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

Debi P Mohapatra† Yang Zhang‡

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Abstract

This paper studies strategic spillovers of regulations intended for a particular market segment to closely related market segments. We study the US pharmaceutical market where market exclusivity is granted to the first over-the-counter (OTC) drug, independent of patents for prescription-drugs. We show that due to the interplay of incentives in the prescription and OTC drug markets, market exclusivity in its current form *reduces* consumer welfare, as it causes many firms to *delay* entry into the OTC drug market until prescription-drug patents expire. An alternative policy that ties OTC exclusivity provision to prescription-drug patent expiry dates improves drug-access and consumer welfare.

Keywords: market exclusivity policy, strategic spillover, access to drugs, pharmaceutical market

1 Introduction

Regulatory policies designed to encourage product entry, improve product variety, and promote competition have been subjects of keen interest for economists, policy-makers, and anti-trust regulators. For example, federal and state governments in the US have adopted subsidy policies to promote electric vehicle sales in the US market (Holland et al. (2016)). To promote the growth of renewable electricity sources, such as wind and solar, governments

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†Dept of Resource Economics, Univ of Massachusetts, Amherst, MA. Email: dmohapatra@umass.edu

‡Dept of Economics, Cornell University, Ithaca, NY. Email: yz656@cornell.edu.

in several countries provide tax credits and investment subsidies to wind and solar electricity generators (Murray et al. (2014), De Groote and Verboven (2019)). Similarly, regarding pharmaceutical and regulated healthcare products, where establishing safety and efficacy is an important requirement for the release of a new product, regulatory policies designed to encourage product entry often take the form of patents and market exclusivity. These policies involve complex design problems and have important implications for consumer welfare. In particular, such policies are often designed by taking only a single market segment into consideration. If firms that are affected by such policies operate in multiple market segments, however, then ignoring spillovers across those segments may lead to unintended consequences and generate inefficiencies.

We investigate these issues by focusing on the design of market exclusivity policies in the context of the release of a new over-the-counter (OTC) drug in the US pharmaceutical market.[1] For prescription (Rx) drugs designed to treat indications that can be self-diagnosed, self-treated, and self-monitored, a pharmaceutical firm may choose to introduce an OTC version of an Rx drug.[2] Many, but not all, molecules that are candidates for an Rx-to-OTC switch have been converted to OTC versions at varying points in their life-cycles. According to the US Food and Drug Administration (FDA), more than 700 OTC drugs have been approved through Rx-to-OTC switches since 1976 (FDA (May, 2016)). An Rx-to-OTC switch improves "access to drugs", as it eliminates the need for a physician's prescription (Scott-Morton and Kyle (2011)). OTC medicines also enable the healthcare system to utilize its limited resources in the diagnosis and treatment of more serious diseases and medical conditions that necessitate the direct involvement of physician while at the same time providing safe, effective, and accessible treatments for a range of conditions to consumers. OTC drug usage is prevalent in the US; in 2018 close to 81% of US adults used OTC medicines as a first-line treatment for minor illnesses and made on average 26 trips a year to purchase OTC drugs compared with three visits to their doctors (PharmaTechFocus (February, 2018)). According to a report issued by the Consumer Healthcare Products Association (CHPA), wider

[1] In the US, a patient can access a drug through the prescription market or through the OTC drug market. A patient can obtain a prescription from a physician and purchase either a branded version of the prescribed drug or a generic version (if generic versions are available) from the prescription market. If the drug is also available with over-the-counter status, however, then the patient does not require a prescription and can purchase the drug directly from a retail store. Both prescription and OTC drugs are regulated for safety and efficacy by the Food and Drug Administration (FDA). Typically, OTC drugs were first sold as branded drugs in the prescription market and then OTC-versions were introduced at some point in the drug's life-cycle. We discuss this in greater detail in Section 2.

[2] The most common agents that meet these requirements include allergy medicines, analgesics, antifungal medicines, drugs used to treat gastrointestinal disorders such as heartburn, acid reflux, diarrhea, and constipation, medicines that treat coughs, colds, and the flu, medicated skin products (including first aid and anti-itch medicines), sleep aids, and smoking-cessation products (Ellery and Hansen (2012)).

availability of OTC medicine may create substantial value for the US healthcare system, totaling approximately $146 billion in savings per year on drug costs and clinical visit costs (CHPA (March, 2019)).

Introducing OTC version of a prescription drug, however, is a costly and uncertain process. Firms that make Rx-to-OTC switches have to undertake risky investments in clinical safety and consumer behavior research and incur the shadow costs when an application fails to obtain approval from the FDA. Additionally, to market such drugs, firms also invest in distribution channels through retailer networks. To help firms recoup their fixed costs and to encourage the introduction of OTC drugs, the FDA provides three-year market exclusivity in the OTC drug market to a firm that makes the first Rx-to-OTC switch with a given drug (following the Drug Price Competition and Patent Restoration Act of 1984, i.e. the Hatch-Waxman Act). During the market exclusivity period, the FDA does not approve any other OTC applications for the same molecule. OTC drug market exclusivity thus allows the first OTC drug to be the only drug in the OTC drug market for the relevant molecule for three years. It is important to highlight that exclusivity in the OTC drug market is granted independently of any patents that the molecule may enjoy in the prescription market.[3]

The goal of providing market exclusivity is to encourage firms to develop and release OTC drugs; does this policy in its current design achieve its goal? In particular, how are incentives that encourage firms to switch to OTC status and timing of switching decisions, affected by a firm's operations in the prescription market? To answer these questions, we develop and estimate a structural model of demand, OTC drug launch decisions, and pricing in the US anti-ulcer prescription and OTC drug markets. Our principal finding is that the current OTC drug market exclusivity policy, which is intended to encourage the development and release of OTC drugs, may actually *reduce consumer welfare* by delaying OTC entry until an Rx drug patent expires. In other words, if the FDA were to eliminate market exclusivity altogether, it would incentivize firms to release the OTC versions of drugs earlier and that would improve consumer welfare. The elimination of exclusivity might, however, weaken firms' incentives to make risky investments in developing OTC products.

Can an alternative design improve access to OTC drugs and enhance consumer welfare? We evaluate an alternative policy that ties OTC drug market exclusivity to Rx patent expiry dates, where market exclusivity is preserved after patent expiration if an OTC drug is introduced more than three years earlier than patent expiration. We find that this alternative design eliminates incentives to engage in strategic delay, protects firms' interests in making

[3]Note that, if a molecule is under patent protection in the prescription market, then only the firm that holds the patents for the molecule is eligible to release the OTC version. However, after the patent expires in the prescription market, other firms are also eligible to make the Rx-to-OTC switch. We discuss this issue in greater detail in Section 2.1.

risky investments and enhances consumer welfare.

The timing of OTC entry is an important aspect of access to OTC drugs. For indications for which OTC drugs are a viable option,[4] the benefits of OTC entry will not materialize until the drug is introduced to the OTC drug market. Our paper shows that the market structure of the prescription drug segment affects the timing of OTC entry decisions, and this spillover effect has significant welfare implications. We study this relationship in the context of the market for anti-ulcer drugs. Several features of this market make it a suitable setting for this study. First, these drugs constitute an important segment of the US pharmaceutical market, with average total annual revenues close to 28 billion USD as measured during our sample period that runs from January 1992 through December 2015. Second, Rx-to-OTC switching is common with these drugs. Our study considers 11 molecules sold in the US, out of which 8 were released in OTC versions at varying points in their life-cycles. Finally, in our data, we observe a subset of branded Rx manufacturers delay launch of OTC drugs until the patent in the prescription market expires. For example, in May 1995 a popular heartburn drug, 'Lansoprazole', was launched by Takeda Pharmaceuticals under the brand name "Prevacid". The Rx patent for Prevacid expired in November 2009. While Takeda could have chosen to launch the OTC version at any time prior to its Rx patent expiry, the OTC version was introduced by Takeda in November 2009 almost precisely when the Rx patent expired. We observe similar behavior involving delayed entry by several branded Rx producers (Tagamet, Zantac, Prilosec, and Nexium) as well. However, we also observe other branded Rx drugs (such as Pepcid and Axid) entering the OTC drug market five to six years prior to Rx patent expiry.[5]

Conditional on releasing an OTC drug, why do some brand Rx firms wait until patent expiration to introduce the OTC, but others introduce OTC versions before patent expiration? Our paper shows that the current design of the three-year market exclusivity policy, whereby exclusivity is granted independently of Rx patent expiry dates, is the key driver of such variations in entry timing. A firm chooses to enter the OTC drug market at a time when three-year OTC drug market exclusivity is most valuable. When an Rx-to-OTC switch is made earlier than Rx-patent expiration, a firm's period of OTC drug market exclusivity overlaps with its Rx patent protection. This overlap creates "cannibalization" if consumers who would have purchased the higher-priced Rx version substitute to the OTC version. On the other hand, releasing an OTC drug early could expand the market and benefit a firm by giving it a first-mover advantage. In addition, the value of market exclusivity will change de-

[4] As mentioned earlier, OTC drugs are a viable option for the class of indications that falls under the category of self-diagnosis, self-monitoring, and self-treatment.

[5] We discuss this data pattern in greater detail in Section 2.2, in connection with Table 1.

pending 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 the first-mover advantage, the market-expansion effect, the degree of cannibalization, the fixed costs incurred to execute the conversion, and differences in the value of market exclusivity over time. If a firm executes an Rx-to-OTC switch early, it gains because of first-mover advantage and the market-expansion effects but loses through cannibalization. When the value of early entry exceeds the value of OTC drug market exclusivity following patent expiration, firms choose to enter early. When the value of OTC drug market exclusivity exceeds the value of early entry, firms choose to delay entry into the OTC drug market. If the fixed entry cost is greater than the profits from either early entry or delayed entry, firms choose not to introduce their OTC products.

To capture these economic factors, the main portion of our paper estimates a structural model of demand, OTC drug launch decisions, and pricing in the US anti-ulcer prescription and OTC drug markets. The model benefits from several key features. First, we capture rich substitution patterns between products by modeling pharmaceutical demand using a discrete-choice framework developed by Bresnahan, Stern and Trajtenberg (1997). The framework allows for correlations across multiple overlapping nests, or clusters, of products. In particular, we allow for preferences to be correlated between products with the same marketing status (Rx or OTC), the same brand status (branded or generic), the same molecule, and the same class.[6] Our framework allows the data to indicate whether (and quantify the extent to which) drugs that vary across one or more of these dimensions are substitutes. The estimated demand parameters therefore capture the key substitution patterns between Rx and OTC products, both within a molecule and across molecules between branded and generic anti-ulcer drugs, enabling us to pin down the spillover effects between the two market segments. Second, we recover marginal costs for drug production using equilibrium first-order conditions resulting from profit maximization under the assumption of a Bertrand-Nash equilibrium in the price-setting game. Third, we embed these implied period profits into a finite-horizon discrete-choice dynamic oligopoly game of OTC entry and estimate its key parameter (the average fixed costs of making an Rx-to-OTC switch), explicitly incorporating the endogenous evolution of market structure. We model the firms' investment decision while developing OTC drugs as a discrete choice between switching to OTC and not switching, with sequential moves between firms and private cost shocks associated

[6]Older anti-ulcer drugs belong to the H2-class and were introduced and marketed in the late 1970s and 1980s. The relatively newer molecules belong to the PPI class and were introduced in the early 1990s. Molecules within a given class (H2 or PPI) are often considered closer substitutes for each other. We discuss this issue in greater detail in Section 2.2.

with each of the dynamic discrete alternatives. For each candidate vector of parameters, we solve this dynamic game for a perfect Bayesian equilibrium (PBE) by backward induction, construct the likelihood of observing the actual choices in the data, and obtain as a maximum likelihood estimate the parameter vector that best rationalizes the observed switching patterns.

The estimated demand and supply parameters enable us to quantify the market-expansion effects and first-mover advantages of releasing an OTC product that improves a firm's profits in the OTC drug market as well as the cannibalization effects of OTC drugs on Rx products that negatively affects profits in the prescription market. In the final step of our empirical analysis, we use the estimated model to conduct counterfactual simulations and evaluate the welfare implications of alternative policy regulations. In particular, we evaluate a counterfactual world that lacks market exclusivity and investigate alternative designs that ties OTC drug market exclusivity provision to prescription drug patent expiry dates, and compare the resulting switching patterns, drug access, and consumer welfare with those from the baseline model under the status-quo policy. To the best of our knowledge, this is the first structural model that provides for joint analysis of two market segments in the US pharmaceutical industry and reveals the spillover effects between the two market segments.

Our demand estimates suggest that there is a strong correlation in preferences for products with similar characteristics. This helps us quantify the cannibalization effects an Rx manufacturer faces while introducing the OTC version. Additionally, we document strong cross-product substitution between drugs within the Rx and OTC drug markets. For example, our results suggest that, if Nexium OTC is removed from a consumer's choice set, the consumer on average is more likely to switch to another product offered in the OTC drug market (for example, Prilosec OTC) rather than switch to the Rx market and opt for Nexium Rx. These cross-substitution patterns play an important role while modeling dynamic OTC drug launch decisions by firms. In particular, this effect suggests that an Rx manufacturer may decide to switch to OTC preemptively even before its own patent expires if it anticipates future competition in the OTC drug market from other molecules. On the supply side, our marginal cost estimates imply that the costs of producing branded Rx drugs are higher than the costs of producing generic Rx and OTC drugs. This finding is in line with findings from Arcidiacono et al. (2013), who also document significantly higher marginal costs for branded products while studying the US anti-ulcer drug market between 1991 and 2010. Finally, our fixed cost estimates suggest that firms on average spend close to 43 million USD to develop, release, and market the OTC versions of their molecules.

Using the estimated parameters, we conduct counterfactual simulations. Our first counterfactual exercise uses the Nexium OTC launch as a case study to establish that the current

provision of the FDA market exclusivity policy may drive firms to delay OTC launches until patent expiration. The branded Nexium drug was introduced by AstraZeneca in February 2001 in the prescription market. Nexium's primary patent in the Rx market expired in May 2014. While AstraZeneca could have chosen to introduce the OTC version at any time earlier than the prescription patent expiry, it chose to release the OTC version in May 2014, just as its primary patent expired. Our counterfactual exercise simulates a world where Nexium 24HR, Nexium Rx's OTC counterpart, was introduced in May 2011, three years prior to the prescription patent expiry, instead of in May 2014. We show that, under *status quo market exclusivity policy*, if AstraZeneca had introduced OTC Nexium earlier, it would have earned higher profits prior to patent expiration, because the first-mover advantage and market expansion effect associated with early-entry dominate the cannibalization effect of OTC releases prior to patent expiration. In the post-patent period, however, the market exclusivity that accompanies delayed-OTC entry at the time of patent expiration provides a window in which AstraZeneca effectively fences off competition from generic products in the OTC drug market. The value of OTC drug market exclusivity at patent expiration is greater than the value at early-entry, which drives AstraZeneca's decision to delay the introduction of OTC Nexium. This finding suggests that the FDA market-exclusivity policy may lead to strategic delays in OTC launches by Rx manufacturers, thereby restricting access to drugs.

Next, we evaluate a counterfactual policy regime where no market exclusivity is granted by the FDA. Eliminating market exclusivity also eliminates a manufacturer's incentive to strategically delay an OTC entry. Doing so may also, however, negatively affect the firm's incentives to undertake risky investments while making the Rx-to-OTC switch and hence may restrict the product variety in the OTC drug market segment. Our counterfactual exercise computes the new industry equilibrium by solving the dynamic OTC entry game and simulates the Rx-to-OTC switching decisions, the timing of the switch for each manufacturer, and consumer welfare in this new regulatory regime. We find that, in the absence of market exclusivity, and conditional on making a switch, all molecules would choose to enter into the OTC drug market earlier than the date of the corresponding patent expiration. In particular, while Tagamet, Prilosec, Prevacid, and Nexium chose to enter immediately following their respective prescription patent expiry in the actual data, they would on average enter the OTC drug market three to four years prior to the patent expiry under a no-exclusivity counterfactual conditional on making the Rx-to-OTC switch. This would improve access to drugs and enhance consumer welfare. In case of Axid, Prevacid, and Zegerid, however, the elimination of market exclusivity makes it highly likely that the corresponding firms would not enter into the OTC drug market, which reduces consumer welfare. Overall, although the no-exclusivity policy provides a weaker incentive to innovate and thereby reduces the

probability of Rx-to-OTC switches with respect to these three molecules, the early entry of other branded and generic OTC products increases overall consumer welfare by 1.4 billion USD over the status-quo policy.

We then evaluate an alternative market exclusivity policy design that ties market exclusivity to Rx-patent expiration dates. We call this alternative policy as "expanded market exclusivity policy" (hereafter "expanded MEP"). In this counterfactual regulatory regime, three years of market exclusivity are granted following the patent expiration, when an OTC is introduced at least three years prior to patent expiry. Because market exclusivity is granted beyond a patent expiration if an OTC drug is introduced early, this policy design eliminates the incentives for strategic delay. Our simulation exercise reveals that, as is the case with the no-exclusivity policy, conditional on making the Rx-to-OTC switch all molecules would be entering into the OTC drug market earlier than the date of the corresponding patent expiration. An additional advantage of this policy regime is that it restores the incentives to innovate and hence is more likely to result in expanded product variety in the OTC drug market. In particular, molecules such as Axid, Prevacid and Zegerid which were not released as OTC drugs under the no-exclusivity regime, are more likely to enter the OTC drug market under the expanded MEP regime. Therefore, the policy does eliminate the incentive to delay strategically without significantly affecting the incentive to innovate. This ensures greater access to drugs and improves consumer welfare. In particular, consumer welfare increases overall by 3.2 billion USD over the status-quo policy. Our analysis shows that the current design of the market exclusivity policy leads to unintended inefficiency and a reduction in consumer welfare, and can be improved significantly by redesigning the market exclusivity structure.

This paper contributes to several strands of literature. The first strand of literature includes studies of pharmaceutical regulation and in particular of the Hatch-Waxman Act and regulatory exclusivity policies (Berndt, Kyle and Ling (2003), Grabowski and Kyle (2007), Ching (2010), Iizuka (2012), Hemphill and Sampat (2012), Arcidiacono et al. (2013), Appelt (2015), Branstetter, Chatterjee and Higgins (2016), Shapiro (2016), Conti and Berndt (2016), Olson and Yin (2017), and Grennan and Town (2020) among others). More generally, this paper contributes to a better understanding of the interplay between the functioning of the market, competition policy, and innovation policy and builds on the work by Aghion et al. (2005), Crawford and Shum (2005), Scott-Morton and Kyle (2011), Ellison and Ellison (2011), Igami (2017), Dubois and Lasio (2018), and Yang (2020) among others. While most studies of regulatory policies in pharmaceutical markets have focused on the prescription market and generic entry following Rx-patent expiry, limited attention has been paid to empirically investigating the combined effects of OTC drug market exclusivity and Rx drug

patents on firms' strategies. Our structural model sheds light on the unintended consequences of ignoring the *interplay* between the Rx and OTC drug markets by analyzing firms' Rx-to-OTC switching decisions and the FDA's three-year OTC drug market exclusivity policy. The second strand of literature to which the paper relates focuses on how innovation and regulatory policies affect strategic product entry decisions (Draganska, Mazzeo and Seim (2009), Seim (2006), Bajari, Benkard and Levin (2007), Fan (2013), Eizenberg (2014), Fan and Yang (2020), Berry, Eizenberg and Waldfogel (2016), Wollmann (2017), Borkovsky (2017), Mohapatra and Chatterjee (2020), Igami (2017), Igami (2018)). Our counterfactual analysis and evaluation of alternative policies provides important insights into the trade-offs that a policy-maker faces while designing intellectual property policies (Pakes (1984), Chaudhuri, Goldberg and Jia (2006), Moser (2013), Dubois et al. (2015)).

Finally, this paper contributes to the strand of literature related to improving access to drugs in the face of sharply rising prescription drug prices in the US (Duggan and Scott Morton (2010), Dafny, Ho and Lee (2022), Dubois, Gandhi and Vasserman (2021)). Among policymakers, the prescription drug market is often cited as being a major source of inefficiency of the US health-care system (Huckfeldt and Knittel (2011)). Given the concern about the rising costs of prescription drugs in the US, wider use of OTC drugs is advocated to expand access to drugs and reduce costs (FDA (2017*b*), C-Span (2018)). Our study contributes to this debate by designing policies that can encourage early introduction of OTC drugs, thereby improving access and consumer welfare while providing manufacturers strong enough incentives to undertake risky investments.

The remainder of the paper is organized as follows. In Section 2 we review the policy background and the anti-ulcer drug market and describe the data. Section 3 provides descriptive evidence pertaining to strategic delays and the first-mover advantage arising from early entry into the OTC drug market. In Section 4 we describe the model. In Section 5 we discuss the identification and estimation strategy and report the estimation results. In Section 6 we describe and report the results of the counterfactual analysis. Section 7 concludes.

2 Policy Background and Data

In this Section, we describe the approval process for Rx-to-OTC switching and the market exclusivity granted by the FDA. We then provide an overview of the OTC anti-ulcer drug market and describe the data.

2.1 Rx-to-OTC Switch and Market Exclusivity

To reduce spending on prescription drugs,[7] the FDA encourages firms to make investments to develop and release OTC alternatives.[8] An 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 to reach an approval decision for an Rx-to-OTC switch. In addition to clinical trials that establish efficacy and safety and side effects, OTC approval also involves randomized control trials to prove that consumers can self-select OTC medications and also read and understand labels and packages. Therefore, these studies incur a fixed cost that firms pay to make the switch in addition to facing uncertainty in approval outcomes.[9]

To help firms recoup their fixed costs and speed up the introduction of OTC drugs, the FDA provides three-year market exclusivity in the OTC drug market to a firm that makes the first Rx-to-OTC switch for a particular molecule independently of patents (following the Drug Price Competition and Patent Restoration Act of 1984 i.e. the Hatch-Waxman Act). OTC drug market exclusivity allows the first OTC drug to be the 'only' drug on the OTC drug market for three years, because during the market exclusivity period, the FDA does not approve any other OTC applications.[10] If a molecule is under patent protection in the prescription market, then only the firm that holds the patents for the molecule is eligible to release the OTC version. After the patent expiry in the prescription market, however, other firms are also eligible to make the Rx-to-OTC switch. Note that, market-exclusivity period in the OTC drug market will overlap with the Rx patent period if a firm that is enjoying patent protection in the prescription market decides to release the drug in OTC version prior to its Rx patent expiry.

2.2 Anti-Ulcer Drug Market

We choose the anti-ulcer drug market to study the effects of market exclusivity and access to drugs.[11] There are two main classes of anti-ulcer drugs—histamine antagonists (H2-

[7] A significant share (for example, close to 17% in 2015) of healthcare spending goes to spending for prescription drugs (Reuters (2016)).

[8] FDA plans to speed up the approval process for over-the-counter medicines (FDA (2017*b*), C-Span (2018)).

[9] In Appendix A.1, we describe the regulatory requirements for Rx-to-OTC switches in greater details.

[10] The 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.

[11] According to *Gale Encyclopedia of Medicine* (Gale-Encyclopedia (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." Anti-ulcer drugs are also used to treat heartburn, gastroesophageal reflux disease (GERD), and hypersecretory syndromes.

blockers), and proton pump inhibitors (PPIs).[12] In Table 1 we report the eleven molecules in the anti-ulcer drug market that we observe in our sample. Four 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 included in Table 1 belong to the PPI class and were introduced in the early 1990s. While the anti-ulcer market has long been one of the top-selling therapeutic classes worldwide, in the US it is an extremely important segment, with average total annual revenue of nearly 28 billion USD as measured between 1992 and 2015.

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	Jul-02	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	May-14	Feb-15	13,042
Omeprazole NaHCO3	PPI	Zegerid	Oct-04	Jul-16	Mar-10	Jul-10	330
Dexlansoprazole	PPI	Dexilant	Feb-09	Jan-23	-	-	2,067

Note: 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.

Given the prevalence of anti-ulcer treatments, the high cost, and the common occurrence of Rx-to-OTC switches, the anti-ulcer drug segment provides an appropriate setting to study the incentives that guide Rx-to-OTC switching decisions. First, 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 peptic ulcers (gastric ulcers or duodenal ulcers).[13] The extensive prevalence of anti-ulcer treatment implies large welfare consequences for consumers. Second, the anti-ulcer treatments are costly. For example, the anti-ulcer drug Nexium Rx cost 2.5 billion USD for 1.5 million Medicare patients, who were given 8 million prescriptions and refills in 2013. Finally, the occurrence of Rx-to-OTC switches in the anti-ulcer drug

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

[13]It is estimated that around 60 million patients in the US suffer from heartburn, (WebMD (2021))and nearly half of the US population has symptoms of GERD at least once a month (WSJ (2012)).

market is common. Firms typically choose to introduce OTC versions in those therapeutic markets, where consumers can self-diagnose, self-treat, and self-monitor, and hence can substitute OTC drugs for Rx versions. Anti-ulcer drugs qualify as one such market.[14] As summarized in Table 1, 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 Rx-to-OTC switches and their timing across molecules. Pepcid, Axid and Zegerid made the switch five to six years before patent expiration. Tagamet, Zantac, Prevacid, Prilosec and Nexium, with relatively higher Rx revenue (as reported in Table 1), made the switch around the time of patent expiration. Two PPI molecules, Aciphex and Protonix, did not make the switch at their patent expirations. Dexlansoprazole, a new drug approved in February 2009 with a long patent term that runs until 2023, did not switch during our sample period.

After receiving approval from the FDA, branded Rx firms usually launch their OTC products in alliance with a consumer product firm that specializes in OTC distribution. For example, in the case of the OTC Nexium 24 HR, Pfizer acquired exclusive global rights from AstraZeneca (the branded Rx firm) to market OTC Nexium 24HR.[15] While interaction between OTC drug producers and marketers may pose interesting economic questions, in our study, to maintain tractability, we abstract from the nature of such joint ventures, assume that their objective is to maximize joint profits, and focus on interaction between exclusivity policy and the release timing of the OTC drugs. Next, we present a brief description of our dataset.

[14]The most common other therapeutic classes that meet these requirements are mild painkillers, allergy medicines, analgesics, anti-fungal medicines, drugs used to treat gastro-intestinal disorders such as heartburn, acid reflux, diarrhea, and constipation, medicines that treat coughs, colds, and the flu, medicated skin products (including first aid and anti-itch medicines), sleep aids, and smoking-cessation products. Note that not all OTC switches are successful, primarily for this reason. For example, Merck and Co experimented with the blockbuster statin Zocor (simvastin) and released the OTC version. However, although the prescription version was a blockbuster drug, the OTC version was launched with only limited success (Ellery and Hansen (2012) chapter 21).

[15]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 in 2003 through a partnership between AstraZeneca and P&G. Zegerid OTC was manufactured by Santarus, Inc., and marketed by Bayer Healthcare LLC. Prevacid manufacturer TAP 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 US and Canada.

2.3 Data

We obtained *The National Sales Perspectives (NSP) data 1992-2015*, and *Integrated Promotional Services (IPS) 1992–2014* from IMS Health. The IMS NSP data monitors every major class of trade and every distribution channel for prescription pharmaceuticals, and OTC products in the US, measuring the monthly volume of dollars and units moving from manufacturers into various outlets within all 50 states. While IMS NSP data do not cover the universe of OTC drugs, its coverage of anti-ulcer OTC drugs at the national level is around 50%, making it a representative sample for studying the OTC drug market. The IMS IPS data record the total monthly spending on promotional activities for pharmaceutical products from office-based and hospital-based physicians as well as direct-to-consumer advertising expenditures.[16]

Several points about the IMS dataset are worth highlighting here. A first challenge with the dataset involves the need to facilitate the comparison across products as the drugs are sold in varying dosages (e.g., once every day, twice every day, and others) and sizes, therefore varying in form (such as tablets and capsules) and efficacy (for example, the daily dosage across molecules may vary). To address this complication, we first consider the milligrams purchased for a given Stock-Keeping-Unit (SKU) for each molecule and use the recommended daily dosage information as a scaling factor to convert it to a patient-month dosage measure.[17] The resulting quantity obtained by dividing the observed quantity with this scaling factor can be interpreted as the number of 'patient-month' if all patients were taking the recommended daily dosage of an active duodenal ulcer medication. We compute the price per patient-month by dividing the total revenue by the number of patient-month for both Rx and OTC drugs. Because our analysis is focused on OTC drug release decisions as well as consumer preferences for the drugs, in our analysis we aggregate SKUs for tablets and capsules for a given firm for a specific molecule and define it as a "product." Therefore, a product is defined as a combination of molecule, brand status (brand vs. generic), market status (OTC vs. Rx) and form (tablet vs. capsule), for example, we define the "branded Rx Omeprazole tablet" (Prilosec) as a product.[18]

A second complication arises with IMS data as the presence of insurance providers com-

[16]Since IPS data end in 2014, we use the average of the product-month specific spending on promotional activities in 2013 and 2014 for a given month in 2015.

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

[18]While we observe sales-quantity and sales-revenue by generic-Rx and generic-OTC manufacturers, a limitation in our data is that generic manufacturers are not separately identified in the IMS database. Thus, if multiple manufacturers are producing a drug by non-proprietary name within the same molecule and formulation in the Rx-market (OTC-market), then they are lumped into one product in the Rx-market (OTC-market).

plicates the interpretation of prices of anti-ulcer drugs. The price used by IMS NSP data 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 post-shipment financial adjustments. In particular, the rebates that are paid by the manufacturer to the third-party payor for favorable formulary placement are not observed in the dataset. This complicates our analysis, as the actual price received by the manufacturer might differ from the price we observe in the data. Additionally, as a result of insurance cost-sharing, the out-of-pocket costs that patients face differ from the price that manufacturers receive. To address the issues of rebate and cost sharing for insurer-patients, we borrow the techniques developed in the literature (Arcidiacono et al. (2013)) used to study the anti-ulcer drug market in the US. We discuss these issues with greater detail in Section 4. Table 2 provides

Table 2: Summary Statistics

	Mean	Standard Deviation
Out-of-Pocket Price per Prescription	18	(7)
Full Price per Prescription	54	(57)
Advertising Expenditure (million $)	3	(8)
Accumulative Advertising Expenditure in last 3 years(million $)	102	(256)
Revenue (million $)	114	(267)
Number of Prescriptions (in millions)	2.5	(5.1)
Market share (market size=35 percent of population)	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)
Number of Observations	5,949	

Note: The unit of observation is month*product. The number of products in each month is different because of product entry and exit. On average, there are 21 products in each market, defined as the national market in a certain month (5949/288 months=20.65). Data source: IMS Health NSP and IPS Data.

the summary statistics for key variables in our empirical analysis. Our data covers the anti-ulcer drug market from 1992 through 2015. The average out-of-pocket price per prescription is 18 USD. The average monthly advertising expenditure is around 2.8 million USD which implies that average accumulative advertising over the previous three years is close to 100 million USD. The number of monthly prescriptions computed using our sample is close to 2.5 million. We also calculate market share conditional on the OTC or Rx categories in which drugs belong. The average conditional share is 9% and the average market share for outside goods is 41%.

Finally, we collected patent and market exclusivity information from historical publications of *The Orange Book* and information on product entries from National Drug Code

data.[19]

3 Descriptive Evidence

In this Section we present suggestive evidence that manufacturers of branded Rx drugs strategically delay releasing the OTC version of a given molecule because of the provision of market exclusivity.

To understand the effects of market exclusivity and patents on OTC drug market entry, we plot the number of firms operating in each molecule in the H2-blocker and PPI categories, respectively, in figure 1. As illustrated in the graphs, the number of firms that manufacture OTC versions in each molecule does not grow initially because of the market exclusivity provision. After the exclusivity period ends, with the entry of generic OTC firms, the number surges to more than 20 firms in less than 3 years. This finding suggests that the exclusivity provision benefits the branded OTC firm (the first entrant) by limiting competition from 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.

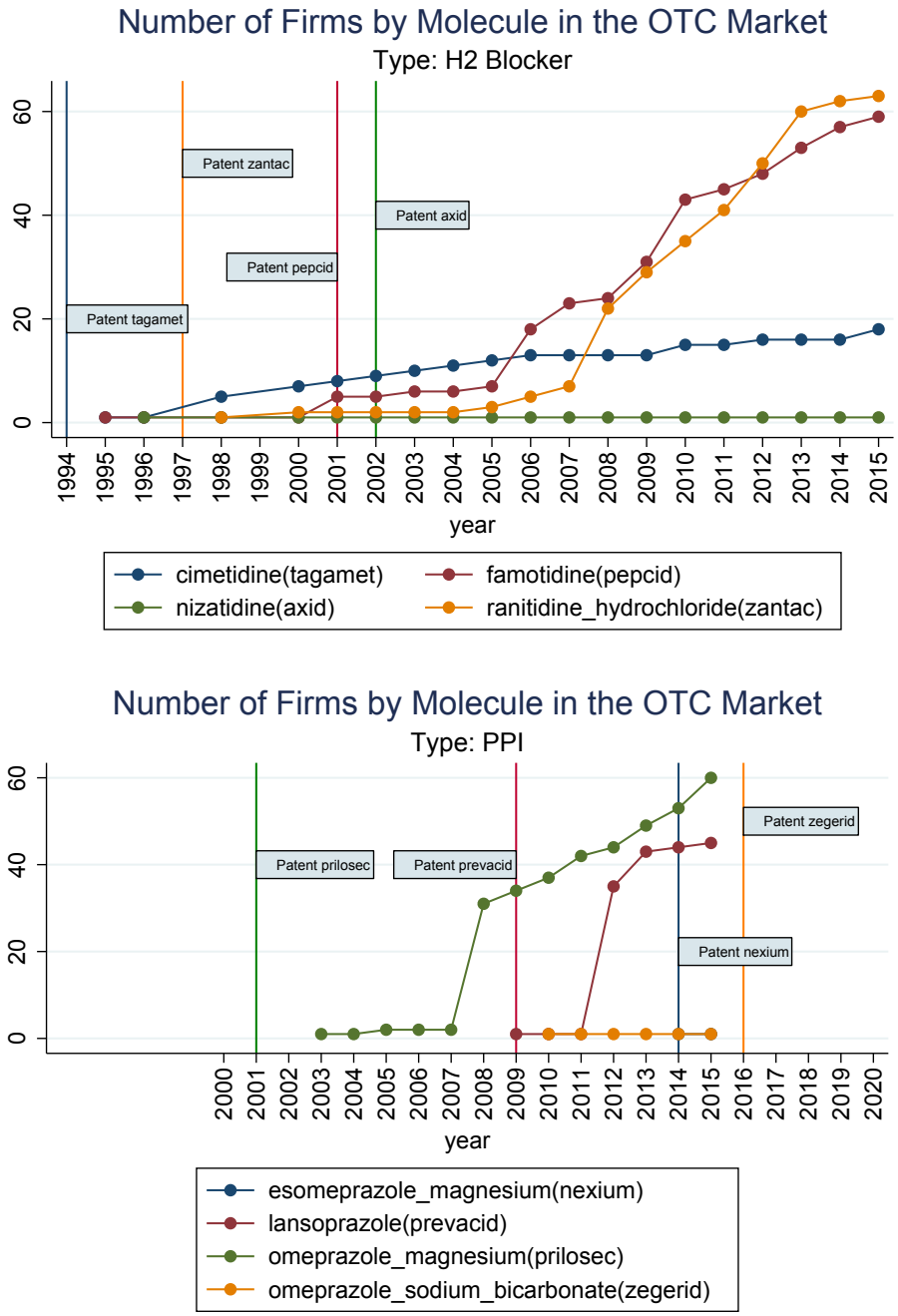
The indirect implication of the FDA's three-year market exclusivity is strategic delays by branded Rx manufacturers. In Table 1, we document the month when the prescription version of the drug was released in the US, the month of patent expiry, and the month in which the first OTC version for the prescription drug was released.[20] Two points are striking here. First, in all cases, whenever an OTC version is released, it is released by the same manufacturer that also sells the 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 the patent for the prescription drug expires.[21] In the other three cases (Pepcid, Axid and Zegerid), the OTC version was released five to six years prior to Rx

[19]The National Drug Code is a unique 10-digit, 3-segment numeric identifier assigned to each medication. The first segment, the labeler code, is 4 or 5 digits long, and identifies the labeler or vendor, any firm that manufactures, repacks or distributes a drug product. The second segment, the product code, is 3 or 4 digits long and identifies a specific strength, dosage form, and formulation for a particular firm. The third segment, the package code, is 1 or 2 digits long and identifies package forms and sizes.

[20]Table 1 reports that, generic Rx for Zegerid first entered the market in July 2010 while the Zegerid patent expired in July 2016. This requires further explanation. Starting in September 2007, Santarus, the manufacturer of branded Zegerid, sued the generics firm Par Pharmaceuticals for patent infringement based on its proposed generic version of Zegerid. The Delaware federal court initially ruled Zegerid's patents invalid on obviousness grounds, and Par launched its generic version in July 2010, based on that decision. However, in September 2012, a federal appellate court reversed the invalidity finding and as a part of the settlement, and the generic version was not distributed until July 2016 when the Zegerid patent expired. (FDA-news (2014))

[21]In the Prilosec case, the NDA for the OTC version was submitted in January 2000. As a result of regulatory delay Prilosec OTC was not approved until June 2003 and was released in September 2003, two years after the Rx patent expiry.

Figure 1: Number of Firms by Molecule in the OTC drug market



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

patent expiry. Note that, prior to the expiry of a patent on a prescription drug, no other firm (except for the patent holder) can release the drug in the OTC drug market. Therefore, the data here suggest that the firm that owns the patent on prescription drug waits until the patent expires; only after that does it release the OTC version and as the first entrant into the OTC drug market, enjoy 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 the OTC version, the patent holder protects its profits from sales of Rx drugs. This is further substantiated by the observation that (as can be seen in the last column in Table 1), the molecules for which the OTC version was released five to six years prior to patent expiry (Pepcid, Axid and Zegerid) also earned relatively lower revenues from the Rx market while, for relatively high-earning molecules, the OTC version was released right around the time of the patent expiry.

The manufacturer also values market exclusivity, however, as it helps the firm build its brand name and enjoy monopoly profits in the OTC drug market. As documented extensively in the existing literature, by spending resources on promotions through physician detailing and/or direct-to-consumer marketing, firms can gain a 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 competition from rivals during the market exclusivity period, firms that make the Rx-to-OTC switch have incentives to invest heavily in promotional and marketing activities to leverage the gain from the three-year period.[22] Therefore, this finding provides suggestive evidence that, to enjoy the FDA's provision of three years of market exclusivity, the firm releases the OTC version right around the time of the patent expiry and uses the exclusivity period to build the OTC brand.

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

[22]For example, Nexium 24HR, introduced in May 2014, aggressively promoted its franchise, reaching more than 70% in units sold through promotions in some months. For the first 12 months following the launch, almost half of all Nexium 24HR units were sold through promotions. Nexium 24HR also boasted the highest number of circular ads. Nexium 24HR reaped $279 million in sales in the first year (Drugstore-news (2015)).

4 Model

In order to evaluate the welfare implications of alternative exclusivity policies, we model how a manufacturer of a branded Rx drug takes into account cannibalization and market expansion effects resulting from OTC switch, and endogenously decides whether to release an OTC version as well as its timing of release in response to changing market conditions. 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 in the anti-ulcer drug market by allowing for four types of product differentiation: (i) between classes (H2 and PPI), (ii) between brands and generics (for example, branded Omeprazole and generic Omeprazole), (iii) between marketing status (for example, Nexium Rx and Nexium OTC), and (iv) between molecules (for example, branded Omeprazole and branded Lansoprazole). This flexible demand model aims at capturing the key substitution patterns among the consumers. First, patients may substitute from branded to the generic version of the same molecule, as pharmacists can typically dispense the generic version of a branded-prescription drug, unless the physician explicitly instructs "dispense as written". Second, as highlighted in Crawford and Shum (2005), physicians might find one molecule as a better fit than another for a given patient through experience and experimentation. Prescription of one molecule versus another may also depend on scientific evidence (Azoulay (2002)), or on information through physician detailing (Berndt et al. (1995), Ching and Ishihara (2010), Ridley (2015)). Hence substitution from one molecule, to a different molecule is also common. The other two substitution patterns (i.e., across marketing status and across class), have received relatively less attention in the literature.[23] Capturing the substitution pattern that varies by marketing status is important for our analysis. We expect anti-ulcer drugs in Rx and OTC drug markets to be substitutes. This is because, in case of anti-ulcer drugs, consumers can self-diagnose, self-treat, and self-monitor, and hence may substitute OTC drugs for Rx versions. Additionally, firms invest heavily in direct-to-consumer advertisement to make the OTC drugs popular among consumers. Our flexible demand specification allows products with the same marketing status to be closer substitutes than those products that are not.

We model the consumer choices using a differentiated-products-discrete-choice demand

[23] In a related work, Carrera and Villas-Boas (2020) studies the substitution patterns between branded OTC and generic OTC by the consumers.

system. 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.[24] A patient may choose from a set of anti-ulcer drugs, or the outside option of forgoing the treatment. Consumer n's conditional indirect utility from choosing drug j in month t is given by

$$\begin{aligned} U_{njt} &= \delta_{jt} + \varepsilon_{njt}, \text{ where,} \\ \delta_{jt} &= \alpha p^c_{jt} + x_{jt}\beta + \zeta_j + \xi_{jt} \end{aligned} \tag{4.1}$$

Equation (4.1) defines the mean utility for a product to depend on p^c_{jt}, the price paid by the patient while purchasing the drug, x_{jt}, a vector of time-varying product characteristics, ζ_j, a product-specific fixed effect that captures any product characteristics (observed or unobserved) that are fixed over time, and ξ_{jt}, a time-varying shock, that captures the unobserved shocks to demand, promotional activity, or changes in brand equity. The error term in the equation, ε_{njt} captures the individual preference heterogeneity, that is independent across consumers, but is assumed to be correlated among products with similar characteristics. To capture the rich substitution patterns across anti-ulcer drugs, we use 'Principles of Differentiation (PD) Generalized Extreme Value (GEV)' model of differentiated products, and allow for a flexible distribution for ε_{njt}. As introduced in Bresnahan, Stern and Trajtenberg (1997), this approach extends the familiar nested logit model of demand, to allow the unobserved preferences to be correlated across multiple nests. For example, the unobserved preference for an OTC branded drug will be correlated with the unobserved preferences for other drugs (both branded and generic) in the OTC drug market, but will also be correlated with the unobserved preferences for other branded drugs in the prescription market. In particular, we assume that the unobserved preference parameters follow a generalized extreme value (GEV) distribution with multivariate cumulative distribution function $F(\varepsilon_{n0t}, \ldots, \varepsilon_{nJt})$. From Proposition 1 of McFadden (1978)

$$F(\varepsilon_{n0t}, \ldots, \varepsilon_{nJt}) = \exp(-G(e^{\varepsilon_{n0t}}, \ldots, e^{\varepsilon_{nJt}})) \tag{4.2}$$

The market share of product j at time t is given by

$$s_{jt} = \frac{e^{\delta_{jt}} G_j(e^{\delta_{n0t}}, \ldots, e^{\delta_{nJt}})}{G(e^{\delta_{n0t}}, \ldots, e^{\delta_{nJt}})} \tag{4.3}$$

[24] 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 Callejas and Mohapatra (2021) among others.

where G_j is the partial derivative of G with respect to the j-th argument. Let L indicate the number of nests, i.e. the (observed) characteristics on which the unobserved preferences may be correlated. In our specification L is equal to 4, as we allow the unobserved preferences to be correlated across the therapeutic class (H2 and PPI), brand and generics status, marketing status (Rx and OTC) and within a specific molecule. Let λ_l denote the possible values of characteristic l, for $l = 1, ..., L$. Following Bresnahan, Stern and Trajtenberg (1997), we can then specify G as

$$G(e^{\delta_t}) = e^{\delta_{0t}} + \sum_{l=1}^{L} \alpha_l \left[\sum_{k \in \lambda_l} \left(\sum_{j=1}^{J} I(j,k,l) e^{\frac{\delta_{jt}}{1-\rho_l}} \right)^{1-\rho_l} \right], \tag{4.4}$$

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

$$\alpha_l = \frac{\rho_l}{\sum_{l=1}^{K}(\rho_l)} \tag{4.5}$$

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

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

$$s_{jt} = \frac{1}{G(e^{\delta_t})} \sum_{l=1}^{L} \alpha_l e^{\delta_{jt}/(1-\rho_l)} \left[\left(\sum_{j'=1}^{J} I(j', k_{jl}, l) e^{\frac{\delta_{jt}}{1-\rho_l}} \right)^{1-\rho_l} \right] \tag{4.6}$$

with the outside good's share given by:

$$s_{0t} = \frac{e^{\delta_{0t}}}{G(e^{\delta_t})} \tag{4.7}$$

Note that, ρ_l captures the degree of correlation between the alternatives in the nest l. As in Bresnahan, Stern and Trajtenberg (1997), when all ρ's go to 0, we move to a multinomial logit model, whereas when all ρ's but one go to 0, we move to a nested logit model.[25]

[25] An alternative to this demand specification is the random coefficients (mixed) logit framework developed by Berry (1994), Berry et al. (1995) (BLP). The advantage of BLP approach is that the model specification does not require an ex-ante choice of nests and also yields flexible substitution patterns. Nevertheless, we believe the Principles of Differentiation Generalized Extreme Value (PDGEV) approach developed by Bresnahan, Stern and Trajtenberg (1997) to be a reasonable choice in our context. This is because the choice

As discussed earlier, presence of health insurance poses a key challenge in quantifying the elasticities. While drug insurance companies do not typically cover spending on OTC drugs, insured patients often pay only a fraction (denoted by p^c_{jt}) 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 would (incorrectly) imply that consumers are insensitive to price and will lead to unreasonably low price elasticities. To address this, we follow the set up in Arcidiacono et al. (2013) which study anti-ulcer drug market in the US from 1991 through 2010 and model the relationship between patient cost sharing and full price as a power function (where the power is less than one). Specifically, following the set up of Arcidiacono et al. (2013), the log of the price paid by patient is assumed to be a linear function of log price for Rx drugs:

$$\begin{aligned} \ln(p^c_{jmt}) &= \phi_0 + \phi_1 ln(p_{jmt}) \text{ (for Rx drugs)}, \\ p^c_{jmt} &= p_{jmt} \qquad\qquad\qquad \text{(for OTC drugs)}, \end{aligned} \tag{4.8}$$

For branded Rx drugs with no generic competition, ϕ_0 is estimated to be 2.558 and ϕ_1 to be 0.113.[26] For generic Rx drugs, we assume that the curvature of the pricing relationship is the same, and adjust the price level such that the average price of generics paid by patients is equivalent to the average reported in Kaiser Family Foundation's 'Employer Health Benefits Survey 2014.' This leads to ϕ_0 to be equal to 2.05 and ϕ_1 to be 0.113 for generic Rx drugs. For branded Rx drugs facing generic competition, we add an indicator variable (where the coefficient of this indicator variable is estimated) to the indirect utility function, implying that facing generic competition may lead to lower cost sharing for branded drugs.[27] Finally, for OTC drugs, we assume that consumers face the same price as the posted price, as OTC drugs are typically not covered by insurance.[28]

of set of nests (or clusters) of products is guided by existing research in health economics, and hence more straightforward compared to other contexts. The relevant product characteristics are almost exclusively binary (for example a product can be either Rx or OTC, and so on). Additionally, as a limitation, we do not have access to rich demographic or multi-market share data that are key to pinning down a more flexible distribution of random parameters. We must exclusively rely on changes over time in the set of available products and their relative prices which may pose challenges for precise estimation of random coefficients while estimating a BLP style model (see Gandhi and Houde (2019) for a discussion on those issues).

[26] 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.

[27] As reported in Table 2, the average out-of-pocket price implied from our calculations is around 18 USD. Note that, according to the Kaiser Family Foundation, in 2002 the average cost shared by patients for insurers with two tiers (generic, brand) was $18.1 (KaiserFamilyFoundation (2013)).

[28] It is worth pointing out that, in this specification, the patient cost sharing 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 impact on the setting of patient cost sharing.

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 by paying 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 non-stationarity 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 value and policy functions to depend on time. In our empirical specification, a firm decides 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.[29]

A brand-name firm producing a molecule 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 Rx-patent status and OTC release status as well as OTC exclusivity status of branded-firm i at period t. We denote firms' average fixed cost of releasing the OTC version by F. 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 a brand-name firm i's patent expiration date for its patented molecule by T_i. We assume that a firm can take active decision about whether to release OTC version at the beginning of a time period $t \leq T_i$. If a brand-name firm chooses to release OTC drug, denote the time of OTC release as T_i^{OTC}. In the beginning of every year t, a branded manufacturer

[29] Note that our demand and marginal cost estimation allows firms to set prices at monthly frequency.

i of a given molecule can be in one of the following situations

(1) Rx-patent active, Rx only,

(2) Rx-patent active, Rx and OTC, with OTC release date T_i^{OTC}

(3) Rx-patent expired, Rx only,

(4) Rx-patent expired, Rx and OTC, OTC exclusivity, with OTC release date T_i^{OTC}

(5) Rx-patent expired, Rx and OTC, no OTC exclusivity.

(4.9)

Case (1), 'Rx-patent active, Rx only' denotes the situation, where the branded firm sells the molecule only in the prescription market, while the Rx-patent for the molecule is still active. Case (2) 'Rx-patent active, Rx and OTC, T_i^{OTC}' denotes the state where the firm sells the molecule both in prescription and OTC drug markets in period t, where $t \leq T_i$. Therefore under this situation, for any $t \leq T_i$, if the molecule enjoys exclusivity in the OTC drug market, it overlaps with Rx-patent protection period for that molecule. T_i^{OTC} denotes the time period of release of OTC version. Note that, although it adds to the computational burden, it is important to keep track of T_i^{OTC}, as the timing of OTC release along with Rx-patent expiry timing determine whether OTC-market exclusivity extends beyond the length of Rx-patent. Case (3), 'Rx-patent expired, Rx only' refers to the state where a branded firm operates only in prescription market and Rx-patent is no more active. Cases (4) and (5) refer to the states where a branded firm operates in both the Rx and the OTC drug market segments and the molecule is no more under Rx-patent protection. In case (4), the branded molecule's OTC-version enjoys market-exclusivity in the OTC drug market whereas in case (5) market exclusivity in the OTC drug market is no longer available. Since under cases (3), (4) and (5) Rx-patent is no longer active, generic Rx entrants may enter the market and hence the branded molecule faces increased competition in the prescription market. Similarly, under cases (3) and (5), where the Rx-patent is expired and market exclusivity is not active in OTC drug market, generic OTC manufacturers may enter the market leading to increased competition in the OTC drug market. We assume that generic-Rx competitors follow the entry patterns that are consistent with the observed data.[30]

Note that, our modeling choice assumes that a brand-name manufacturer can decide to release its OTC version only while its Rx-patent is still active. In other words, if a firm chooses not to switch to OTC prior to its Rx-patent expires, it loses its opportunity to release the OTC version. This assumption is consistent with our empirical setting where

[30]We discuss our modeling assumptions in more detail in Section 5.3.2. In particular, we run a robustness check that relaxes the assumption that the Rx-patent expiry and generic Rx entry timings are fixed. The results from this robustness check are reported in Section A.4.

brand-name Rx-manufacturers introduce OTC-versions when Rx-patent is still active.[31] As highlighted in figure 1, several generic OTC versions of different molecules enter the OTC drug market right after the end of market exclusivity period. Consistent with this, we assume that firms face competition from generic OTC after market exclusivity (as well as Rx patent) period is over. Additionally, our model rules out possibility of exit from Rx and OTC drug markets, as we do not observe any exit during our sample period.

In period t, if the brand-name firm arrives with states (2), (3), (4) or (5), (that is the brand-name firm already operates in both prescription as well as in the OTC drug markets, or the branded manufacturer operates only in Rx-market, but Rx-patent is no more active,) then the firm only decides on the period price for the offered products, and realizes the period profit. If a firm arrives at time t with the state (1) 'Rx-patent active, Rx only', then the firm can choose to take one of the two actions:

$$\{\text{Release OTC, Not Release OTC}\} \tag{4.10}$$

Since market exclusivity in OTC drug 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 if $T_i^{OTC} = T_i$, or $T_i - 1$, or $T_i - 2$), then depending on the year of release, the firm enjoys market exclusivity of one to three years in the OTC drug 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.[32]

As discussed earlier, in order to avoid cannibalization from its OTC alternative, and protect the profit in the Rx market, a brand-name 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, the firm may face competition from rival generic firms in the OTC drug market after the patent expiry. Therefore, in order to avoid this competition, the branded-Rx-manufacturer may choose to release the OTC drug prior to patent expiry and avail the monopoly status in the OTC drug market 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, a Rx manufacturer may anticipate future competition in the OTC drug market from other molecules that are

[31] As an exception, we observe Prilosec releasing its OTC version *after* patent expiry. However, important to note here is that the new drug application (NDA) for OTC version was submitted in January 2000 (FDA (2003)) while the Rx patent expired in October 2001. Prilosec OTC entry was delayed due to delay in the approval process.

[32] We discuss the transition of a brand-name firm from period t to $t+1$ in greater detail in Section A.5.

close substitutes, and hence may decide to switch to OTC preemptively even before its own patent expires and enjoy first-mover advantage in the OTC drug market. For example, Pepcid, the third entrant in the H2-Blocker Rx-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 drug 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. If the brand-name firm already operates in both prescription as well as in the OTC drug markets, or the branded manufacturer operates only in Rx-market, but Rx-patent is no more active (*i.e.* the brand-name manufacturer arrives in period t with states (2), (3), (4) or (5)), then the firm only decides on the prices for the offered products, and realizes the period profit. Similarly, every period, generic Rx-manufacturers (for molecules where Rx-patent has expired) and generic OTC manufacturers (for molecules where Rx-patent and OTC exclusivity has expired) also maximize period profit by choosing corresponding prices. We assume that these industry wide features are common knowledge.

- After the period competition, each brand-name manufacturer with state (1) 'Rx-patent active, Rx only' draws alternative-specific iid private fixed-cost shock vector given by $\{\vec{\varepsilon_{it}}\}$. These brand-name manufacturers with state (1) move sequentially and decide whether to release OTC version or continue producing the Rx version only.

- In our baseline model, branded manufacturers 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 an upfront fixed cost. This action is observed by all other firms, and other firms move in the sequential order.[33]

- 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, we assume that firms know

[33]The assumption of sequential move ensures existence and uniqueness of equilibrium in the entry model. In our robustness check, we allow alternative rules of sequential entry and check for the sensitivity of our result to this specification.

the distribution of these shocks. Hence, firms can compute the future expected period profit, when making 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 used while studying the innovation in hard-disk industry in Igami (2017) and Igami (2018). Because different brand-name 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. These shocks capture all factors that affect a firm's OTC drug launch decision but are not captured in the expected revenue or cost functions assumed by the model. 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, scaled by a parameter θ_ε that can take different values for different molecules.[34]

B. Dynamic Optimization

When their turns to move arrive, firms make 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 state (1) Rx-patent active, Rx only) are characterized by the following Bellman equation:

$$V_t^{i,Rx}(s_t,\varepsilon_{it}) = \pi_t^i(s_t^i, s_t^{-i}) + \max\Big\{\beta E\left[V_{t+1}^{i,Rx}\left(s_{t+1},\varepsilon_{it+1}|s_t,\varepsilon_{it}\right)\right] + \varepsilon_{it}^1, \\ \beta E\left[V_{t+1}^{i,Rx+OTC}\left(s_{t+1},\varepsilon_{it+1}|s_t,\varepsilon_{it}\right)\right] + \varepsilon_{it}^2 - F\Big\} \tag{4.11}$$

where $V_{t+1}^{i,Rx}$ stands for value function under 'Rx only' in the next period (due to the action 'not release OTC'), $V_{t+1}^{i,Rx+OTC}$ stands for value function under 'Rx + OTC' in the next period (due to the action 'release OTC'). F stands for the fixed cost of switching to the OTC version from the Rx version of the drug. The expectations in the equation (4.11) are over the other firms' choices and hence over the realizations of their private cost shocks. Besides the components of period profit functions, the key parameter of this dynamic discrete

[34]In estimation, molecules with similar revenue in branded Rx market also assumed to have the same scaling parameter leading to three different scaling parameters. This is done to keep the computational burden of estimation manageable. Similar scaling parameters that vary with market size, are also used while estimating the dynamic product positioning game in Sweeting (2013).

game is given by F, 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 Perfect Bayesian equilibrium (PBE) in pure strategies. Assumptions taken in this model are important to ensure computational feasibility and avoid multiplicity of equilibria. First, firm's payoff is affected by its rivals' cost shocks only through their actual choices, and not by the specific realizations of $\varepsilon_{i,t}$, 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 effectively solves 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.

By the end of our sample period, except for Dexlansoprazole (a new drug approved in February 2009 with a long patent term till 2023), all remaining patent protections had already ended. Given the long patent term of Dexlansoprazole, and since our sample ends in 2015, we exclude the strategic OTC entry decision of Dexlansoprazole from our analysis. Additionally, from 2015 to 2017, Nexium branded OTC enjoyed exclusivity in the over-the-counter market. We assume that for the end of 2017, for the rest of the periods after 2017, the world becomes stationary. The terminal values associated with each molecule is given by

$$V_T^{i,Rx} = \sum_{t=T}^{\infty} \beta^t \pi_T^{i,Rx}(s_T); \quad V_T^{i,Rx+OTC} = \sum_{t=T}^{\infty} \beta^t \pi_T^{i,Rx+OTC}(s_T) \tag{4.12}$$

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

$$\begin{aligned} \max \Big\{ & \beta E \left[V_T^{i,Rx} \left(s_T | s_{T-1} \right) \right] + \varepsilon_{i,T-1}^1, \\ & \beta E \left[V_T^{i,Rx+OTC} \left(s_T | s_{T-1} \right) \right] + \varepsilon_{i,T-1}^2 - F \Big\} \end{aligned} \tag{4.13}$$

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.

$$E_{\varepsilon_{i,T-1}}[V_{T-1}^{i,Rx}(s_{T-1},\varepsilon_{i,T-1})|s_{T-1}] = \pi_{T-1}^{i}(s_{T-1}) + \theta_\varepsilon \left\{ \gamma + \ln \left[\exp\left(\frac{\beta E\left[V_T^{i,Rx}\left(s_T|s_{T-1}\right)\right]}{\theta_\varepsilon} \right) + \exp\left(\frac{\beta E\left[V_T^{i,Rx+OTC}\left(s_T|s_{T-1}\right)\right] - F}{\theta_\varepsilon} \right) \right] \right\} \tag{4.14}$$

where γ is Euler constant and θ_ε is the logit scaling parameter. 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 OTC drug release 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 favorable formulary placement. While typically 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 follow the specification used in Arcidiacono et al. (2013) while studying US anti-ulcer drug market, and assume that all firms selling Rx drugs pay the rebate at the rate set by Medicaid program (15.1% before 2010 and 23.1% after 2010) prior to generic entry and adjust to a rebate rate of 48.3% upon the generic entry.[35] The key intuition in this set up is that, since increasing rebate above the Medicaid rebate share (15.1% prior to 2010 and 23.1% after 2010) of its average price to any insurer, also entailed the obligation of increasing its rebate to the US government, a manufacturer could credibly pursue an insurer, that it was too costly to offer a rebate above the Medicaid rebate rate off its average price. The institutional details of the specification and the approximations followed by Arcidiacono et al. (2013) is discussed in Appendix A.2.

[35] Under Medicaid Drug Rebate Program, branded drug manufacturers must either give the US government their best price or a fixed rebate rate (set at 15.1% prior to 2010 and 23.1% after 2010) off their average price. The 15.1% discount was established by the Omnibus Budget Reconciliation Act of 1990. The rebate was increased to 23.1% under the Patient Protection and Affordable Care Act of 2010.

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

$$\pi_{it} = \sum_{j \in J_{it}} ((1 - r_{jt}) * p_{jt} - mc_{jt}) M_t * s_{jt}(p) \tag{4.15}$$

J_{it} denotes the set of products offered by firm i at time t, p_{jt} denotes price of product j at time t. Similarly, mc_{jt} denotes marginal cost of producing the drug j at time t. M_t denotes market size at time t, and s_{jt} denotes market share of product j at t. r_{jt} denotes the rebate charged by the firm which takes value 0 for OTC products and takes values 15.1% before 2010, and 23.1% after 2010 in pre-generic entry time periods and 48.3% post-generic-entry for Rx-drugs. The first order conditions are given by

$$0 = (1 - r_{jt}) s_{jt}(p) + ((1 - r_{jt}) p_{jt} - mc_{jt}) \frac{\partial s_{jt}(p)}{\partial p_{jt}} \tag{4.16}$$

We model the log of marginal cost for a product j in molecule m at a time period t to depend linearly on the observed cost shifters, w_{jt} and on an additive error term ω_{jt}.

$$\log(mc_{jt}) = w_{jt}\gamma + \omega_{jt} \tag{4.17}$$

where γ is the parameter vector to be estimated.

5 Identification, Estimation, and Results

5.1 Demand and Marginal Cost

The identification and estimation of the demand model closely resemble Berry et al. (1995), Nevo (2000) and Gandhi and Houde (2019). We construct moments using equations (4.1) and (4.17), and estimate the parameters using the Generalized Method of Moments.[36] Since we assume that in every period firms strategically determine price after (ξ_{jt}, ω_{jt}) are realized, in the demand model price can be potentially endogenous. We construct two types of instruments to address the endogeneity problem: BLP instruments and the differentiation instruments (following Gandhi and Houde (2019)).[37] The validity of our estimation

[36] We discuss more details of demand estimation in Appendix Section A.6.1.

[37] 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 generic 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 generic 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.

strategy relies on the timing assumption, that firms do not know demand and marginal cost shocks (ξ_{jt}, ω_{jt}), when 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 any time-invariant product-specific effects through product dummies, as well as time-varying factors 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.

The IMS health data are available at the monthly (national) level, so for the purpose of demand estimation, we define a month as a market. As we do not observe the market size, we multiply the 'prevalence rate' by the total US population at a given point in time to compute market size. We assume the prevalence rate to be 35%.[38] Our demand specification allows for four overlapping nests that flexibly capture substitution patterns across different products. In the utility specification (specified in equation (4.1)), we include product fixed-effects, where a product is defined at the manufacturer-molecule-marketing status(Rx-OTC)-form(tablet-capsule) level. Any time-invariant characteristics will be subsumed by those product-specific fixed effects. We also allow for a rich set of time-varying product characteristics (x_{jt}) in our demand specification that may affect consumer utility. These time-varying characteristics include cumulative log advertising at the molecule-manufacturer-month level which varies between Rx and OTC drugs. As discussed in Section 2.3, the 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 branded-OTC drugs.[39] 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 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 used in the existing literature (for example, see Arcidiacono et al. (2013) and Shapiro, Hitsch and Tuchman (2021)). Additionally, we include a set of time-since-entry-dummy variables for each of the thirty-six months (three years) after product entry that varies by class (H2 and PPI) and also by marketing status (Rx and OTC). These dummies would account for any tendency to advertise more intensely during the initial introduction phase and also captures any differences in advertisement effects between Rx and OTC drug markets. Additionally, these dummies may capture product availability and other aspects of consumer awareness during the initial months of product

[38] Gelhot and Scott (1999) estimates the lifetime prevalence of Gastroesophageal Reflux Disease to be 25 to 35 percent in the US population. Similarly, Antunes, Aleem and Curtis (2017) estimates the prevalence rate in the US to be between 18.1% to 27.8%.

[39] Advertisement expenditure is kept at zero for generic-Rx and generic-OTC products.

release. We also include time-dummies and allow those to vary by class (H2 and PPI) and by marketing status (Rx and OTC). Finally, we include an interaction of price paid by patient with OTC dummy and generics dummy in our utility specification. Note that, for OTC drug, the price paid by patient is identical to the posted price, as typically insurance providers do not cover the consumer expenses on the OTC drugs. By allowing for different price slopes in the demand specification, we allow for the fact that, the consumers may respond differentially while making purchase decisions in the Rx and OTC drug markets.

In the marginal cost specification, covariates (w_{jt}) in equation (4.17) include product dummies that capture cost differences across different products, and time dummy for Rx and OTC drugs that captures cost differences over time by marketing status. Finally, we control for time-since-entry dummies for 36 months and allow it to vary by class (H2 and PPI) and also by marketing status (Rx and OTC).

Table 3: **Nesting Parameters**

	Coefficient	Standard error
Molecule	0.46***	(0.04)
Marketing (Rx and OTC)	0.63***	(0.12)
Brand (Brand and Generics)	0.50***	(0.23)
Class (H2 and PPI)	0.51***	(0.21)
Number of Observations: 5,949		

Note: This Table reports the estimated nesting parameters from the PD-GEV (Principles of Differentiation Generalized Extreme Value) demand estimation. Each of those estimates represents the degree of correlation between the alternatives in the given nest.

We report key parameter estimates from the demand model in Tables 3, and 4. The non-linear, or nesting, parameters, which drive cross-product substitution, are presented in Table 3. A value of a nesting parameter closer to 1 reflects a higher degree of correlation between the alternatives within a given nest. The four nesting parameters range from 0.46 to 0.63, reflecting strong correlation across products within a given nest. The correlation is strongest along the marketing status dimension, reflecting strong cross-product substitution between products in the Rx and in the OTC drug market segments. In other words, the estimate of marketing-specific nesting parameter suggests that, if Nexium OTC is removed from the market, consumers are more likely to switch to Prilosec OTC rather than switch to Rx market and opt for Nexium Rx. Similarly, the estimate of molecule-specific nesting parameter captures the tendency of consumers to substitute Nexium OTC for Nexium Rx. These cross-substitution patterns play an important role in the dynamic decision making

of the firms while releasing the OTC version of the drugs. In particular, a brand-name Rx manufacturer may anticipate future competition in the OTC drug market from other molecules that are close substitutes, and hence may decide to switch to OTC preemptively even before its own Rx-patent expires. The fact that all of our estimated nest parameters are both economically and statistically significant highlights the importance of adopting a flexible framework, because imposing either of the possible extreme assumptions (i.e. perfect substitutes or non-substitutes) would have prevented us from explaining regularities in the data.

Table 4 presents selected linear parameters from the demand estimation. The price and advertising coefficients indicate –not surprisingly– that consumers buy products with low prices and heavy advertising, all else equal. Our estimates reveal that advertising has slightly higher impact for PPIs compared to H2 class drugs. For branded Rx drugs facing generic competition, an indicator variable is added to the indirect utility function, allowing that facing generic competition may lead to lower patient cost sharing for branded prescription drugs. The estimated value comes out to be negative (-0.27) and statistically significant. We also allow for different price sensitivities for OTC versus Rx drugs, and for generics versus branded drugs that capture differential consumer responses in Rx and OTC drug markets.

Table 5 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 33 dollars, whereas it costs 12 dollars to produce the same amount of generic prescription medication. This finding is in line with findings from Arcidiacono et al. (2013), who document significantly higher marginal costs for branded anti-ulcer drug between 1991 and 2010. Similarly, it costs 20 dollars for one month supply of brand OTC medication, and 9 dollars for generic OTC medication on average. Finally, the differences in the Rx and OTC marginal cost estimates may reflect the different distribution costs emanating from the different distributional channels of Rx and OTC drugs, among other factors.

5.2 A Model of Advertisement Expenditure

Our dynamic estimation requires us to compute period profit for each product under every market structure.[40] Therefore, to compute the period profit of a drug for different market structures, we need to compute the predicted advertisement spending for the product. As discussed earlier, while generic Rx and generic OTC products typically do not advertise, branded Rx and OTC products invest heavily in promotional and marketing activities, es-

[40]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.

Table 4: **Demand Results: PD-GEV Estimation**

	(Estimates)
Covariates in equation (4.1)	
Price Paid by Patient	-0.55***
	(0.04)
Constant	16.8***
	(1.2)
Log Cumulative Advertisement	0.14***
	(0.02)
Log Cumulative Ad x PPI Class dummy	0.11***
	(0.03)
Level change in Price Paid by Patient	-0.27***
(for Branded Rx after Generic Entry)	(0.06)
Price Paid by Patient x Generics Dummy	-0.78***
	(0.09)
Price Paid by Patient x OTC Dummy	0.35***
	(0.08)
Included Dummies in x_{jt} in equation (4.1)	
(1) Product(firm-molecule-marketing status-form) Dummy	
(2) Time Since Entry Dummy (upto 36 months)	
(3) Time Since Entry Dummy x PPI Dummy	
(4) Time Since Entry Dummy x OTC Dummy	
(5) Time Since Entry Dummy x generic OTC Dummy	
(6) Time Dummy by Class	
(7) Time Dummy x OTC dummy	
Included Dummies in w_{jt} in equation (4.17)	
(1) Product(firm-molecule-marketing status-form) Dummy	
(2) Time Since Entry Dummy (upto 36 months)	
(3) Time Since Entry Dummy x PPI Dummy	
(4) Time Since Entry Dummy x OTC Dummy	
(5) Time Since Entry Dummy x generic OTC Dummy	
(6) Time Dummy x OTC dummy	
(7) Dummy for Rx-patent expiry by molecule	
Number of Observations: 5,949	

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

Note: This Table reports the result from demand estimation. The parameters are estimated using the Generalized Method of Moments where we construct moments using equations (4.1) and (4.17).

pecially during the initial introduction phases. Therefore, we estimate a reduced form policy function for advertising for branded Rx and branded OTC products.[41] Our advertisement

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

Table 5: **Estimated Marginal Costs by Brand and Marketing Status**

Brand and Marketing status	Average Price	Average Estimated MC	SD of Estimated MC
Brand Rx	101	33	19
Generic Rx	20	12	21
Brand OTC	25	20	7
Generic OTC	10	9	3
Number of Observations: 5,949			

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.

specification is given by

$$adv_{jt} = w_{jt}^{adv}\gamma^{adv} + \omega_{jt}^{adv} \tag{5.1}$$

where adv_{jt} refers to the advertisement spending on product j in period t. We flexibly model the advertisement decision by including time dummy varying by drug class, OTC drug dummy varying by class, time since entry dummies for 36 months varying by class, as well as firm-molecule-form fixed effects in w_{jt}^{adv}. These estimates are used to predict the advertisement spending for branded Rx and OTC products and to compute period profit when estimating the dynamic product entry model. We report the parameter estimates in Table 6. The results show that advertisement expenditures are lower for branded OTC drugs than the branded Rx drugs.

5.3 Fixed Cost of Switching from Rx to OTC

The static demand, marginal cost and advertisement model estimates from Sections (5.1) and (5.2) 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 brand-name manufacturer into the OTC drug market during the period when cannibalization effect of the OTC drug has large negative effects on own Rx-products. Since we observe different branded prescription drug manufacturers making OTC drug entry choices at varying points during their Rx-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

Table 6: **Advertisement Model Parameter Estimates**

	(Estimates)
Constant	2.38***
	(0.40)
Branded OTC Dummy	-0.12**
	(0.06)
Branded OTC Dummy x PPI Dummy	-2.10***
	(0.12)
Included Dummies	
(1) Firm-Molecule-Form Dummy	
(2) Time Since Entry Dummy (upto 36 months)	
(3) Time Since Entry Dummy x PPI Dummy	
(4) Time Dummy by Class	
Number of Observations: 5949	

Note: This table reports the coefficient estimates and standard errors from estimation of advertisement model (see Equation 5.1).

the fixed cost of entry while estimating the dynamic model.

We embed the variable profit estimates into a dynamic discrete game model and solve it for a perfect Bayesian equilibrium (PBE) by following backward induction. Our goal here is to estimate the dynamic parameter (F) that represents the average fixed cost of a brand-name manufacturer while releasing the OTC product. Additionally, we estimate the scaling parameters for the logit error draws. Using each candidate parameter vector, we compute the stream of period profits for a given manufacturer for every market structure. Hence each candidate parameter vector implies a specific expected value OTC drug entry for each brand-name manufacturer, in each state-year, as well as optimal choice probabilities of releasing the OTC drug. The maximum-likelihood estimate maximizes the likelihood of observing the actual choice probabilities in the data.

An industry state vector at period t contains information on the Rx-patent status, OTC release status, as well as OTC exclusivity status of all branded-manufacturers for different molecules. In the beginning of period t, a brand-name manufacturer i of a given molecule can be in one of the states as described in (4.9). For estimation purposes, we assume that, a brand-name firm does not enter into the OTC drug market in the first four years after its Rx drug is introduced. Starting from the fifth year of Rx drug's life, the firm starts taking active decision whether to enter into the OTC drug market. The reason for this assumption is twofold: first, it is reasonable for a certain amount of time to pass between the release of Rx-version and the introduction of OTC-version, as getting through clinical trials to prove

safety and efficacy of the OTC drug takes time. Second, adding this restriction reduces the state space and helps achieve computational feasibility. Similar assumption has been used by Shapiro (2016) to study the introduction of a reformulation of an original molecule where he assumes that reformulations can enter at least five years after the original molecule entry.

In period t, if the brand-name firm arrives with states (2), (3), (4) or (5) (as specified in 4.9, these states imply that either the brand-name firm already operates in both prescription as well as in the OTC drug markets, or the branded-manufacturer operates only in Rx-market, but Rx-patent is no longer active,) then the firm only decides on the period price for the offered products, and realizes the period profit. For a brand-name manufacturer that enters the period t with state '(1) Rx-patent active, Rx only', the action space is given by (4.10), where the firm may either choose to release the OTC version at period t, or may delay the OTC introduction by not releasing at period t. Corresponding policy function p_t^i denotes the manufacturer i's probability of releasing OTC drug at period t. 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

$$p_t^i = \exp\left(\frac{\beta E_\varepsilon V_{t+1}^{i,Rx+OTC}(s_{t+1}) - F}{\theta_\varepsilon}\right)/B \tag{5.2}$$

where

$$B = \exp\left(\frac{\beta E_\varepsilon V_{t+1}^{i,Rx}(s_{t+1})}{\theta_\varepsilon}\right) + \exp\left(\frac{\beta E_\varepsilon V_{t+1}^{i,Rx+OTC}(s_{t+1}) - F}{\theta_\varepsilon}\right)$$

The ML estimator for the mean fixed cost maximizes the joint likelihood of observing the actual data from $t = 0, 1, ..., T-1$.[42]

Table 7 reports the results from the maximum likelihood estimation. Note that, during our sample period, Aciphex, Protonix and Dexilant did not introduce OTC version of the prescription drug. Dexilant patent was approved in February 2009 with a long patent term till 2023. Given the long patent term of Dexilant, and since our sample ends in 2015, we exclude the strategic OTC entry decision of Dexilant from our analysis.[43] For Aciphex and Protonix, the patent ended in 2013 and 2011 respectively. For our modeling assumption, we need to take a stand on the decisions made by Aciphex and Protonix. In particular, we can assume that, (i) those two molecules are not potential candidates for Rx-to-OTC switch, or (ii) those two molecules are potential candidates for Rx-to-OTC switch, but *chose* not to introduce the OTC version. The attributes of Aciphex and Protonix are similar to other anti-ulcer drugs in the PPI-class that made the Rx-OTC switch. We did not however, find

[42] We describe further details on implementing the nested fixed point algorithm to estimate the dynamic model in Appendix Section A.6.2.

[43] Additionally, since in our model, we assume that a firm does not release OTC in the first four years of Rx drug's life-cycle, we are effectively ignoring active strategic decision making of Dexilant only for one year while estimating the likelihood.

Table 7: **Maximum Likelihood Estimates of the Fixed Cost**

Fixed Cost	42.9***	56.5***
	(10.1)	(11.9)
Scale of ε's		
Molecules with low avg Rx Rev	3.6***	2.1***
	(0.8)	(0.3)
Molecules with medium avg Rx Rev	1.4***	1.4***
	(0.5)	(0.3)
Molecules with high avg Rx Rev	0.9**	0.4***
	(0.4)	(0.1)
Log Likelihood	-9.5	-13.4
Assumption:	Model *does not allow* Aciphex & Protonix to release OTC	Model *allows* Aciphex & Protonix to release OTC
Assumed Order of Move: More Experienced firm moves first		

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. The left panel reports the results from maximum likelihood estimation where model does not allow Aciphex and Protonix to release OTC versions. The right panel reports the results from maximum likelihood estimation where model allows Aciphex and Protonix to release OTC versions. Standard errors are reported in the parentheses.

any news articles (or any information) from doing a web search which mentioned about new drug applications for OTC-drugs by the manufacturers of Aciphex and Protonix. Therefore, instead of picking one assumption over the other, in Table 7 we report fixed cost results under both sets of assumptions.

The left panel reports the results from maximum likelihood estimation where model does not allow Aciphex and Protonix to release the OTC version. Average estimated fixed cost of releasing the OTC version is close to 43 million USD under this assumption. The right panel in Table 7 reports the results from maximum likelihood estimation where model allows both molecules to release the OTC version, and the estimated fixed cost is around 57 million. Intuitively, under the second assumption (where the two molecules could have released the OTC drug, but *chose* not to do so), a higher estimated fixed cost rationalizes the no-switch decision of the two molecules. For the purpose of counterfactual analysis, we use the fixed cost estimates from the first assumption (43 Million USD) as our specification.

Note that, the estimated fixed cost of introducing an OTC drug includes clinical research costs, the cost of distribution through retailer networks, the shadow cost of an application failing to obtain the FDA approval, other unobserved costs incurred by the firms, as well as the opportunity costs of the firm making those risky investments. The cost of clinical trials is one of the major components of R&D cost and hence a key contributor to the fixed cost.

To get a sense of 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 switch 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 subject from Berndt and Cockburn. (2014), we can compute that, just the consumer clinical trial may cost around 10 million dollars.[44] Our fixed cost estimates obtained from the estimation of dynamic game, that includes other accounting as well as economic costs, in addition to the clinical trial costs, are in line with the industry estimates.

In our baseline model, we assume a specific order of move while solving the dynamic game under backward induction, that firms move in the order of closeness (in terms of time) to respective dates of patent expiry. Hence, the more experienced firm being closest to patent expiry moves first. As a robustness check, we assume an alternative specification where the least experienced firm moves first, and report the results in Table A1 in Appendix Section A.3. Our results indicate that the fixed cost estimates are robust to the order-of-entry assumption as the overall change in magnitude of fixed cost estimate is negligible with most of the differences in the estimates occurring in the third decimal point.

5.3.1 Model Fit

Table 8 shows that the predictions from the model fit the data reasonably well by replicating the entry decisions of OTC molecules. For this exercise, we use the estimated model and run 20,000 simulations of the industry history.[45] In Table 8, we report the probability of not switching to OTC version. We also report the average number of years a branded Rx and its branded OTC version overlap before Rx-patent expiry conditional on introduction of the OTC version. Here, the average is taken over the 20,000 simulation draws. The column 'Pr(no OTC entry)' reports the share of the simulations for which the Rx molecule chooses not to release the OTC version in the predicted world. Consistent with the observed data pattern, the model predicts that all molecules will introduce OTC versions at some point in their respective life-cycles with high probability. Additionally, the model predicted year of entry matches closely with the actual year of entry observed in the data. Therefore, as can be seen in the Table, the model predicted number of years for which branded Rx and

[44] 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) (Battelle-Technology (2015)).

[45] While running these simulations, we use assumption 1 from entry estimation (that Aciphex and Protonix are not allowed to release OTC version of the drug during their life cycle - see Section (5.3) for a detailed discussion).

branded OTC are jointly sold in the market before the branded Rx patent expires, closely replicates the observed data patterns.

Table 8: **Model Fit**

		# years Branded Rx & Branded OTC overlap *before* patent expiry		
		Data	Estimated Model	
Brand	Molecule	# Yrs	# Yrs	Pr(no OTC entry)
Tagamet	Cimetidine	0	0.7	14%
Zantac	Ranitidine	1	1.1	10%
Pepcid	Famotidine	5	3.9	13%
Axid	Nizatidine	6	4.8	22%
Prilosec	Omeprazole	0	0.8	0%
Prevacid	Lansoprazole	0	0.7	0%
Aciphex	Rabeprazole	No OTC Entry	-	-
Protonix	Pantoprazole	No OTC Entry	-	-
Nexium	Esomeprazole	0	0.9	0%
Zegerid*	OmeprazoleNaHCO3	0	0.2	25%
Dexilant	Dexlansoprazole	No OTC Entry	-	-
In simulations, model *does not allow* Aciphex & Protonix to release OTC				

Note: The Table reports the OTC entry patterns by molecule as observed in the data, as well as predicted by the model. In the data column, the Table reports the number of years branded Rx and branded OTC are jointly sold in the market before the branded Rx patent expires. 'No OTC Entry' in case of Aciphex, Protonix, and Dexilant refers to the case where the branded Rx does not release its OTC version. The column Pr(no OTC entry) refers to the share of the simulations for which the OTC version is not released in the predicted world. While simulating the industry history, we assume that Aciphex and Protonix would not release OTC versions (assumption 1 - see Section 5.3 for a detailed discussion).
∗Note that, while Zegerid patent was scheduled to expire in July 2016, it was challenged and the patent was ruled invalid by the federal court in July 2010. Please refer to Section 3 for more discussion on this.

5.3.2 Further Discussion on Modeling Choice

The structural model makes two key assumptions which deserve more discussion. First, we assume that, the arrival timing of a branded-Rx drug evolves exogenously and does not strategically respond to the introduction of an OTC drug by a different molecule. The assumption implies that, for example, Nexium's decision of when to release the branded-Rx drug in the prescription market, is independent of a rival molecule's timing decision of releasing an OTC drug. Note that, the R & D process and the patent approval process

for branded-Rx drugs are quite lengthy and uncertain. Therefore, once a drug gets market exclusivity in the Rx-market through patent protection, it is in the best interest of a firm to release the prescription drug at the earliest to maximize the profits during the patent protection period. Hence, it is unlikely that the firm would choose to strategically delay entry of a new branded prescription drug because of a rival's OTC drug launch.

Second, we assume that the timing of Rx-patent expiry is exogenously given and is independent of OTC entry decisions. An incumbent in the prescription market, however, may face challenges from generic counterparts before the expiration of a patent relating to its brand name drug.[46] Therefore, ex-ante an incumbent with Rx-patent faces an *inherent* probability of losing its patent protection in a given period. In some cases, the incumbent may strike a pay-for-delay settlement with the generic Rx producers where the generic manufacturer agrees to refrain from entering into the Rx market for a given period of time in exchange for a payment from the incumbent.[47] Our model abstracts away from modeling those incidents. Instead, we take the equilibrium outcome of such interactions between branded and generics firms in the Rx-market as given, and model the dynamic incentives involved in the OTC entry decisions taking both within-molecule, and between-molecule interactions into consideration.[48] While we do not include those additional factors to keep the model tractable and estimation feasible, we run a robustness check to show that our key counterfactual results are robust to this assumption. In the robustness check, we consider the case of Nexium and relax the assumption that the expiration timing of Nexium's Rx-patent is fixed. Instead, we assume that Nexium's Rx-patent may expire with a given probability due to generic challenge in each period.[49] We solve for a new equilibrium in the dynamic game under this

[46] In particular, under the Hatch-Waxman Act, a generic manufacturer may file an Abbreviated New Drug Application (ANDA) with Paragraph IV (Para-IV), prior to the patent expiry of a branded product. By filing a Para-IV entry certification, the generic maker declares that its product does not infringe on a patent or that patent is invalid (Li, Lo and Thakor (2021)).

[47] For example, in 2008, an agreement between AstraZeneca (the manufacturer of Nexium Rx) and generics firm Ranbaxy Laboratories Ltd. was reached to delay Ranbaxy's launch of a generic version of AstraZeneca's patented heartburn drug Nexium until 2014.

[48] Our estimation and counterfactual results highlight that consideration of between-molecule interactions is important for rationalizing the observed entry patterns in OTC drug market. In particular, in order to reap the first-mover advantages a molecule may preemptively enter into the OTC drug market to become the first drug within a specific therapeutic class. For example, Pepcid, the third entrant in the Rx H2-Blocker class, became the first entrant in the H2-Blocker OTC drug market, and managed to maintain its position as the OTC drug market leader within the H2-Blocker class for several years.

[49] This counterfactual exercise mimics a real-world situation where a brand-name Rx manufacturer faces an inherent probability of losing its Rx-patent. This is because a generic entrant's challenge and litigation following it may lead to a decision where Rx-patent is deemed as invalid. On the other hand, a firm that holds the Rx-patent may strike a settlement agreement (such as a pay-for-delay agreement) with the generic entrant. In our framework, such an agreement is interpreted as an action that may lower the inherent probability of Rx-patent getting invalid in a given period. While we do not observe (or estimate) such probabilities in our framework, for the robustness check, we assume the probability to take a range of values

assumption and simulate OTC entry decisions for the expanded MEP counterfactual world. Our results show that the key conclusions are robust to this assumption. We discuss this counterfactual exercise in more detail in Appendix Section A.4.

6 Counterfactual Analysis

Using the estimates from our structural model, we first address the question of whether the FDA market exclusivity policy *may lead* to strategic delay in the OTC launch. 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.

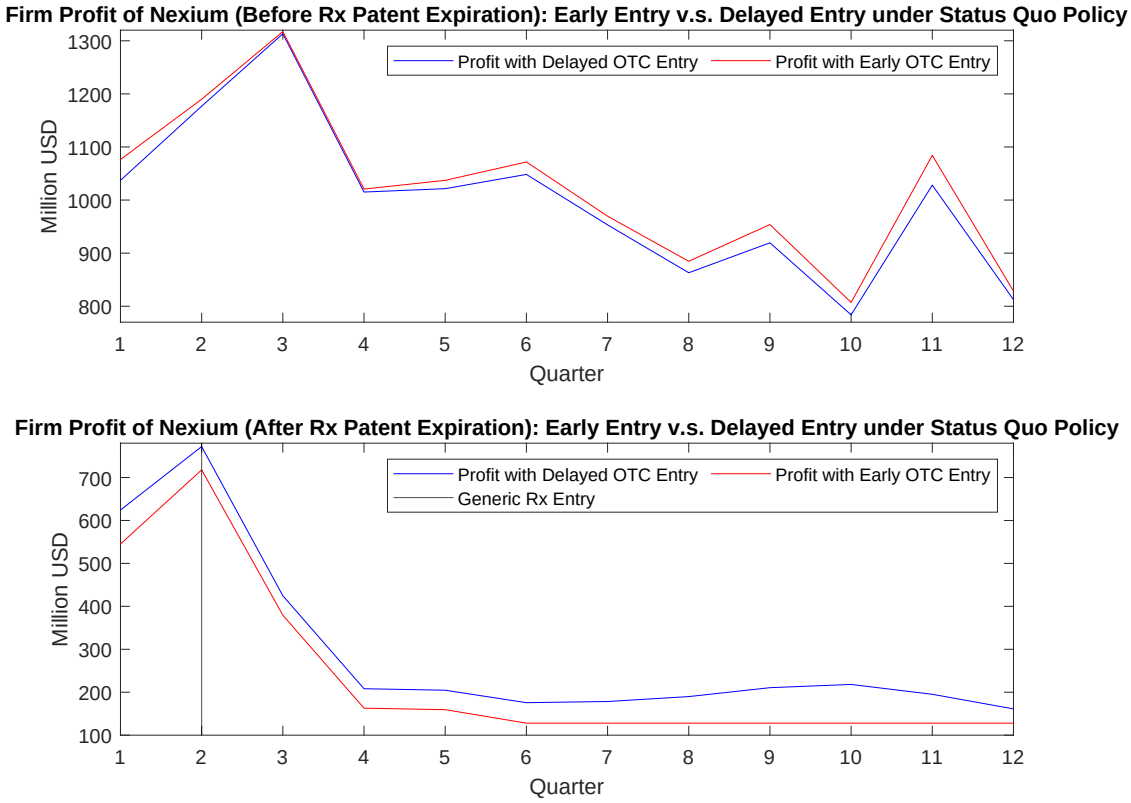
6.1 The Value of OTC drug market Exclusivity and Delayed OTC Entry: The Case of Nexium

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 before patent expiration) and the value of OTC drug market exclusivity (i.e. 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 exceeds cannibalization (and negative otherwise). When the value of early entry is negative, brand prescription drug manufacturers either delay the OTC release or choose not to release OTC. Positive value of early entry implies that firms have an incentive to enter early, therefore if OTC is delayed, it suggests the value of OTC drug 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. 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. 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, where the equilibrium OTC release decisions are solved by solving the full dynamic equilibrium model.

to accommodate inherent probability and (possibly) lower probability of expiry due to settlement agreements.

Figure 2: Firm Profit of Nexium: Early Entry v.s. Delayed Entry under Status Quo Policy



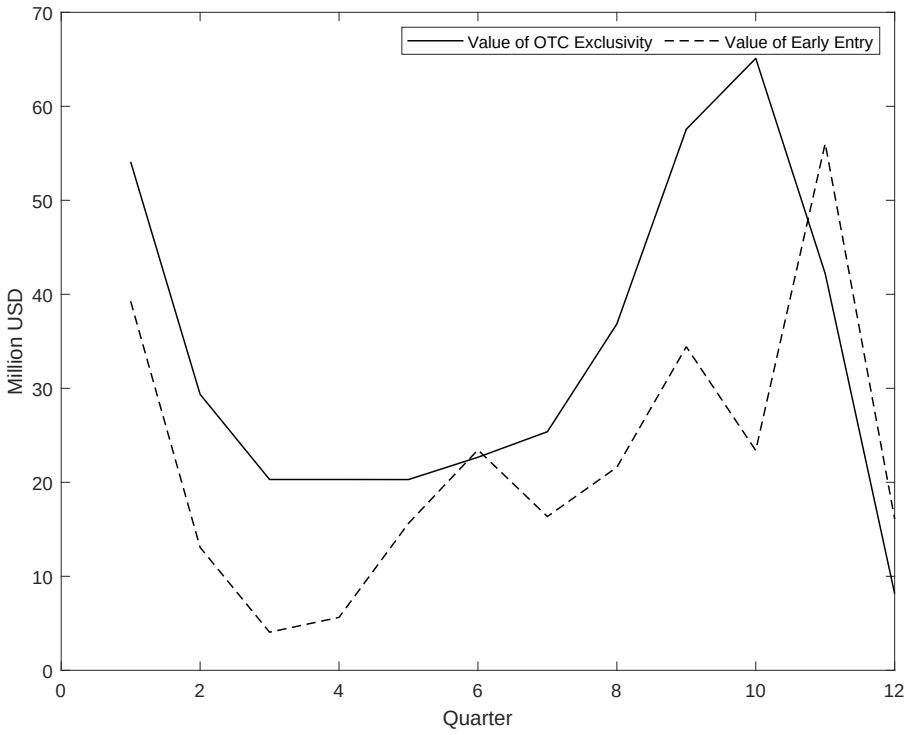
Note: The upper graph plots the firm profit of Nexium for the 3 years (12 quarters) prior to patent expiration. The bottom graph plots the firm profit of Nexium for the 3 years (12 quarters) after the patent expiration. The blue line and the red line plot the Nexium quarterly profit for delayed entry (as observed in actual data) and early entry (our counterfactual exercise) of Nexium OTC under Status Quo exclusivity policy. The vertical line in the bottom graph indicates the date when the first Nexium Rx generic entered the market.

Figure 2 compares the firm profit of Nexium under delayed entry (blue line) with early entry (red line). The upper plot covers three years (twelve quarters) prior to the patent expiration. The bottom plot covers the three years period (twelve quarters) after the Nexium Rx patent expires. In the case of Nexium, the generic Rx enters in the second quarter after the Nexium Rx patent expires, as indicated by the black vertical line. As is clear from the bottom graph, the overall profit of Nexium falls significantly after the entry of generic products in the prescription market. Prior to patent expiry, Nexium's overall profit was around 800-900 million dollars; within two quarters after the generic Rx entry, it went down to around 200 million dollars per quarter.

The simulation shows that if Nexium chose to introduce OTC in May 2011, it would make a higher profit during the three years before patent expiration. As reflected in the gap between the red line and the blue line in the upper plot, market expansion effect and first-mover advantage exceed cannibalization when the Nexium OTC enters early, i.e., the

value of early entry is positive. However, the bottom plot shows that OTC drug market exclusivity creates greater value for the firm in case of delayed entry. The blue line in the bottom figure exceeds the red line suggesting that Nexium OTC brings higher profit even after generic Nexium Rx entry in the second quarter after Rx patent expiry. Thus, absent the strategic consideration for market exclusivity, it would be profitable for Nexium to introduce its OTC earlier. The reason for the delay is that the three-year 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.

Figure 3: Value of Early Entry and Value of OTC Exclusivity for Nexium under StatusQuo Policy



Note: The solid line plots the value of OTC exclusivity (measured by the quarterly profit increase for AstraZeneca during three years post patent expiration, in million dollars) when Nexium is introduced at patent expiration. The dotted line plots the value of early entry (measured by the quarterly 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.

Figure 3 plots the value of early entry pre-patent expiration (denoted by the dotted line) versus the value of OTC drug market exclusivity post patent expiration (denoted by the

solid line).[50] The value of OTC drug market exclusivity is almost always greater than the value of early entry. Finally, we estimate the consumer welfare loss caused by the delay of Nexium OTC launch. Our results suggest that early entry of Nexium OTC would have increased consumer welfare by around 230 million dollars each year on average before patent expiration. The welfare enhancement arises from increased product variety and tougher competition that arrive earlier.

6.2 Restructuring of Market Exclusivity

If three-year market exclusivity induces strategic delay and welfare loss under the current policy, can a redesign of the market exclusivity provision solve the problem? We consider two alternatives to the status quo policy. First, we consider the removal of the exclusivity provision. Removing the exclusivity policy weakens the incentive to undertake risky investments while introducing an OTC version, and hence may reduce the variety of OTC drugs offered in the market. On the other hand, without any incentive for strategic delay, a branded-manufacturer may introduce the OTC drug earlier than its Rx-patent expiration in order to enjoy a first-mover advantage during the patent period. The net welfare effect of no-exclusivity policy is ambiguous.

Second, we consider an "expanded market exclusivity policy (expanded MEP)" that can potentially eliminate the delay incentive and enhance consumer welfare. Under expanded MEP, three-year market exclusivity is granted to an OTC drug following the molecule's Rx-patent expiration regardless of the OTC release date, only if the OTC-version is introduced early. In particular, a brand-name firm will enjoy full three-year exclusivity period being the first entrant in the OTC drug market, only if the OTC version is released three or more years prior to the prescription drug patent expiry; the first entrant will enjoy two (or one) years of market exclusivity, if the OTC version is released two (or one) year in advance; no exclusivity will be granted if the OTC-version is released right at prescription drug patent expiry. This policy differs from the status quo policy, where three-year market exclusivity granted to the first firm that introduces the OTC version, following the date of OTC drug approval. By ensuring that the market exclusivity in the OTC drug market is granted beyond patent expiration if OTC drugs are introduced early, this policy removes the incentives for strategic delay. As a result, we expect the number of OTC drugs in the market should not decrease relative to the status quo policy, additionally due to elimination of incentives for strategic

[50] 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 drug 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.

delay, 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. This is because, when it is in the firm's own interest to introduce the OTC version before the patent expiration without this provision, the market-exclusivity provision reduces consumer welfare by deterring generic OTC entry, and hence limiting competition for 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, the firm may face potential competition from generic OTC entrants. 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 (FDA (2017*a*)). However, due to the three-year market exclusivity policy, the review and approval of generic OTC were 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 OTC entry decisions as well as the timing of OTC entry of each manufacturer in this new regulatory regime. As discussed earlier, we exclude the strategic entry decision of Dexilant from our analysis, because Dexilant patent was approved in February 2009 with a long patent term till 2023. Additionally, for counterfactual exercise, we assume that Aciphex and Protonix (the other two molecules that did not switch to OTC during our sample period) would not release OTC in the counterfactual world. In other words, in our counterfactual exercise, we assume that those two molecules are not potential candidates for introduction of OTC versions.[51] Note that, allowing Aciphex and Protonix to release OTC drugs may lead to higher number of products and hence higher consumer welfare in the counterfactual world. Hence, our assumption is conservative, and our welfare estimates would serve as an informative lower bound under the alternative assumption.

We simulate the entry decisions of the brand-name firms over the entire life cycle of the prescription drugs for the period 1982-2017 to capture the entry decisions of the molecules in the anti-ulcer market. Operationally, we consider an alternative counterfactual regime (in our case – 'no-exclusivity' or 'expanded MEP'), and solve the model for a new PBE in

[51]Note that, we did not find any news articles (or any information) from doing a web search which mentioned about new drug applications (NDA) for OTC-drugs by the manufacturers of Aciphex and Protonix.

this counterfactual environment. We use the equilibrium choice probabilities from the new regulatory regime to run 20,000 simulations of industry history. For each simulation draw, we focus on the timing of the OTC switch for each manufacturer, and the length of time for which the branded prescription and its OTC-version are available to consumers prior to Rx-patent expiry. We report the results from our counterfactual analysis in Table 9.

For each of the molecules, we focus on the length of the period for which branded OTC version overlaps with the branded prescription drug, prior to branded prescription patent expiry. For example, in case of Nexium, since Nexium-OTC was released right at the patent expiry, the length of the period for which Nexium-OTC overlapped with the branded drug in the prescription market, prior to the Nexium prescription patent expiry, is equal to 0. In the column 'Status Quo (Data)', we document the *observed* overlap periods for each molecule in our data. As discussed earlier, incentives to strategically delay the OTC entry, under the current policy, leads to no overlap periods in five out of the eight molecules that we consider for counterfactual analysis. We expect that elimination of such incentives in the counterfactual world, may lead to earlier entry and hence longer overlap periods. Additionally, for each simulation, a branded manufacturer may also choose not to release the OTC version. Hence, in Table 9 for each molecule, for both counterfactual policy designs, we report the average number of years for which the branded OTC and branded prescription drug overlap in the market, as well as the probability that there will be no entry of OTC-version.[52]

Two key points are worth highlighting in the 'no exclusivity' counterfactual. First, under no exclusivity policy, three brand-name manufacturers (Axid, Prevacid and Zegerid) choose not to release corresponding OTC-versions with high probability in the equilibrium. Our results show that, Axid, Prevacid and Zegerid may choose not to release the OTC versions with 47%, 45% and 42% probabilities respectively. This is driven by the fact that, without market exclusivity in the new policy regime, these three molecules do not find it profitable to invest in the fixed cost of developing an OTC product due to lower expected profit. Axid and Zegerid, two of the H2-blocker drugs are also relatively less popular drugs in the prescription market with low average revenues (as can be seen in Table 1). The profit margin of those two products is further reduced by early OTC entry decisions of other molecules that belong to the same class. Similarly, in the PPI class, early entry of OTC versions by other popular molecules negatively affects Prevacid's expected profit from releasing the OTC drug. This also highlights the advantages of our modeling choice, where we capture such inter-dependencies in the joint decision-making of all molecules by a dynamic discrete-

[52]For a given counterfactual simulation, we compute the Pr(no OTC entry) by taking the ratio:
[(# simulations for which a manufacturer chooses not to release the OTC version)/(# of total simulations)]

Table 9: **Results from Counterfactual Analysis: Alternative Exclusivity Designs**

		# years Branded Rx & Branded OTC overlap *before* patent expiry				
		Status Quo (Data)	No Exclusivity CF		Expanded MEP CF	
Brand	Molecule	# Yrs	# Yrs	Pr(no OTC entry)	# Yrs	Pr(no OTC entry)
Tagamet	Cimetidine	0	1.7	26%	1.9	20%
Zantac	Ranitidine	1	1.5	10%	1.6	9%
Pepcid	Famotidine	5	3.6	26%	3.8	18%
Axid	Nizatidine	6	4.7	47%	4.6	26%
Prilosec	Omeprazole	0	3.0	0%	3.8	0%
Prevacid	Lansoprazole	0	3.4	45%	3.5	21%
Aciphex	Rabeprazole	No OTC Entry	-	-	-	-
Protonix	Pantoprazole	No OTC Entry	-	-	-	-
Nexium	Esomeprazole	0	3.4	0%	3.6	0%
Zegerid*	OmeprazoleNaHCO3	0	0.3	42%	0.3	34%
Dexilant	Dexlansoprazole	No OTC Entry	-	-	-	-
Δ in consumer welfare compared to status-quo policy			1.4 Billion USD		3.2 Billion USD	

Note: The Table reports the results from counterfactual analysis. For the data (under the status quo policy), as well as for counterfactual worlds, the Table reports the number of years branded Rx and branded OTC are jointly sold in the market before the branded Rx patent expires. The column 'Status Quo (Data)' denotes the number of years of branded Rx and branded OTC are sold in our sample before branded Rx patent expires. 'No OTC Entry' refers to the case where the branded Rx does not release its OTC version. The 'No Exclusivity CF' column refers to the counterfactual exercise where the three year FDA market exclusivity is removed. The 'Expanded MEP CF' 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, two years of exclusivity are granted when the OTC is released two years prior to patent expiry, and one year market exclusivity is granted when the OTC is released one year prior to patent expiry. The column Pr(no OTC entry) refer to the probability that the OTC version is not released in the counterfactual world.
∗Note that, while Zegerid patent was scheduled to expire in July 2016, it was challenged and the patent was ruled invalid by the federal court in July 2010. Please refer to Section 3 for more discussion on this.

choice oligopoly game. Our simulations reveal that popular OTC drugs such as Prilosec and Nexium would enter the market with 100% probability even without market exclusivity, leading to expanded access to drugs. Other molecules (Tagamet, Zantac, and Pepcid) would release the OTC version with relatively high probability (74%, 90%, and 74%, respectively). This suggests that, due to the high expected variable profit from releasing the OTC drug, the firms with those five molecules would find it profitable to invest in the fixed cost of developing OTC products even without exclusivity.

Second, under no-exclusivity, conditional on introducing the OTC version, all molecules would choose to enter into the OTC drug market earlier, compared to the date of the corresponding patent expiration. This leads to a longer overlap period between Rx and OTC products prior to Rx patent expiry. While Tagamet, Prilosec, Prevacid, and Nexium choose to enter right after respective patent expiry in the actual data, they would on average enter three to four years prior to the 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 the introduction of the OTC version. Therefore, early entry in the OTC drug market leads to an overall increase in firm profit. In the status-quo policy regime, those molecules chose to strategically delay the OTC release to avail market exclusivity, and hence removing the exclusivity leads to early entry of branded OTC drugs and improves access. Removing exclusivity also improves access to the generic OTC drugs, as market exclusivity under the existing policy, along with strategic entry of those molecules right around the patent expiry, blocks the entry of generic OTC drugs for three years. In case of Pepcid and Axid, under status quo policy, the two molecules enter five and six years prior to patent expiry; in the no exclusivity counterfactual world, they would continue to enter four to five years early conditional on introducing the OTC version. Overall, although the no-exclusivity policy provides less incentive to innovate and leads to lower probability of introduction of OTC versions for three molecules, due to early entry of other branded and generic OTC products, the overall consumer welfare increases by 1.4 billion dollars, compared to the status-quo policy.

In the expanded MEP regime, the incentive to innovate is protected by providing market exclusivity regardless of approval date. However, the full three-year exclusivity is granted only if the branded manufacturer decides to introduce the OTC version at least three years prior to its prescription patent expiry.[53] The results from this exercise is reported in the columns under the heading 'Expanded MEP CF'. By redesigning the exclusivity policy, incen-

[53]Note that, two years of exclusivity are granted when the OTC is released two years prior to patent expiry, and one year market exclusivity is granted when the OTC is released one year prior to patent expiry under this exclusivity design.

tives to strategically delay the OTC entry are eliminated. Hence, similar to the no-exclusivity policy, conditional on introducing the OTC version, all brand-name manufacturers would choose to enter into the OTC drug market earlier compared to the date of corresponding Rx-patent expiration. This leads to longer overlap period between Rx and OTC products prior to Rx patent expiry, and hence expanded access to drugs. Additionally, the reported probabilities of no OTC entry under expanded MEP are lower (as reported in the last column of the Table 9), compared to the no-exclusivity design. This suggests that this alternative design restores the incentives to innovate and hence ensures access to all OTC drugs with higher probability. In particular, Axid and Prevacid OTC are released with substantially higher probability (74% and 79% respectively), compared to the no-exclusivity case (with probabilities 53% and 55% respectively). Under expanded MEP however, Zegerid chooses not to introduce OTC-version at a high probability (34%). This is because Zegerid has low profit margin which is further lowered under the expanded MEP world due to early OTC introduction by other molecules in the PPI class. Therefore, even after restoring exclusivity, Zegerid may still find it unprofitable to invest in the introduction of OTC-version with a higher probability. Overall, restoring the incentives to innovate leads to higher probability of introduction of OTC versions for all molecules, and due to early entry of OTC products, the overall consumer welfare increases by 3.2 billion dollars than the status-quo policy. Therefore, our counterfactual exercise suggests that status-quo policy leads to inefficient market outcomes and a redesign of the exclusivity policy can benefit consumers by fostering competition and improving access to drugs.

7 Concluding Remarks

This paper evaluates the impacts of FDA's market exclusivity policy on a pharmaceutical manufacturer's incentives to develop and release the OTC drugs. We study this in the context of US anti-ulcer drug market. This paper contributes by showing that, the current FDA market exclusivity policy creates unintended inefficiency as it ignores the spillover effects of the exclusivity policy designed for the OTC-market segment on the prescription-market segment. To address this, we develop and estimate a structural model of demand, OTC introduction decisions, and pricing in the US anti-ulcer prescription and OTC drug markets. Our principal finding is that the current OTC drug market exclusivity policy, which is intended to encourage the development and release of OTC drugs, may reduce consumer welfare and access to drugs by delaying OTC entry until an Rx drug patent expires. We evaluate alternative exclusivity policies using the estimated model. We show that if the FDA were to eliminate market exclusivity altogether, it would incentivize firms to release

the OTC versions of drugs earlier and that would improve consumer welfare. The elimination of exclusivity might, however, weaken firms' incentives to make risky investments while developing OTC products. We propose and evaluate 'expanded MEP' policy, an alternative market-exclusivity policy, that ties OTC drug market exclusivity to Rx-patent expiry dates, where market exclusivity is preserved after patent expiration to an OTC drug that is introduced more than three years earlier than patent expiration. We find that this alternative design eliminates incentives to engage in strategic delay, protects firms' interests regarding risky investments and enhances consumer welfare.

This paper contributes to the literature that studies the unintended effects of intellectual property policies on competition by considering interactions between two segments of the pharmaceutical market– prescription drugs and OTC drugs. Our counterfactual exercise also contributes to the research on the optimal design of the intellectual property and competition policy. Our study demonstrates that maintaining a delicate balance between the incentives of different players in the pharmaceutical market can have important welfare implications. The lesson from the paper 'that policy in one market (OTC drug) can have (unintended) consequences in another (prescription drug) market', may have broader relevance in other economic settings.

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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 [54] 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: (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.

[54] 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.

A.2 Rebate specification

The extensive use of rebates by the manufacturers to maintain favorable formulary placement with the insurer creates another complication for our estimation. Information about rebates, however, are not publicly available and also vary by third party payor (Kyle and Ridley (2007)). While rebate data are not public, we follow the institutional details highlighted in Arcidiacono et al. (2013) to infer rebates. Under Medicaid Drug Rebate Program, branded drug manufacturers must either give the US government their best price or a fixed discount rate (set at 15.1% prior to 2010 and 23.1% after 2010) off their average price. The 15.1% discount was established by the Omnibus Budget Reconciliation Act of 1990. The rebate was increased to 23.1% under the Patient Protection and Affordable Care Act of 2010. Therefore, increasing rebate to any insurer above the Medicaid rebate also entailed the obligation of increasing a manufacturer's rebate to the US government. Given this intuition, we assume a rebate of 15.1% for time period before 2010 (and 23.1% after 2010) for a molecule prior to generic entry. In other words, we assume that prior to generic entry, manufacturers attempt to keep rebates at 15.1% (or 23.1%) to limit the best price obligation to Medicaid. After patent expiration, the Medicaid penalty constraint is relaxed because sales to Medicaid becomes a much smaller share of business as a result of Medicaid's switches to generics (state Medicaid programs typically don't pay for a branded drug when a generic version is available). We follow the approximation suggested in Arcidiacono et al. (2013), and assume that all manufacturers adjust to a higher rebate percentage of 48.3% upon generic entry.

A.3 Additional Robustness Check 1: Order of Entry in Dynamic Estimation

In our baseline model, we assume a specific order of move while solving the dynamic game under backward induction, that firms move in the order of closeness (in terms of time) to respective dates of patent expiry. Hence, the more experienced firm being closest to patent expiry moves first. As a robustness check, we assume an alternative specification where the least experienced firm moves first, and report the results in Table A1 in Appendix Section A.3. As can be seen, the overall change in magnitude of fixed cost estimate is negligible with most of the differences in the estimates occurring in the third decimal point. This suggests that order-of-entry assumption may not play a decisive role in estimating a multi-period dynamic model as compared to a static two-period model.

Table A1: **Maximum Likelihood Estimates of the Fixed Cost**

	Assumed Order of Move		Assumed Order of Move	
	More Experienced 1st	Less Experienced 1st	More Experienced 1st	Less Experienced 1st
Fixed Cost	42.9***	42.9***	56.5***	56.6***
	(10.1)	(10.2)	(11.9)	(11.9)
Scale of ε's				
Molecules with low avg Rx Rev	3.60***	3.63***	2.14***	2.14***
	(0.8)	(0.8)	(0.31)	(0.31)
Molecules with medium avg Rx Rev	1.40***	1.40***	1.39***	1.39***
	(0.5)	(0.5)	(0.27)	(0.27)
Molecules with high avg Rx Rev	0.90**	0.91**	0.36***	0.36***
	(0.4)	(0.4)	(0.06)	(0.06)
	Model *does not allow* Aciphex & Protonix to release OTC		Model *allows* Aciphex & Protonix to release OTC	
Log Likelihood	-9.5	-9.5	-13.4	-13.4

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. The left panel reports the results from maximum likelihood estimation where model does not allow Aciphex and Protonix to release OTC versions. The right panel reports the results from maximum likelihood estimation where model allows Aciphex and Protonix to release OTC versions. Standard errors are reported in the parentheses.

A.4 Additional Robustness Check 2: Timing of Rx-patent expiry

In this robustness check, we consider the case of Nexium and relax the assumption that the expiration timing of Nexium's Rx-patent is fixed. Instead we assume that, every period (independent of other periods) conditional on Rx-patent being active, Nexium's Rx-patent may expire with a given probability due to generic challenge. This counterfactual exercise mimics a real-world situation where a brand-name Rx manufacturer faces an inherent probability of losing its Rx-patent. This is because a generic entrant's challenge and litigation following it may lead to a decision where Rx-patent is deemed as invalid. On the other hand, a firm that holds the Rx-patent may strike a settlement agreement (such as a pay-for-delay agreement) with the generic-Rx producers under which the generic manufacturer agrees to refrain from entering into the Rx market for a given period of time in exchange for a direct payment from the incumbent. Note that, ex-ante, the possibility of such an agreement can be interpreted as an action that may *lower* the probability of Rx-patent getting invalid in a given period. While we do not observe (or estimate) such probabilities in our framework, for the robustness check, we assume the probability to take a range of values to accommodate inherent probability and (possibly) lower probability of expiry due to settlement agreements.

Therefore, to understand how our counterfactual results under expanded MEP get af-

fected under different probabilities, we assume that the probability can take values 1%, 5% and 10%. We solve for new equilibrium in the dynamic game for each of those probabilities and simulate OTC entry decisions for the expanded MEP counterfactual world. Our results show that the key conclusions of our analysis are robust to this assumption. In particular, both when Nexium Rx-patent faces no uncertainty (the baseline model) and when Nexium Rx-patent may expire with a given probability (1%, 5%, 10%) every period, Nexium chooses to enter into OTC drug market 4 to 5 years early under expanded MEP. This confirms that our key finding (i.e., expanded MEP policy eliminates the incentives for strategic delay and leads to early introduction of OTC versions) remains valid even when Nexium Rx-patent faces uncertainty in its expiry date. Uncertainty however alters the probability that Nexium releases its OTC version. As reported in Table A2, when Nexium Rx-patent may expire with 1% probability in a given period, with 4% probability, Nexium may choose not to introduce its OTC version. This probability increases to 12% and 15% respectively when the uncertainty faced by Nexium increases to 5% and 10% respectively. Note that, as Nexium chooses to enter into OTC drug market with a lower probability, Prevacid's probability of introduction of its OTC version increases. While in the baseline case, Prevacid does not introduce its OTC version with 21% probability, it chooses to enter with close to 100% probability when Nexium's probability of entry into OTC drug market goes down as its faces more uncertainty.

Table A2: **Results from Robustness Check: Expanded MEP with Varying Rx-Patent Expiry Timing**

		# years Branded Rx & Branded OTC overlap *before* patent expiry							
				Every period Nexium Rx-patent expires with					
		Baseline		1% prob		5% prob		10% prob	
Brand	Molecule	# Yrs	Pr(no OTC entry)	# Yrs	Pr(no OTC entry)	# Yrs	Pr(no OTC entry)	# Yrs	Pr(no OTC entry)
Tagamet	Cimetidine	1.9	20%	1.9	20%	1.9	20%	1.9	20%
Zantac	Ranitidine	1.6	9%	1.6	9%	1.6	9%	1.6	9%
Pepcid	Famotidine	3.8	18%	3.8	18%	3.8	18%	3.8	18%
Axid	Nizatidine	4.6	26%	4.6	26%	4.6	26%	4.6	26%
Prilosec	Omeprazole	3.8	0%	3.8	0%	3.8	0%	3.8	0%
Prevacid	Lansoprazole	3.5	21%	3.7	21%	5.4	4%	5.4	0%
Aciphex	Rabeprazole	-	-	-	-	-	-	-	-
Protonix	Pantoprazole	-	-	-	-	-	-	-	-
Nexium	Esomeprazole	3.6	0%	4.0	4%	4.7	12%	4.4	15%
Zegerid*	OmeprazoleNaHCO3	0.3	34%	0.3	34%	0.4	35%	0.4	35%
Dexilant	Dexlansoprazole	-	-	-	-	-	-		

Note: The Table reports the results from robustness check where Nexium patent may expire with a given (1%, 5% or 10%) probability under Expanded MEP counterfactual regime. For each of the probability values, the Table reports number of years branded Rx and branded OTC are jointly sold in the market before the branded Rx patent expires. Column Pr(no OTC entry) refers to the probability that the OTC version is not released in the counterfactual world. Column 'Baseline' denotes the number of years branded Rx and branded OTC are jointly sold under Expanded MEP counterfactual where Nexium Rx-patent expiry does not face any uncertainty. Columns '1% prob', '5% prob', '10% prob' reports results from the cases where every period Nexium Rx-patent may expire with probabilities 1%, 5% and 10% respectively.
∗Note that, while Zegerid patent was scheduled to expire in July 2016, it was challenged and the patent was ruled invalid by the federal court in July 2010. Please refer to Section 3 for more discussion on this.

A.5 Dynamic Game: Transition of brand-name firms

Note that, we denote a brand-name firm i's patent expiration date for its patented molecule by T_i, and assume that a firm can take active decision about whether to release OTC version at the beginning of a time period $t \leq T_i$. As highlighted in equation 4.9 in Section 4.2.1, in the beginning of every year t, a branded manufacturer i of a given molecule can be in one of the five situations. The transition from period t to $t+1$ is given in Table A3.

Table A3: State transition from t to $t+1$

State at t	Action	State at $t+1$
(1) Rx-patent active, Rx only	Release OTC	(2) Rx-patent active, Rx and OTC, $T_i^{OTC} = t+1$, if $t < T_i$ (4) Rx-patent expired, Rx and OTC, OTC exclusivity, $T_i^{OTC} = t+1$ if $t = T_i$
	Not Release OTC	(1) Rx-patent active, Rx only, if $t < T_i$ (3) Rx-patent expired, Rx only, if $t = T_i$
(2) Rx-patent active, Rx and OTC, T_i^{OTC}	No action	(2) Rx-patent active, Rx and OTC, if $t < T_i$ (4) Rx-patent expired, Rx and OTC, OTC exclusivity, if $t = T_i$, $T_i^{OTC} \geq T_i - 3$ (5) Rx-patent expired, Rx and OTC, no OTC exclusivity, if $t = T_i$, $T_i^{OTC} < T_i - 3$
(3) Rx-patent expired, Rx only	No action	(3) Rx-patent expired, Rx only
(4) Rx-patent expired, Rx and OTC, OTC exclusivity, T_i^{OTC}	No action	(4) Rx-patent expired, Rx and OTC, OTC exclusivity, T_i^{OTC}, if $t \leq T_i^{OTC} + 3$ (5) Rx-patent expired, Rx and OTC, no OTC exclusivity, if $t > T_i^{OTC} + 3$
(5) Rx-patent expired, Rx and OTC, no OTC exclusivity	No action	(5) Rx-patent expired, Rx and OTC, no OTC exclusivity

A.6 More Details on Estimation

A.6.1 Demand Estimation Details

Steps for estimation of demand parameters following PD-GEV specification are similar to estimation of BLP model (Berry (1994), Berry et al. (1995)). The estimation procedure requires one to compute the errors $e_{jt} = (\xi_{jt}, \omega_{jt})$ as specified in equations (4.1), and (4.17). We start with a candidate parameter vector that takes into account the nesting parameters and price coefficients $\theta^d = (\rho_1, \rho_2, \rho_3, \rho_4, \vec{\alpha})$. In equation (4.1), define the part of mean utility excluding price as

$$\tilde{\delta}_{jt} = x_{jt}\beta + \zeta_j + \xi_{jt} \tag{A.1}$$

The model predicted market share $s_{jt}(x_{jt}, p^c_{jt}, \tilde{\delta}_{jt}, \theta^d)$ is given by equations (4.3) and (4.4). We match the model predicted market share vector with the observed market shares given in vector form:

$$\vec{s}(x_{jt}, p^c_{jt}, \tilde{\delta}_{jt}, \theta^d) = \vec{S} \tag{A.2}$$

where $\vec{S}$ denotes the *observed* market shares. Given a fixed value of θ^d, we invert this equation to retrieve a vector of mean utility levels ($\tilde{\delta}_{jt}$) by using BLP contraction mapping. After recovering $\tilde{\delta}_{jt}$, the demand-side unobservables (ξ_{jt}) can be computed by:

$$\xi_{jt} = \tilde{\delta}_{jt} - x_{jt}\beta - \zeta_j \tag{A.3}$$

Using first order conditions (4.16), we recover marginal cost (mc_{jt}). Marginal cost unobservables (ω_{jt}) are recovered using (4.17) and is given by

$$\omega_{jt} = \log(mc_{jt}) - w_{jt}\gamma \tag{A.4}$$

Given the instruments matrix Z, we define the GMM objective function. We search for parameter vector θ^d that minimizes this GMM objective function.

A.6.2 Algorithm to solve Dynamic Game

We employ the nested fixed-point (NFXP) algorithm for the estimation of the dynamic parameters, the average fixed cost of OTC launch (F) and scaling parameters for error draws (θ_ε). For each candidate vector of parameters, we solve the dynamic game for a Perfect Bayesian Equilibrium (PBE) by backward induction, construct the likelihood of observing the actual choices in the data, and obtain as a maximum likelihood estimate the parameter vector that best rationalizes the observed OTC release-timing patterns. The operational details of this computation are as follows:

- We set discount factor β at 0.88, and the initial values for the parameters to be estimated, $(F, \theta_\varepsilon^1, \theta_\varepsilon^2, \theta_\varepsilon^3)$.

- We run a numerical search for the parameter values that maximize the log likelihood of observing the OTC switching patterns by branded-manufacturers in the data. The optimization routine employed here constitutes the "outer loop" of the NFXP algorithm for parameter search. The outer loop follows a maximum likelihood estimation method.

- The "outer loop" estimation repetitively calls for the likelihood objective function to be maximized. The "inner loop" consists of this likelihood function, which takes as input a vector of candidate parameter values, and returns as output a scalar (i.e., the joint log likelihood).

- For a given candidate parameter values, the inner loop proceeds by backward induction. Note that, from equation (4.12), we assume the state vector that brand-name manufacturers reach at period T is an absorbing state. We start the backward induction calculation from period $T-1$. For period $T-1$, denote the values from next period (period T) as V'.

- For each state vector in period $T-1$, we consider all brand-name manufacturers who are with state '(1) Rx-patent active, Rx only,' as defined in equation (4.9). For those brand-name manufacturers with the given state, we find a fixed point of the optimal choice probabilities of releasing OTC versions. We store these policy functions from period $T-1$.

- We compute the ex-ante value as specified in equation (4.14) for period $T-1$ and state vector s. This will serve as V' when we move to period $T-2$.

- We repeat this process for each $t = T-1, T-2, \ldots, 2, 1$. We then calculate the joint likelihood of observing the given OTC release patterns, and return this log-likelihood value to the "outer loop" for further parameter search.

- The NFXP procedure is complete when the "outer loop" determines the parameter values that maximize the likelihood. These values constitute our maximum likelihood estimates.