Does Market Exclusivity Improve Access to Drugs? The Case of US Anti-Ulcer Drug Market

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(Please find the most recent draft [here])

Abstract

Over-the-counter (OTC) versions of prescription drugs can improve access and affordability, and potentially reduce spending on healthcare. To incentivize firms to conduct the R & D process required for converting prescription (Rx) drugs to OTC status, the first firm to gain approval for OTC sales of a prescription (Rx) drug enjoys three years of market exclusivity granted by the Food and Drug Administration (FDA), independent of patents. Firms usually, but not always, delay OTC entry until the end of their Rx patent protection. Using US anti-ulcer drug market as a case study, this paper shows that the FDA provision of market exclusivity, intended to encourage innovation and increase the number of OTC drugs, actually *hurts consumers* by delaying OTC entry until an Rx drug patent expires. We propose an alternative policy in which market exclusivity is preserved after patent expiration to an OTC drug that is introduced more than three years earlier than patent expiration, and find that the policy eliminates the incentive of strategic delay, and enhances consumer welfare.

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1 Introduction

Intellectual property policy must strike a balance between innovation and competition. The US pharmaceutical industry provides an ideal setting to study the complex consequences of innovation policies, where patents and market exclusivity are granted by the government to encourage and reward innovation. In the long run, innovation generates new drugs and treatments that benefit consumers (i.e. dynamic efficiency); in the short run, the policies to encourage innovation may limit competition and harm consumers' welfare (i.e. static inefficiency). The inefficiency is aggravated when innovation policies provide the incumbents with the opportunity to exploit their old discoveries. The net effects of such policies on consumer welfare have been constantly debated.

In this paper, we focus on these policy issues in the context of prescription (Rx) to over-the-counter (OTC) switch in the US anti-ulcer drug market. According to the US Food and Drug Administration (FDA), more than 700 OTC drugs have been approved through Rx-to-OTC switch since 1976.[1] Many, but not all, molecules that are candidates for Rx-to-OTC switch have been converted at varying points in their lifecycle. Converting Rx drugs to OTC status improves access to drugs by removing the need for a physician's prescription and also reduces their costs to consumers. However, firms that make Rx-to-OTC switches have to undertake several risky investments that include clinical research cost, distribution through retailer network, as well as the risk of application being rejected. To help firms recoup their fixed costs and to speed up the introduction of OTC drugs, the FDA provides three-year market exclusivity in the OTC market to the firm that makes the first Rx-to-OTC switch (following the Drug Price Competition and Patent Restoration Act of 1984 i.e. Hatch-Waxman Act). OTC market exclusivity allows the first OTC drug to be the 'only' drug in the OTC market for three years, because during the market exclusivity period, the FDA does not approve any other OTC application.

The goal of providing market exclusivity is to encourage firms to develop and release the OTC drugs; does this policy achieve its goal? Can it be designed better to improve the access to OTC drugs and consumer welfare? This paper focuses on these very important policy questions by developing and estimating a structural model of anti-ulcer market that recognizes imperfect substitution between Rx and OTC drugs and allows endogenous pricing as well as OTC entry decisions by the manufacturers. We show that the current OTC market exclusivity policy, which is intended to encourage the release of OTC drugs, may actually reduce consumer welfare by delaying OTC entry until an Rx drug patent expires. For example, with no market exclusivity, AstraZeneca would have introduced Nexium OTC in

[1] http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143547.htm

2007 instead of at patent expiry in 2014. We evaluate an alternative policy in which market exclusivity is preserved after patent expiration to an OTC drug that is introduced more than three years earlier than patent expiration, and find that the policy eliminates the incentive of strategic delay, and enhances consumer welfare.

The timing of OTC entry has significant welfare implications. As OTC drugs become a viable option for both the uninsured and insured, consumer surplus is enhanced by Rx-to-OTC switch through lower price and increased access. However, these benefits will not materialize until the drug is introduced to the OTC market. Why do some brand Rx firms wait till patent expiration to introduce the OTC ('delayed entry'), but others introduce OTC before patent expiration? The key policy that drives the variation in the timing of entry is the three-year market exclusivity. Firms choose to enter the OTC market when the three-year OTC market exclusivity is most valuable. When an Rx-to-OTC switch is made earlier than a patent expiration, a firm's period of OTC market exclusivity overlaps with its Rx patent protection. This overlap creates 'cannibalization' if consumers who would have purchased the higher-priced Rx version switch to the OTC version. However, the early entry into the OTC market may benefit the firm by giving it a first-mover advantage. In addition, the value of the market exclusivity will change depending on what other products are available in the market at the same time: an OTC drug introduced at patent expiry will compete against generic Rx versions of the same molecule. The timing of the Rx-to-OTC switch depends on the net impact of first-mover advantage, degree of cannibalization, and differences in the value of market exclusivity at different periods. Whether a drug is converted at all depends on the fixed costs the firm incurs to make the conversion.

To understand and evaluate alternative exclusivity policies, this paper estimates a structural model of firms' Rx-to-OTC decisions for the anti-ulcer market. First, we use the data on aggregate prices, quantities and advertisement spending to estimate a discrete choice demand model. The estimated substitution patterns between Rx and OTC drugs will determine the extent of potential cannibalization when a Rx manufacturer decides to release the OTC version. Second, we recover marginal costs for drug production using equilibrium first-order conditions resulting from firms' profit maximization. Finally, we embed the implied period profits from demand and marginal cost estimates into a dynamic oligopoly game of OTC entry and estimate the fixed cost of converting Rx drug into OTC status using the panel data of manufacturers' decisions.

Our estimates suggest that consumers derive significant additional utility when a prescription drug switches to OTC status. Similarly, firms by advertising a product can gain higher market share. We observe strong competition effects between the branded and generic drugs in the Rx market. Additionally, our demand estimates reveal strong cannibalization

effect of OTC version on the molecule's Rx counterpart. Our marginal cost estimates show that the cost of branded Rx drugs are much higher compared to the generic Rx and OTC drugs. Finally, our fixed cost estimates suggest that, firms on average spend close to 16 million USD to develop and release the OTC version.

Using the estimated parameters, we first evaluate the effect of the current provision of three-year market exclusivity and then evaluate alternative policies. First, using Nexium OTC launch as a case study, we show that our model rationalizes AstraZeneca's decision to delay introduction of OTC Nexium until patent expiry. We then evaluate alternative market exclusivity policies: no market exclusivity, and market exclusivity that lasts until three years after Rx patent expiry regardless of the timing of OTC introduction.

We show that under status quo market exclusivity policy, if AstraZeneca had introduced OTC Nexium in May 2011, three years earlier than its actual introduction in May 2014, it would earn higher profit prior to patent expiration. We find that the first mover advantage and market expansion effect in case of early entry dominate the cannibalization effect due to OTC release prior to patent expiration. However, in the post-patent period, market exclusivity that accompanies the delayed OTC entry at the time of patent expiration provides a window when AstraZeneca effectively fences off competition from generic Nexium. Thus the value of market exclusivity is higher in the delayed entry case than the early entry case. The value of OTC market exclusivity at patent expiration is greater than the value of early entry, which drives AstraZeneca's decision to delay introduction of OTC Nexium. The delay of Nexium OTC entry causes consumers to lose at least 500 million dollars each year on average. This suggests that the FDA market exclusivity policy may lead to strategic delay in the OTC launch by Rx manufacturers leading to lower access to drugs.

We then consider the policy regime where was no market exclusivity is granted by the FDA. In this scenario, lessened incentive to innovate may reduce the variety of OTC drugs, while firms that decide to introduce the product may introduce the OTC drug before patent expiration. In our counterfactual exercise, we solve the dynamic entry game, and simulate the equilibrium entry decisions as well as timing of entry of each manufacturer in this new regulatory regime. We find that in the absence of market exclusivity, Prilosec, Prevacid and Nexium would choose to enter the market seven to eight years prior to patent expiry improving access and consumer welfare. On the other hand, in case of Axid and Zegerid, the removal of market exclusivity drives them not to enter the OTC market, which creates a loss of consumer welfare. We find that, even with lower variety, overall consumer welfare increases compared to the status-quo policy.

Finally, we evaluate an alternative market exclusivity policy: three year market exclusivity is granted following the patent expiration, when an OTC is introduced at least three

years prior to patent expiry. Under this policy, market exclusivity is granted beyond patent expiration if OTC drugs are introduced early, and hence the strategic delay incentives are removed. Our simulation exercise reveals that indeed the Rx-to-OTC switches that occur under status-quo policy also hold in this new policy regime. Additionally, firms tend to enter early. We find that the policy does eliminate the incentive of strategic delay without affecting the incentive to innovate. This leads to higher access and higher consumer welfare. Our analysis reveals that current policy is inefficient and can be improved by redesigning the exclusivity structure.

This project makes several contributions. Our structural model analyzes firms' Rx-to-OTC switch decisions and economic evaluation of the FDA's three-year OTC drug market exclusivity policy. Our analysis sheds light on the interplay between Rx and OTC markets, and estimates substitution patterns between Rx and OTC versions of the same molecule. We additionally estimate the fixed cost of Rx-to-OTC switch and in our counterfactual exercise, provide the first evidence of a plausible FDA alternative policy that eliminates the incentive to delay, and compute the value to consumers under the alternative policy. Given the sharply rising prescription drug spending in the US, wider use of OTC drugs are advocated to expand access lower the healthcare costs. Our study contributes to this debate by designing policies that can encourage early introduction of OTC drugs.

This paper is closely related to a strand of literature that studies generic entry and Hatch-Waxman act (Appelt (2015), Berndt, Kyle and Ling (2003), Huckfeldt and Knittel (2011), Shapiro (2016), Grabowski and Kyle (2007), Hemphill and Sampat (2012), Arcidiacono et al. (2013)), and regulatory exclusivity (Olson and Yin (2017), Yin (2015)). More generally, this paper contributes to a better understanding of the interplay between market, competition policy and innovation policy and builds upon the work by Crawford and Shum (2005), Dubois and Lasio (2018), Aghion et al. (2005), Chaudhuri, Goldberg and Jia (2006) and Igami (2017) among others. The literature on the specific setting of Rx-to-OTC switches has investigated the spillover effects of marketing and cannibalization effect of Rx-to-OTC switch (Berndt, Kyle and Ling (2003) and Ling, Berndt and Kyle (2002)), physician and patients response (Neyaz (2007)), payer policies (Sullivan and Nichol (2004)) and firms' strategies (Jain and Conley (2012), Cavusgil, Deligonul and Calantone (2011) , Shih, Prasad and Luce (2002)). However, limited attention has been paid to empirically investigate the combined effect of OTC drug market exclusivity with Rx drug patent on firms' strategies. This paper contributes by studying the unintended effects of intellectual Property policies that regulate two segments of pharmaceutical market- Rx drug market and OTC drug market.

The remainder of the paper is organized as follows. Section 2 reviews the policy background, the anti-ulcer drug market and describes the data. Section 3 provides descriptive

evidence on strategic delay and first-mover advantage arising from the early entry into OTC market. Section 4 describes the model. Section 5 discusses the identification and estimation strategy and reports the estimation results. Section 6 reports counterfactual analysis. Section 7 concludes.

2 Industry Background and Data

In this section, we describe the approval process for Rx-to-OTC switch and the market exclusivity granted by Food and Drug Administration (FDA). We then provide an overview of OTC anti-ulcer drug market and present a description of the data.

2.1 Rx to OTC switch and market exclusivity

In order to lower the spending on prescription drugs,[2] the FDA encourages firms to make investments to develop and release over-the-counter (OTC) alternatives.[3] Converting prescription (Rx) drugs to over-the-counter (OTC) status improves access to drugs by removing the need for a physician's prescription and also reduces their costs to the consumers. The application for an Rx-to-OTC switch follows the 'New Drug Application' (NDA) process required for the approval of a prescription drug. The FDA requires studies that involve a hybrid of clinical safety and consumer behavior research in reaching an approval decision for Rx-to-OTC switch. In addition to clinical trials to establish efficacy, safety and side effects, OTC approval also involves randomized control trials to prove that consumers can self select OTC medication and also read and understand the label and package. Therefore, these studies incur a fixed cost for firms that make the switch, in addition to the uncertainty in the approval outcome that the firms face.[4]

To help firms recoup their fixed costs and to speed up the introduction of OTC drugs, the FDA provides three-year market exclusivity in the OTC market to the firm that makes the first Rx-to-OTC switch independent of patents (following the Drug Price Competition and Patent Restoration Act of 1984 i.e. Hatch-Waxman Act). OTC market exclusivity allows the first OTC drug to be the 'only' drug in the OTC market for three years, because during

[2] A significant share (for example, close to 15% in 2015) of the healthcare spending goes to spending for retail prescription drugs. According to a report by Kaiser Family Foundation, the total US prescription drug spending is expected to rise almost by two times in next 5 years making it the fastest-growing healthcare category.

[3] Food and Drug Administration (FDA) plans to speed up the approval process for over-the-counter medicines. https://www.whitehouse.gov/briefings-statements/remarks-president-trump-lowering-drug-prices/

[4] In appendix A, we describe more details about the regulatory requirements for Rx-to-OTC switch.

the market exclusivity period, the FDA does not approve any other OTC application.[5]

2.2 Anti-Ulcer Drug Market

We choose the anti-ulcer drug market to study the effect of market exclusivity and access to drugs. According to Gale Encyclopedia of Medicine (2008), 'anti-ulcer drugs are a class of drugs, exclusive of the antibacterial agents, used to treat ulcers in the stomach and the upper part of the small intestine.'[6] Anti-ulcer drugs are also used to treat heartburn, gastroesophageal reflux disease (GERD), and hypersecretory syndromes. There are two main categories of anti-ulcer drugs - histamine antagonists (H2 blockers), and proton pump inhibitors (PPIs).[7] Table 1 reports the eleven molecules in the anti-ulcer drug market that we observe in our sample. Molecules - Cimetidine, Ranitidine, Famotidine, and Nizatidine belong to the H2 blocker class and were introduced and marketed in the late 1970s and 1980s. The other seven molecules in the table 1 belong to the PPI class and were introduced in early 1990s. While the anti-ulcer market has long been one of the top-selling therapeutic classes worldwide, anti-ulcer market in the US is one of the important segments with average total annual revenue close to 35 billion USD as measured between 2007 and 2015.

[Table 1 around here]

Given the prevalence of anti-ulcer treatment, high cost, and common occurrence of Rx-to-OTC switches, the anti-ulcer drug segment provides an appropriate setting to study the incentives that guide the switching decisions. Anti-ulcer treatment is prevalent; 8.4% of the subjects in the National Health Interview Survey (NHIS) between 1997 and 2003 reported a history of pepcid ulcer (gastric ulcer or duodenal ulcer). It is estimated that around 60 million patients in the US suffer from heartburn[8], and nearly half of the U.S. population has symptoms of GERD at least once a month.[9] The extensive prevalence of anti-ulcer treatment implies large welfare consequences for consumers. In addition, the anti-ulcer treatment is costly. For example, the anti-ulcer drug Nexium Rx cost 2.5 billion for 1.5 million medicare patients, who filled 8 million prescriptions and refills in 2013. Finally, the occurrence of Rx-to-OTC switches in the anti-ulcer drug market is common. As summarized in table 1,

[5]Exclusivity policy prevents the submission or effective approval of ANDAs (Abbreviated New Drug Application) or applications described in Section 505(b)(2) of the Food Drug & Cosmetic Act.

[6]Anti-ulcer Drugs. (n.d.) Gale Encyclopedia of Medicine. (2008). Retrieved May 11 2018 from https://medical-dictionary.thefreedictionary.com/Antiulcer+Drugs

[7]H2 blockers inhibits the secretion of gastric acid by stopping the action of histamine on the gastric parietal cells, and may achieve 75-79% reduction in acid secretion. PPI block the secretion of gastric acid by the gastric parietal cells and are more effective than H2 Blockers.

[8]http://www.webmd.com/heartburn-gerd/guide/understanding-heartburn-basics

[9]https://www.wsj.com/articles/SB10001424127887323894704578115031699278010

all four H2 blocker molecules have made the Rx-to-OTC switch, while four out of seven PPI molecules have made the switch during our sample period. We also observe variations in the Rx-to-OTC switch across molecules. Pepcid, Axid and Zegerid made the switch five to six years before patent expiration. As reported in table 1, the average Rx revenue from these molecules were also relatively lower compared to other molecules. Tagamet, Zantac, Prevacid, Prilosec and Nexium, with relatively higher Rx revenue, made the switch around the time of patent expiration. Two PPI molecules, Aciphex and Protonix did not make the switch at their patent expiration. Additionally, Dexlansoprazole, a new drug approved in February 2009 with a long patent term till 2023, did not make a switch during our sample period.

After receving approval from FDA, brand Rx firms usually launch their OTC products in alliance with a consumer product firm, who specializes in OTC distribution. For example, in the case of the OTC Nexium 24 HR, Pfizer acquired the exclusive global rights from AstraZeneca (the brand Rx firm) to market over-the-counter Nexium 24HR.[10] While interaction between OTC drug producers and marketers may pose interesting economic questions, for tractability, in our study, we abstract from the nature of such joint ventures, assume that their objective is to maximize the joint profit, and focus on the interaction of exclusivity policy with the release timing of the OTC drugs. Next, we present a brief description of our dataset.

2.3 Data

We obtained our primary dataset, *The National Sales Perspectives (NSP) data 1992-2015* from IMS Health. The IMS National Sales Perspectives monitors every major class of trade and channel of distribution for prescription pharmaceuticals, over-the-counter products and select, self-administered diagnostic products in the United States, measuring volume of dollars and units moving from manufacturers into various outlets within all 50 states. IMS health NSP data captures 100% of prescription pharmaceutical market, measuring sales at actual transaction prices rather than using an average wholesale price. While IMS NSP does

[10]Under the agreement, Pfizer made an upfront payment of $250 million. Additionally, AstraZeneca was eligible to receive milestone and royalty payments based on product launches and sales. Similarly, Prilosec OTC was brought to the market through partnership between AstraZeneca with P&G in 2003. Zegerid OTC was manufactured by Santarus, Inc, and marketed by Bayer Healthcare LLC. Prevacid manufacturer TAP was partnered with Novartis Consumer Health, Inc to produce and market Prevacid 24HR. Pepcid AC and Pepcid Complete were launched in 1995 and 2000 by Johnson & Johnson–Merck Consumer Pharmaceuticals, a joint venture between Merck and J&J formed in 1989 to develop, manufacture, market and distribute certain OTC consumer products in the U.S. and Canada.

not cover the universe of OTC drugs,[11] its coverage for anti-ulcer OTC drug at the national level is quite high making it a representative sample for studying OTC market. The sales data include units (for example, number of pills), and the dollar value for sales of prescription and OTC drugs sold at retail pharmacies from 1992 to 2015.

The second major data source is *Integrated Promotional Services (IPS) 1992-2014* that we obtained from IMS Health. This dataset records the total promotional activity for pharmaceutical products from office-based and hospital-based physicians as well as direct-to-consumer advertising expenditures at molecule-manufacturer-month level. Several additional pieces of information complete the dataset. We collect the patent and market exclusivity information from the historical publication of the Orange Book. Finally, the information on product entry are collected from National Drug Code data.

Given our IMS health data is available at monthly (national) level, we define a month as a market. Since we do not observe the market size, we multiply the prevalence rate (around 30%) with the U.S. population to compute the market size. A few points about the dataset need to be highlighted here. A first challenge in the dataset is to facilitate the comparison across products as the drugs are sold in different dosages (once every day, twice every day, and others) and sizes, therefore varying in the form (such as tablets and capsules) and efficacy (for example, daily dosage across molecules may vary). To address this, we first consider the milligrams purchased for a given Stock-Keeping-Units (SKU) for each molecule and use the recommended daily dosage information as a scaling factor to convert it to a patient-day dosage measure.[12] The resulting quantity obtained by dividing the observed quantity with this adjustment factor can be interpreted as the number of prescriptions if all patients were taking the recommended active duodenal ulcer daily dosage. We compute the price per prescription by dividing the total revenue by the numbers of prescriptions for both Rx and OTC drugs. Since our analysis is focused on OTC drug release decisions of the firms as well as consumer preferences for the products, in our analysis, we aggregate SKUs for tablets and for capsules for a given firm for a specific molecule and define it as a "product". Therefore, a product is defined as the combination of molecule, brand status (brand v.s. generic), market status (OTC v.s. Rx) and form (tablet v.s. capsule), for example, we define brand Rx Omeprazole tablet (Prilosec) as a product.

A second complication arises as the presence of insurance providers complicate the interpretation of prices of the anti-ulcer drugs. The price used by the IMS National Sales

[11] Coverage of OTC market is around 50%. While for products like vitamins, herbals supplements the coverage is lower, for products that are generally accepted as medicines, especially ones that have been prescription based (such as anti-ulcer drugs) the data has better coverage.

[12] We collect the recommended daily dosage information for active duodenal ulcer treatments from Physicians' Desk Reference (PDR). We multiply this by 30 days and use that as the scaling factor.

Perspectives is an average invoice price from the wholesaler to the purchasing outlet (retailing and non-retailing including pharmacies, hospitals, clinics, etc.). This price does not reflect the post-shipment financial adjustments. In particular, the rebates that are paid by the manufacturer to the insurer to remain in a lower copayment tier, is not observed in the dataset. This complicates our analysis, as the actual price received by the manufacturer might be different from the price we observe in the data. Additionally, due to insurance cost sharing, the out of pocket costs that the patients face (the copay) is different from the price that the manufacturers receive. To address the issues of rebate and copay, we borrow the techniques developed in the literature (Arcidiacono et al. (2013)) used to study the anti-ulcer drug market. We discuss the details in the section 4.

[Table 2 around here]

Table 2 provides the summary statistics for key variables in our empirical analysis. Our data covers anti-ulcer drug market from 1992 to 2015. The average price per prescription in our sample is 24 dollars. The average monthly advertising expenditure is around 2.8 million dollars, which implies that average accumulative advertising in last three years is close to 100 million dollars. The number of monthly prescriptions computed from our sample is close to 2.5 millions. We also calculate market share conditional on OTC or Rx category drugs belong to. The average conditional share is 9%. The average market share for outside goods are 40.8%.

3 Descriptive Evidence

In this section, we present some suggestive evidence that manufacturers of branded Rx drugs strategically delay releasing the OTC version of the molecule due to the provision of market exclusivity.

To understand the effect of market exclusivity and patents on the entry of firms in the OTC market, we plot the number of firms operating in each molecule in the category of H2 blocker and PPI respectively in figure 1. As illustrated in the graphs, the number of firms that manufacture OTC version in each molecule does not grow initially due to the market exclusivity provision. After the exclusivity period ends, with entry of generic OTC firms, the number surges to more than 20 firms in less than 3 years. This suggests that the exclusivity provision benefits the branded OTC firm (the first entrant) by limiting the competition from the generic OTC competitors, in other words, without the exclusivity, the first manufacturer that makes the Rx-to-OTC switch would face significant competition from rival entrants.

[Figure 1 around here]

The indirect implication of the FDA three year market exclusivity is the strategic delay by the branded Rx manufacturer. In table 1, we document the month when the prescription version of the drug was released in the US, the month of patent expiry and the month on which the first OTC version for the prescription drug was released. Two things are striking here, first, in all cases, whenever an OTC version is released, it is released by the same manufacturer which also sells Rx version of the molecule. Second, in five out of the eight cases (Tagamet, Zantac, Prilosec, Prevacid, and Nexium) the OTC version is released around the same time as when the patent for the prescription drug expires.[13] In other three cases (Pepcid, Axid and Zegerid), the OTC version was released five to six years prior to the Rx patent expiry. Note that, prior to the expiry of patent of the prescription drug, no other firm (except for the patent holder) can release a drug in the OTC market. Therefore, the data here suggests that the firm that owns the patent of the prescription drug waits until the patent expires; only after that it releases the OTC version and being the first entrant into the OTC market enjoys market exclusivity. It is important to note here that, if released during the patent period, the OTC version will compete with the Rx version of the same molecule. Therefore, by strategically delaying the entry of OTC version, the patent holder protects its profits from sales of Rx drugs. This is further substantiated by the observation that, (as in the last column in table 1) the molecules for which OTC version was released five to six years prior to patent expiry (Pepcid, Axid and Zegerid) also earned relatively lower revenue from Rx market while for relatively high-earning molecules, the OTC version was released right around the patent expiry.

However, the manufacturer also values market exclusivity, as it helps the firm to build its brand-name and enjoy monopoly profit in the OTC market. As well documented in the existing literature, firms by spending on promotions through physician detailing and/or direct-to-consumer marketing can gain first mover advantage (for example, see Avery et al. (2007), Avery, Eisenberg and Simon (2012), Ching and Ishihara (2012), Hellerstein (1998), Hurwitz and Caves (1988), Iizuka (2004), Iizuka and Jin (2005), Crawford and Shum (2005), Shapiro (2018) among others). Therefore, in the absence of rival competition during market exclusivity period, firms that make the Rx-to-OTC switch have incentives to invest heavily in promotion and marketing activities to leverage the gain from the three-year period. In figure 2, we plot the annual national advertising spending and the total revenue of four PPI OTC drugs (Prilosec, Prevacid, Zegerid and Nexium) from 2006 to 2014 and in figure 3 we plot the advertising-revenue-ratio.

[13] In case of Prilosec, the NDA for OTC version was submitted in January 2000. While typical NDA approval process takes around 10 months, due to regulatory delay Prilosec OTC was approved in June 2003 and was released in September 2003, two years after the Rx patent expiry.

[Figure 2 around here.]

[Figure 3 around here.]

As expected, the trend suggests that firms invest more in advertising during the period of market exclusivity, and advertising-revenue-ratio is high when a product is first introduced to the market.[14]. Therefore, this provides suggestive evidence that to enjoy FDA's provision of three years of market exclusivity, the firm releases the OTC version right around the patent expiry and use the exclusivity period for building the OTC brand.

Does the policy of market exclusivity, designed to encourage the development and release of OTC version actually harm consumers by delaying the OTC entry? In other words, if FDA gets rid of the market exclusivity altogether, whether it would incentivize the firm to release the OTC version earlier and improve consumer welfare, and whether there is a better way to design the market exclusivity policy. To answer these questions, we develop and estimate a structural econometric model of US anti-ulcer drug market which we describe next.

4 Model

To evaluate welfare implications of alternative exclusivity policies, we need to model how the manufacturer of a branded Rx drug endogenously decide on the OTC release in response to changing market conditions while taking into account the cannibalization effect. This section presents a finite-horizon dynamic discrete game that describes firm's decisions on offering the OTC version in the market, setting prices of the offered products as well as consumers' decisions on choosing among those available products.

4.1 Demand

We capture the substitution patterns across anti-ulcer drugs using a nested logit model of differentiated products. Similar discrete choice modeling has been used in Arcidiacono et al. (2013), Crawford and Shum (2005), Dubois and Lasio (2018) while studying anti-ulcer drug market in the US, in Italy and in France respectively.[15] A patient with heartburn may choose

[14]For example, according to the Drug Store News, Nexium 24HR, introduced in May 2014, aggressively promoted its franchise, reaching more than 70% in units sold on promotion in some months. For the first 12 months after launch, almost half of all Nexium 24HR units were sold on promotion. Nexium 24HR also boasted the highest number of circular ads. Nexium 24HR reaped $279 million in sales in the first year. http://www.drugstorenews.com/article/nexium-hr-sells-well-promotion

[15]A growing number of studies use discrete choice model to estimate demand in pharmaceutical drug markets including Ching (2010), Dunn (2012), Björnerstedt and Verboven (2016), and Branstetter, Chatterjee and Higgins (2016) among others.

from a set of anti-ulcer drugs, or the outside option defined as not treating the heartburn. Consumer n's conditional indirect utility from choosing drug j that belongs to molecule m in month t is given by

$$U_{njmt} = \underbrace{\alpha p^c_{jmt} + x_{jmt}\beta + \xi_{jmt}}_{\delta_{jmt}} + (1-\sigma)\varepsilon_{njmt} \tag{4.1}$$

In equation (4.1), ε_{njmt} follow independent and identically distributed (i.i.d.) type-1 extreme value distribution. The term σ captures the degree of correlation between the alternatives in the nest. In our demand specification, all products (branded Rx, branded OTC, generic Rx, generic OTC) in a given molecule belong to the same nest, hence allowing different versions of the same molecule to be closer substitutes of each other. For example, in most states a pharmacist can substitute branded lansoprazole to its generic version, unless expressly forbidden by the physician (Arcidiacono et al. (2013)) allowing a closer substitution of products inside a molecule.[16] As the parameter σ approaches 1, the within-molecule correlation of utility levels goes to 1, and as σ approaches 0, the within-molecule correlation of utilities goes to 0. Equation (4.1) defines the mean utility for a product to depend on x_{jmt}, a vector of time-varying product characteristics, p^c_{jmt}, the price paid by the patient, and ξ_{jmt}, a product-level shock that includes unobservable product-specific variables that could affect utility.

As discussed earlier, presence of health insurance poses a key challenge in quantifying the elasticities. While drug insurance companies do not cover spending on OTC drugs, insured patients pay only a fraction (copayment denoted by p^c_{jmt}) of the full price for Rx products. Therefore, for Rx drugs, the relevant price that the patients face is typically much lower than the posted price recorded in the national datasets. Ignoring this distortion would (incorrectly) imply that consumers are insenstive to price. To address this, we borrow the existing literature, follow the set up used in Arcidiacono et al. (2013) while studying anti-ulcer drug market in the US (between 1991 and 2010) and assume log copayments as a linear function of log price for Rx drugs. In particular,

$$\begin{aligned} \ln(p^c_{jmt}) &= \phi_0 + \phi_1 ln(p_{jmt}) \quad \text{(for Rx drugs)} \\ p^c_{jmt} &= p_{jmt} \qquad\qquad\qquad \text{(for OTC drugs)} \end{aligned} \tag{4.2}$$

[16] While modeling demand for US anti-ulcer drug market Arcidiacono et al. (2013) allow for even more flexible substitution patterns through generalized nested logit structure. However, their estimates suggests that the nesting parameter capturing the substitution patterns inside a molecule is the key determinant of overall substitution patterns. Hence, even though we consider a conservative model with one nesting parameter, our demand model still captures the key cross product substitution patterns in the data. In robustness checks, we allow more flexible forms of demand model and compare sensitivity of estimated elasticities across models.

Following the specification in Arcidiacono et al. (2013), we allow ϕ_0 to be equal to 2.558 and ϕ_1 to be 0.113. The details of the specification and calibration followed by Arcidiacono et al. (2013) is discussed in appendix B.

In this framework, the well-known formulas for market shares are given by

$$s_{jt|m} = \frac{e^{\delta_{jmt}/(1-\sigma)}}{D_{mt}}; \text{ where } D_{mt} = \left[\sum_{h \in S_m} e^{\delta_{hmt}/(1-\sigma)}\right] \tag{4.3}$$

In the above expression, $s_{jt|m}$ denotes the conditional probability of choosing a product j given the choice of molecule m at time t. The probability of choosing molecule m is given by

$$s_{mt} = \frac{D_{mt}^{1-\sigma}}{\left[1 + \sum_k D_{kt}^{1-\sigma}\right]} \tag{4.4}$$

Finally, the model predicted market share of product jmt is given by

$$s_{jmt} = s_{mt} s_{jt|m} \tag{4.5}$$

4.2 Supply

We model the entry decisions of the OTC version as a finite-horizon, sequential move, dynamic discrete game with private information. In our setting, the branded Rx products are already developed and marketed before the manufacturer considers Rx-to-OTC switch. Additionally, the patent term for the branded Rx product is exogenously given. Therefore, in our model, at every time period until patent expiry, each manufacturer with a given branded Rx drug for a molecule (and no OTC drug) first decides whether to release the OTC version and pay the fixed cost. The manufacturer's value function is jointly determined by its own action and its rivals' actions in the industry equilibrium. In every period, having observed the OTC release decisions of all firms, the manufacturer decides on the prices of the offered products.

4.2.1 Stage 1: Switching Decision

A. Timing

Time is discrete with finite horizon $t = 0, 1, 2, ..., T$. This modeling choice is important in our context, as it permits the solution of a dynamic game without ignoring the presence of fundamental nonstationarity in the data induced by innovation in the market. Non-stationarity in our data arises as patents of different molecules expire at different time periods, leading to non-stationarity of demand and costs. To accommodate this, we allow values and policies to

depend on time. In our empirical specification, we allow each firm to decide whether to release the OTC version in the beginning of every year. This allows us to lower the dimensions of the state space and keep the problem computationally tractable.[17]

A firm is indexed by i. The industry state consists of $(t, (s^i)),\ i = 1, 2, ..N$, where t denotes period t and s_t^i denotes the OTC release status of firm i at period t. We denote firms' average fixed cost of releasing the OTC version by FC. In addition, in the beginning of every period, each firm gets a draw of entry cost that is private information of the given manufacturer. Firms observe their private cost shocks and form expectations about the future stream of profits contingent on the action taken.

Denote firm i's patent expiration date by T_i. Prior to patent expiration, in the beginning of every year ($t \leq T_i$), firm i arrives with one of the two states

$$\{\text{Rx only, Rx and OTC}\}$$

where 'Rx only' denotes the case, when the firm only produces the patented molecule in Rx form, while 'Rx and OTC' denotes the state where the firm operates both in prescription as well as in the OTC markets in the beginning of period t. In our model, if the firm already operates in both prescription as well as in the OTC markets, then the firm only decides on the period price, and hence, transits to the state {Rx and OTC} in the next period with probability 1. Note that, our modeling choice assumes that the manufacturer can decide to switch to its OTC version only while its Rx patent is still active. Additionally, our model rules out possibility of exit from Rx and OTC markets. These choices are consistent with our empirical setting, where we do not observe any exit in OTC market during our sample period and we observe manufacturers in our sample switching to OTC market only during the Rx patent period in order to avail market exclusivity.[18]

If a firm arrives at time t with the state 'Rx only', then the firm can choose to take one of the two actions

$$\{\text{Release OTC, Not Release OTC}\}$$

Since market exclusivity in OTC market is granted for 3 years, if a firm decides to release the OTC version less than 3 years prior to patent expiry (that is $t = T_i$ or $t = T_i - 1$ or $t = T_i - 2$), then depending on the year of release, the firm enjoys market exclusivity in the OTC market after patent expiry. However, if a firm releases the OTC version before $T_i - 3$, then no exclusivity period is left for the firm after the patent expiry. In our model we assume

[17] Note that our demand and marginal cost estimation uses data at monthly level.

[18] Note that, while we observe Prilosec releasing its OTC version *after* patent expiry, the new drug application (NDA) for OTC version was submitted in January 2000. A typical NDA approval process takes around 10 months.

that, if the firm releases OTC, then after market exclusivity period is over, a generic OTC version enters the market with probability 1. Otherwise, if the firm chooses not to release the OTC version during the patent period of the Rx drug, then the generic OTC enters with probability 1 at the end of patent expiry. This assumption is consistent with our empirical observation in figure 1, where we observe several generic OTC versions of different molecules entering the market right after the end of market exclusivity period.

Note that, in order to avoid cannibalization from its OTC alternative, and protect the profit in the Rx market, a firm would choose to strategically delay the release of the OTC version until the patent expiry. However, there are countervailing economic forces that would incentivize the firm to release the OTC version prior to patent expiry. First, without branded OTC entry, in the absence of any exclusivity restrictions, rival generic firms will enter the OTC market after the patent expiry. Therefore, in order to avoid this competition, the branded Rx manufacturer may choose to release the OTC drug before patent expiry and avail the monopoly status through market exclusivity. Additionally, due to entry of generic alternatives in the Rx market, delaying the OTC switch until after the patent expiry poses competition for OTC drugs from generic Rx competitors as well. Finally, Rx manufacturers in other molecules (that are close substitutes) may decide to switch to OTC and enjoy first mover advantage in the OTC market. For example, Pepcid, the third entrant in the Rx H2-Blocker market, became the first entrant in the H2-Blocker OTC market, and managed to maintain its leading position for many years. Therefore, to avoid competition from generic Rx alternatives and OTC alternatives of other molecules, a manufacturer may choose to switch to OTC market prior to patent expiry.

The timing of the game is as follows. Each year t starts with realization of demand and marginal cost shocks (ξ and ω) and period competition among the current products in the market, from which each firm earns period profit $\pi_t^i(s_t^i, s_t^{-i})$ given the industry wide demand and cost conditions. We assume that these industry wide features are common knowledge.

- After the period competition, each firm with patent protection and with state 'Rx only' draw a private cost shock $\{\varepsilon_{it}\}$. These firms move sequentially to decide whether to release OTC version or continue producing the Rx version only.

- In our baseline model, firms move in the order of closeness (in terms of time) to respective patent expiry. Hence, the firm closest to patent expiry moves first, decides whether to release the OTC version or not. If the firm releases OTC version, then it pays a upfront fixed cost denoted by FC which is common across all firms. This action is observed by all other firms, and other firms move in the sequential order.[19]

[19]The assumption of sequential move ensures existence and uniqueness of equilibrium in the entry model.

- Firms for which patent has expired before time t or who have already released the OTC version prior to time t, only maximize period profit and transit to the same state with probability 1.

- On the basis of these actions of firms, market structure transits from time t to time $t+1$. The demand and cost conditions including arrival of new molecules as well as patent expiry evolve exogenously. All firms have rational expectations regarding the evolution of demand and cost conditions. While the demand and marginal cost shocks (ξ and ω) are realized in the beginning of every period, the firms with the knowledge of distribution of these shocks can compute the expected period profit and accordingly take the switching decisions.

The order of move in the above represents another important assumption of the model to facilitate the computation of its solution as well as estimation. Similar assumptions are also used while studying the innovation in hard-disk industry in Igami (2017) and Igami (2018). Because different types of firms move sequentially, each firm is effectively solving a single-agent problem at its turn. Private cost shocks reflect each firm's informational, managerial, and organizational conditions of transient nature. We focus on pure strategy equilibrium which maps these cost draws to a discrete choice, in the spirit of a static entry game with private information similar to Seim (2006). To facilitate both the solution and the estimation of the model, we assume that ε_{it} is iid extreme value.

B. Dynamic Optimization

When their turns to move arrive, firms make their dynamic discrete choices of releasing or not releasing the OTC version to maximize their expected values. They discount their future stream of profits by a factor $\beta \in (0,1)$ with rational expectations regarding the endogenous evolution of market structure and perfect foresight regarding the exogenous evolution of demand and supply conditions.

The dynamic programming problems of active firms (firms with patent protection with state (Rx only) are characterized by the following Bellman equation:

$$V_t^{i,Rx}(s_t,\varepsilon_{it}) = \pi_t^i(s_t^i, s_t^{-i}) + \max\left\{\beta E\left[V_{t+1}^{i,Rx}\left(S_{t+1}|S_t\right)\right] + \varepsilon_{i,t}^1, \beta E\left[V_{t+1}^{i,Rx+OTC}\left(S_{t+1}|S_t\right)\right] + \varepsilon_{i,t}^2 - FC\right\} \tag{4.6}$$

Where V^{Rx} stands for value function under Rx only action, V^{Rx+OTC} stands for value function under the action 'Rx + OTC', $\varepsilon_{i,t}$ follow extreme value type 1 distribution, and FC stands for the fixed cost of entry. Besides the components of period profit functions, the

In our robustness check, we allow alternative rules of sequential entry and check for the sensitivity of our result to this specification.

key parameter of this dynamic discrete game is given by FC, that denotes the fixed cost of switching to the OTC version from the Rx version of the drug.

C. Equilibrium

We solve this finite-horizon, sequential-move dynamic discrete game with private information for a PBE in pure strategies. Assumptions taken in this model are important to ensure computational feasibility and avoid multiple equilibria. First, firm's payoff is affected by its rivals' cost shocks only through their actual choices, and not by the specific realizations of ε_i^t, so firms hold perfect information on the payoff-relevant part of past history. Second, firms move sequentially after observing the choices of earlier movers. At its turn to move, the firm is effectively solving a single-agent problem based on its expectation over the subsequent evolution of market structure. Third, these two features and the finite-horizon formulation allow us to solve the model by backward induction.

We assume that at the end of our sample, all remaining patent protection ends, and for each molecule, a generic OTC enters the market (if it has not entered earlier). Hence, for the rest of the periods after our sample ends, the world becomes stationary. The terminal values associated with each molecule is given by

$$V_T^{i,Rx} = \sum_{t=T}^{\infty} \beta^t \pi_T^i(s_T^{i,Rx}); \quad V_T^{i,Rx+OTC} = \sum_{t=T}^{\infty} \beta^t \pi_T^i(s_T^{i,Rx+OTC}) \tag{4.7}$$

If the firm chooses not to release the OTC version in period T, then it incurs $\pi_T^i(s_T^{i,Rx})$ for the rest of the periods. Similarly, if the firm chooses to release the OTC version, then it incurs $\pi_T^i(s_T^{i,Rx+OTC})$ for the rest of the periods. In year $T-1$, an active firm's problem (apart from maximizing its period profit) is given by

$$\begin{aligned} \max \Big\{ & \beta E\left[V_T^{i,Rx}\left(S_T|S_{T-1}\right)\right] + \varepsilon_{i,T-1}^1, \\ & \beta E\left[V_T^{i,Rx+OTC}\left(S_T|S_{T-1}\right)\right] + \varepsilon_{i,T-1}^2 - FC \Big\} \end{aligned} \tag{4.8}$$

We follow Rust (1987) and exploit the property of logit error and their conditional independence over time, to obtain a closed-form expression for the expected value before observing ε.

$$\begin{aligned} E_{\varepsilon_{i,T-1}}[V_{T-1}^{i,Rx}] = & \pi_{T-1}^i(s_{T-1}) + \gamma + \exp(\beta E\left[V_T^{i,Rx}\left(S_T|S_{T-1}\right)\right] + \varepsilon_{i,T-1}^1) \\ & + \exp(\beta E\left[V_T^{i,Rx+OTC}\left(S_T|S_{T-1}\right)\right] + \varepsilon_{i,T-1}^2 - FC) \end{aligned} \tag{4.9}$$

where γ is euler constant. In this manner, we can write the expected value functions from year T all the way back to year 0. The associated choice probabilities (policy functions) will provide a basis for the maximum likelihood estimation (MLE).

4.2.2 Stage 2: Price competition

The second stage decision of the firm involves setting the prices for the products offered in the market following the switching decisions in stage 1. We assume that the price is decided following a static oligopolistic model of price competition. A key complication that arises in the context of pharmaceutical competition is the extensive use of rebates paid by the Rx manufacturer to the insurer in return for a low copayment tier. While there is no such provision for OTC drugs, presence of rebates creates a disconnect between the price observed in the data and the actual payoff to the producer for Rx products. Rebates are not directly observed and information about rebates are not publicly available, however, ignoring this would distort the implied costs faced by the suppliers. To address this, we borrow the existing literature, follow the specification used in Arcidiacono et al. (2013) while studying US anti-ulcer drug market, and assume that all firms selling Rx drugs charge 15.1% rebate prior to generic entry and adjust to a new common rebate of 48.3% upon the generic entry. The details of the specification and the calibrations followed by Arcidiacono et al. (2013) is discussed in appendix C. In our robustness checks, we allow alternative rebate values and check the sensitive our key results to this choice of rebate values.

Incorporating the rebate rate, the profit function of a multi-product firm i is as follows:

$$\pi_{it} = \sum_{j \in J_i} ((1 - r_{jt})p_{jmt} - mc_{jmt})M * s_{jmt}(p) \tag{4.10}$$

J_i denotes the set of products offered by firm i, p_{jmt} denotes price of product j in month t that belongs to molecule m. Similarly, mc_{jmt} denotes marginal cost of producing the drug j at time t where the product belongs to molecule m. M denotes market size, and s_{jmt} denotes market share of product j in month t for molecule m. r_{jt} denotes the rebate charged by the firm, takes value 0 for OTC products and takes values 15.1% and 48.3% in pre and post generic entry time periods for Rx drugs. The first order conditions are given by

$$0 = (1 - r_{jt})s_{jmt}(p) + ((1 - r_{jt})p_{jmt} - mc_{jmt}) \frac{\partial s_{jmt}(p)}{\partial p_{jmt}} \tag{4.11}$$

5 Identification, Estimation, and Results

5.1 Demand

The identification and estimation of the demand model closely resembles Berry et al. (1995), Nevo (2000) and Gandhi and Houde (2019). Since we assume that in every period firms strategically determine price after ξ_{jmt} are realized, in the demand model price can be po-

tentially endogenous. An additional source of price endogeneity arises from the construction of product price as we obtain the product price by aggregating and taking the average across drugs of different dosages and packages (i.e. different stock keeping unit, or SKU).[20] We construct two types of instruments to address the endogeneity problem: BLP instruments and the differentiation instruments (following Gandhi and Houde (2019)).[21] The validity of our estimation strategy relies on the timing assumption, that firms do not know demand shocks (ξ_{jmt}), while they choose product characteristics. Such timing assumptions are made in, for example, Eizenberg (2014), Wollmann (2017), and Fan and Yang (2020). In our demand estimation, we control for systematic molecule, brand as well as time effects using various fixed effect controls. Hence, though imperfect, it seems reasonable to assume that any product-time specific shocks are uncorrelated with contemporaneous product characteristics.

We allow for a rich set of product characteristics (x_{jmt}) in our demand specification that may affect consumer utility. We include firm-molecule-form-specific fixed effects that captures any product characteristics (observed or unobserved) that are fixed over time. Our time-varying characteristics include cumulative log advertising at the molecule-manufacturer-month level which varies between Rx and OTC drugs. As discussed in the data section, our advertisement dataset records the total promotional activity that includes physician detailing as well as the direct-to-consumer advertising which occurs for branded Rx and OTC drugs. In our specification all forms (tablets or capsules) of the same molecule receive the same gain in utility from advertising. It is worth pointing out that, we treat advertising as exogenous to demand shocks. This is guided by our institutional setting where advertising schedules and budgets are typically laid out far in advance and hence do not react to the monthly demand shocks to demand that constitute our econometric error. Hence, controlling for a full set of product fixed effects, we assume that the variation in advertising is independent of the demand error term. Similar assumptions are also used in the existing literature (for example, see Arcidiacono et al. (2013) and Shapiro, Hitsch and Tuchman (2019)). Additionally, we include a set of time-since-entry-dummy variables for each of the twelve months after product entry. These dummies would account for any tendency to advertise more intensely during the initial introduction phase. Additionally, these dummies may capture product availability and other aspects of consumer awareness during the initial months of product release. We

[20]The SKU sales are implicitly used as weight in calculating product price. We do not model the choice on the SKU level, but SKU sales share is likely to be correlated with the unobserved product attributes ξ.

[21]In particular, we include the number of molecules for the same form, the number of molecules of the same form in the same class, whether generic Rx is present in the same form, whether generics Rx is present in the same molecule, the number of generic Rx present of the same form, the number of generic Rx present of the same form in the same class, whether generic OTC is present in the same form whether generics OTC is present in the same molecule, the number of generic OTC present of the same form, the number of generic OTC present of the same form in the same class as instruments.

also include time-dummies and allow those to vary by class (H2 and PPI).

[Table 3 around here.]

We report the key demand side parameter estimates in the table 3. In our IV specification, the coefficient of copay (the relevant price to a consumer) is negative and significant suggesting that consumers derive disutility from higher prices. The nesting parameter, the key driver of cross-product substitution is estimated to be 0.43, suggesting that products inside a molecule are closer substitutes of each other. The positive coefficient of advertisement suggests that firms by advertising can increase the market share its products. The dummy of OTC products picks a positive coefficient suggesting that consumers derive additional utility from access to the OTC version of a molecule. The negative coefficient of branded Rx product interacted with generic Rx suggests that branded products with generic competition see lower demand. Similarly, the negative coefficient of brand Rx interacted with OTC implies that a branded Rx product with own OTC version faces lower demand, suggesting cannibalization of between Rx and OTC versions of the same molecule.

5.2 Marginal Costs and a model for Advertisement

From the demand estimates and firms' first order conditions, we infer marginal costs of production.

[Table 4 around here]

Table 4 summarizes the marginal cost by marketing status and brand status. It shows that on average the marginal cost of producing one month supply of brand prescription medication is 68 dollars, while it only costs 17 dollars to produce the same amount of generic prescription medication. Similarly, it costs 22 dollars for one month supply of brand OTC medication, and 9 dollar for generic OTC medication on average.

Note that, our dynamic estimation would require us to compute specific period profit for each molecule under every market structure.[22] Hence, having estimated the marginal costs, we model the log of marginal cost for a product j in molecule m in a time period t to depend linearly on the observed cost shifters, w_{jmt} and on an additive error term ω_{jmt}.

$$log(mc_{jmt}) = w_{jmt}\gamma + \omega_{jmt} \tag{5.1}$$

[22]For example, while nexium released its OTC product in 2014, while estimating our model, we need to compute its period profits in periods prior to 2014 (say 2013) when we do not observe nexium OTC in our sample.

where γ is the parameter vector to be estimated. We include brand-molecule-form specific dummies to capture cost differences across different products. To capture the cost differences over time varying by class, we allow time dummy by class in the set of controls. Finally, we control for time since entry dummies for 12 months. The R-square is 0.92. We report a subset of parameter estimates in the table 5. Our estimates suggest that, relative to Rabeprazole capsules, other products have lower marginal costs. Among other products Nizatidine capsules are particularly costly, while Esomeprazole capsules are relatively cheaper.

[Table 5 around here]

Finally, to compute the period profit of a drug for different market structures, we need to compute the predicted advertisement spending for the product. We estimate a reduced form policy function for advertising for branded Rx and OTC products.[23] Our advertisement specification is given by

$$adv_{ijmt} = w_{ijmt}\gamma^{adv} + \omega^{adv}_{jmt} \tag{5.2}$$

where adv_{imt} refers to the advertisement spending made by manufacturer i in period t for product j that belongs to molecule m. We flexibly model the advertisement decision by including time dummy varying by class, time since entry dummies for 12 months, as well as firm-molecule-form fixed effects in w_{ijmt}. These estimates are used to predict the advertisement spending and compute the period profit while estimating the dynamic model.

5.3 Fixed cost of switching from Rx to OTC

The static demand, marginal cost and advertisement model estimates from previous two steps imply specific period profit for each molecule, in each year, under each market structure. These static estimates together with observed timing of entry choices during the life cycle of the drugs in the panel data of pharmaceutical manufacturers, constitute the key inputs for identification of fixed cost in the dynamic model. For example, a large fixed cost of switching would lower the predicted value of entry of a manufacturer into the OTC market during the period when cannibalization effect of the OTC drug has large negative effects on own Rx products. Since we observe different manufacturers making entry choices at varying points during their patent period (for example, nexium switched to OTC right at patent expiry, while axid released its OTC version six years prior to the expiry of its patent), this variation helps us to identify the switching cost while estimating the dynamic model.

In the final step, we embed these variable profit estimates into a dynamic discrete game model and solve it for a perfect Bayesian equilibrium (PBE) by following backward induc-

[23] Similar approach has been followed by Shapiro (2016) while studying the market for Ambien CR.

tion. Our goal here is to estimate the dynamic parameter (FC) that represents the average switching cost of a manufacturer while releasing the OTC product. Using each candidate parameter value, we can compute the stream of period profits for a given manufacturer for every market structure. Hence each parameter value implies a specific expected value for each manufacturer, in each state-year, as well as optimal choice probability of releasing the OTC drug. The ML estimate maximizes the likelihood of observing the actual choice probablities in the data.

Consider a molecule with Rx drug under patent protection. In the beginning of period t, a molecule can enter in two different states {Rx only, Rx and OTC}. The states of all the 11 molecules determine the state space at time t, denote by $\{S_t\}$. A typical state space looks like:

$$S_t = \{Rx_1, Rx_2, Rx_3 + OTC_3, \cdots, Rx_{10} + OTC_{10}, Rx_{11}\}$$

where molecule 1 and 2 enter period t with the state Rx only while molecule 3 enters the period t operating both in Rx and OTC markets. If the molecule is in state Rx only, then action space is given by

$$\{\text{No Switch, Switch to OTC}\}$$

Corresponding policy function p_t^i denotes the manufacturer i's probability of not releasing OTC drug in period t and $(1 - p_t^i)$ denotes the probability that i releases the OTC version in period t. If the molecule is in state $(Rx + OTC)$, the molecule transits to the state $(Rx + OTC)$ in the next period with probability 1. Once all firms decide on the actions, $\{S_t\}$ moves to $\{S_{t+1}\}$. Policy function (p_t^i) for firm i at period t is given by

$$p_t^i = \exp\left[\beta EV_{t+1}^{i,Rx}(S_{t+1})\right]/B \tag{5.3}$$

where

$$B = \exp\left[\beta EV_{t+1}^{i,Rx}(S_{t+1})\right] + \exp\left[\beta EV_{t+1}^{i,Rx+OTC}(S_{t+1}) - FC\right]$$

The ML estimator for the mean fixed cost maximizes the joint likelihood of observing the actual data from $t = 0, 1, ..., T - 1$.

Table 6 reports the results from the maximum likelihood estimation. Average estimated fixed cost of releasing the OTC version is close to 15.9 million USD. In our baseline model, we take the discount factor (β) to be equal to 0.88. Additionally, we assume a specific order of move, that firms move in the order of closeness (in terms of time) to respective date of patent expiry. Hence, the more experienced firm being closest to patent expiry moves first. As a robustness check, in the second column, we assume an alternative specification where the least experienced firm moves first. As seen in table 6, the overall change in magnitude

of fixed cost estimate is negligible suggesting that order-of-entry may not play a decisive role in estimating a multi-period dynamic model as compared to a static two-period model. In table 7, we report the sensitivity analysis with respect to choice of different values of discount factor (β). While we set $\beta = 0.88$ in our baseline model, here we consider values of β to be equal to 0.75, 0.8 and 0.92. With increase in the β values, we observe an increase in the estimated value of fixed cost, and the estimate ranges between 13 to 19 million USD.

Note that, the fixed costs of making Rx-to-OTC switch include clinical research, distribution through retailer networks, the risk of application being rejected, as well as other unobserved costs incurred by the firms. The clinical trials are the major component of R&D cost and hence a key contributor to the fixed cost. To get a sense whether our estimated fixed cost is in line with the industry estimates, we refer to information from external sources. It is worth pointing out that, the cost of clinical research for Rx-to-OTC research is less studied than the clinical trial cost for prescription drugs. Typically, the length of the consumer research is shorter (1-2 weeks) for OTC drugs. Using the estimates of average cost per subjects from Berndt and Cockburn. (2014), the consumer clinical trial cost falls in the range of 4-10 million dollars.[24] Our fixed cost estimate obtained from our dynamic optimization, that includes clinical trial and other costs are in line with the industry estimates of OTC switching costs.

6 Counterfactual Analysis

Using the estimates from our structural model, we first address the question whether the FDA market exclusivity policy *may lead* to strategic delay in the OTC launch by Rx manufacturers leading to lower access to drugs. Using Nexium OTC launch as a case study, we find that the answer to this question is *yes*. We then evaluate alternative market exclusivity policies and their effects on product offerings and consumer welfare.

6.1 The Value of OTC Market Exclusivity and Delayed OTC Entry: The case of Nexium

This exercise uses Nexium OTC as a case study to show that the FDA market exclusivity policy may drive firms to delay the OTC launch until patent expiration. In this analysis, we simulate the value of early entry (i.e. the value of first mover advantage and market expansion minus cannibalization pre-patent expiration) and the value of OTC market exclusivity (i.e.

[24] Anti-ulcer consumer clinical research typically involves 165-651 human subjects. The average cost per subject is estimated at $16,566 per patient in 2014 (Berndt and Cockburn. (2014)), and $16,500 per patient for phase zero and phase IV in 2013 according to Cutting Edge Information (CEI) (Reference Link).

the value of preventing generic OTC entry post patent expiration). The value of early entry is positive if the value of market expansion and first mover advantage is greater than cannibalization, and negative otherwise. Negative value of early entry can drive delay in OTC release or may result in no entry. Positive value of early entry implies firms' incentive to enter early, and therefore if OTC is delayed it suggests the role of OTC market exclusivity: the value of OTC market exclusivity in the delayed entry scenario must be greater than the value of early entry.

The simulation exercise done here is as if Nexium 24HR, Nexium Rx's OTC counterpart, was introduced in May 2011, instead of in May 2014, when its primary patent expired. Nexium's rivals are assumed to follow their equilibrium strategy path when Nexium launches OTC in May 2011. This assumption is taken only for simplification purpose and is relaxed in the full counterfactual simulation in the next counterfactual exercise, where the equilibrium OTC release decisions are solved by solving the full dynamic equilibrium model. We simulate the profit for Rx and OTC Nexium by re-solving price equilibrium and market share with the new market structure brought by early entry.

[Figure 4 around here]

Figure 4 compares the firm profit of Nexium under delayed entry (Blue line) with early entry (Red line). The horizontal axis covers three years before patent expiration and three years after patent expiration, hence plots Nexium firm profit for 24 quarters. The first horizontal line at 12th quarter shows the time period when patent expires. In case of Nexium, the generic Rx enters in February 2015 (15th quarter in our graph) and is shown by the green vertical line. As is clear from the graph, overall profit of Nexium falls significantly after generic entry post patent expiry. The simulation also shows that if the Nexium OTC enters early, then market expansion effect and first mover advantage exceed cannibalization, therefore the value of early entry (measured by the gap between red line and the blue line) is positive. This implies, if Nexium chose to introduce OTC in May 2011, it would make higher profit before patent expiration. However, OTC market exclusivity creates greater value for the firm in the case of delayed entry. As shown in the figure, post patent expiration, in the delayed entry case (the blue line), Nexium OTC brings firm higher profit even after generic Nexium entry in February 2015 (in 15th quarter shown by vertical green line). It would be profitable for Nexium to introduce its OTC earlier, absent the strategic consideration for market exclusivity. The reason for delay is that the three market exclusivity offers a window when Astrazeneca's profit would be higher if Nexium OTC, protected by market exclusivity, managed to absorb its brand Rx consumer who would have been lost to generic rivals and attract consumers from its rivals.

[Figure 5 around here]

Figure 5 plots the value of early entry pre-patent expiration (denoted by the red line) versus the value of OTC market exclusivity post patent expiration (denoted by the blue line).[25] The value of OTC market exclusivity is almost always greater than the value of early entry. Finally, we calibrate the consumer welfare loss caused by the delay of Nexium OTC launch. Our calculations suggest that early entry of Nexium OTC increases consumer welfare by around 500 million dollars each year on average before patent expiration. The welfare enhancement arises from increasing variety of products and tougher competition. More importantly, after patent expires, consumers gain by an even larger amount because of the generic OTC entry.

6.2 Restructuring of Market Exclusivity

If three year market exclusivity induces the strategic delay and welfare loss under the current policy, can a redesign of the market exclusivity provision solve the problem? We consider two different alternatives to the status quo policy. First, we consider the removal of the exclusivity provision. Removing the exclusivity policy, lowers the incentive to innovate and hence may reduce variety of OTC drugs offered in the market. On the other hand, without any incentive for strategic delay, firms that decide to develop the product may introduce the OTC drug earlier than patent expiration in order to enjoy first-mover advantage during the patent period. The net welfare effect of no-exclusivity is ambiguous.

Second, we consider an alternative policy that can potentially eliminate the delay incentive and enhance consumer welfare. Under this policy, three year market exclusivity is granted following the patent expiration, regardless of approval date only if OTC drugs are introduced early.[26] This policy differs from the one in practice where three year market exclusivity to the first firm that makes Rx-to-OTC switch follows the date of OTC drug approval. By ensuring that the market exclusivity in the OTC market is granted beyond patent expiration if OTC drugs are introduced early, this policy removes the incentives for strategic delay. As a result, the number of Rx-to-OTC switches should not decrease relative to the status quo and firms would choose to enter early. While this may serve as a better policy compared to the current provision, this is still a second-best policy as, when it is firms' own interest to introduce the OTC before the patent expiration without this provision, the market exclusivity provision reduces consumer welfare by limiting competition for

[25] Note that, the value of early entry pre-patent expiration is computed by taking the difference between counterfactual profit from early entry and observed profit from delayed entry in the pre-patent expiry period. Similarly, the value of OTC market exclusivity is computed by taking the difference of observed profit from delayed entry and counterfactual profit from early entry in the post-patent expiry period.

[26] A similar proposal is discussed in Shapiro (2016).

three years. Next we discuss in detail the two counterfactual policies and their implications on access to OTC products and consumer welfare through simulation exercise.

Under counterfactual policy of 'no exclusivity', the FDA market exclusivity provision is removed. Therefore, if a manufacturer does not release the OTC version during the Rx patent period, after the patent expiry, a generic OTC may enter the market without any delay. For example, in case of Nexium 24HR (the branded OTC version of Nexium Rx), the OTC version was released and was granted market exclusivity by the FDA in March 2014. The Nexium Rx patent expired in May 2014. The first generic OTC application was also submitted to FDA for review in May 2014 after the Rx patent expiration.[27] However, due to the three year market exclusivity policy, the review and approval of generic OTC was delayed, and the first generic OTC entered the market in August 2017. Under 'no exclusivity' policy, conditional on regulatory approval, the generic OTC would have entered the market in 2014 instead of 2017.

In our counterfactual exercise, we modify the exclusivity provision, solve the dynamic entry game, and simulate the equilibrium entry decisions as well as timing of entry of each manufacturer in this new regulatory regime. Operationally, we solve the model for a new PBE in this counterfactual environment, and use the equilibrium choice probabilities to run 10,000 simulations of industry history. For each simulation draw, we solve for the timing of the OTC switch for each manufacturer, and report the median entry date across all simulation draws. In table 8, the column 'patent expiration' refers to the year of Rx patent expiry for the molecules observed in the sample. The column 'branded OTC entry' refers to the actual year of entry observed in our sample for each molecule. In the column denoted by 'no exclusivity', we report the results from the case where exclusivity is removed. The column 'alt exclusivity' refers to the case where alternative exclusivity model is considered. Note that, earlier release of OTC version increases the consumers' access to drugs while 'no switch' leading to no release of OTC version results in reduced access to drugs.

[Table 8 around here]

Three key points are worth highlighting in the 'no exclusivity' counterfactual. First, our results show that, five molecules will choose not to release the OTC drug in equilibrium under this new policy. While in the actual data, we observe 'no switch' for three out of eleven molecules, two additional products (Axid and Zegerid) would choose to not release the OTC drug when exclusivity provision is removed, leading to lower access to drugs. This is driven by the fact that, in the new policy regime, without exclusivity, Axid and Zegerid do not find it profitable to invest in the fixed cost of developing OTC product due to lower expected

[27] Reference: Link to the application letter in the FDA website [Link]

profit. The profit margin of those two products are further lowered due to early switching decisions of other molecules that belong to the same class. Second, compared to the date of corresponding patent expiration, four molecules: Pepcid, Prilosec, Prevacid and Nexium would choose to enter the OTC market earlier. While Prilosec, Prevacid and Nexium choose to enter right after respective patent expiry in the actual data, they would enter seven to eight years prior to patent expiry in this counterfactual world with no exclusivity. In case of these molecules, the market expansion and the first mover advantage effects dominate the cannibalization effect from introduction of OTC version. Therefore, early entry in the OTC market leads to overall increase in firm profit. In the status-quo policy regime, those three molecules chose to strategically delay the OTC release, and hence removing the exclusivity leads to early entry and improves access. Third, Tagemet and Zantac would enter into OTC market right around patent expiry when exclusivity is removed. For these two molecules, the cannibalization effect dominates the market expansion effect, therefore leading to lower overall profit when OTC version is introduced during the patent period. However, with patent expiry and generic Rx entry, even without market exclusivity, these molecules find it profitable to invest the fixed cost to develop the OTC version. Note that, these two molecules also choose to enter right around patent expiry in the actual data suggesting that market exclusivity harms the access to generic OTC drugs by limiting competition for three years. Although, no-exclusivity policy provides less incentive to innovate leading to no release of five OTC drugs, due to early entry of other products, the overall consumer welfare increases by 350 Million USD on average per year.

In the alternative policy regime, however, the incentive to innovate is protected by providing market exclusivity regardless of approval date. However, the exclusivity is granted only if the molecule chooses to enter at least three years prior to patent expiry. The results from this exercise is reported in the column 'Alt Exclusivity'. As is clear from the table, all the molecules that chose to switch to OTC version under status-quo policy (as observed in the data) also chose to enter the OTC market in this new policy regime. Additionally, except for Tagamet, all other molecules entered much earlier compared to patent expiry year in order to avail the market exclusivity.[28] Therefore, by redesigning the exclusivity policy, incentives to strategically delay are eliminated. This leads to higher overall access to drugs and hence, higher consumer welfare. Therefore, our counterfactual exercise suggests that status-quo policy leads to inefficient outcome and a redesign of the exclusivity policy can benefit consumers by improving access and welfare.

[28]In case of Tagamet, the cannibalization from OTC dominates the benefits from exclusivity leading to the delay in entry in different policy regimes.

7 Concluding Remarks

This paper evaluates the impacts of FDA's market exclusivity policy on pharmaceutical manufacturers' incentives to develop and release the OTC version in the context of US anti-ulcer drug market. This paper contributes by showing that, the current FDA market exclusivity policy is inefficient, *may lead* to strategic delay in the OTC launch by Rx manufacturers, resulting in lower access to drugs and reduced consumer welfare. To address this, we develop and estimate a structural model of demand and supply for US anti-ulcer drug market, and evaluate alternative exclusivity policies. We show that removing the exclusivity policy may actually *improve* consumer welfare. However, no exclusivity may lead to lower incentives to innovate and hence may lower access to OTC drugs, as some manufacturers may choose not to release the OTC version. We also evaluate another counterfactual policy where market exclusivity is granted beyond patent expiration, if OTC drugs are introduced early. We find that the policy eliminates the incentives for strategic delay while protecting the incentives for innovation, hence improves access to drugs and increases overall consumer welfare.

This paper contributes to the literature that studies the unintended effects of IP policies by considering interactions between two segments of the pharmaceutical market- Prescription drug and OTC market. Our counterfactual exercise also contributes to the research on the optimal design of the IP policy. Our study demonstrates that maintaining a delicate balance between the incentives of different players in the pharmaceutical market can have important welfare implications while designing the OTC drug exclusivity policy.

8 Tables and Graphs

Table 1: Entry of Anti-ulcer Drugs by Molecule

Molecule name	Class	Brand name	Brand entry	Patent expiration	1st OTC entry	1st Generic Rx entry	Avg Rx Revenue
Cimetidine	H2-Blocker	Tagamet	Aug-77	May-94	Aug-95	May-94	1,491
Ranitidine	H2-Blocker	Zantac	Jul-83	Jul-97	Apr-96	Jul-97	5,165
Famotidine	H2-Blocker	Pepcid	Nov-86	Oct-00	Jun-95	Apr-01	1,641
Nizatidine	H2-Blocker	Axid	May-88	Apr-02	Jul-96	Oct-98	925
Omeprazole	PPI	Prilosec	Oct-89	Oct-01	Sep-03	Nov-02	7,205
Lansoprazole	PPI	Prevacid	May-95	Nov-09	Nov-09	Nov-09	7,957
Rabeprazole	PPI	Aciphex	Sep-99	May-13	-	Nov-13	2,837
Pantoprazole	PPI	Protonix	Apr-00	Jan-11	-	Dec-07	4,820
Esomeprazole	PPI	Nexium	Feb-01	May-14	Mar-14	Feb-15	13,042
Omeprazole NaHCO3	PPI	Zegerid	Oct-04	July-16	Mar-10	Jul-10	330
Dexlansoprazole	PPI	Dexilant	Feb-09	Jan-23	-	-	2,067

Notes: Each row in this table corresponds to a molecule used as an Anti-ulcer drug. The column 'Brand entry' refers to the release of branded prescription drug. The columns '1st OTC entry' and '1st Generic Rx entry' refers to the time-line of over-the-counter version and generic Rx version respectively. The Average Rx revenue is reported in Million USD.

Table 2: Summary Statistics

	Mean	Standard Deviation
Out-of-Pocket Price per Prescription	24	(15)
Full Price per Prescription	58	(85)
Advertising Expenditure (million $)	3	(8)
Accumulative Advertising Expenditure (million $)	390	(877)
Accumulative Advertising Expenditure in last 3 years(million $)	102	(256)
Revenue (million $)	112	(265)
Miligrams (in millions)	6036	(1.2e+04)
Number of Prescriptions (in millions)	2.5	(5.1)
Market share (market size=30 percent of popuation)	0.02	(0.05)
Outside Option Market Share	0.41	(0.18)
Within Group Market Share (H2 v.s. PPI)	0.10	(0.17)
Within Group Market Share (Brand v.s. Generic)	0.09	(0.17)
Within Group Market Share (Rx v.s. OTC)	0.09	(0.13)
Population (in millions)	299	(17)
Observations	6116	

Note: The unit of observation is month*product. The number of products in each month is different because of product entry and exit. The market is defined as the national market in a certain month. On average, there are 21 products in each market (6065/288 months=21.06). Data source: IMS Health NSP and IPS 1992m1-2015m12.

Table 3: Demand Results: Nested Logit Estimation

	(OLS)	(IV)
Copay	-0.06***	-0.28***
	(0.002)	(0.06)
Nesting Parameter	0.91***	0.43***
	(0.01)	(0.04)
Constant	1.95***	3.52***
	(0.2)	(0.89)
BrandRx x generic competition	-0.27***	-1.1***
	(0.04)	(0.13)
OTC Dummy	0.73***	4.6***
	(0.12)	(1.17)
BrandRx x OTC	-0.39***	-0.36***
	(0.05)	(0.12)
Generic Rx x OTC	-0.67***	-0.11
	(0.1)	(0.19)
Log Cumulative Advertisement	-0.02***	0.13***
	(0.01)	(0.03)
Log Cumulative Ad x PPI Class dummy	0.08***	0.17***
	(0.01)	(0.05)
Observations	6,116	6,116
Firm-Molecule-Form FE	Yes	Yes
Time Since Entry Dummy (upto 12 months)	Yes	Yes
Time Since Entry Dummy x PPI Dummy	Yes	Yes
Time Dummy by Class	Yes	Yes

(standard errors in parentheses)
*** p<0.01, ** p<0.05, * p<0.1

Table 4: **Estimated Marginal Costs by Brand and Marketing Status**

Brand and Marketing status	Price	Average Estimated MC	SD of Estimated MC
Brand Rx	111	68	55
Generic Rx	20	17	18
Brand OTC	25	22	6
Generic OTC	11	9	7
No of Obs: 6116			

Note: This table reports the average and standard deviation of estimated marginal costs for different brand and marketing status. The numbers are reported in USD.

Table 5: **Marginal Cost Parameter Estimates**

		Coefficient	S. Error
Cimetidine	Tablet	-1.2	(0.13)
Dexlansoprazole	Capsule	-1.7	(0.06)
Esomeprazole	Capsule	-1.9	(0.06)
Famotidine	Tablet	-1.2	(0.13)
Lansoprazole	Capsule	-1.8	(0.06)
Lansoprazole	Tablet	-1.7	(0.06)
Nizatidine	Capsule	-0.9	(0.13)
Nizatidine	Tablet	-1.2	(0.13)
Omeprazole	Capsule	-1.3	(0.06)
Omeprazole	Tablet	-1.7	(0.07)
OmeprazoleNaHCO3	Capsule	-1.7	(0.06)
Pantoprazole	Tablet	-1.5	(0.06)
Rabeprazole	Tablet	-1.2	(0.06)
Ranitidine	Capsule	-1.1	(0.13)
Ranitidine	Tablet	-1.2	(0.13)
Time Dummy by Class			Yes
Time Since Entry Dummy			Yes
Brand-Molecule-Form Dummy			Yes
R-squared			0.92
The base product is Rabeprazole in capsule form			
No of Obs: 6116			

Note: This table reports the coefficients and standard errors from estimation of marginal cost model (see equation 5.1.

Table 6: **Maximum Likelihood Estimates of the Fixed Cost**

	Assumed Order of Moves	
	More Experienced First	Less Experienced First
Fixed Cost of Releasing OTC	15.86***	15.99***
	(3.528)	(3.501)
Log Likelihood	-67.10	-67.26

Note: The fixed cost figures reported here are in million USD. The numbers here are estimated for the case where the discount factor(β) is assumed to be 0.88. Standard errors are reported in the parentheses.

Table 7: **Sensitivity of Fixed Cost to Choice of β**

	$\beta = 0.75$	$\beta = 0.8$	$\beta = 0.92$
Fixed Cost of Releasing OTC	13.21**	14.79	18.83*
	(6.963)	(12.41)	(11.09)
Log Likelihood	-61.88	-63.63	-69.82

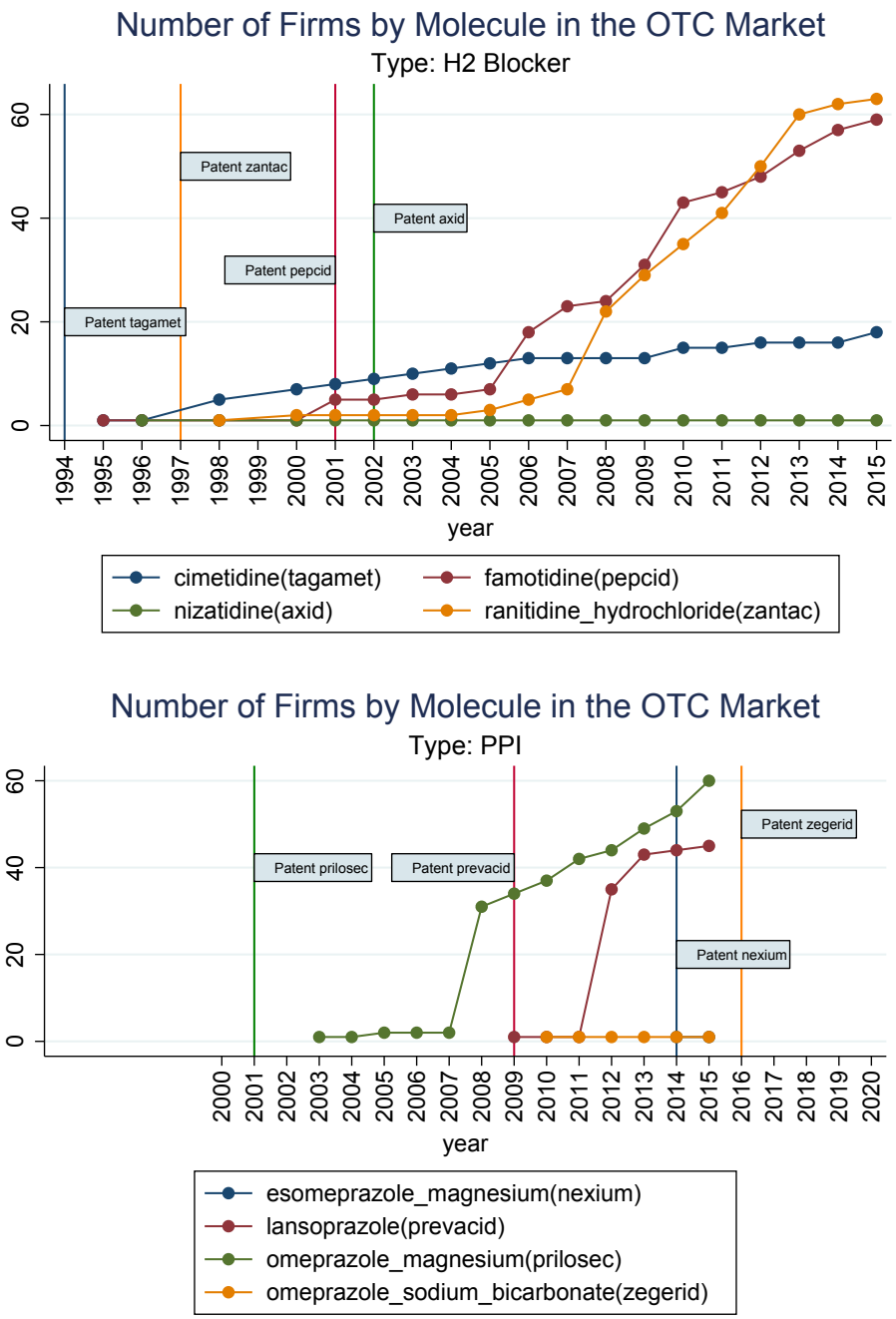
Note: The fixed cost figures reported here are in million USD. Standard errors are reported in the parentheses.

Table 8: **Results from Counterfactual Analysis: Alternative Exclusivity Designs**

		Patent	Branded OTC	Counterfactual Results	
Brand	Molecule	expiration	entry (in data)	No Exclusivity	Alt. Exclusivity
Tagamet	Cimetidine	1994	1995	1994	1994
Zantac	Ranitidine	1997	1996	1997	1994
Pepcid	Famotidine	2000	1995	1995	1995
Axid	Nizatidine	2002	1996	No Switch	1995
Prilosec	Omeprazole	2001	2003	1996	1995
Prevacid	Lansoprazole	2009	2009	2001	2001
Aciphex	Rabeprazole	2013	No Switch	No Switch	No Switch
Protonix	Pantoprazole	2011	No Switch	No Switch	No Switch
Nexium	Esomeprazole	2014	2014	2007	2007
Zegerid	OmeprazoleNaHCO3	2016	2010	No Switch	2010
Dexilant	Dexlansoprazole	2020	No Switch	No Switch	No Switch
	Δ in Consumer Welfare (per-year) compared to status-quo policy			350 Million	430 Million

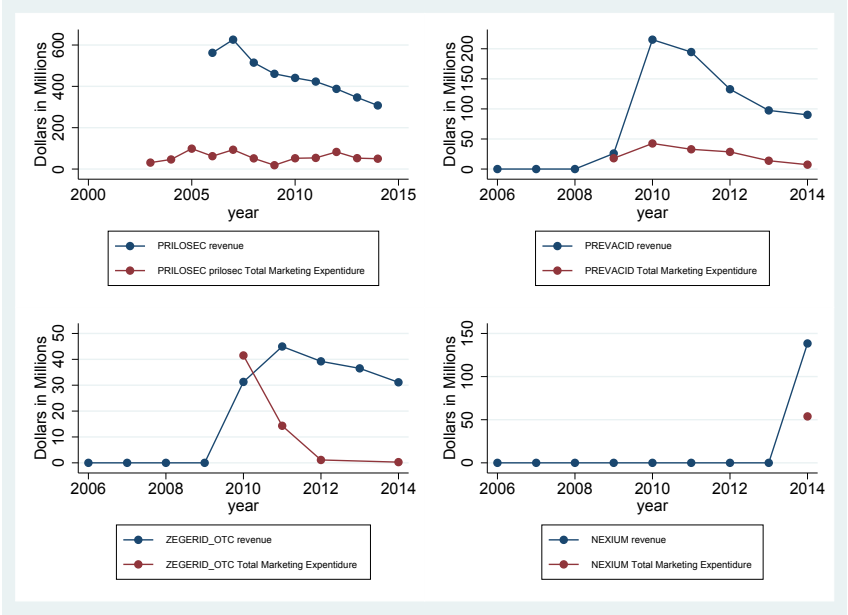
Note: The table reports the results from counterfactual analysis. The column 'Patent expiration' denotes the year of Rx patent expiry for the molecules observed in our sample. The column 'Branded OTC entry' denotes the year of entry of the branded OTC products that we observe in the data. 'No Switch' refers to the case where the branded Rx does not release its OTC version. The 'No Exclusivity' column refers to the counterfactual exercise where the three year FDA market exclusivity is removed. The 'Alt. Exclusivity' column refers to the case where three year exclusivity is granted only if the molecule is released more than three years prior to patent expiry.

Figure 1: Number of Firms by Molecule in the OTC Market



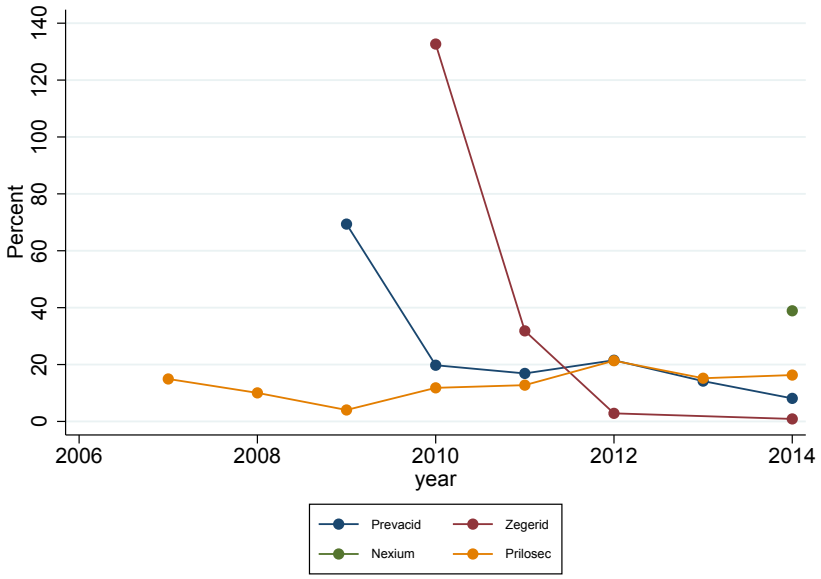
Note: The vertical lines indicate the date of patent expiration for each molecule. The number of firms that manufacture each molecule does not grow initially due to market exclusivity. After the exclusivity period, it surges to more than 20 firms in less than 3 years. Two out of four H2 blocker molecule (Tagamet and Zantac) entered the OTC market at their patent' expirations. Three out of four PPI molecules (with the exception of Zegerid) entered the market at their patent expiration. Source: National Drug Code.

Figure 2: Advertising Expenditure and Total Sales by OTC Brand



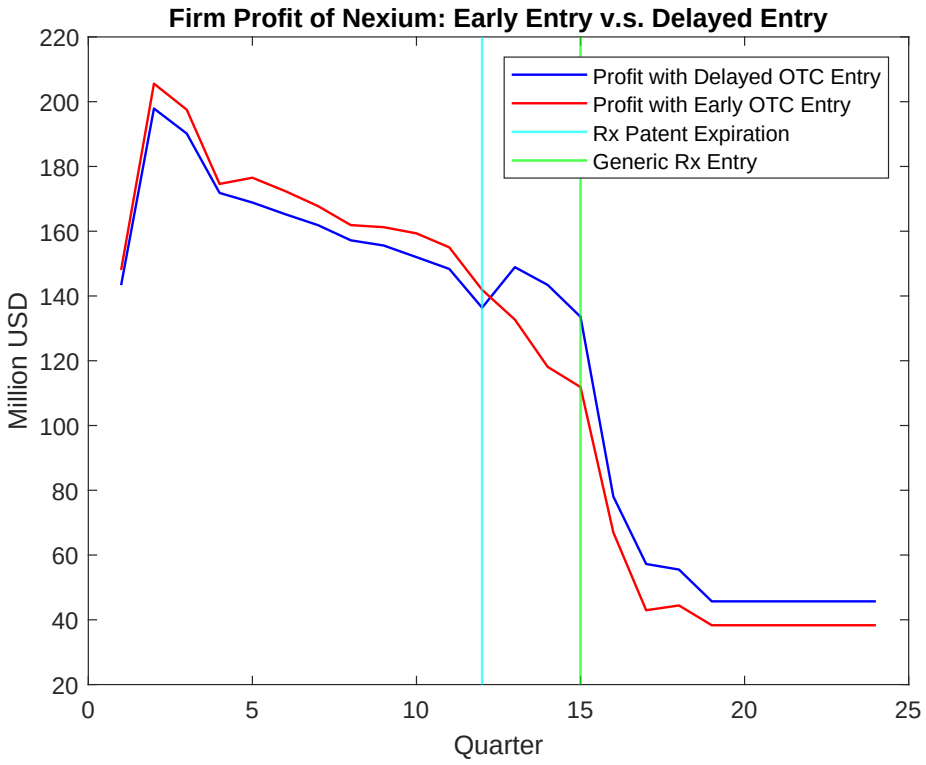
Source: Ad$Summary from TNS Multimedia Intelligence, and Nielsen Retailer Scanner Data

Figure 3: Ad-Sales Ratio by OTC Brand



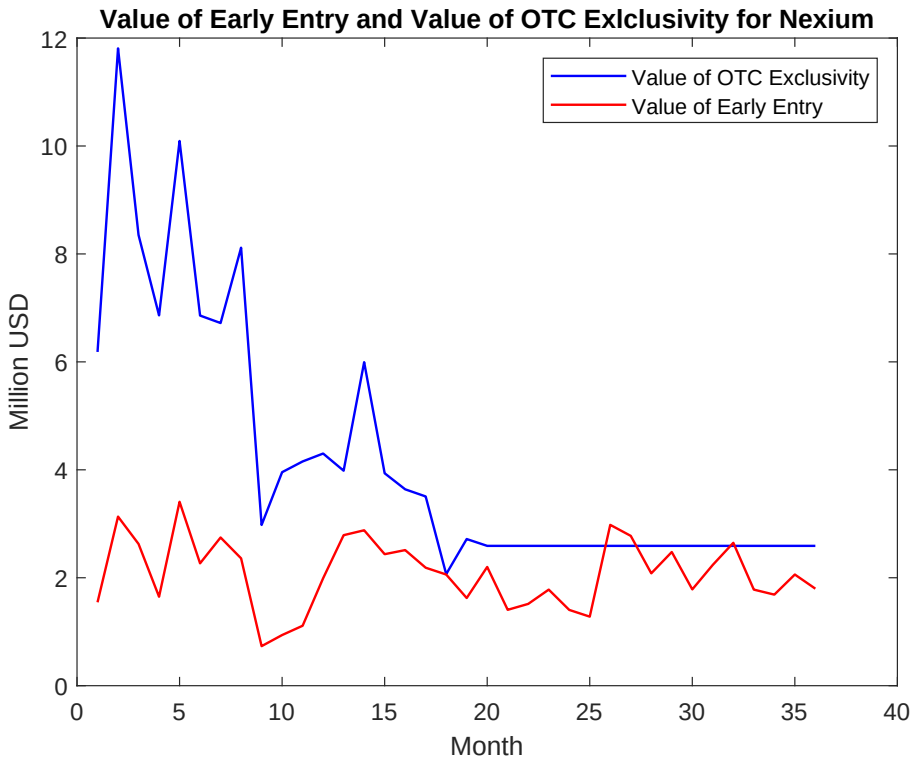
Source: Ad$Summary from TNS Multimedia Intelligence, and Nielsen Retailer Scanner Data

Figure 4: Firm Profit of Nexium: Early Entry v.s. Delayed Entry under Status Quo Policy



Note: The blue line and the red line plot the Nexium quarterly profit for delayed entry (as observed in actual data) and early entry (our counterfactual exercise) of Nexium OTC under Status Quo exclusivity policy. The cyan vertical line indicates Nexium Patent expiration date, and the green vertical line indicates the date when the first Nexium Rx generic entered the market.

Figure 5: Value of Early Entry and Value of OTC Exclusivity for Nexium under StatusQuo Policy



Note: The blue line plots the value of OTC exclusivity (measured by the monthly profit increase for AstraZeneca during three years post patent expiration, in million dollars) when Nexium is introduced at patent expiration. The red line plots the value of early entry (measured by the monthly profit increase for AstraZeneca during three years before patent expiration, in million dollars) when Nexium is introduced early. Nexium OTC entry was delayed until patent expiration because the value of OTC exclusivity exceeds the value of early entry.

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A Appendix: For On-line Publication Only

A.1 Regulatory Requirement for Rx-to-OTC Switch

Rx drugs need to be supervised by licensed medical practitioners, while OTC drugs do not, as explicitly established in Durham-Humphrey Amendment in 1951. The application for an Rx-to-OTC switch follows the New Drug Application (NDA) process [29] required for the approval of a prescription drug. The FDA requires studies that involve a hybrid of clinical safety and consumer behavior research in reaching an approval decision for Rx-to-OTC switch.

There are no clear standards for how to conduct or evaluate the studies. Generally speaking, Rx-to-OTC studies involve the following objectives:

- Clinical trials to prove efficacy: to prove efficacy for OTC use (based on evidence from Rx clinical trials or conduct new Phase III trials)
- Clinical trials to prove safety and side effects: (based on evidence Rx clinical trials, and from post-marketing surveillance for Rx drugs or new clinical studies),
- Label comprehension studies: to prove that consumer can read and understand the label and package
- Consumer self-selection studies: to prove that patients can self-select OTC medication,
- Compliance and actual use studies

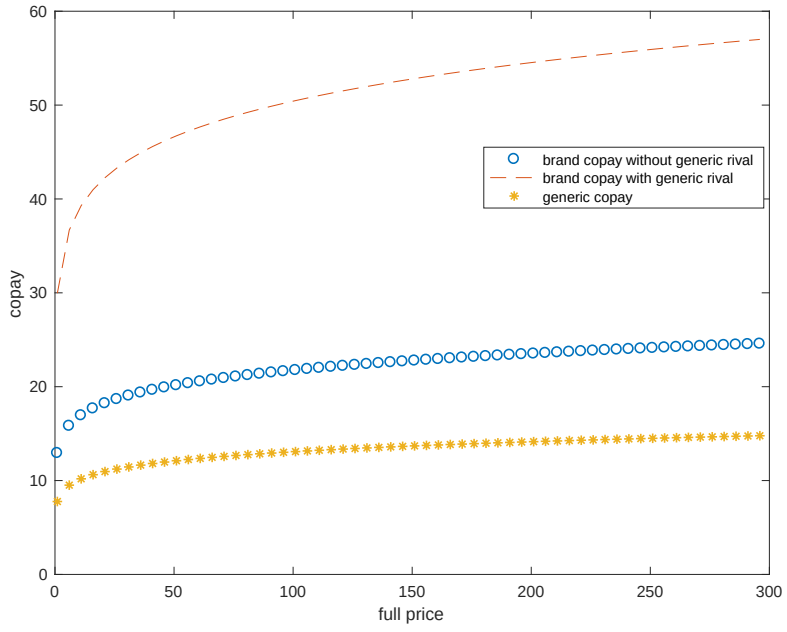
Data to support the switch are derived from randomized controlled clinical trials in the original prescription NDA, as well as post marketing safety surveillance, and literature reports. New efficacy and safety data from controlled clinical trials need to be included if the OTC indications or strengths are different from those for the prescription drug. Some studies are unique to the OTC setting, such as the comprehension of the proposed labelling studies, and the studies to evaluate consumer behavior in an OTC setting by conducting actual use and self-selection studies. These studies incur a fixed cost for firms that make the switch, in addition to the uncertainty in the approval outcome firms face. A different process through which many other OTC products are regulated is the OTC Drug Monograph system for drug active ingredients that are Generally Recognized As Safety and Effective (GRASE), such as aspirin.

[29] NDA Chemical Type 8 refers to Rx-to-OTC switch. Other types are: 1 New molecular entity (NME); 2 New active ingredient (new salt, new noncovalent derivative, new ester); 3 New dosage form; 4 New combination; 5 New formulation or new manufacturer; 6 New indication [no longer used]; 7 Drug already marketed without an approved NDA; 8 OTC (over-the-counter) switch; 9 New indication submitted as distinct NDA, consolidated with original NDA after approval; 10 New indication submitted as distinct NDA - not consolidated.

B Copayment specification

Arcidiacono et al. (2013) estimate a copay function for branded Rx drugs without facing generic competition in anti-ulcer category using SDI Health data and AdvancePCS copayment data. Similar to their assumptions, we assume that the curvature of the pricing relationship is the same for generic drugs and branded drugs with generic competitors, and adjust the price level such that the average price of generics/ branded drugs with generic competitors is equivalent to the average price of generics/non-preferred brand drugs given in Kaiser Family Foundation's report 'Employer Health Benefits Survey 2014.' It is worth pointing out that, in this specification, the copay function is treated as exogenous. In particular, we abstract away from the bargaining between drug manufacturers and insurers. Drug insurance plan is generally structured based on all prescription drugs, and any particular drug or class of drugs may only have limited effects on the setting of copay and other insurance features.

Figure 6: Copay Function



Source: Arcidiacono et al. (2013), SDI Health data and AdvancePCS copayment data, Kaiser Family Foundation's report 'Employer Health Benefits Survey 2014'

C Rebate specification

[To be added]