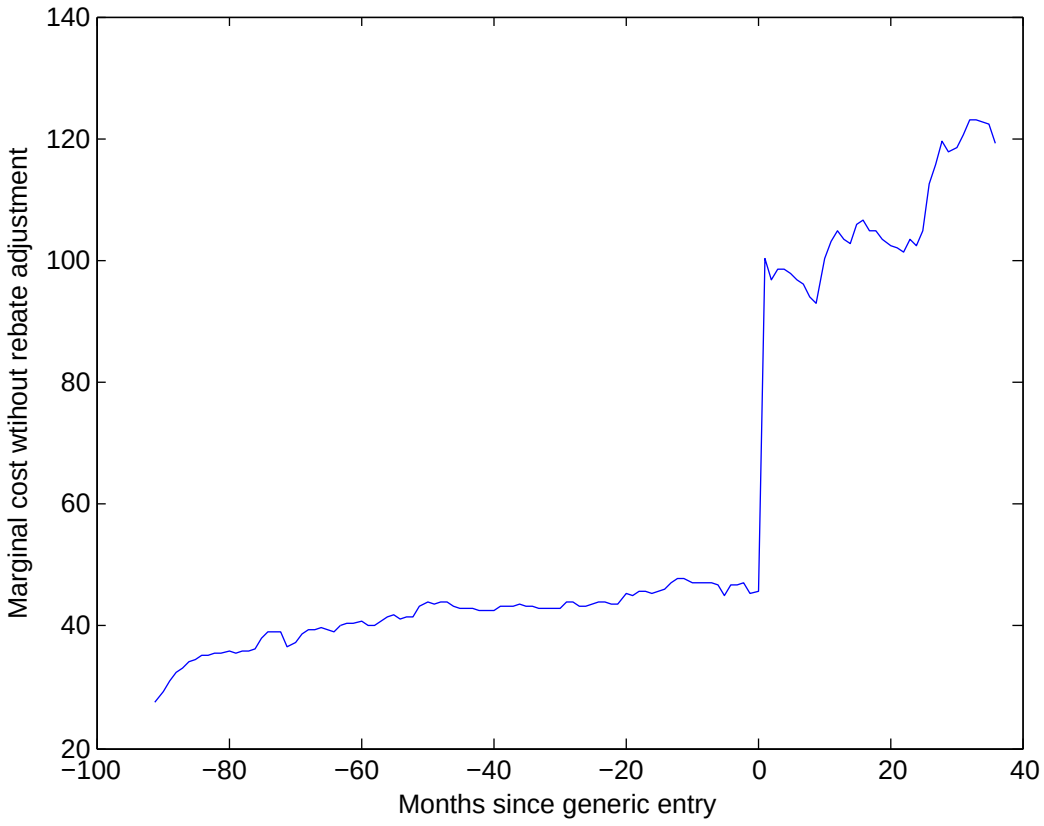


Figure 6: Marginal cost as a function of time since first generic entrant for pantoprazole.

6 Counterfactuals

6.1 Value of Eliminating Pharmaceutical Followers

We can now combine our supply- and demand-side estimates to calculate how equilibrium prices and shares will change under various hypothetical scenarios. We begin by considering three such counterfactuals: (1) no generics, (2) no me-too molecules (only the first in class), and (3) no PPIs.[38] Table 9 lists shares for all molecule-brand/generic combinations in December 2010 for the base case and for the three counterfactuals. In each of the counterfactuals, products are removed, and we consider both the effect when prices adjust and when prices do not adjust. This allows us to differentiate between the price and variety effects.

For each counterfactual, we assume the number of manufacturers is fixed for each of the molecule-brand/generic combinations that are not removed, so that the remaining manufacturers neither enter nor exit. For example, even when generics are removed, we assume that branded drugs that previously exited (branded cimetidine and nizatidine) do not return. We also ran the simulations with those manufacturers returning, but it did not change our results because these were relatively low-quality drugs and would have garnered low market shares regardless of the policy regime.

Removing generic competition cuts the total number of prescriptions by over half. The H2 market, which is dominated by generics, falls to less than one twentieth of its original size. If branded manufacturers did not raise their prices in response to generic exit, then their share would rise from 4.8 to 7.8 percent. With branded manufacturers able to raise price, branded share rises to 7.0 percent instead.

Removing me-too molecules causes an even larger drop in utilization than removing generics. Removing me-toos increases the share of generic omeprazole. However, utilization falls slightly for generic PPIs as a a whole, and falls substantially for generic H2s and branded PPIs. When PPIs are removed from the market, utilization falls about 80%. While generic H2s increase their share by close to a percentage point, this is small compared to the 12 percentage point drop in share purchasing any drug.

The large drops in utilization when generics, me-too molecules, or PPIs are removed might seem dramatic. However, the results make sense given the evolution of the market. As shown in Figure 1, PPIs dramatically expanded the prescription market, suggesting H2s are not particularly good substitutes for PPIs. Further, at the end of our sample period many of the H2s and some of the PPIs were available over-the-counter. In this sense, we may be underestimating the importance of me-too molecules and PPIs due to the accrued benefits once the drug can be obtained without a prescription.

Using the coefficient on copayment from the demand-side estimation and the formulas for ex-

[38] Note that when we remove generics we turn off the brandXgeneric competition variable in Table 5 which adjusted for how copayments for branded drugs are affected by generic competition.

pected utility in a GEV model, we can calculate welfare changes for our counterfactuals. For the counterfactuals, we hold insurance premiums fixed. Given our outside good assumption, consumer surplus changes moving from regime r to r' can be expressed as differences in the log probabilities of choosing the outside good in the two regimes divided by the coefficient on copayment (Arcidiacono and Miller, 2011):

$$\Delta E(CS) = \frac{\ln(s_{0r}) - \ln(s_{0r'})}{\alpha}$$

We express consumer surplus changes in annual terms, taking twelve times the expected individual change and multiplying by the number of afflicted people. Table 10 gives annual spending by insurers, spending by consumers on copayments, variable costs, and profits gross of fixed costs.[39]

If generics are removed, prescriptions fall by over 50%, yet total revenue increases. Revenue increases because the price per prescription increases. Also, without competition from generics, rebates fall. Profit (gross of fixed cost) increases by $1.4 billion. Consumer welfare falls $125 million. Copayments drop because of the fall in prescriptions, but total insurance spending rises because of the increase in price per prescription.

If me-too drugs are removed, annual drug manufacturer profit falls from over $4.5 billion to $354 million. Profit is low because there are fewer drugs, and all remaining drugs face generic competition. Insurance spending falls by $7 billion. Holding insurance premiums constant, consumer welfare loss is $135 million. The consumer welfare loss is small relative to the insurer gains. Some of these gains to insurers could be passed to consumers in lower premiums, higher wages (due to savings in employer-provided insurance), and lower taxes (due to savings in government insurance programs).[40]

[39] Profits gross of fixed costs refers to revenues from insurance companies and consumers minus variable costs. Note that the revenues from insurance companies are net of rebates.

[40] We can compare the counterfactual estimates from Table 10 to the plot of prescriptions from Figure 2. In the base case from Table 10, revenue from H2s and PPIs is over $9 billion in 2010. In Figure 2 in 2010, brand PPI prescriptions are 3 million per month multiplied by $200 per prescription and 12 months per year or over $7 billion. Generic PPI prescriptions are 5 million per month multiplied by $40 per prescription and 12 months per year or over $2 billion. Revenue from H2s in 2010 is negligible because prescriptions and prices are much smaller than PPIs. Hence, the $9 billion from Table 10 is consistent with Figure 2 if we convert from monthly to annual and multiply by price.

Table 9: Simulated Shares (%)

			Prices Adjust			Prices Do Not Adjust		
	Molecule	Base	No Generic	No Me-Too	No PPI	No Generic	No Me-Too	No PPI
H2 Brand	famotidine	0.0	0.0		0.0	0.0		0.0
	ranitidine	0.0	0.1		0.0	0.1		0.0
	Subtotal	0.0	0.1		0.0	0.1		0.0
H2 Generic	cimetidine	0.1		0.1	0.1		0.1	0.1
	famotidine	0.6			0.7			0.8
	nizatidine	0.0			0.0			0.1
	ranitidine	1.4			2.1			2.1
	Subtotal	2.1		0.1	2.9		0.1	3.0
PPI Brand	dexlansoprazole	0.4	0.4			0.5		
	esomeprazole	3.4	3.7			4.4		
	lansoprazole	0.1	0.8			0.6		
	omeprazole	0.0	0.1	0.0		0.1	0.0	
	omeprazole $NaHCO_3$	0.0	0.0			0.1		
	pantoprazole	0.4	1.1			1.4		
	rabeprazole	0.5	0.7			0.6		
	Subtotal	4.8	6.9	0.0		7.7	0.0	
PPI Generic	lansoprazole	1.0						
	omeprazole	5.6		6.2			6.9	
	omeprazole $NaHCO_3$	0.1						
	pantoprazole	1.5						
	Subtotal	8.2		6.2			6.9	
	Total	15.1	7.0	6.3	2.9	7.8	7.1	3.0

Table 10: Simulated Welfare, Spending, and Profit in US Market in 2010 ($US millions)

		Prices Adjust			Prices Do Not Adjust		
	Base	No Generic	No Me-Too	No PPI	No Generic	No Me-Too	No PPI
Revenue	9179	9471	1211	283	9747	1255	289
Variable cost	4675	3564	857	158	4018	958	168
Copayments	1401	814	872	197	1356	554	202
Insurer spending	7778	8657	339	86	8391	702	87
Profit gross of fixed cost	4504	5908	354	125	5729	297	120
Consumer welfare change	0	−125	−135	−183	−113	−123	−183

Table 11: Simulated Generic Esomeprazole as a Function of the Number of Generic Manufacturers

Long run (3 years)					
Number of generic manufacturers	0	1	2	3	4
Branded esomeprazole share (%)	3.4	1.2	0.6	0.5	0.5
Generic esomeprazole share (%)	0.0	3.5	11.2	13.5	15.3
Others (%)	11.7	10.9	10.0	9.5	9.1
Branded esomeprazole price ($US)	205	215	265	268	270
Generic esomeprazole price ($US)		103	56	55	55
Consumer welfare change ($US millions)		7	110	142	167

Short run (3 months)					
Number of generic manufacturers	0	1	2	3	4
Branded esomeprazole share (%)	3.4	2.0	0.6	0.6	0.5
Generic esomeprazole share (%)	0.0	4.2	8.4	10.3	11.7
Others (%)	11.7	10.5	10.5	10.1	9.7
Branded esomeprazole price ($US)	205	172	263	265	267
Generic esomeprazole price ($US)		88	70	69	69
Consumer welfare change ($US millions)		26	73	97	115

The short run differs from the long run because of falling marginal costs and rising perceived quality for generic esomeprazole.

6.2 Forecasting Generic Esomeprazole

Our next set of counterfactuals examine how the entry of generic manufacturers of esomeprazole affects equilibrium prices, shares, and welfare. We focus on esomeprazole —Nexium, the quintessential me-too drug — because it is one of the top-selling drugs of all time and faces generic competition beginning in 2014.

In the long run (greater than 3 years), generics have been on the market sufficiently long so that their perceived quality and marginal costs have stabilized. To perform this counterfactual, we set the quality and marginal cost for generic esomeprazole. Marginal cost for generic esomeprazole is set to $23.65 less than branded esomeprazole, corresponding to estimates in Table 8. For quality, we looked at differences in branded and generic quality for PPIs that faced generic competition, using the median difference.[41] The same quality and marginal cost parameters are used for each of the generics for the cases in which there is more than one generic entrant. The results are reported in Table 11.

Entry of the first generic has little effect on long-run consumer welfare. This occurs for two

[41]If we instead used the average difference in quality between all branded drugs (H2's and PPI's) our estimated consumer welfare gains and generic shares would be even higher, with generic shares rising up to 25%. This would suggest our estimates are lower bounds. However, the outside option may also improve as more drugs move to over the counter. To the extent the outside option improves, we will be over-estimating the effects of generic esomeprazole.

reasons. First, branded esomeprazole must now pay large rebates to the insurers, making it less competitive. Branded prices rise, both because of the increase in the rebate paid and because of incentives for the branded manufacturer to focus on customers who strongly prefer branded drugs. Second, without other generic competitors of the same molecule, the remaining generic esomeprazole is sufficiently differentiated that it can set a higher price. Total utilization changes only slightly with the addition of the first generic.

Adding another generic has a substantial effect on consumer welfare, primarily due to price competition between the generics, as generic prices fall by half. The price cut results in tripling of generic esomeprazole prescriptions. The annualized consumer welfare change is more than $100 million. Gains from additional generic entries are smaller, in part because a single generic provides sufficient price competition. Adding more generics has little effect on prices.

The second panel shows results in the short-run case where generic esomeprazole has been on the market for three months, implying a lower perceived quality (Table 5) and higher marginal costs (Table 8). The results for the short-run case are very different from the long-run case. Here, the decreased generic quality and higher marginal cost means that branded esomeprazole is a closer substitute. Hence, the addition of a generic entrant increases welfare more in the short run than the long run. When there is only one generic, the increased branded competition results in a lower generic price (relative to the case of one generic in the long run). Additional generics beyond the first have smaller marginal welfare effects, as the market was reasonably competitive when there was only one generic entrant. When multiple generic manufacturers are present, the branded manufacturer stops trying to compete and raises its price to focus on consumers with a strong taste for the branded product. With multiple generics, the branded price rises and its market share falls.

7 Conclusion

We estimate the demand and supply of antiulcer drugs, accommodating rich substitution patterns across classes, brand/generic status, forms, and molecules. We deal with two challenges caused by insurance. First, the prices we see in the data are not the prices paid by consumers due to insurance subsidies. Second, firm revenues are distorted because firms pay sizable rebates to insurance companies.

The estimates of the demand and supply models allow us to perform two sets of counterfactuals. First, we show consumer welfare losses and changes in insurance payments and profits when drugs are removed from the market. Removing generics or me-too drugs leads to annual losses of consumer welfare of $125 and $135 million dollars respectively, holding insurance premiums constant. The changes in insurance payments and firm profits are more dramatic. While removing generics would increase insurance payments by a billion dollars annually, removing me-too drugs would decrease insurance payments by over $7 billion dollars annually.

Although me-too drug Nexium (esomeprazole) increased insurance spending by tens of billions

of dollars since 2001, it will be available as a generic in 2014. We examine generic esomeprazole in our second set of counterfactuals. We find that generic esomeprazole will expand utilization in the class after enough generic manufacturers enter, with annual consumer welfare gains of over $100 million.

While me-too drugs provide price competition, we find that the net effect of me-too drugs is to increase pharmaceutical spending, in part because of the added variety. This has implications for health policy. First, the President's proposed budget for 2013 includes speeding biosimilars to market, but if biosimilars behave like these me-too drugs, they are likely to increase spending, rather than decrease spending as the President predicts. Likewise, the priority review voucher (Ridley et al., 2006) which speeds me-too drugs to market would be expected to increase spending. Conversely, the Indian policy of not patenting me-too drugs like Glivec would decrease spending. Of course, such effects on spending also have implications for innovation incentives which we leave for future work.

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