DISCUSSION PAPER SERIES

DP11813

THE UNEXPECTED CONSEQUENCES OF ASYMMETRIC COMPETITION. AN APPLICATION TO BIG PHARMA

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INDUSTRIAL ORGANIZATION and PUBLIC ECONOMICS

ISSN 0265-8003

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Discussion Paper DP11813
Published 27 January 2017
Submitted 27 January 2017

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JEL Classification: D22, I11, L13

Keywords: Asymmetric competition, Pharmaceutical industry, Generic entry

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Acknowledgements
We would like to thank Laurent Bouton, Guilhem Cassan, Christopher Cotton, Margaret Kyle, Patrick Legros, Alessandro Lizzeri, Laurent Mathevet, Jacopo Perego, R egis Renault, Patrick Rey, Pablo Querubin, Tobias Salz, Fiona Scott Morton, Denni Tommasi, and PhilippeWeil, as well as seminar participants at Oxford University, ECARES, the Paris School of Economics, Queen's University, Universidad Carlos III, Universit é de Cergy-Pontoise, Universit é de Lausanne, EARIE2016, and CRETE2016. Siotis gratefully acknowledges the nancial support from the Ministerio Econom ía y Competitividad (Spain) grants Beca I3 2006/04050/011, ECO2015-65204-P, MDM 2014-0431, and Comunidad de Madrid grant MadEco-CM (S2015/HUM-3444). Castanheira gratefully acknowledges financial support from FRS-FNRS (Belgium).

The Unexpected Consequences of Asymmetric Competition. An Application to Big Pharma*

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January 24, 2017

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This paper shows that a pro-competitive shock leading to a steep price drop in one market segment may benefit substitute products. Consumers move away from the cheaper product and demand for the substitutes increases, possibly leading to a drop in consumer surplus. The channel leading to this outcome is non-price competition: the competitive shock on the first set of products decreases the firms' ability to invest in promotion, which cripples their ability to lure consumers.

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§Universidad Carlos III de Madrid and CEPR. Georges Siotis gratefully acknowledges the financial support from the Ministerio Economía y Competitividad (Spain) grants Beca I3 2006/04050/011, ECO2015-65204-P, MDM 2014-0431, and Comunidad de Madrid grant MadEco-CM (S2015/HUM-3444).

¶Maria-Ángeles passed away before being able to complete this project. We owe a lot to her inspiration and enthusiasm, and dedicate this paper to her memory.

1 Introduction

A common belief is that forces that stimulate competition must improve market outcomes. Abstracting from situations in which market failures are obvious (*e.g.*, significant information asymmetries), economic theory has identified only a few exceptions where increasing competition would fail to improve market efficiency and welfare. Hence, these are typically considered as such: exceptions, oddities.

This paper contends, instead, that the link from competitiveness to allocative efficiency is weaker than that belief suggests. To attract customers, firms do not only cut prices. They also use non-price instruments, such as advertising and investments in brand management. We show that the mere presence of these instruments affects, or even reverses, the way that competitive shocks alter market outcomes. This happens when the competitive shock disproportionately impacts some of the incumbent firms: even though the price of their products (call them A) drop, consumers end up shifting to more expensive products (call them B). The firms producing B can even profitably increase their price along with their market share, and consumer welfare may drop as a result. The reason for this outcome is that the competitive shock cripples the former firms' capacity to invest in non-price instruments.

This is more than a theoretical construct: using a data trove tracking prices, advertising, and quantities sold, we show that competition by generics in the trillion-dollar pharmaceutical market generally fails to put effective pressure on the drugs that remain protected by a patent. Despite price drops as high as 45% for the drug experiencing generic entry, it is the market share of *competing molecules* that increases. The volume market share of the molecule that is now cheaper–the originator drug *plus its generic bioequivalents*–drops, on average, by 31% in the pharmacy channel and by 26% for drugs sold in hospitals. Both our theoretical and empirical findings show that, quite counter-intuitively, this phenomenon is more pronounced when molecules are close substitutes and when market size is large. By extension, these results raise questions for markets in which some products become (almost) free. Note, also, the difference from the effects of competition on innovation identified by Aghion *et al.* (2005), among others. Although the issues addressed in Sutton's (1998) seminal contribution are fundamentally different, endogenous sunk costs in the form of advertising play a central

role in shaping our model's equilibrium outcomes (see, also, Sutton (2007) for an overview).

To clarify the forces at play, we propose a stylized model in which two firms, A and B, each produce a differentiated product. Consider, first, the situation in which they compete only in price. Following standard intuition, the more substitutable the goods, the lower the initial prices will be. Then, firm A is confronted with the entry of a new competitor that sells a direct substitute for its product. Absent capacity constraints, this competition shock drives the price of A down to marginal cost and forces B to also react with a lower price. In this situation, "competition works": even though this asymmetric competition shock need not improve allocative efficiency,[1] consumer surplus must increase.

What happens when the two firms also rely on non-price instruments such as advertising to attract consumers? In this setting, A's reduced profitability also induces it to cut down investment in the non-price instrument. This produces a demand shift opposite to that of the reduced price: it favors B. Whenever the non-price shock dominates the price shock, B sees its residual demand expand. B can then increase both price and market share. We show that, even when the non-price instrument has no direct impact on utility, consumer surplus may drop as a result.

Under which conditions does this *reverse competition effect* dominate? Quite surprisingly, the problem is more acute when A's and B's products are *closer substitutes*. The reason is that the more substitutable the two goods are, the more aggressively A and B compete before the entry of the third firm (*generic entry* in the case of the pharmaceutical industry). This translates into initially lower prices and higher "promotion" (the non-price instrument that we can measure in our data). In that situation, generic entry has a comparatively small impact on prices; the reduction in promotion dominates.

High levels of differentiation have the opposite effect: prices are initially high and promotion low. Then, generic entry affects primarily prices: both A's and B's prices drop. This is an important cautionary tale for competition policy and for empirical IO scholars, who often rely on the observed reactions to price shocks to evaluate cross-price elasticities and/or establish market boundaries. Under the conditions described above, such estimates are bound

[1] For instance, if the two products are symmetric (for a given price $p_A = p_B$, 50% of the consumers prefer A to B and 50% have the opposite preference), then the steeper price drop of A than of B would increase A's market share above 50%.

to be heavily biased, unless one can track the firms' investments in non-price instruments over time.

Theory also informs us on the expected effects of demand elasticity and market size. Our model tells us that a lower price elasticity of demand increases the likelihood that B benefits from stiffer competition faced by A. The same goes for market size: the reverse competition effect is more likely to hold in large markets because B maintains a high level of promotion.

The pharmaceutical industry is a fertile testing ground for evaluating these predictions. First, it is oligopolistic and differentiated – both horizontally and vertically. Second, it is large, with worldwide sales totaling nearly a trillion USD in 2013, while the US market stood at 374 billion USD in 2014.[2] Third, non-price instruments are central to the firms' competitive strategies: in the case of Big Pharma, promotion to physicians represents 15% to 20% of total sales, about the same as R&D investments.[3] Fourth, the price elasticity of demand varies across distribution channels – we will exploit the difference between hospitals and pharmacies to assess the role played by the elasticity of demand. Fifth, and most important, asymmetric competition shocks are rife: firms benefit from a 20-year period (or longer) of exclusivity between patent filing and generic entry.[4] Given this long time span, actual market size and the degree of substitutability of competing products cannot be predicted ahead of actual launch. This produces substantial exogenous variation across episodes of generic entry that we exploit in our regressions.[5]

Focusing on the changes that occur around the Loss of Exclusivity (LoE) at the end of these 20 years, and thanks to an extended database that tracks the majority of prescription

[2]Source: http://www.statista.com/statistics/263102/pharmaceutical-market-worldwide-revenue-since-2001/ and http://www.statista.com/statistics/238689/us-total-expenditure-on-medicine/

[3]In the *Oxford Handbook of the Biopharmaceutical Industry*, Harrington (2012) estimates the R&D to be at 17.9% of total net sales for the period 2001-2005, and Kenkel and Mathios (2012) report that the advertising-to-sales ratio was 18% in 2005 in the U.S. As points of comparison, they highlight that, in 2010, advertising stood at 4.5% of total net sales for General Motors (a car producer), 9.5% for Anheuser Busch (a beer producer) and 10.8% for Kellogg (breakfast cereals). The figures are typically smaller for most other R&D-intensive industries. For instance, in 2013, Apple spent 3% of its total net sales on R&D and 0.4% on advertising (Apple 2013: 10-K SEC submission).

[4]Patent filing is followed by lengthy clinical trials and regulatory approval processes. This effectively reduces the post-launch patent protection period to 8-12 years.

[5]Generic competition could be less than fully effective because some patients and physicians fear that generics are not an exact bio-equivalent (*e.g.*, due to dosage problems) to the original drug. Yet, if this were the primary reason for poor generic penetration, we should observe that they are also – perhaps mainly – toothless against the original, branded molecule. The opposite is observed in the data.

sales in the U.S. between 1994Q1 and 2003Q4 (40 quarters), we can study the effects of 95 episodes of generic entry spread over 53 different therapeutical classes ("ATC3 markets"). The scattered distribution of these competition shocks, across both markets and time, should be sufficient to rule out confounding factors.

In Section 2, we document that firms start reducing their promotional efforts three years before they lose exclusivity (see, also, Caves *et al.* (1991)).[6] After generic entry, the price of the molecule drops, on average, by about 45% after three years. Yet, the market share of the molecule drops by around 25-30%. That is, the cumulated sale volume of the original brand plus its generic competitors drops, even though these markets are typically growing. We show that this market "anomaly" is due to a drop in the flow of promotion drops by 85% (or more).

The size and granularity of our product-level dataset also allow us to address the numerous limitations of the previous empirical literature on generic entry and competition in the pharmaceutical industry. The existing literature has focused either on inter-molecular competition amongst patent-protected drugs or on the intra-molecular competition shock associated with generic entry. As far as we can tell, our paper is the first to study the knock-on effects of intra-molecular competitive shock on inter-molecular competition. The benefit of this exercise is that we can exploit (large and exogenous) changes in competitive strategies associated with LoE to identify the coefficients of the demand function. This contrasts with former analyses that had to focus on marginal changes in prices and advertising around their equilibrium values.

As shown in Section 5, this econometric approach leads to higher–and more reasonable–estimates of price and promotion elasticities than those found in the existing literature.[7] At the same time, our results identify a difference between the price elasticities in the pharmacy and hospital channels that is consistent with the differential evolutions of market shares following patent expiration. They also confirm that generic entry does not affect demand

[6] One might object that firms often develop new generations of molecules to anticipate their LoE, a strategy dubbed "evergreening". We checked the robustness of our results by running the same regressions as in Section 5, but keeping only the 75 drugs (out of 95) for which there was no instance of evergreening. All of our substantive results remained unchanged.

[7] Kremer *et al.* (2008) provide a meta-analysis of the detailing elasticity of demand and report that, on average, point estimates are below unity.

beyond the change in the price and promotion effort for the drug experiencing LoE, dispelling the possibility that aversion towards generics could explain the shift towards other patent-protected molecules.

After controlling for other possible sources of heterogeneity, our econometric estimates indicate that generic entry alone causes an *increase* in market share of about 12% for molecules that remain on patent. The effect is smaller in the hospital channel: the higher price elasticity reduces the magnitude of this effect by about 3%. We also propose a novel measure of product differentiation for the pharmaceutical industry based on the number of modes of action within a therapeutic class. We claim that the existence of different modes of action to treat a particular condition is indicative of more differentiation. We find that differentiation knocks another 4% off the market share gain of the competitors. Finally, the market share gain is further reduced by 7% in "small" markets. Each of these observations is in line with the theoretical predictions sketched out above.

Related literature. The existing literature on competitive interactions in the pharmaceutical industry has produced a complex picture. One group of papers analyses inter-brand competition when drugs are still patent-protected (see, for instance, Brekke and Kuhn (2006) for a theoretical model and Dave and Safer (2012) for empirics). de Frutos, Ornaghi and Siotis (2013) present a model of inter-brand competition in which the proportion of brand-loyal consumers is endogenously determined by promotional effort; the main results are then empirically tested. Another strand focuses on intra-molecular competition following loss of exclusivity — *i.e.*, when a generic bioequivalent drug can legally come to market (*e.g.* Scott Morton (2000)).[8] It was in that context that the "generic entry paradox" — that the price of the originator drug often goes up following the launch of a competing bioequivalent generic, has been unearthed. This empirical finding has been thoroughly documented (see *a.o.* Caves *et al.* (1991); Regan (2008); Vandoros and Kanavos (2013)). The more recent literature has focused on the relative importance of the persuasive and informative role of promotional effort (Ching and Ishihara (2012)) and on whether detailing and direct-to-consumer advertising have a market expansion effect (Ching *et al.* (2016); Fischer and Albers (2010)).

[8] See Grabowski and Kyle (2007) for a description of generic entry in the US in the period 1995-2005 and Berndt and Dubois (2016) for a comparison of generic penetration across OECD countries for the period 2004-2010.

The few papers that have attempted to simultaneously analyze pre- and post-LoE competition have produced conflicting results. For instance, Stern (1996) provides evidence of intense inter-molecular competition. By contrast, Ellison *et al.* (1997) reports strong intra-molecular rivalry between the originator and the generic version of the drug, as well as weak (or insignificant) inter-molecular competition. There is little empirical evidence on the reaction of still on-patent branded producers when a competing drug experiences generic entry.

Our model provides a unifying framework to understand inter- and intra-molecular competition, in that it covers both pre- and post-LoE environments. This helps reconcile the conflicting findings in the literature and sheds new light on the pre- and post-generic market share movements observed in the data.

The remainder of the paper is organized as follows. Section 2 presents some surprising facts that spur the paper's central research question. Section 3 presents the model and derives testable implications. Section 4 describes the data, while Section 5 presents the empirical results. Section 6 discusses some welfare considerations and concludes.

2 Generic competition: some empirical regularities

2.1 Price, patents, and quantities

The pharmaceutical industry brings together many characteristics of interest for Industrial Organization scholars. It is oligopolistic, regulated, and differentiated – both horizontally and vertically. It is also unique in combining high R&D and high promotion intensity. From a public policy perspective, the cost of drugs is an important component of growing health care costs – a concern for health insurers and public authorities alike. Encouraging competition with generic bioequivalents is a potential key to moderating these ballooning costs.

Once on the market, the life cycle of a patent-protected pharmaceutical drug can be broken in two distinct stages. The first covers the period spanning market launch until the firm loses exclusivity, which usually stems from patent expiry. During that phase, the producing firm has exclusive rights over the production and distribution of the drug and, thus, can thus exercise market power. The second phase begins after loss of exclusivity (LoE), when generic equivalents can enter the market to compete with the originator firm.

The introduction of a bioequivalent competitor produces a dramatic change in the nature of competitive interaction. Generics are typically sold at a fraction of the price of their branded equivalent and exert strong competitive pressure on the original branded product: Grabowski *et al.* (2014) show that, for branded drugs facing first generic entry in 2011-2012, brands retained, on average, only 16% of the molecule market after one year.

The light-grey curves in Figure 1 below illustrate the evolution of the mean and median price and quantity for 95 molecules that experienced generic entry in the U.S. during the period 1994-2003. Time is expressed in quarters, and we denote as "date 0" the quarter in which firms lose exclusivity. We normalize to 1 values at quarter -12.[9] Before patent expiration (quarters -8 to 0), the price of the original molecule is slightly increasing. Then, within a year of the loss of exclusivity (LoE), mean (respectively, median) prices drop by about 30% (20%). Within three years, the drop reaches about 50% (40%).[10]

Figure 1 identifies the unexpected piece of evidence mentioned in the introduction: despite being sold at a fraction of the original price, the *genericized molecule actually experiences a drop in volume* after LoE (black curves): the average and median quantities drop by 25% three years after patent expiry. In other words, after LoE, the *combined* volumes of the branded and generic producers are substantially below the volume of the single branded drug when it is sold at a price embodying monopoly power.

Another perplexing feature surrounding generic entry is that the price of the other molecules – those still patent-protected – does not decrease (see Section 5 and Jena *et al.* (2009);[11] Gonzalez *et al.* (2008)). And yet, in many instances, they experience a gain in mar-

[9] We control for the fact that not all molecules are observed in all quarters (for instance, if a patent expires four quarters before the end of the data, we have only four data points after patent expiration) by: i) computing the price change over two consecutive periods for all available molecules; ii) computing the average of these variations for each quarter before and after patent expiration; and iii) constructing an index that starts at 1 and that varies over time following the average variations computed at stage (ii). We follow the same approach to compute the median price and all the other statistics in this graph.

[10] Although the *average price of the molecule* (displayed) falls following generic entry, this is not always the case for the price of the branded drug (not separately depicted in Figure 1). Sometimes, the latter remains constant or even *increases*; this is the so-called *generic entry paradox* (for empirical evidence, see Regan (2008) for the U.S. and Vandoros and Kanavos (2013) for the EU). This behavior is usually attributed to the fact that a subset of patients insists on purchasing the brand, even at a higher price. This allows branded producers to keep extracting rents on a (shrinking) subset of patients.

[11] The authors track price and quantity evolutions in five therapeutic classes. They interpret the absence of price reaction by competitors and/or demand shifting towards generics as evidence of single molecule markets, without actual substitutability.

Figure 1: Price and Quantity around generic entry

ket share. Put differently, few new patients are directed to the cheap genericized molecule, and a number of existing patients switch to competing molecules at the time that their initial treatment becomes cheaper (European Commission, 2009). Neither the rationales for the so-called *generic entry paradox* (*cf.* footnote 10) nor co-payment by health insurances explain why cross-price elasticities suddenly seem to take the "wrong sign".

Taken together, these facts show that generics display two different faces: while they are fierce competitors for the branded drug that lost exclusivity, they appear to be toothless challengers with respect to the remaining patent-protected drugs.

2.2 Loss of Exclusivity and Promotion Intensity

Competitive interactions in the pharmaceutical industry are richer than the changes in prices and quantities documented above. LoE also triggers major shifts in the firms' promotional effort–we will use the terms *detailing, promotion* and *advertising* as synonymously. Using data from IMS-Health, we measure the firms' drug-specific spending on personalized visits to general practitioners and hospital specialists, free samples dispensed to physicians, and

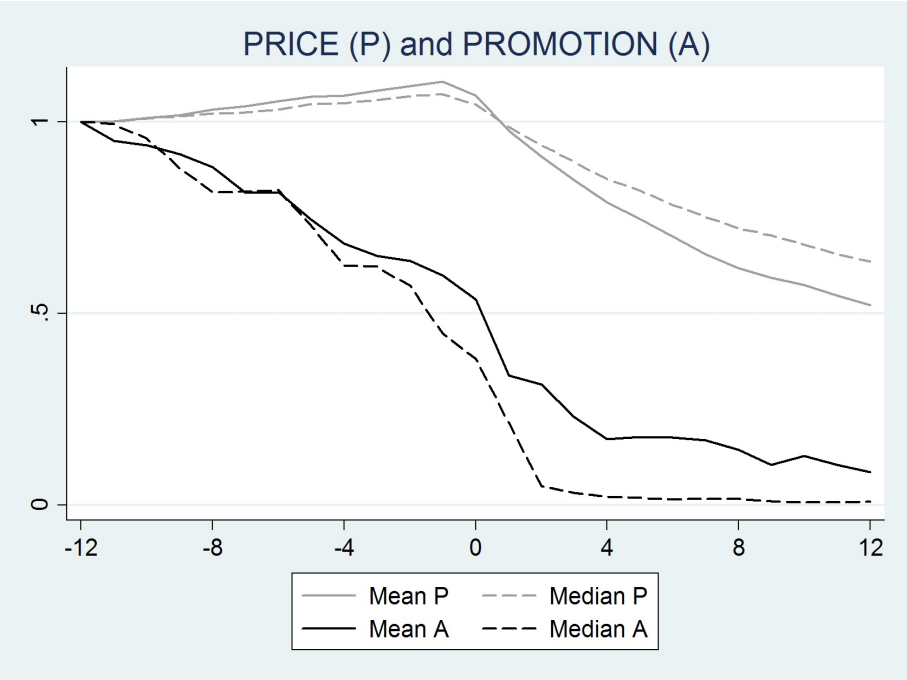

Figure 2: Price and Promotion around generic entry

advertising in professional journals. All these instruments affect the physicians' incentives to prescribe one drug rather than another to their patients.[12]

Figure 2 shows how total spending on these three channels evolves around the time of LoE for the molecules that are actively promoted before their patent expires. Our data reveal that promotion falls continuously over the 12-quarter period before patent expiration, with a sharp acceleration around the time of LoE. At time 0, promotion effort has dropped by 50%. Within three years, the median spending is zero. The average lies above the median because some molecules continue to be promoted.[13]

The fact that physicians reduce prescriptions when promotion drops (see Section 5.1

[12]Inderst and Ottaviani (2012) propose a seminal model of competition through commissions and kickbacks which can be applied to describe the physicians' role as intermediaries between patients and pharmaceutical companies. Iizuaka (2012) provides evidence that physicians respond to economic incentives in their prescription decisions. The association between payments to physicians and their prescription behavior can also be assessed on the basis of publicly available data (Grochowski, Jones, and Ornstein, 2016).

[13]For instance, high levels of promotions are observed for Prozac (fluoxetine) because Eli Lilly & Co. introduced weekly delayed release capsules of the drug just before LoE in an attempt to stem the post-patent decrease in sales of their daily dosage. Similarly, we observe positive spending for Zantac (ranitidine) and Tagamet (cimetidine), probably because some of their lower-dosage tablets are available over-the-counter (no prescription required).

for more empirical evidence) clearly suggests that promotion is principally of a "persuasive nature" around LoE –unless one believes that doctors forget what they have been prescribing for years shortly before the drug's patent expires. We are not claiming that promotion does not provide information leading to market expansion. Rather, the underlying assumption is that the informative component is more relevant earlier in a molecule's life cycle, while the persuasive dimension dominates around LoE, which is the time window we focus on (see Ching and Ishihara (2012) Ching *et al.* (2016) and Fischer and Albers (2010) for a more precise decomposition of the informative and persuasive components). Note that Caves, Whinston and Hurwitz (1991) also observe that "generic entry brings with it two offsetting effects: first, generic entrants offer significantly lower prices, which tend to expand overall sales of the drug, but their arrival also leads to a significant reduction in the level of advertising for the drug, which acts to counterbalance this price effect". However, they do not explore the matter further, either theoretically or empirically.

The literature has identified cases in which one or the other of these opposing effects dominates. Berndt et al. (1996, 2003) report instances where the market share of the molecule losing exclusivity experiences a fall, while Aitken *et al.* (2009, 2013) find the opposite. Our model identifies the forces that drive these different outcomes, making it possible to derive a series of of testable hypotheses. The latter are taken to the data; the empirical results provide strong support for the model's central results.

3 The model

Our first contribution is to propose a model that sheds light on the competitive interactions that appear when (1) firms compete through price and non-price instruments; (2) purchasing behavior is mediated through an intermediary who can be persuaded to modify his or her recommendations of either good and; (3) one good faces the entry of a direct substitute.

Formally, we focus on what is initially a duopoly situation: two firms, A and B, compete both in prices and in "advertising,"which increases fixed costs. Starting from that initial situation, what are the effects of the entry of a third firm, G, that produces a perfect substitute for firm A's product? Intuitively, substitutability implies that A's advertising effort produces

a positive spillover on G's demand (the way that a brick and mortar store's advertising for a given product also stimulates online demand for the same product). Under these circumstances, competition between A and G implies that both the price and advertising effort of A must drop substantially. Our central question is: what happens to the demand for B? Clearly, stiffer price competition on the side of A will exert negative pressure on B's demand schedule. But, at the same time, less advertising by A will buoy B's demand.

Shifting to a terminology adapted to the pharmaceutical industry, consider a market in which two firms' molecules compete for physicians' prescriptions. We want to capture the firms' *detailing* and *pricing* strategy given the quality θ_J of their molecule, the heterogeneity of treatment responses across patients, e,[14] and the price sensitivity δ of the patients' demand (which depends on insurance co-payment).[15] It is important to note that the patient's demand is intermediated through an agent: her physician (Inderst and Ottaviani, 2012).

Consider the case of a patient who goes to her physician with a condition that requires treatment. The patient/physician pair (PPP) i's intrinsic utility from using treatment A or B is, respectively (we introduce detailing below):

$$U_A^i = \theta_A - \delta p_A + \varepsilon^i, \tag{1}$$

$$U_B^i = \theta_B - \delta p_B - \varepsilon^i, \tag{2}$$

where p_J is the price of molecule $J \in \{A, B\}$; $\varepsilon^i \sim \mathsf{U}\left[-\frac{e}{2}, \frac{e}{2}\right]$ is the relative efficiency of drug A as opposed to B to treat patient i's condition; and U denotes the uniform distribution.[16] A larger value of e implies that patients are more heterogeneous and, hence, that the two molecules are *more distant substitutes*. A larger co-payment by the patient's health insurance makes the PPP less price sensitive: it reduces δ.

[14] These parameters directly relate to vertical and horizontal product differentiation in classical Industrial Organization analyses. However, product differentiation is not a choice variable in our model.

[15] This modeling choice fits the industry's description provided by Berndt (2002): "Within many therapeutic classes of drugs, a number of possible substitute medications exist, and in such cases, the market structure is more appropriately depicted by the differentiated product oligopoly framework. In such a setting, it is useful to envisage the optimal profit maximizing price as equaling marginal cost plus a positive margin, where the margin depends on benefits and attributes (including prices) the firm's own drug relative to other drugs in the therapeutic class, on attributes of non-drug therapies, patient heterogeneity and other demand-side considerations."

[16] Focusing on a single random variable ε that can be either positive or negative implicitly eliminates patients with negative valuations of the two molecules, who have no reason to consume either of the two drugs. Issues of aggregate under- or over-prescription are, thus, beyond what this model can capture.

Note that assumptions such as the linearity of the demand schedule and the uniform distribution of patients would be inappropriate if we were to estimate the model structurally. However, our data (see Section 4) do not allow us to track the demand of individual consumers, and our questions are rather orthogonal to the ones that structural estimations are meant to address. We thus choose to simplify the model as much as possible without losing track of the main trade-offs we want to capture. In Section 5, we only test the model's resulting predictions. If the data were to reject these, we would have to revisit the model's specific assumptions. As will be seen, however, this does not appear to be an issue.

To limit the number of cases, we focus on the situation in which all patients who require a treatment receive one.[17] This requires that the quality θ_J of both molecules is sufficiently high relative to the equilibrium prices–formally, $\theta_A + \theta_B > 2e$ (see Appendix 1). Therefore, patients with a sufficiently good fit with drug A (*i.e.*, with ε^i sufficiently large) buy treatment A, and all the others buy drug B. For lower drug qualities, prices would also affect market size, which complicates the algebra. Letting μ denote market size (or the number of afflicted patients), we identify the patient who is indifferent between A and B to determine quantities in the absence of detailing, and we find that:

$$\begin{aligned} Q_A &= \left(1 - F\left[\frac{\Delta\theta_B - \delta\Delta p_B}{2}\right]\right) \times \mu \\ Q_B &= F\left[\frac{\Delta\theta_B - \delta\Delta p_B}{2}\right] \times \mu, \end{aligned}$$

where F represents the CDF of ε^i, $\Delta\theta_B \equiv \theta_B - \theta_A$ and $\Delta p_B \equiv p_B - p_A$. We associate drug A with the oldest molecule, while B is more recent: firm A loses exclusivity before B. For the sake of the argument, we focus on the case $\Delta\theta_B \geq 0$, since more recent drugs (here: B) are expected to be more effective than older drugs (here: A). However, all the results extend to the complementary case of $\Delta\theta_B < 0$. Thus, when they *cannot promote their drugs*

[17] Generalizing the model to include possible corner solutions in which all patients buy treatment, or some do not, because the price of A, or that of B, or both are too high, makes the model a lot less tractable and muddies the message, without adding any interesting insights. See also footnote 14.

(superscript ND for the "No Detailing" case), firms' respective profits are:

$$\pi_A^{ND} = p_A \times \left[\frac{1}{2} - \frac{\Delta\theta_B - \delta\Delta p_B}{2e}\right] \times \mu, \quad (3)$$

$$\pi_B^{ND} = p_B \times \left[\frac{1}{2} + \frac{\Delta\theta_B - \delta\Delta p_B}{2e}\right] \times \mu, \quad (4)$$

where the terms between brackets are, respectively, the equilibrium market shares of A and B when we substitute for the value of F under the uniform distribution.[18]

Generic Entry. Until now, we assumed a duopoly market: each firm's patent gives it exclusivity for the production of its molecule. Here, we turn to the effects of A losing that exclusivity (LoE), while firm B retains its patent protection and monopoly power – that is, we are now 20 years after A registered its patent, and B patented its molecule after A.

The first case we study is the one in which there is *no detailing.* In the absence of detailing, an equilibrium is characterized by a pair of prices in which firms maximize profits in $(3) - (4)$. Loss of exclusivity implies that generic bioequivalents can compete directly for A consumers. Based on the evidence (see *a.o.* Grabowski *et al.*, 2014), we let competition among generic producers reduce the price of A down to marginal costs, which we normalize to zero without loss of generality – we empirically verify this assumption in Section 5.2.

In the absence of detailing, a post-generic-entry equilibrium is characterized by the price that maximizes B's profits when $p_A = 0$. Unsurprisingly, the results in Appendix 1 show that generics competition for the A market can only drive down the price and market share of drug B. We also find that, in an interior equilibrium, price sensitivity determines the magnitude of the price reduction, but does not influence market shares.

Detailing. As documented above, the pharmaceutical industry stands out for its high promotional intensity. Through their *detailing* activity, pharmaceutical companies devote substantial resources to inform physicians and provide them with a number of perquisites, sometimes contingent on their prescription behavior. Often, companies invest in field studies to further

[18] Formally:

$$F(\varepsilon) = \begin{cases} 0, \forall \varepsilon < -e/2 \\ \frac{\varepsilon + e/2}{e} = \frac{1}{2} + \frac{\varepsilon}{e}, \forall \varepsilon \in [-e/2; e/2] \\ 1, \forall \varepsilon > e/2. \end{cases}$$

and the PDF is $f(\varepsilon) = 1/e, \ \forall \varepsilon \in [-e/2; e/2]$.

document the merits of their drugs. As seen in Section 2, this non-price competition component is also dramatically modified upon generic entry: price competition amongst producers typically brings detailing down to 0.

Here, we focus on the case in which detailing operates like *persuasive* advertising: it stimulates prescriptions without affecting the patient's intrinsic utility (1) − (2). Hurwitz and Caves (1988) and Rizzo (1999) provide extensive evidence pertaining to the persuasive nature of pharmaceutical detailing (see Bagwell (2007) for a review of the advertising literature). The fact that physicians shift away from A after LoE (see Figures 1 and 2) is additional evidence that the dominant effect around LoE is the persuasive component of detailing (the informative component is probably more relevant earlier in the molecule's life cycle–see also Ching and Ishihara (2012) for a more detailed decomposition). Formally, when firm J spends $C(a_J) \equiv a_J^2/2$ on detailing, it produces an autonomous increase in the demand for drug J from θ_J to $\theta'_J = \theta_J + a_J$.

Given an action profile $\{a_A, a_B, p_A, p_B\}$, the resulting demands are then:

$$\begin{aligned} Q_A^D &= \left(1 - F\left[\frac{\Delta\theta_B + \Delta a_B - \delta\Delta p_B}{2}\right]\right) \times \mu, \\ Q_B^D &= F\left[\frac{\Delta\theta_B + \Delta a_B - \delta\Delta p_B}{2}\right] \times \mu, \end{aligned}$$

where superscript D denotes *Detailing* and $\Delta a_B \equiv a_B - a_A$. The firms' profits become:

$$\begin{aligned} \pi_A^D &= p_A \times \left[\frac{1}{2} - \frac{\Delta\theta_B + \Delta a_B - \delta(p_B - p_A)}{2e}\right] \times \mu - \frac{a_A^2}{2}, \\ \pi_B^D &= p_B \times \left[\frac{1}{2} + \frac{\Delta\theta_B + \Delta a_B - \delta(p_B - p_A)}{2e}\right] \times \mu - \frac{a_B^2}{2}. \end{aligned}$$

3.1 Equilibrium analysis

Before generic entry, each PPP has a choice between two branded molecules. Each firm chooses its price and promotion intensity to maximize its profits. Taking first-order conditions

yields the implicit solutions:

$$p_J^D = \frac{2e}{\delta}\frac{Q_J}{\mu}, \tag{5}$$

$$a_J^D = \frac{1}{\delta}Q_J, \tag{6}$$

which, in turn, imply:

Testable implication 1 *The price p_J^D is increasing in the molecule's market share (Q_J/μ), and promotion intensity a_J in quantity Q_J. Both are decreasing in the PPP's price sensitivity δ.*[19] *Moreover, prices (but not promotion) are increasing with the degree of "horizontal differentiation" e.*

In Appendix 2, we solve for the firms' equilibrium market shares and find that when the two molecules are closer substitutes (smaller e), the market share of the superior drug decreases towards 50%, because firm B invests less in promotion, whereas A invests more. Conversely, a larger market size (μ) magnifies the gap between B and A: with higher potential profits, B invests in promotion more aggressively and, hence, increases its market share.

3.2 The effects of generic entry

After LoE, generic entry drives the price of molecule A to $p_A = 0$, and the dissipation of profits produces a drop in detailing: $a_A = 0$. As a consequence, firm B's post-entry profit function becomes:

$$\pi_B^G = p_B \times \left[\frac{1}{2} + \frac{\Delta\theta_B + a_B - \delta p_B}{2e}\right] \times \mu - \frac{a_B^2}{2}.$$

Where superscript G stands for *Generics*: firm B, which still benefits from market power, faces stiffer price competition but looser non-price competition from molecule A. We find:

Proposition 1 *For $Q_A^D, Q_A^G > 0$, the loss of exclusivity on molecule A allows B to* ***increase*** *its market share, promotional effort, and price iff $2\delta e < \mu$.*

[19] This result is in line with, *e.g.*, de Frutos *et al.* (2013) or Brekke and Khun (2006), who write that "*detailing, DTCA and price (if not regulated) are complementary strategies for the firms. Thus, allowing DTCA induces more detailing and higher prices.*" Similarly, Grossman and Shapiro (1984) find that more competitive markets reduce both prices and advertising in a model in which the purpose of advertising is to inform consumers of a product's existence.

Proof. *From Propositions 2 and 3 in Appendix 2, after some tedious algebra, one finds that* $Q_B^G - Q_B^D$, $a_B^G - a_B^D$, *and* $p_B^G - p_B^D$ *are all a multiple of* $(2\delta e - \mu)(\delta(\Delta\theta_B - 3e) + \mu)$, *where the second factor is negative whenever* Q_A^D *is positive (see proof of Proposition 2).* ■

It is striking that it is precisely when A and B are closer substitutes (e small enough) that stiffer price competition by the generic versions of A allows B to increase its market share. Conversely, only if the two molecules are sufficiently distant substitutes or if market size μ is small, will price competition have the (*a priori* expected) effect of boosting the sales of molecule A.

The rationale for this result stems directly from firm A's pre-LoE behavior. When market size is large and/or the two firms sell close substitutes, competition becomes intense: A invests a lot in promotion and keeps its price low. As a consequence, generic entry will substantially loosen non-price competition (a_A dropping from a high level to 0) and have a comparatively smaller effect on price competition (p_A dropping from a low level to 0). Conversely, when market size is small and A and B are distant substitutes, competition is lax pre-generic entry (*i.e.*, prices are higher and promotion lower). In that case, generic entry produces a comparatively stronger price drop, which dents the demand for B, and forces the latter to react by adopting a more aggressive pricing strategy:

Testable implication 2 *Generic entry should produce lower gains in market share for* B *in markets when price sensitivity* δ *is higher.*

Testable implication 3 *Generic entry should produce larger gains in market share for* B *in markets where horizontal differentiation* e *is lower.*

Testable implication 4 *Generic entry should produce larger gains in market share for* B *in larger markets.*

The equilibrium outcome whereby close substitutes in large markets are most heavily promoted fits nicely with one empirical observation. Based on Donohue *et al.* (2007), who identify the products most heavily advertised through Direct to Consumer Advertising (DTCA), Kenkel and Mathios (2012) note that a "striking feature of the US Top 20 list was the number

of competing products for the same medical condition."In New Zealand, the other country where DTCA is allowed, the composition of the Top 20 list was different: only four drugs appeared on both countries' lists. This is due to reimbursement rules: in New Zealand, only one product per therapeutic class is subsidised (hence, it makes little sense to advertise the non-subsidised product via DTCA). There is, however, one condition–erectile dysfunction– for which New Zealand's Pharmaceutical Management Agency (Pharmac) does not subsidize *any* drug. This is also *the* exception in the respective Top 20 lists: contrary to the other product categories, two close substitutes, Viagra and Cialis, are heavily advertised in both countries.

In Appendix 3, we extend the model to study efficiency and welfare. Our first main result relates to allocative efficiency: we find that generic entry increases the market share of B when it is already too large compared to the pre-LoE first best, and it decreases its market share when it is initially too low. In other words, it always distorts the market allocation farther away from the first best. Banning promotion overall would not solve this issue: the results are identical in the absence of promotion. The reason is that the highest quality drug tends to be sold at a higher markup, and generic entry reduces the price of only one molecule, generating inefficient, lopsided competition.

The second result aims at evaluating when generic entry increases or decreases *consumer (patient) surplus*. Based on the logic of Inderst and Ottaviani (2012), we acknowledge that promotion effort influences the behavior of the intermediary (the physician) but, with a focus on patients, we calculate consumer surplus using the utility functions (1) and (2). This implies that promotion does *not* enter in the definition of consumer surplus directly. It enters only indirectly, through its impact on prescription behavior.

We find that the final consumer welfare effects of generic entry vary on a case-by-case basis: even though allocative efficiency worsens, patients benefit from the lower prices of A and, in some cases, of B. We identify that a drop in Q_B is a *sufficient* condition for patients' utility to increase. Conversely, for $\Delta\theta_B = 0$, welfare decreases only if the market share of B increases strongly. We return to these points in the conclusion, once we have assessed actual market responses in the data.

4 The Data

This section describes our dataset and additional stylized facts about the changes in competitive conditions that occur upon generic entry. The empirical results are in Section 5.

We have data on quarterly dollar revenues and physical quantities for hundreds of branded and generic prescription drugs sold in the U.S. in several therapeutic areas over the 40-quarter period 1994q1 to 2003q4. These have been obtained from the proprietary database IMS-Health, one of the most important medical-information companies (IMS-MIDAS). We compute deflated revenues (R) by dividing nominal value of sales by the producer price index for the pharmaceutical industry published by the Bureau of Labor Statistics. Quantities (Q) are reported in standard units that represent the number of dose units sold for each product; this corresponds to one capsule or tablet of the smallest dosage or five milliliters of a liquid (*i.e.*, one teaspoon). Standard units allow comparison across different drug forms and dosages, as all different packages are subsumed into the same unit of observation. We then compute the average price of a molecule (P) by dividing R–*i.e.*, the revenues for all the different packages–by total Q.[20] An important feature of our data is that we observe R and Q for two different distribution channels: hospital (HO) and pharmacies (PH).

For a subsample of therapeutic classes, we also observe product-level expenditures for promoting drugs to doctors over the entire period. These promotional data, also obtained from IMS-Health, include three main components: visits to office-based practitioners and hospital specialists (this component is generally known as "detailing"); free samples dispensed to physicians (their cost being estimated as the sales price of the drug); and advertising in professional journals. IMS Health data on detailing are constructed using a representative panel of physicians who track their contacts with sales representatives. The amount spent on free samples is based on a panel of approximately 1200 office staff members in medical practices, while expenditures on advertising in professional journals are computed by tracking ads placed in approximately 400 medical journals and then adding the publisher's charge for those ads. The empirical analysis assumes that promotion to office-based practitioners affects sales in pharmacies, while promotion to hospital physicians affects the use of drugs in

[20] This produces a price per standard unit. Note that our empirical specifications control for unobserved differences, such as quality and Defined Daily Dose (DDD), across molecules.

hospitals.

The promotion level used in the demand specifications reported in Section 5 is computed with the perpetual inventory method, commonly used for physical capital:

$$A_{it} = (1 - \rho)\ A_{it-1} + I_{it},$$

where I_{it} is the quarterly expenditure in promotion retrieved from IMS, and ρ is the quarterly depreciation rate, assumed to be 0.1–*i.e.*, about 35% per year.[21]

Table 1 reports descriptive statistics for these variables, distinguishing between hospitals and pharmacies. Note that competitors' promotion refers to the sum of the promotion of all other drugs in the ATC3 market, each computed according to the equation above. At the same time, the competitors' price refers to the average price of all the other molecules in the market, including generics, and it is computed as the ratio between total revenues and total quantities in the ATC3 market, after subtracting the revenues and quantities of drug i.

Variables	**Channel**	**Mean**	**SD**	**Min**	**Max**
Market Shares	Hosp	0.117	0.173	0.01	1
	Phar	0.134	0.183	0.01	1
# Competitors	Hosp	13.2	8.17	0	46
(other Molecules)	Phar	12.1	6.62	0	41
Own Price	Hosp	16.73	70.31	0.02	902.8
	Phar	16.78	71.23	0.05	910.1
Own Promotion	Hosp	3269	8101	0	59469
	Phar	11165	24592	0	198027
Competitors' Price	Hosp	8.86	28.32	0.02	197.29
(average price in ATC3)	Phar	4.15	15.19	0.02	122.13
Competitors' Promotion	Hosp	16315	37402	0	231144
(total promotion in ATC3)	Phar	55871	124654	0	891515

Table 1. Summary Statistics

For the main econometric analysis (which focuses on pre-LoE competition), the sample we use includes 227 drugs initially covered by patent protection, 95 of which lost patent protection between 1994 and 2003.[22] All the drugs are classified according to the Anatomical

[21] All the results reported in Section 5 are robust to setting $\rho = 0.25$.

[22] While data on sales from IMS-MIDAS allow us to retrieve 123 branded drugs experiencing generic entry, we could match only 95 of these drugs to the data on promotion expenditures. According to IMS-Health, 61 of

Market Descriptive Statistics		**Molecule Descriptive Statistics**	
# ATC3	53	# molecules	227
# ATC4	75	# LoE	95
#ATC4 in ATC3	**%age obs'ns**	**#Gen. entries**	**#Markets in sample**
1	56.8%	1	22
2	20.2%	2	8
3	13.3%	3	8
4	4.3%	4	3
5	3.7%	5	3
6	1.7%	6	1

Table 2. Therapeutical Markets, Molecules and Generic Entry

Therapeutic Chemical (ATC) classification system. The "ATC3 level" corresponds to a market: it groups the drugs that target a given condition. As shown in Table 2, drugs in our sample are divided into 53 ATC3 markets, some of which are further subdivided into ATC4 sub-classes. 46 of the ATC3 markets see the entry of at least one new generic molecule during the observed time window, with one market experiencing LoE for six of its branded drugs. Compared to previous studies, our sample includes a much larger number of drug classes, including lipid regulators, antidepressants, anti-ulcerants and hypertension drugs.[23] The complete list of therapeutic markets can be found in Appendix 5.

For illustrative purposes, Table 3 below reports the list of (plain) lipid regulators for the main two ATC4 subclasses of anti-cholesterol drugs: statins and bile acid sequestrants.[24] The former has six different competing molecules, while the latter has four. Thus, in total, there are up to ten different prescription possibilities for a physician who has a patient with excess cholesterol. The last column identifies either the quarter in which the drug lost its patent

these molecules are actively advertised. Note that we also report the result of a complementary exercise (whose focus is on post-LoE competition) with a larger sample made up of all drugs that faced generic substitutes – see Section 5.2.

[23]For instance, Regan (2008) investigates the effect of generic entry on prices using a sample of eighteen drugs, divided amongst 6 therapeutic markets. Half of the drugs in her sample are from the cardiovascular market, while five others treat diseases/conditions affecting the central nervous system.

[24]Statins (C10A1) lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Bile Acid Sequestrants (C10A3) increase the elimination of bile acids which the liver can replace only by converting cholesterol, thus reducing its level in the blood. Note that there are other ATC4 groups in the therapeutic market C10A, such as Fibrates (C10A2). Although we observe quantities and prices for Fibrates, we have promotional data only for the most important ATC4 markets. In fact, quarterly sales of Fibrates in 2000 were around ten millions dollars compared to quarterly sales of more than a billion dollars for Statins.

protection (4th quarter of 2001 in the case of Mevacor, for instance) or the date on which the company decided to withdraw the molecule from the market (lethal secondary effects triggered the early withdrawal of Lipobay in 2001).

To get an initial grasp of the differences between hospitals and pharmacies, the upper part of Table 4 shows that the average quantity dispensed in pharmacies is three times as high as in hospitals. The bottom part reports two different statistics for the drop in volume market shares following generic entry:[25] i) the simple average and ii) the average where each molecule has been weighted by the advertising intensity of competitors in the same ATC3. Table 4 suggests that quantity drops observed after LoE are more pronounced in pharmacies and in markets in which promotion is more prevalent. We will exploit these dimensions of heterogeneity in the econometric analysis.

5 Empirical Results

In this section, we first estimate the demand equation prior to LoE (section 5.1). This allows us to assess whether the PPPs' demand behavior matches the main hypotheses underlying the model. We find that the elasticity of demand with respect to both a company's and competitors' price and promotion are large and significant. Several results vindicate our

ATC3 class	ATC4 class	Description	Molecule Name	Brand Name	Patent Expiry
C10A	C10A1	Statins	Atorvastatin	Lipitor	
			Cerivastatin	Lipobay	withdrawn 2001
			Fluvastatin	Lescol	
			Lovastatin	Mevacor	2001q4
			Pravastatin	Pravachol	
			Simvastatin	Zocor	C10A
C10A	C10A3	Bile Acid Sequestrant	Colestipol	Colestid	
			Cholestyramine	Questran	1996q3
			Aspartame+ colestyramine	Prevalide	
			Colesevelam	Welchol	

Table 3. Classification of Anti-cholesterol Drugs

[25]The changes are calculated based on the evolution between three years before and after patent expiration. When patent expiration is either closer to the beginning or to the end of the sample period 1994q1-2003q4, we take the first (last) available observation for the pre-expiration (post-expiration) period.

approach. First, generic entry into a competitor's molecule does not appear to affect the parameters of the demand function. Second, the estimated elasticities of demand with respect to promotional effort and price *before* LoE are consistent with the average observed drop in the molecule's market share *after* LoE. In particular, the empirical results correctly predict that, despite their substantially lower price, molecules losing patent protection experience a decrease in quantity and (volume) market shares of the molecule – *i.e.*, the original brand plus all generics, taken together.

We then focus on competitive interactions post-LoE (section 5.2) – *i.e.*, when a molecule has become generic. For each substance, our dataset distinguishes between the originator (branded) product and generic producers. In the model, we assume that generic entry leads to a Bertrand outcome, driving the price of A down to the marginal cost of production. In the data, we find that price elasticities for generics increase up to 9, which is compatible with near-Bertrand outcomes. We also observe some residual within-molecule market segmentation: while cross-price elasticities are high among generic producers of the same molecule, it is not significantly different from zero with respect to the originator drug, a finding compatible with the existence of the "generic entry paradox". We also find that the intense pre-LoE inter-molecular rivalry becomes subdued post-LoE.

In Sections 5.3 and 5.4, we test the model's main predictions. Section 5.3 checks the pre-LoE prediction that firms with higher-quality products should gain market share, increase their prices, and promote more intensely (testable implication 1). Section 5.4 assesses how on-patent drugs' market shares react when a competitor faces generic entry. We verify testable

Distribution of $Q_{PH}/(Q_{PH}+Q_{HO})$		
Mean	0.75	
Median	0.86	
Percentage Change in Market Shares	*PH*	*HO*
Simple Mean	-0.31	-0.26
Weighted by Drug-A Sales	-0.36	-0.25
Weighted by ATC3 Promotion	-0.40	-0.35
Drop in Price (%)	-0.44	-0.45
Drop in Advertising Flow (%)	-0.89	-0.85

Table 4. Distribution: Pharmacists (PH) & Hospitals (HO)

implications 2, 3, and 4, which state that it will depend on the price sensitivity of demand (δ), horizontal differentiation (e), and market size (μ). Note that, while Proposition 1 extends the predictions to prices and promotion, we focus here on market shares. The main reason is that identification is weak with regard to the other variables, and the results (available upon request) are rarely significant. This may be due to the measurement errors for prices and promotion.[26]

5.1 Patients-Physicians' demand schedule

We start our empirical analysis by evaluating the parameters of the demand side of the market to assess the relative importance of promotion. We conduct the exercise separately for hospitals and pharmacies to unearth potential heterogeneity in market share responses following generic entry across the two channels. This section focuses on the pre-LoE stage. The post-LoE stage is covered in the next section.

Since we focus on the pre-LoE period, we estimate the demand using an unbalanced panel of active ingredients until one quarter before we observe entry of generic versions of the same molecule.[27] This means that all firms in this subsample face competition only from imperfect substitutes (which can be branded or generic).

Our specification estimates the elasticity of a given branded drug's market share with respect to its own price and promotion effort, as well as the cross-elasticities with respect to the same variables for competing drugs. We use this simple econometric framework as opposed to other models of differentiated products demand – *e.g.* Almost Ideal Demand System (AIDS), nested logit or random coefficient models in the spirit of Berry *et al.* (1995) – for different reasons. First, we do not have consumer-level purchase data nor do we observe product characteristics that have a straightforward economic meaning (unlike engine horsepower, a 10mg dosage is not necessarily superior to a 5mg one). Recall that our aim behind estimating the demand function is to understand how (own and cross) price elasticities compare to promotion elasticity across a large sample of branded drugs, several of which are in their final years

[26] We thank Fiona Scott Morton for drawing our attention to the acuteness of this issue.

[27] The results reported below have been obtained with quantity market shares (relative quantity in the ATC3 market) as the dependent variable. The results with (absolute) quantity as the dependent variable are similar and available upon request. Our preference for relative quantity is that most of these markets are growing in both value and volume.

of patent protection. Our aim is not to retrieve price-cost margins, to measure the intensity of competition or to carry out merger simulations. Second, and perhaps most importantly, the empirical results strongly suggest that the competitive constraints that drugs exercise on each other vary with exclusivity.[28] In that context, it would make little sense to fix the nest structure *a priori*.

Defining a market as a given ATC3 group, equation (7) describes the PPPs' demand for a particular molecule i at time t. In this and all the other estimations reported in the remainder of this paper, errors have been clustered at the ATC3 level.

The demand equation is estimated in first-differences in order to remove all time-invariant, drug-specific fixed effects, such as quality differences:[29]

$$\begin{aligned} \Delta ms_{i,t} = \quad & \alpha_0 + \alpha_1 \Delta p_{i,t} + \alpha_2 \Delta p_{-i,t} + \alpha_3 \Delta a_{i,t} + \alpha_4 \Delta a_{-i,t} \\ & + \alpha_5 GEN_{-i,t} + TE_{i,t} + \varepsilon_{i,t} \end{aligned} \tag{7}$$

where $\Delta ms_{i,t}$, $\Delta p_{i,t}$ and $\Delta a_{i,t}$ refer to the quarterly growth of, respectively, the quantity market share, price, and the promotion effort of branded drug i in the ATC3 market (to repeat, our unbalanced panel includes molecules i until one quarter before LoE). Similarly, $\Delta p_{-i,t}$ and $\Delta a_{-i,t}$ are the competing molecules' evolution of prices and promotion in the same ATC3 market (to repeat, the products in $-i$ may either be branded or generic). All of these variables are in logarithms, implying that the coefficients can be interpreted as elasticities. $GEN_{-i,t}$ is the number of these competing molecules in the ATC3 market that lost exclusivity during the observed time period. We do *not* expect it to be significant: according to our hypotheses, generic entry affects demand only through its effect on prices and promotional effort. Finally, the variable $TE_{i,t}$ (Time to Expiration) counts the number of quarters left to patent expiration, to account for the impact of the drug's life cycle on demand.[30]

The regressors are likely affected by two different problems. The first one is that feedback from market-share shocks to future prices and advertising may produce endogeneity issues

[28] This could explain the somewhat conflicting results among papers that empirically analyse both inter- and intra-molecular competition (*e.g.* Stern 1996 and Ellison *et al.* 1997).

[29] Results using FE are qualitatively similar, but we could not identify a set of instruments that simultaneously pass the relevant tests for under-identification/weak-identification and the Hansen J test for the exogeneity (orthogonality) of the instruments.

[30] We use negative values so that the variable is increasing as we approach patent expiration. For instance, -10 and -1 refer, respectively, to ten quarters and one quarter before LoE.

(reverse causality). The second problem is errors in the measurement of both prices and promotion effort. The price actually paid may differ from the price we observe in the IMS database because the latter does not reflect off-invoice ex-post rebates that pharmaceutical companies grant to large buyers in return for some performance component, such as reaching a target volume of sales (see Berndt (2012)). Errors in the measurement of promotion effort stem from the difficulty to observe and quantify monetarily the work of sales representatives when they visit physicians. Both measurement errors are likely to create an attenuation bias when estimating (7) using OLS.[31]

To address these two problems, we follow the literature by instrumenting prices and advertising with: the number of packages (linear and squared);[32] the average price of drugs sold by firm i in quarter t in other ATC3 markets ("Hausman" instruments); and a dummy indicating whether a branded drug has experienced the entry of a generic competitor before LoE, following a successful "Paragraph IV" challenge.[33] This choice of instruments is validated by the Kleibergen-Paap rk-statistic (K-P) for under-identification, the Angrist-Pischke (A-P) F-test for weak instruments, the Hansen J-test for the orthogonality conditions, and the C-statistic to test the exogeneity (endogeneity) of one or more instruments (regressors).[34]

We estimate the empirical model in (7) separately for hospitals and pharmacies in order

[31] In the words of Griliches and Hausman (1986), "Errors of measurement will usually bias the first difference estimators downward (toward zero) by more than they will bias the within estimators." This problem has been largely discussed in the empirical literature on the estimation of production function (see Griliches and Mairesse (1995), among others). It is not by coincidence that the estimation of the demand elasticity to promotion is affected by the same problem of the elasticity of production with respect to capital. In fact, in both cases, econometricians need to construct a measure of "effective stock" looking at account data on past and present expenditures on physical capital or promotional effort.

[32] The number of packages has been used by Chaudhuri, Goldberg and Jia (2006) and Branstetter, Chatterjee and Higgins (2014), among others. The variable is related to the average price p, as variations in p stem in part from variations in the set of packages available in each period. First-stage results show that this variable is also highly correlated with promotion. This is because the introduction of a new posology or delivery mode is often accompanied by a resurgence in promotional effort. For instance, Ely Lilly started a huge marketing campaign to promote Prozac Weekly, a once-weekly formulation of Prozac. Anther example is Paxil CR, a controlled-release version of Paxil. Other examples abound.

[33] Paragraph IV of the Hatch-Waxman Act allows generic manufacturers to attempt to enter the market before patent expiration of the original branded drug, either by claiming non-infringement or invalidity of the branded product's patent. A successful Paragraph-IV challenge represents an exogenous shift in the promotional effort of branded drugs uncorrelated with demand shocks or measurement errors. Branstetter, Chatterjee and Higgins (2011) investigate the welfare effect of accelerated generic entry via Para-IV challenges for hypertensive drugs.

[34] These tests lead us to use slightly different instruments for the two channels. Concretely, the average firm prices in other markets can be used only for hospitals, while for the pharmacy channel we use the price of the molecule sold in hospitals.

to unearth possible channel-specific idiosyncrasies.[35] Columns (1a,b) of Table 5 report the estimates obtained without instrumenting for prices and promotion. Comparing these results with those in Columns (2a,b) confirms the existence of an attenuation bias due to errors in measuring prices and promotion intensity.

5.1.1 Regression results

A number of interesting findings emerge from the results in Column 2a—the results pertaining to Column 2b are discussed below. First, the estimated elasticities *w.r.t.* own-price and own-promotion are higher than those reported in most of the literature. For instance, Dave and Saffer (2012) report price estimates below unity, a finding difficult to reconcile with profit maximization in the absence of a binding price cap. By contrast, our point estimates in Column (2a) are compatible with price-cost margins in the 40-55% range. This order of magnitude is in line with the price reductions observed following generic entry, and it is also close to the results obtained by Rizzo (1999). At the same time, Dave and Saffer (2012) find elasticities *w.r.t.* detailing to physicians and advertising to customers that vary between 0.2 and 0.5. The meta-analysis by Kremer *et al.* (2008) also reports low average elasticities.

We speculate that there are two reasons for this large difference: 1) Our sample includes a larger number of drugs losing patent protection. Patent expiration represents a substantial (exogenous) shock that produces a larger than usual variation in prices and drop in promotional effort (*cf.* Section 2). Our identification strategy relies on using this rich source of variation to delineate the effect of price and promotion on market shares. 2) We use a richer set of instrumental variables: our initial estimates in columns (1a)-(1b) display significantly lower estimates for promotion elasticities. This is largely due to measurement errors stemming from the difficulty of observing promotion efforts and assigning it a monetary value. Moreover, around one third of the drugs in our sample are not actively promoted on the basis of IMS data, which may also contribute to biasing the estimates towards zero. Our instruments appear to address these issues particularly well.

Second, we find that the elasticity of demand *w.r.t.* prices is higher in hospitals than

[35] Berndt (2002) provides a detailed explanation as to why arbitrage between different (cf. hospitals and retail pharmacies) cannot occur.

Table 5. Demand of Branded Drugs in Hospital and Pharmacy channel

Depend Vbl: Market Shares		**Hospital**				**Pharmacies**			
Specification:		FD	FD	FD-IV	FD-IV	FD	FD	FD-IV	FD-IV
	Coeff.	(1a)	(1b)	(2a)	(2b)	(1a)	(1b)	(2a)	(2b)
Own Price	α_1	−1.280***	−1.377***	−2.629*	−2.607**	−1.003***	−1.029***	−1.725***	−1.784***
		(0.18)	(0.18)	(1.55)	(1.28)	(0.22)	(0.22)	(0.65)	(0.67)
Price_Comp	α_2	0.844***		0.914***		0.260**		0.310*	
		(0.15)		(0.25)		(0.13)		(0.17)	
Price_Comp_Brand	$\alpha_{2.1}$		0.749***		0.951***		0.257		0.338
			(0.14)		(0.28)		(0.26)		(0.35)
Price_Comp_Generic	$\alpha_{2.2}$		0.022		0.003		0.053		0.066
			(0.02)		(0.07)		(0.04)		(0.09)
Own Promotion	α_3	0.084***	0.084***	1.994***	2.062***	0.096***	0.096***	1.998***	2.016***
		(0.02)	(0.02)	(0.48)	(0.51)	(0.04)	(0.04)	(0.71)	(0.71)
Promotion_Comp	α_4	-0.061***	-0.061***	-1.436***	-1.472***	-0.067**	-0.067**	-1.528***	-1.542***
		(0.02)	(0.02)	(0.36)	(0.38)	(0.03)	(0.03)	(0.54)	(0.55)
Generic Entry	α_5	0.005***	0.005***	0.002	0.002	0.004**	0.003**	-0.001	-0.002
		(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
Nmb of Competitors	α_6	-0.031**	-0.028**	-0.002	0.013	-0.033**	-0.032**	-0.005	-0.005
		(0.01)	(0.01)	(0.02)	(0.02)	(0.01)	(0.01)	(0.02)	(0.02)
Time to Expiration		-0.004***	-0.004***	-0.003***	-0.003***	-0.003***	-0.003***	-0.001*	-0.001*
		(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
Observations		5046	5046	5046	5046	5032	5032	5032	5032
K-P Underidentification[a]				.0101	.0053			.0124	.0123
AP_F-test - Promotion[b]				.0020	.0013			.0102	.0100
AP_F-test - Price[b]				.0324	.0221			.0082	.0078
Hansen J test (df)[c]				.362 (3)	.361(3)			.511 (3)	.514 (3)
C-test - Endogeneity[d]				<.0001	<.0001			.0013	.0012
C test - Exogeneity[d]				.5027	.3614			.3449	.5144

Notes: Robust standard errors clustered at market level in parentheses. * significant at 10% level; ** significant at 5%; *** significant at 1%. All specifications in First Differences. Endogenous variables: Own price and promotion. Five instruments: #Packages (linear and squared), Average Price charged by same firm, Dummy for new products by same firm, Indicator for Paragraph IV challenges. [a] P-value for the Kleibergen-Paap rk statistics testing the null hypothesis that the model is underidentified. [b] P-value for the Angrist-Pischke F-test for excluded instruments testing for weak instruments in the first stage regressions of promotion and price. [c] Hansen J test of overidentifying restrictions with degrees of freedom reported in parentheses. [d] P-value of C (GMM distance) test of endogeneity for own price and promotion and test of exogeneity for price and promotion of competitors.

in pharmacies: in specification (7), a Wald test rejects the hypothesis that the coefficients of the company's price and competitors' price could be the same for the two channels (p-value: 0.01).[36] This probably reflects the following difference: private practice doctors do not directly benefit when patients buy a cheaper alternative (possibly, they even lose some perks offered by pharmaceutical companies). At the same time, these patients pay only a fraction of the drug's price, thanks to third-party payer coverage. In contrast, hospitals are residual claimants: their margin depends one-for-one on procuring drugs at a discount since they then charge the patient a pre-determined reference price. There are, thus, two opposite effects that magnify the differences between hospital and pharmacies. Of course, how they affect welfare remains a different question.

Third, the coefficient pertaining to the price of competitors ($Price\_Comp$) is of the right sign and significant for both channels. However, it is about three times as large in the hospital channel and more precisely estimated. This reinforces the message that hospitals are more price-sensitive than private practice doctors.

Fourth, in column (2b), we decompose the rivals' price index into a sub-index for branded competitors ($Price\_Comp\_Brand$) and another one for generic competitors ($Price\_Generic\_Comp$).[37] That is, we test how the demand for an on-patent drug is affected by the price of other branded molecules (whether they are still on-patent or not) and that of generics producers present in the same ATC3 market. We observe that the coefficients for $Price\_Comp\_Brand$ are close to the coefficients for $Price\_Comp$ in column (2a), whereas the coefficients for $Price\_Comp\_Generic$ are much smaller and nowhere close to statistical significance. This is further evidence that, even though generics are fierce competitors for their branded bioequivalent, they are toothless challengers with respect to the remaining patent-protected drugs.

Fifth, the coefficients for own- and cross-promotion elasticity are of the right sign, large, and precisely estimated in both channels. When instrumented, the point estimates increase substantially, confirming the extent to which this variable is affected by endogeneity prob-

[36] This is in line with what Berndt (2002) reports: "Next lowest are prices to hospitals (...) prices charged pharmacies for their cash-paying customers are discounted off "list" price the least".

[37] Doing the same for promotional effort would not make much sense since generic drugs are not actively promoted through detailing.

lems. The point estimates barely change when we split the price index (2a *vs.* 2b). These results indicate that short-term strategic interactions in the pharmaceutical industry cannot be understood without properly accounting for promotional effort.

Sixth, the coefficient on the headcount of genericized molecules is statistically insignificant once we properly control for endogeneity (and economically minute in columns (1a) and (1b)). In other words, the regression confirms our initial hypothesis that generic entry affects demand exclusively through the price and promotion of a given molecule. Beyond these effects, generic entry does not modify the effective number of products on the market or the level of the demand for the other molecules.

To the best of our knowledge, these are the first results that identify the relative importance of price and non-price instruments in determining market shares separately for hospitals and pharmacies for a large set of prescription drugs sold in the US. While the data samples are quite different, Anderson *et al.* (2015) also identify the importance of comparative advertising for analgesics sold over the counter (OTC).

5.1.2 Out-of-sample prediction

To test our model's predictive capacity, we carry out some "back-of-the-envelope" calculations to gauge how well our pre-LoE point estimates are able to predict post-LoE (*i.e.* out of sample) developments. The exercise runs as follows: first, we use the evidence in Table 4, which indicates that LoE produces an average price drop of about 45% and 44%, and an average drop in the *flow* of promotion by about 85% and 89% in hospitals and in pharmacies, respectively. We calculate that, once converted into *stocks*, these correspond to a drop of 69.4% and 72.9%, respectively, 3 years after LoE. Now, using the regression results in Table 5, column (2b), we have that the own-price elasticity is around -2.6 in hospitals and -1.78 in pharmacies, whereas the own-advertising elasticities are around 2.06 and 2.02. Piecing these elements together, in hospitals, the predicted change in market share is:[38]

$$-2.607 \cdot (-0.45) + 2.062 \cdot (-0.694) = -0.258,$$

[38] This ignores the reaction of the other firms, but the latter is small in absolute value.

which compares to an actual average drop of about -0.26 (see Table 4). Following the same procedure for pharmacies, the predicted evolution is:

$$-1.784 \cdot (-0.44) + 2.106 \cdot (-0.729) = -0.684,$$

which compares to an actual average drop about -0.31. Thus, the regression results predict (i) a drop in market shares for both segments and (ii) a larger drop for pharmacies, which is in line with what is observed in the data. Table 5 shows that this difference in responses is driven mainly by the higher price sensitivity in the hospital segment.[39]

5.2 Competitive environment post genericization

The analysis above has focused on drugs that are still patent-protected. The demand estimation confirmed the central role played by promotion. In this sub-section, we analyze whether the model's assumptions are also supported for the post-generic entry universe.

In the model, it is assumed that price will converge to marginal cost as Bertrand competition kicks in following the entry of a bioequivalent substitute. Since the only difference between products is residual (different excipient, packaging or colors), and the choice between varieties is made by the physician/pharmacist (these are prescription drugs), we expect intra-molecule competition to converge to the Bertrand outcome in the absence of capacity constraints. However, during the initial stages of generic entry, the stock of past promotion may still drive PPPs' choices because depreciation is not immediate.

In contrast to the estimations in Section 5.1, we now focus on the molecules that have experienced generic entry. Our sample includes 409 such molecules with a mean of around seven molecules per ATC3 market. The median and mean numbers of generic producers for the same molecule are 7 and 12, respectively.

This sample is used to estimate the following specification in first differences, with errors

[39] We experimented with different estimating techniques and specifications. Once endogeneity is dealt with, the finding of a volume market share drop is consistent across specifications and/or estimation techniques. We also compared the results with our estimations with that reported in column (1) of Table 2 of Dave and Saffer (2012). Interestingly, their ratio of price elasticity to detailing elasticity is not too far from the one we find in our sample. However, an out-of-sample prediction derived from their point estimates would significantly undershoot actual developments.

clustered at the ATC3 level:

$$\begin{aligned}\Delta ms_{g,j,t} &= \delta_1 \Delta p_{g,t} + \delta_2 \Delta p_{-g,t} + \delta_3 \Delta p_{b,t} + \delta_4 \Delta p_{og,t} + \delta_5 \Delta p_{ob,t} \\ &\quad + \delta_6 \Delta a_{b,t} + \delta_7 \Delta a_{ob,t} + X_{it} + \varepsilon_{j,t},\end{aligned}$$

where ms_g is market share of a generic molecule produced by firm g (*e.g.* TEVA Fluoxetine) in the ATC3 market j; $p_{g,t}$ is the corresponding price of that firm; p_{-g} is the average price set by the other generic producers of the same molecule (*e.g.*, MYLAN fluoxetine, BARR fluoxetine, etc..); p_b is the price of the original branded drug (*i.e.* ELI LILLY fluoxetine sold under the brand name *Prozac*); and p_{og} and p_{ob} refer to the price index of other generic antidepressants (*e.g.* amytriptilyn), and other still-on-patent antidepressants (*e.g.* sertraline, brand name *Zoloft*),respectively. Finally, a_b and a_{ob}, for "brand" and "other brand", pertain to the promotion associated with the originator drug and other on-patent drugs in the ATC3 (*i.e.* respectively, *Prozac* and *Zoloft* in our example). All variables are in logarithms.

The thrust of the results reported in Table 6 is that generic entry essentially leads to a undifferentiated Bertrand outcome. Focusing on column (2), where endogenous variables (own price and market promotion of on-patent drugs) have been instrumented for.[40] The first salient fact is the four-to-fivefold increase in the price elasticity of demand as compared to the results reported in Table 5. By any standard, this is a quantum change.

Second, the most significant competitive price pressure is exercised by other generic producers of the same molecule. The cross-price elasticity pertaining to other generic versions of the same molecule is significant and of the right sign. It is about six times smaller than the company's price elasticity, which is in line with the fact that the median number of generic competitors for a given molecule is seven.

Third, the cross-price elasticity *w.r.t.* the originator brand has the right sign, but it is small and statistically insignificant. This finding is compatible with instances of the generic entry paradox, whereby the sales of a particular molecule are directed at two different consumer segments. Fourth, the cross-price elasticity *w.r.t.* other generics in the same ATC3 has the

[40]The instruments are: the number of generic producers of the same molecule; the number of competing generic molecules; the number of competing molecules that are branded; the size of the market; and the time since patent expiration. Note the effectiveness of the IV strategy: while the coefficient δ_7 appears with the wrong sign in column (1), instrumentation leads to a negative and significant point estimate.

Dep't vbl: Market Shares		**Hospital**		**Pharmacies**	
	Coeff.	FD (1)	FD-IV (2)	FD (1)	FD-IV (2)
Own Price	δ_1	-0.448***	-9.234***	-0.539***	-8.706***
		(0.04)	(1.97)	(0.03)	(2.17)
Price Generics	δ_2	0.005	1.566***	-0.054	1.392***
(same molecule)		(0.04)	(0.43)	(0.04)	(0.41)
Price Brand	δ_3	0.012	0.059	-0.031	0.139
(same molecule)		(0.03)	(0.08)	(0.03)	(0.11)
Price Other Generics	δ_4	0.143***	0.588***	0.035	0.212**
		(0.03)	(0.18)	(0.02)	(0.09)
Price Other Brands	δ_5	0.308***	0.275*	0.038	-0.359
		(0.06)	(0.16)	(0.10)	(0.28)
Promotion Brand	δ_6	0.061*	0.229*	0.031	0.304**
(same molecule)		(0.03)	(0.12)	(0.03)	(0.14)
Promotion Other Brands	δ_7	0.149***	-1.578**	0.164***	-1.930**
		(0.03)	(0.71)	(0.04)	(0.83)
Observations		61443	61443	61260	61260
K-P Underidentification[a]			$< .0001$		.0025
AP F-test - Promotion[b]			$< .0001$		.0003
AP F-test - Price[b]			$< .0001$		$< .0001$
Hansen J test (df)[c]			.512 (3)		.755 (3)
C-test - Endogeneity[d]			$< .0001$		$< .0001$
C test - Exogeneity[d]			.3289		0.8572

Notes: Robust standard errors clustered at molecule level. *, **, *** significant at 10%, 5% and 1%, respectively. Endogenous variables: own price and market promotion of on-patent drugs. Five instruments in specification (2): #generic producers of same molecule, #competing generic molecules, #competing brand molecules, total size of the ATC3 market and time since patent expiration (all IVs in period t-1). [a]P-value for the Kleibergen-Paap rk statistic testing the null that the model is underidentified. [b]P-value for the Angrist-Pischke F-test for excluded instruments testing for weak instruments in 1st-stage regressions. [c]Hansen J-test of overidentifying (df). [d]P-value of C (GMM distance) test of endogeneity for own price and prom and of Exogeneity for price of generics and brands for the same molecule.

Table 6. Demand function of a generic drug (*e.g.* Mylan fluoxetine)

right sign and is significant, but its magnitude is small. Fifth, other branded products barely have an influence (the point estimates are very small and are barely significant only in the case of the hospital channel). Sixth, we observe that the relative importance of detailing is greatly diminished.Promotion for the branded drug (same molecule) has a positive, but small, effect on market share. This reflects the positive externality stemming from the brand's stock of promotion on the generic bioequivalent. Last, we observe that promotion by other on-patent drugs within the same ATC3 does exercise a negative influence on a generic's market share.

This is in line with the previous results that the competing molecules acquire additional market shares by sustaining promotional effort.

Thus, overall, our results suggest that, while competition is *inter*-molecular while drugs are on patent, and shifts to chiefly *intra*-molecular after LoE. Within the sub-market for the molecule experiencing LoE, the share of the originator drug progressively fades into insignificance, while the generic bio-equivalents are engaged in Bertrand competition. In that post-LoE context, the originator brand may maintain some residual promotion, but it is typically insufficient to compensate the loss in molecule market share, since promotion for competing brands does not abate.

5.3 Firms' strategic behavior prior to LoE (testable implication 1)

While Sections 5.1 and 5.2 estimate demand functions pre- and post-LoE, this section and the next test the main theoretical predictions found in Section 3. Here, we focus on strategic interactions among firms when they still benefit from exclusivity (testable implication 1). Then, Section 5.4 examines the effects of LoE (testable implications 2-4).

Based on testable implication 1, we expect that a producer with a higher-quality molecule will (a) sell more, (b) charge a higher price, and (c) promote its molecule more intensely than its lower-quality competitors. In addition, (d) both promotional effort and price should be decreasing in price sensitivity δ. Given the differences in price elasticities that we identified in the previous section, we expect lower prices in hospitals than in pharmacies. Last, (e) prices should be increasing in the degree of "horizontal" differentiation.

To test prediction (e), we construct a measure of horizontal differentiation for each ATC3 market based on each molecule's therapeutic categorization. As detailed in Section 4, the ATC3 class is associated with a pathology, while each of the ATC4 therapeutic sub-groups within the same ATC3 corresponds to different modes of action to treat that pathology. Our conjecture is that the higher the number of ATC4 sub-groups in the same ATC3, the more differentiation there is in that market. We define MoA (for *Modes of Action*) as the number of ATC4 sub-groups in each ATC3 market, minus 1. That is, for each drug, it identifies the number of rival modes of action to treat the same pathology.

Empirically, the first set of predictions (a-c) compare different molecules/firms in a particular market. However, we cannot directly observe the relative quality or other unobserved differences between molecules. Hence, we use a specification in first-differences and test implication 1 by checking whether an increase in market share is, indeed, associated with higher promotion and prices (note that similar results are obtained using the FE estimator). To test (d), we exploit the higher price elasticity in hospitals that we estimated in Section 5.1: we expect β_2 to be negative in equation (8) below.

Firm i's behavior in market j at quarter t is described by the following equation:

$$\Delta y_{i,t} = \beta_0 + \beta_1 \Delta q_{i,t} + \beta_2 Hosp + \beta_3 MoA_{j,t} + X_{i,t} + \varepsilon_{i,t}, \tag{8}$$

where, based on equations (6) and (7) in Section 3.1, y is promotion (resp. price) and q is quantity (resp. markets share). $Hosp$ is a dummy taking value 1 for the hospital channel and zero otherwise. $MoA_{j,t}$ has been defined above, and control variables X include a trend that identifies the number of quarters before patent expiration of brand i (time to expiration, TE), and a complete set of time dummies.

Table 7 reports the results obtained when we limit the sample to branded drugs until one quarter before LoE for the two channels. Column (1) tests (a-c) by looking at the relationship between quantity and promotion. Column (2) tests for the same relation between prices and promotion and column (3) between market shares and prices. The last specification suffers from the classic identification problem that both demand and supply influence that relationship. To address this issue, we exploit the results in Section 5.1, which showed that promotion produces an outward shift of demand. In column (4), therefore, we use promotion as an instrument to isolate supply-side effects.

In line with testable implication 1, we find that prices, promotion and market shares co-move positively over time.[41] Next, the price response is lower in hospitals (prediction d), although the effect for promotion is not significant. In line with the theoretical model, e does not directly influence promotion. However, in contrast with our predictions, we do not

[41] In column (3), we observe that the demand side of the ledger dominates the raw correlation between prices and market shares. Once market shares are properly instrumented for in column (4), the coefficient changes sign and is precisely estimated.

	Dep. Variable:	**Promotion**	**Promotion**	**Price**	**Price-IV**
	Coeff.	FD(1)	FD(2)	FD(3)	FD(4)
Quantity	β_{1q}	0.251***			
		(0.054)			
Market-Shares	β_{1ms}			-0.037***	0.038**
				(0.008)	(0.020)
Price	β_{1p}		0.339**		
			(0.184)		
Hospital	β_2	-0.006	-0.001	-0.003***	-0.005***
		(0.005)	(0.004)	(0.001)	(0.002)
Modes of Action: "e"	β_3	-0.070	-0.067	-0.006**	-0.003
		(0.061)	(0.058)	(0.003)	(0.004)
Time to Expiration		-0.001	-0.002**	-0.001	0.001***
		(0.001)	(0.001)	(0.001)	(0.000)
Observations		10345	10345	10345	10345
R-squared		.235	.228	.050	
Under-identification[a]					< 0.001
Hansen J-test (df)[b]					0.438 (1)

Notes: Robust standard errors clustered at ATC3-market level in parentheses. * significant at 10% level; ** significant at 5%; *** significant at 1%. In Model (4), we control for endogeneity of price using promotion and number of competitors as demand shifters. [a]P-values of F-test for excluded instruments in the first stage. [b]P-value of Hansen J-test of overidentification.

Table 7. Market Share, Price and Promotion under Patent Protection

find a significant impact of e on price. This is not so surprising, given that most of the data variation for Modes of Action comes from differences across markets and not over time.[42]

5.4 The effects of LoE (testable implications 2-4)

This section looks at the effects of competing molecules losing exclusivity on drugs that remain on patent. According to testable implications 2-4, the reaction of branded drug B (the one that remains patent-protected) when molecule A loses patent protection should depend on three elements: (i) the price sensitivity of demand δ; (ii) the degree of horizontal differentiation e; and (iii) market size μ. The purpose of this section is to test these predictions

[42]Only ten of the 53 ATC3 markets register an increase in the number of *Modes of Action* during the time window we consider.

using the following specification:

$$\begin{aligned} ms_{i,t} &= \rho\, ms_{i,t-4} + \gamma_1 GEN_{-i,t} + \gamma_2 Hosp\; GEN_{-i,t} + \gamma_3 MoA_t\; GEN_{-i,t} \\ &\quad + \gamma_4 S_{i,t}\; GEN_{-i,t} + \beta' X_{i,t} + \gamma_i + \varepsilon_{i,t}, \end{aligned}$$

where $ms_{i,t}$ is the market share of the patent-protected drug in the ATC3 market, and $GEN_{-i,t}$ counts the number of molecules that lost exclusivity in the same market. $Hosp$ is a dummy for the hospital channel, and MoA_t is our proxy for horizontal differentiation, defined in the previous section. To proxy the importance of drug i, we identify the top 25% selling drugs during the entire time period and define the indicator variable S (for small) for drugs that do *not* belong to that blockbuster group. The specification includes the one-year lag of the dependent variable (*i.e.*, four quarters) to capture dynamic autoregressive processes. The set of control variables X includes the number of competing branded molecules to proxy the intensity of competition, a time trend (TE), and a complete set of time dummies. As for other specifications, the data for $ms_{i,t}$ pertain to branded drugs until one quarter before patent expiration.

With respect to testable implication 2, the market share of a B-molecule should increase less (or decrease more) if δ is higher. Using the results of Section 5.1, where we found that the elasticity of demand is higher in hospitals, we expect γ_2 to be negative. According to testable implication 3, we also expect γ_3 to be negative: the market share of molecule B should increase less (or decrease more) if the ATC3 market features more differentiation. Finally, according to testable implication 4, we expect on-patent drug B to be more likely to lose market share if the revenue it generated is small prior to LoE (as indicated previously, the results for prices and promotion are rarely significant, probably due to measurement errors in the data).

In Table 8 (columns 1 and 2), we first report standard random and fixed effects estimations without instrumenting. As expected, the more precise estimates are the ones that control for drug-level fixed effects. However, because of the presence of the lagged dependent variable, the use of fixed effects leads to a downward bias (generally known as "Nickell bias") in the point estimate of ρ, which can be transmitted to the other coefficients. To tackle this problem, we use the GMM estimator with the forward orthogonal deviation (FOD) transformation

		GEN				GEN^{IMP}	
	Coeff.	RE (1)	FE (2)	FOD-IV(3) (3)	FOD-IV(4) (4)	FOD-IV(1) (5)	FOD-IV(2) (6)
GEN	γ_1	0.068**	0.158***	0.123***	0.131***	0.237***	0.243***
		(0.03)	(0.04)	(0.04)	(0.04)	(0.04)	(0.04)
Hosp*GEN	γ_2	-0.021	-0.016	-0.035*	-0.030*	-0.089***	-0.082***
		(0.02)	(0.02)	(0.02)	(0.02)	(0.03)	(0.03)
Modes_of_Action*GEN	γ_3	-0.006	-0.038***	-0.041***	-0.041***	-0.084***	-0.081***
		(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)
Small*GEN	γ_4	-0.023	-0.098***	-0.063*	-0.071**	-0.164***	-0.172***
		(0.04)	(0.04)	(0.04)	(0.04)	(0.05)	(0.05)
Time to Expiration		-0.003	-0.016***	-0.018***	-0.018***	-0.017***	-0.017***
		(0.00)	(0.01)	(0.00)	(0.00)	(0.00)	(0.00)
Number of Competitors		-0.015	-0.013	-0.012	-0.013	-0.014	-0.014
		(0.01)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Lagged Dependent Variable	ρ	0.635***	0.551***	0.754***	0.708***	0.771***	0.732***
		(0.04)	(0.05)	(0.11)	(0.10)	(0.11)	(0.10)
Hosp		-0.004					
		(0.06)					
Modes_of_Action		-0.225					
		(0.14)					
Small		-0.726***					
		(0.12)					
Observations		8622	8622	8622	8622	8622	8622
Hansen J-test (df)a				0.333 (9)	0.697 (69)	0.348 (9)	0.999 (69)

Notes: Robust standard errors clustered at ATC3-market level in parentheses. *significant at 10% level; **significant at 5%; ***significant at 1%. Endogenous variable: lagged dependent vbl one year before. Instrument: lags of number of competitors and market concentration. a P-value of Hansen J-test of overidentifying restrictions with degrees of freedom reported in parentheses

Table 8. Effect of a competitor's genericization on on-patent drugs

proposed by Arellano and Bover (1995). The reason for preferring the FOD over the First Difference estimator is that some of the regressors do not vary (*e.g.* $Hosp$) or vary little over time (*e.g.* MoA). Accordingly, taking these regressors in First Difference would not capture the transition from the pre-entry to post-LoE equilibrium as defined in our theoretical model.[43]

The instruments we use are composed of lags of the number of competitors and market concentration measured by the Herfindahl-Hirschman index. Because the number of instruments generated by our GMM framework is quadratic in T, we try to avoid the well known problem of using "too many weak instruments" by experimenting with two approaches. In column (3), we use lags of the instruments from period $t-4$ to $t-8$, but we collapse them as in Rodman (2006). In column (4) we use the standard (un-collapsed) instruments, but we limit the lags to period $t-4$.

The IV strategy leads to an increase in the point estimate of the lagged dependent variable. Estimates for the coefficients of interest are consistent with our testable implications. The first finding is that we observe mainly instances of branded drugs increasing their volume market share following the genericization of a competitor. Indeed, the coefficient γ_1 is positive and precisely estimated. As already discussed, the reason is that generic entry also drastically reduces promotional effort, which more than compensates for the price drop. Important, and in line with the higher elasticity of demand estimated in Section 5.1, is that this effect is more limited in the hospital channel: in both columns (3) and (4), the interaction between the two dummies ($HOSP*GEN$) is significantly negative, reducing by roughly a quarter the market share gain for the drugs remaining on patent. The negative coefficient γ_3 confirms that markets characterized by a higher degree of horizontal differentiation experience a smaller increase in market share.[44] The interaction between the revenue size indicator variable and the generic count (γ_4) is also significant and of the expected sign.

To check the robustness of these findings, we define an alternative generic entry count variable that considers LoE experienced by only the most important molecules. More pre-

[43]Moreover, an advantage of FOD is that, unlike first differencing, which introduces a moving average structure in the error term, lack of correlation in the transformed errors is preserved if the original ones are not autocorrelated.

[44]Recall that $Modes\_of\_Action = 0, 1, 2...$ when there are $1, 2, 3...$ ATC4 subclasses in the same ATC3.

cisely, the new variable $GEN^{IMP}_{-i,j,t}$ pertains only to the LoE of the 20 drugs (out of 95 drugs) with the largest average sales over the sample period.

Estimating the same regression with this new variable yields the results in Columns 5 and 6 of Table 8. We note that coefficient signs do not change when we focus solely on these "important" drugs. In line with the intuition, the absolute value of the point estimates increases substantially. Yet note that the relative magnitude of the different coefficients remains similar. Interestingly, the precision of the estimates improves markedly as compared to columns (3)-(4).

6 Conclusions and welfare implications

This paper analyzes the consequences of asymmetric competition in imperfectly competitive markets. Our research question was prompted by the puzzling observation that intense intra-molecular price competition following generic entry typically proves ruinous for the molecule that experiences Loss of Exclusivity (LoE).

Why would substantially lower prices end up repelling consumers? Is that phenomenon related to specificities of generic competition or caused by broader forces? We posit that the key to this "reverse competition" effect is the presence of non-price instruments combined with an asymmetry in the competitive shock associated with generic entry. Our model shows that a product selling at much reduced price-cost margins may end up selling less, simply because the firm hit by stiffer competition stops promoting its product (or, by extension, reduces its investments in non-price instruments).

This phenomenon helps explain why, despite generics accounting for 75-90% of the market for the molecules that have lost exclusivity,[45] their overall effect on the market has fallen short of expectations. Legislators on both sides of the Atlantic have had to actively promote generic penetration, and yet expenditures on drugs kept on rising, pouring cold water on the initial (high) hopes of market competition being a silver bullet.

The issue of promotion and asymmetric competition is extremely salient in the pharma industry: Harrington (2012) and Kenkel and Mathios (2012) document that Big Pharma

[45] Source: http://pharmaphorum.com/views-and-analysis/greek_nhs_the_battle_continues_to_rage/

posts a 15%-20% promotion-to-revenue ratio, which is high by any standard, particularly for an R&D intensive industry. Using data covering the universe of prescription drugs in the U.S. for the period 1994 to 2003, we confirm that the originator producer loses most of its market power. Price elasticities are as high as 9 for generics. The originator firm's market share for that molecule then plummets: on the face of it, competition works.

Yet, the drop in promotion associated with generic entry decreases the physicians' incentive to prescribe this particular drug. This typically more than compensates the lower price of generics.

The model also identifies the circumstances under which the molecule facing generic entry will *not* experience a market share drop. This occurs when the market is small in size, the price elasticity of demand is high and, strikingly, when horizontal product differentiation is significant. Under such a constellation, pre-LoE promotion intensity is low, and the pro-competitive effects of generic entry dominates the competition-softening drop in promotion. These theoretical predictions are largely confirmed by our empirical analysis.

Going one step further, the model allows us to infer some welfare implications. In Appendix 3, we extend the analysis to patient/consumer surplus. Following the logic in Inderst and Ottaviani (2012), our model reckons that promotion does influence physicians' prescription behavior. But this influence may not directly benefit patients. Using a definition of consumer surplus that does not attribute any *direct* benefit of promotion to the patients, we find that a sufficient condition for patient (consumer) surplus to increase after generic entry is that the market share of molecules remaining on-patent decreases *in equilibrium* (the price of both molecules then falls). As we saw, this condition is rarely met in practice, meaning that asymmetric competition typically *hurts* patients according to that definition of surplus. The model also allows us to assess when the change in market shares produced by generic entry brings the market allocation closer to the first best (Proposition 5 in Appendix 3). The answer is *never*, and a ban on promotion would not resolve the problem.

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Appendix 1: Benchmark. The effects of generic entry in the absence of promotion

This section presents the case in which firms cannot use detailing and can compete only on prices. One of the main reasons for promoting generics is to make drugs more affordable. The expectation is two-pronged: first, the entry of a generic version of molecule A should put substantial pressure on the price of molecule A. As we saw in Section 2, this effect is unquestionably present. Thus, we assume that generic entry does produce such strong competition on molecule A that the price of drug A drops to the marginal cost of production, which we normalized to 0. This is the direct effect of generic entry.

The second, indirect, effect is the price reaction of firm B. We can check how each of these effects operates when firms can compete only on prices–that is when we impose that firms cannot use promotion: $a_A = a_B \equiv 0$.

Deriving firms' respective reaction functions is straightforward:

$$p_A = \frac{1}{2\delta}\left(e - \Delta\theta_B + \delta\ p_B\right) \tag{9}$$

$$p_B = \frac{1}{2\delta}\left(e + \Delta\theta_B + \delta\ p_A\right). \tag{10}$$

Hence, in the pre-entry equilibrium:

Pre-entry benchmark: *Before generic entry and in the absence of detailing, for* $\theta_A + \theta_B > 2e$, and $|\Delta\theta_B/e| \leq 3$, *the equilibrium is such that:*

$$p_A = \frac{1}{\delta}\left(e - \frac{\Delta\theta_B}{3}\right) \text{ and } Q_A = \left(1 - \frac{\Delta\theta_B}{3e}\right) \times \frac{\mu}{2},$$

$$p_B = \frac{e}{\delta} + \frac{\Delta\theta_B}{3\delta} \text{ and } Q_B = \left(1 + \frac{\Delta\theta_B}{3e}\right) \times \frac{\mu}{2}.$$

The drug with highest quality θ_J, *sells more and at a higher price. Moreover, both prices increase in patient heterogeneity* e *and decrease in price elasticity,* δ.

In that benchmark, the condition $\theta_A + \theta_B > 2e$ is necessary and sufficient to ensure that all patients obtain their treatment in equilibrium. For lower values of θ_J, some patients would find both treatments unaffordable. Note that this condition does not depend on price sensitivity δ because, in the absence of price constraints, firms vary their price exactly to compensate a variation in price sensitivity. In other words, if health insurances double their intervention, total prices will double as well, and the patient will pay the same final price. Second, the condition $|\Delta\theta_B/e| \leq 3$ ensures that both firms sell positive quantities for the price levels derived in benchmark 1.

Upon generic entry, the price of A falls to 0. As a consequence, by (10) , the equilibrium becomes:

Post-entry benchmark: *After generic entry and in the absence of detailing, an interior equilibrium is such that:*

$$p_A = 0 \text{ and } Q_A = \left(\frac{3}{2} - \frac{\Delta\theta_B}{2e}\right) \times \frac{\mu}{2},$$

$$p_B = \frac{e + \Delta\theta_B}{2\delta} \text{ and } Q_B = \left(\frac{1}{2} + \frac{\Delta\theta_B}{2e}\right) \times \frac{\mu}{2}.$$

Note that for any interior solution (*i.e.*, for $0 < \Delta\theta_B/e < 3$), the price of B must decrease, and the market share of A must increase in comparison to the pre-entry benchmark. Hence, the only question is the magnitude of this change: the more vertically superior is molecule B, the less generic entry influences market shares and equilibrium prices.

Appendix 2: equilibrium before and after generic entry in the presence of promotion

We derive the explicit solutions for the equilibrium levels of prices, promotion, and quantities before and after generic entry. We work under the following condition, which ensures that solutions are interior (*i.e.*, the market share of A before entry is strictly positive):

Condition 1 $\mu < (3e - \Delta\theta_B)\,\delta$.

Equilibrium before generic entry

Letting $K_J \equiv 1 + \frac{\theta_J - \theta_{-J}}{3\delta e - \mu}\delta$ and solving explicitly yields:

Proposition 2 *Under Condition 1, the equilibrium* prior to generic entry *is unique and such that:*

$$p_J^D = \frac{e}{\delta}K_J \tag{11}$$
$$a_J^D = \frac{\mu}{2\delta}K_J \tag{12}$$
$$Q_J^D = \frac{\mu}{2}K_J, \tag{13}$$

for $J \in \{A, B\}$. Hence, the most advanced molecule, B, has a higher price, advertisement level and market share than A.

Proof. *Everything follows directly from the FOCs:*

$$\begin{aligned}\frac{\partial \pi_A}{\partial a_A} &= \frac{\mu p_A}{2e} - a_A = 0\\ \frac{\partial \pi_B}{\partial a_B} &= \frac{\mu p_B}{2e} - a_B = 0.\end{aligned}$$

Hence:

$$\Delta a_B = \frac{\mu}{2e}\Delta p_B.$$

Next:

$$\begin{aligned}\frac{\partial \pi_A}{\partial p_A} &= \left[\frac{1}{2} - \frac{\Delta\theta_B + \Delta a_B - \delta\,(p_B - 2p_A)}{2e}\right] \times \mu = 0 \Leftrightarrow p_A = \frac{e}{\delta}\left[\frac{1}{2} - \frac{\Delta\theta_B + \mu\frac{p_B - p_A}{2e} - \delta p_B}{2e}\right]\\ \frac{\partial \pi_B}{\partial p_B} &= \left[\frac{1}{2} + \frac{\Delta\theta_B + \Delta a_B - \delta\,(2p_B - p_A)}{2e}\right] \times \mu = 0 \Leftrightarrow p_B = \frac{e}{\delta}\left[\frac{1}{2} + \frac{\Delta\theta_B + \mu\frac{p_B - p_A}{2e} + \delta p_A}{2e}\right]\end{aligned}$$

Solving jointly for p_A and p_B yields:

$$\begin{aligned}p_A &= \frac{e}{\delta}\left(1 - \frac{\Delta\theta_B\delta}{3\delta e - \mu}\right)\\ p_B &= \frac{e}{\delta}\left(1 + \frac{\Delta\theta_B\delta}{3\delta e - \mu}\right)\end{aligned}$$

Finally, Condition 1 follows from the fact that $Q_A \geq 0$ iff:

$$\begin{aligned}
1 &\geq \frac{\Delta\theta_B + \Delta a_B - \delta\left(p_B - p_A\right)}{e} \\
e &\geq \Delta\theta_B + \frac{\mu}{2e} 2\frac{e}{\delta}\frac{\Delta\theta_B\delta}{3\delta e - \mu} - 2\delta\frac{e}{\delta}\frac{\Delta\theta_B\delta}{3\delta e - \mu} \\
\frac{e}{\Delta\theta_B} &\geq 1 + \frac{\mu}{3\delta e - \mu} - \frac{2\delta e}{3\delta e - \mu} = \frac{3\delta e - \mu + \mu - 2e\delta}{3\delta e - \mu} = \frac{\delta e}{3\delta e - \mu} \\
\Delta\theta_B &\leq \frac{3\delta e - \mu}{\delta}
\end{aligned}$$

■

Equilibrium after generic entry

Profit maximization yields:

Proposition 3 *Post generic entry, the unique equilibrium is given by:*

$$\begin{aligned}
p_A^G &= a_A^G = 0 \\
p_B^G &= 2e\frac{\Delta\theta_B + e}{4\delta e - \mu} \\
a_B^G &= \frac{\mu}{2e} p_B^G \\
Q_B^G &= \frac{\mu}{2}\left[1 + \frac{2\delta\Delta\theta_B - (2\delta e - \mu)}{4\delta e - \mu}\right]
\end{aligned} \tag{14}$$

Proof. Perfect competition amongst generics implies that $p_A = a_A = 0$. Taking first-order conditions of the maximization of π_B with respect to p_B and a_B yields the Proposition. ■

Appendix 3: Outcome Efficiency and Consumer Welfare

The results in Section 3.2 can be exploited to analyze how generic entry influences static allocative efficiency and patient welfare. The fact that our results focus on *static* efficiency is important to note: our analysis considers firm behavior for pre-existing molecules, around the time of patent expiration. As we know, patents are essential to provide the incentives to pharmaceutical firms to develop these molecules in the first place. Yet, extending the analysis to dynamic allocative efficiency and welfare would require accounting for the endogenous R&D investments by different firms, which is beyond the scope of this paper.

Keeping this in mind, static efficiency is reached when both firm A and B face perfect competition. In this first-best case (FB), the price of both molecules is driven down to marginal costs, $p_A^{FB} = p_B^{FB} = 0$, and promotion consequently drops to zero: $a_A^{FB} = a_B^{FB} = 0$. The resulting quantities are:

$$Q_J^{FB} = \frac{\mu}{2}\left(1 + \frac{\Delta\theta_J}{e}\right), \tag{15}$$

and consumer surplus is maximized.

Quite trivially, we would reach first best as soon as all molecules have lost exclusivity; it is just a matter of time. In reality, new vintages of old treatments (so-called "me too" drugs) and new treatments appear constantly. In our quarterly data, for instance, there is at least one molecule still under patent protection for all "anatomic therapeutic classes" and periods. That is, reality is best described either by situation D or situation G that we analyzed above. Our purpose here will be to identify when the movement from D (only patent-protected molecules) to G (some patent-protected molecules) improves market efficiency and/or consumer welfare. We find that:

Proposition 4 *Whether a pharmaceutical firm can (D), or cannot (ND), use detailing, generic entry* ***never*** *brings the market equilibrium closer to the first-best allocation* (15).

Proof. First, let us concentrate on the case in which firms can use detailing and focus on the quantities sold by B, since A serves the rest of the market. Consider, first, the case in which $q_B^D > q_B^{FB}$ – *i.e.*, B sells too much prior to generic entry. By (13) and (15) this only happens if:

$$\frac{\delta}{3\delta e - \mu} > \frac{1}{e} \Leftrightarrow 2\delta e < \mu,$$

which is the exact condition in Proposition 1 for $q_B^G > q_B^D$. Hence, generic entry produces an increase in the quantities sold by B precisely when convergence to the first best requires a drop. By the same token, the reverse is true for $2\delta e > \mu$.

Second, let us turn to the case in which firms cannot use detailing. As shown in Appendix 1, the quantities before and after generic entry are, respectively:

$$\begin{aligned} Q_B^D &= \frac{\mu}{2}\left(1 + \frac{\Delta\theta_B}{3e}\right) \\ Q_B^G &= \frac{\mu}{4}\left(1 + \frac{\Delta\theta_B}{e}\right) = \frac{Q_B^{FB}}{2}, \end{aligned}$$

and the condition for Q_B^D and Q_B^G to be less than the whole market (μ) is: $\Delta\theta_B < 3e$. It is straightforward to check that, for such parameter values, we always have $Q_B^G < Q_B^D < Q_B^{FB}$. ■

The main reason for this result is the same as for Proposition 1: generic entry produces a very lopsided market, in which one molecule becomes cheaper but is no longer promoted. As we saw, when molecules are distant substitutes and/or market size is small ($2\delta e > \mu$), the genericization of A intensifies competition for B, which loses market share, and cuts down prices and promotion as a result. This is exactly the intended purpose of generic competition. The problem is that this happens precisely when B's market share is initially lower than in the first best.

Conversely, when the two molecules are close substitutes and/or market size is large ($2\delta e < \mu$), the genericization of A actually relaxes the competitive pressure on B. This allows firm B to actually gain market power and market share. In this case, firm B also grabs the opportunity to increase its prices and its detailing effort. This only happens when B's market share was already initially too high.

Interestingly, prohibiting detailing altogether would not be a panacea. In that case, the market share of the more advanced molecule B is *always* too low (except in the corner solutions in which it grabs 100% of the market), and the genericization of A further reduces it.

From a policy perspective, being confronted with explosive expenditures on healthcare, authorities have actively promoted the use of generics, partly in an effort to contain the costs borne (directly or indirectly) by patients. In addition, competition authorities have, de facto, adopted a *consumer surplus standard*. We define consumer surplus as their utility minus the price they pay for the molecule they actually buy. Importantly, their utility depends on the actual quality of the molecule, θ_J, whereas which molecule they actually buy also depends on promotion effort, which is rather targeted at the physicians or is spent on the representatives' wages, etc. Thus, we calculate consumer surplus as the integral of the patients' utilities (1-2) when they actually consume the quantities Q_J^D before, and Q_J^G after, generic entry.[46] We find that:

Proposition 5 *Generic entry necessarily increases consumer welfare when B's market share (weakly) decreases after generic entry* (i.e., *for $\mu < 2\delta e$). For $\Delta\theta_B = 0$, consumer surplus decreases upon generic entry when $\mu > \frac{2\delta e}{3}\left(7 - \sqrt{10}\right) \simeq 2.56\ \delta e$, in which case B gains substantial market share, and increases prices and promotion intensity.*

[46] The derivations of consumer surplus are available upon request. We do not present them here because they are tedious but rather straightforward.

Proof. After tedious algebra (see supplementary material), we find that:

$$2\delta e = \mu \Rightarrow CW^G - CW^D = \frac{(e-1)^2}{2} \geq 0,$$

where CW^D is consumer surplus when both A and B benefit from patent protection, and CW^G is consumer surplus when only B still benefits from patent protection. When μ is smaller, prices must be decreasing for all consumers, and their welfare increases.

Imposing $\Delta\theta_B = 0$ for the sake of tractability, one can also identify the value of μ for which this difference in consumer surplus is zero. The threshold is: $\mu = \frac{2\delta e}{3}\left(7 - \sqrt{10}\right)$. For any values of μ below that threshold, consumer surplus increases upon generic entry. ■

Appendix 4: Supplementary tables

Table A1: list of ATC3 markets

ATC3	*ATC4*	*ATC4_name*	*ATC3*	*ATC4*	*ATC4_name*
A10B	A10B1	Sulphonylurea Antidiabetics	J1D	J1D1	Cephalosporins,Oral
A10B	A10B2	Biguanide Antidiabetics	J1G	J1G1	Oral Fluoroquinolones
A10B	A10B3	Comb Sulph+Biguan Antidiabetics	J2A	J2A0	Syst Antifungal Agents
A10B	A10B4	Thiazolinedione Antidiabetics	J4A	J4A1	Anti-Tb, Single Ingred
A10B	A10B5	Alpha-Gluc.Inhib. Antidiabetics	J5B	J5B0	Antivirals Excl Anti-Hiv
A10B	A10B9	Other Oral Antidiabetics	L1A	L1A0	Alkylating Agents
A2B	A2B1	H2 Antagonists	L1B	L1B0	Antimetabolites
A2B	A2B2	Acid Pump Inhibitors	L1C	L1C0	Vinca Alkaloids
A2B	A2B9	All Other Antiulcerants	L1D	L1D0	Antineoplas. Antibiotics
B1C	B1C2	Adp Recep Antag Plat Inhibitors	L1X	L1X1	Adj Prep For Cancer Ther
B1C	B1C4	Pl Camp Enh Plat Ag Inhibitors	L1X	L1X2	Platinum Compounds
C10A	C10A1	Statins - Hmg-Coa Reduct. Inhibitors	L1X	L1X9	All Oth. Antineoplastics
C10A	C10A3	Bile Acid Sequestrant	L2B	L2B1	Cyto Anti-Oestrogens
C10A	C10A9	All Oth Chol/Triglyc Red	L2B	L2B2	Cyto Anti-Androgens
C1B	C1B0	Antiarrhythmics	L2B	L2B3	Cytostat Aromatase Inhibitors
C1F	C1F0	Positive Inotropic Agent	L4A	L4A0	Immunosuppressive Agents
C1X	C1X0	All Other Cardiac Preps	M1A	M1A1	Antirheumatics Non-S Pln
C2A	C2A1	Antihyper.Pl Mainly Cent	M1A	M1A3	Coxibs
C2A	C2A2	Antihyper.Pl Mainly Peri	M1C	M1C0	Spec Antirheumatic Agent
C3A	C3A2	Loop Diuretics Plain	M5B	M5B1	Oral Bisph Bone Calc Reg
C3A	C3A3	Thiazide+Analogue Plain	N1A	N1A2	Inject Gen Anaesthetics
C4A	C4A1	Cereb/Periph Vasotheraps	N2A	N2A0	Narcotic Analgesics
C7A	C7A0	B-Blocking Agents,Plain	N2B	N2B0	Non-Narcotic Analgesics
C8A	C8A0	Calcium Antagonist Plain	N3A	N3A0	Anti-Epileptics
C9A	C9A0	Ace Inhibitors Plain	N4A	N4A0	Anti-Parkinson Preps
C9B	C9B1	Ace Inhibitors Comb+A-Hyp/Diur	N5A	N5A1	Atypical Antipsychotics
C9B	C9B3	Ace Inhibitors Comb+Calc Antag	N5B	N5B1	Non-Barbiturate Plain
D10A	D10A0	Topical Anti-Acne Preps	N5C	N5C0	Tranquillisers
D11A	D11A0	Other Dermatological Prd	N6A	N6A1	Antidepress.Excl Herbals
D1A	D1A1	Topical Dermat Antifung	N6B	N6B0	Psychostimulants
D6D	D6D1	Topical Antivirals	P1D	P1D1	Antimalarials Single Ing
D6D	D6D9	Oth Top Prds Viral Inf	R1A	R1A1	Nasal Cortic W/O Anti-inf
D7A	D7A0	Top.Corticosteroid Plain	R1A	R1A6	Nasal A-Allergic Agents
G4A	G4A1	Urinary Antibiot/Sulphon	R1B	R1B0	Systemic Nasal Preps
G4B	G4B3	Erectile Dysfunction Prd	R3G	R3G4	A-Chol+B2-Stim Comb,Inh
G4B	G4B4	Urinary Incontinence Prd	R6A	R6A0	Antihistamines Systemic
G4B	G4B9	All Oth Urological Prods	S1D	S1D0	Anti-Viral Agents -Eye
J1C	J1C1	Brd.Spect.Penicill.Oral			

TABLE A2: List of Branded Drugs losing patent protection

Brand Name	*Generic Name*	*Quarter Generic Entry*
anafranil	clomipramine	1996q4
ansaid	flurbiprofen	1994q2
augmentin	amoxicillin+clavulanic acid	2002q3
axid	nizatidine	2001q3
betapace	sotalol	2000q2
blenoxane	bleomycin	1996q3
bumex	bumetanide	1995q1
buspar	buspirone	2001q2
capoten	captopril	1995q4
capozide	captopril+hydrochlorothiazide	1997q4
carafate	sucralfate	1996q4
cardene	nicardipine	1996q3
cardura	doxazosin	2000q4
ceclor	cefaclor	1994q4
cerubidine	daunorubicin	1998q2
ciproxin	ciprofloxacin	2003q2
clarinase	loratadine+pseudoephedrine	2002q3
claritine	loratadine	2002q3
condylox	podofilox	2002q1
cordarone	amiodarone	1998q2
cyclocort	amcinonide	2002q2
cylert	pemoline	1999q2
daypro	oxaprozin	2001q1
diprivan	propofol	1999q2
dormicum	midazolam	2000q2
drogenil	flutamide	2001q3
dtic-dome	dacarbazine	1998q4
duricef	cefadroxil	1996q1
eldepryl	selegiline	1996q3
elocon	mometasone	2002q1
floxstat	ofloxacin	2003q3
floxyfral	fluvoxamine	2000q4
glucophage	metformin	2002q1
glucotrol	glipizide	1994q2
heitrin	terazosin	1999q3
imuran	azathioprine	1995q3
inocor	amrinone	1998q3
lariam	mefloquine	2002q2
leponex	clozapine	1997q4
lodine	etodolac	1997q1
loniten	minoxidil	1996q2
losec	omeprazole	2002q4
mevacor	lovastatin	2001q4
mexitil	mexiletine	1995q2
micronase	glibenclamide	1994q2
mutamycin	mitomycin	1995q2
myambutol	ethambutol	2000q2
navelbine	vinorelbine	2003q1

Brand Name	Generic Name	Quarter Generic Entry
nizoral	ketoconazole	1999q2
nolvadex	tamoxifen	2002q4
normodyne	labetalol	1998q3
pepcidine	famotidine	2001q2
permax	pergolide	2002q4
pevaryl	econazole	2002q4
platinol	cisplatin	1999q4
prostin vr	alprostadil	1998q1
prozac	fluoxetine	2000q3
psorcon	diflorasone	1998q2
questran	colestyramine	1996q3
relifex	nabumetone	2001q3
retin-a	tretinoin	1998q2
rivotril	clonazepam	1996q3
rynatan mepo	chlorpheniramine+mepyramine	1994q4
sandimmun	ciclosporin	1998q4
sectral	acebutolol	1995q2
seroxat	paroxetine	2003q3
serzone	nefazodone	2003q3
somnatrol	estazolam	1997q3
stadol	butorphanol	1997q2
staril	fosinopril	2003q4
sufenta	sufentanil	1996q1
tagamet	cimetidine	1994q2
talwin nx	naloxone+pentazocine	1997q2
tambocor	flecainide	2002q1
taxol	paclitaxel	2000q4
temovate	clobetasol	1994q3
tenex	guanfacine	1995q4
ticlid	ticlopidine	1999q2
toradol	ketorolac	1997q2
trental	pentoxifylline	1997q3
ultram	tramadol	2002q2
unat	torasemide	2002q2
univasc	moexipril	2003q2
vaseretic	enalapril+hydrochlorothiazide	2001q3
vasotec	enalapril	2000q3
viroptic	trifluridine	1996q2
voltaren	diclofenac	1995q3
wytensin	guanabenz	1994q3
zantac	ranitidine	1997q3
zaroxolyn	metolazone	2003q3
zavedos	idarubicin	2002q3
zestoretic	hydrochlorothiazide+lisinopril	2002q2
zestril	lisinopril	2002q2
zinnat	cefuroxime axetil	2002q1
zovirax	aciclovir	1997q2