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Identifying Industry Margins with Price Constraints: Structural Estimation on Pharmaceuticals[†]

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We develop a structural model to investigate the effects of pharmaceutical price regulation on demand and on manufacturers' price-setting behavior in France. We estimate price-cost margins in a regulated market with price constraints and infer whether these constraints are binding, exploiting cost restrictions across drugs, which come from observing the same drugs in potentially price-constrained markets (France) and in markets where prices are unregulated (United States and Germany). Our counterfactual simulations suggest that price constraints generated modest savings for anti-ulcer drugs in 2003–2013 (2 percent of total expenses), relative to a free pricing scenario, and shifted consumption from generic to branded drugs. (*JEL* C51, D24, I18, L13, L51, L65)

Understanding the role played by regulatory constraints is of major importance in, for example, the pharmaceuticals industry, where regulation is pervasive throughout all stages of drug development and commercialization, but where countries differ significantly in their regulatory approach. For instance, manufacturers in the United States are allowed to freely choose prices for prescription drugs, while France regulates the price of pharmaceuticals covered by public health insurance. The French system of price regulation was revised in the 2000s, as part of a broader reform intended to control rising drug expenditures. The regulatory changes targeted both demand and supply, by affecting the drug choices of prescribers, pharmacists, and patients and the pricing decisions of firms. These changes include a cap on reimbursement for branded drugs after generic entry and stricter requirements on price levels and their evolution over time. Difference-in-differences evidence on the effects of the price cuts introduced in 2006 suggests that prices declined

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significantly as a consequence of this reform, on average by 30 percent for the drugs subject to this policy.

This paper develops a structural model to investigate the effects of price regulation in France. We estimate price-cost margins in a regulated market where the regulator imposes price constraints, and we infer whether these constraints are binding. Once the shape of demand is recovered, the identification strategy relies on assumptions on the price competition game played by firms and on cost restrictions across drugs and markets, which exploit the presence of some markets that are not price constrained, as prices are not regulated. Using IMS data on drug sales, we investigate whether the current price-setting regulation in France imposed binding constraints on the prices of anti-ulcer drugs between 2003 and 2013, using the United States and Germany as unconstrained markets. We then evaluate the counterfactual free pricing equilibrium in which all price regulation is removed and a different, regulated equilibrium based on external reference pricing, a policy that was recently implemented in France. These comparisons allow us to quantify changes in prices, demand, and spending due to price regulation.

Estimating demand is the first step of our analysis and requires a flexible yet tractable model able to capture the differentiation of anti-ulcer drugs, as well as the heterogeneity in preferences (Ching 2010a, b). Following the standard approach in empirical IO (Berry 1994; Berry, Levinsohn, and Pakes 1995; Nevo 2000, 2001) and some recent applications to pharmaceuticals (Dunn 2012, Björnerstedt and Verboven 2016), we use a random coefficient logit model to account for heterogeneity in preferences over drug characteristics and price disutilities. Our demand specification controls for quality, by including quality-related drug characteristics, and for advertising (primarily in the form of detailing, the practice of sending pharmaceutical sales representatives to physicians). We find that demand for anti-ulcer drugs is price elastic, particularly for drugs subject to the maximum reimbursement rule in France. Even after controlling for detailing, which positively affects sales, brand-name drugs are preferred to generics, although there is significant estimated variation in preferences. Consistent with medical knowledge, we find that anti-ulcer drugs are highly differentiated and that substitution occurs mostly (but not entirely) at the level of the molecule or subclass.

Once we have identified demand and substitution patterns, we explore the impact of regulation on prices and margins, in a setting where firms strategically choose prices given the constraints imposed by the regulator, which amount to price caps. The magnitude of these price ceilings imposed on firms is unknown to the econometrician, but our identification strategy allows us to infer when price constraints are binding across drugs and periods. Under the assumption that firms compete à la Bertrand, the identification is obtained by the use of unconstrained markets (the United States and Germany, where drug prices are not regulated) and by restrictions on the costs of drugs across markets, which allow us to recover such constraints.

We find that some but not all drugs are significantly constrained and that regulation has spillover effects on drugs not directly subject to price cuts, as prices chosen by manufacturers are affected by the regulatory constraints on their closest substitutes through the equilibrium conditions. Counterfactual simulations suggest that the current price controls reduced prices relative to a free pricing scenario, especially in years in which prices were cut. Such declines in prices, especially

for high-quality drugs, shifted consumption toward branded drugs at the expense of generics, which experienced a smaller decrease in price, in both absolute and percentage terms. Once the difference between the branded and the generic price is reduced, the preference for the branded drug (captured by our demand estimates) leads to substantial losses for generic manufacturers, as profits would be 23 percent higher in a free pricing scenario, compared to an increase of only 15 percent for branded firms. Nevertheless, price constraints generate some modest savings, approximately 2 percent of total expenses, on average, over the 11 years of data and increase consumer surplus, due to the greater utilization of cheaper and preferred branded drugs. To avoid the increased consumption of branded drugs in favor of generics, the regulator could instead cap prices at the level of other countries (so-called external reference pricing), a rule introduced in France for other drugs in 2004. Our simulations suggest that under this policy, prices would decline even more and demand would increase but less than proportionally, leading to additional savings. Contrary to the regulation in place for anti-ulcer drugs during the period 2003–2013, generic penetration would increase (one of the objectives of the French regulator), due to the significant reductions of generic prices and margins. However, while in the short run consumer surplus would be higher than under the current regulatory setting, this alternative regulation may hinder the survival of generics in the long run.

Our work contributes to different strands of the literature. First, we contribute to the broad research on demand for pharmaceuticals, which has employed different approaches to estimate preferences for drugs and substitution patterns, from log-log models (as in Berndt et al. 1995, 1996; Rizzo 1999; and Berndt, Kyle, and Ling 2003), to AIDS and multistage budgeting (as in Ellison et al. 1997 and Chaudhuri, Goldberg, and Jia 2006). Our approach more closely resembles the works that use discrete choice models (logit in Azoulay 2002, Berndt, Pindyck, and Azoulay 2003, and Crawford and Shum 2005; and nested logit in Stern 1996, Donohue and Berndt 2004, and Arcidiacono et al. 2013). Our random coefficient logit model is similar to Ching (2010a, b) and Björnerstedt and Verboven (2016), as we explicitly account for heterogeneity in price sensitivity, although we do not incorporate consumer learning.

Our study explores the role of price controls and shows their different effects on branded and generic drugs, in line with previous works documenting how price controls may render generic competition ineffective or even counterproductive (Danzon and Chao 2000). Our results suggest that external reference pricing may avoid this effect in France in the short run, although similar policies linking prices across countries have been shown to discourage or delay drug introduction (Danzon, Wang, and Wang 2005; Kyle 2007; Danzon and Epstein 2008) and to affect drug entry decisions beyond the role of market size and firm characteristics (Scott-Morton 1999; Kyle 2006), leading to large welfare losses at a global scale (Filson 2012). Nevertheless, price controls may be welfare-improving when used to counterbalance the welfare losses from other regulatory measures (see Chaudhuri, Goldberg, and Jia 2006 on TRIPS product patents in India). However, alternative regulations may dominate price controls. For example, policies that impose additional copayments on patients demanding high-priced branded drugs can be more effective than price caps in lowering drug prices and provide incentives for pharmacists to promote generic sales

(see Brekke, Grasdal, and Holmås 2009 and Brekke, Holmås, and Straume 2011, 2013 on Norway).

Our work also illustrates how standard IO methods can be combined with cost restrictions across markets to recover the price-cost margins in a setting where firms may be constrained by regulation but where these constraints are unobserved by the econometrician. In a similar vein, Goldberg (1995) studies the car industry and the role of trade policy, such as voluntary export restraints, that imposed a quota on Japanese cars in the US market in the 1980s. The Lagrange multipliers associated with the quantity constraints on imported cars are identified by exploiting observations from the truck market, which was not subject to the same quota constraints. In Goldberg (1995), quantity constraints are observed, while we do not observe the implicit price caps that the regulator imposes on firms. Salvo (2010) addresses a similar problem in estimating market power in the Brazilian cement industry, where firms are constrained in price setting due to the threat of entry by foreign producers, which poses an observable ceiling for the price that domestic competitors can set. Salvo (2010) predicts the price ceiling based on observed costs. Brenkers and Verboven (2006) study how constraints on international markup differentials introduced after liberalizing the distribution of cars in Europe affect the market equilibrium. After estimating the demand for cars before liberalization and thus without price constraints, they simulate a new price equilibrium by imposing a given maximum difference in markups across countries. We use the variation across countries and markets to generate the cost restrictions needed for identification. Our identification strategy could be used in the context of markets where prices may be affected by inequality constraints on markups across markets. A recent paper by Ching, Hayashi, and Wang (2015) explores the role of capacity constraints and excess demand in the nursing home market. Their identification strategy relies on observing the unconstrained demand of private-pay consumers (who never face capacity constraints because they are given priority) to identify the extent of excess demand due to Medicaid patients and test whether the constraints bind. Hence, they use demand-side variation, while we exploit cost restrictions across markets.

Section I describes the market for anti-ulcer drugs and the data used; it also illustrates how price regulation operates in France and provides difference-in-differences evidence of its impact on prices. Section II presents our identification of price-cost margins in an oligopoly model when demand is known, provided that both constrained and unconstrained markets are observed. Thereafter, Section III explains the particular demand model estimated as a first step of the supply-side estimation. The results are discussed in Section IV. Section V reports counterfactual price equilibrium and savings calculations in the absence of the price setting regulation in France (Section VA) or with external reference pricing (Section VB). Finally, Section VI concludes the paper.

I. Market, Data, Regulation, and Difference-in-Differences Evidence

A. *Regulatory Framework in France*

The consumption of pharmaceuticals in France has historically been high, due to low regulated prices relative to other comparable European markets (Nguyen-Kim

et al. 2005), a generous public drug reimbursement system, covering nearly the entire French population, and high rates of complementary health insurance. In the early 2000s, pharmaceutical expenses in France represented one-fifth of total public expenditures on health and doubled with respect to the previous decade (reaching 30 billion euros in 2004), increasing more rapidly than anywhere else in Europe (Nguyen-Kim et al. 2005). This situation accelerated a project to reform the pharmaceutical regulatory system intended to reduce public expenditures on drugs. The policies introduced targeted both the demand and the supply of drugs, ranging from public campaigns to encourage the use of generics, to financial incentives for generic substitution to pharmacists (see additional details in Section IIIA), to new guidelines for physicians to prescribe primarily drugs for which generic alternatives are available, and to a thorough review of the list of reimbursed drugs that reduced or removed completely public coverage for those with insufficient therapeutic value.

Major changes were made to the rules that govern drug reimbursement. In 2003, a maximum reimbursement price was introduced (Tarif Forfaitaire de Responsabilité (TFR)) when generic penetration does not reach a certain threshold defined by the Ministry of Health. In such a case, coverage for these drugs is only up to the TFR price, which is a function of generic prices.[1] Manufacturers can keep the price above this TFR price, but the difference is paid out of pocket by the patient.

The reform also addressed the process of price setting, which in France is regulated by the Economic Committee for Health Products (Comité Economique des Produits de Santé (CEPS)). The price proposed by companies must be approved by the regulator, and it depends on the therapeutic improvement of the drug, on the anticipated sales volume, and on the price of existing comparable reimbursed drugs (further details on price setting are reported in Section IIB). In 2004, the criterion that prices of new drugs need to be in line with prices in Italy, Germany, the United Kingdom, and Spain was added (so-called external referencing). In 2006, the CEPS declared a price cut on all drugs based on the same molecule when generics become available or when they have been on the market for at least 24 months. The rule for price cuts has evolved over time (both in terms of the percentage of the price to be cut and time since generic entry) but can still be applied to markets not subject to TFR (TFR and price cuts being mutually exclusive).

Table 1 summarizes the regulatory changes that affected both the demand and the supply side of the anti-ulcer drug market in France between 2003 and 2013. Our work focuses on the impact of price cuts (which directly affect six drugs in our sample since 2006), accounting for the role of TFR in demand. We will then explore the effect of external referencing in our counterfactual simulations.

B. *The Anti-Ulcer Drugs Market*

We define the anti-ulcer prescription drugs market using the A02B category of the international World Health Organization ATC classification. The absence of real

[1] The regulator decides which molecules are subject to TFR based on the rate of generic penetration. In general, TFR can be introduced when the market share of generics for a molecule is below 60 percent after 18 months or 65 percent after 2 years since generic entry. These percentages and timing have changed slightly over time and unexpectedly, and the regulator has total power over this issue, meaning that it can make exceptions and unilaterally decide to define a TFR.

Table 1—Regulatory Changes Affecting the Anti-Ulcer Market in France since 2003

Date	Description
Panel A. Regulatory changes affecting the demand side	
September 2003	Introduction of maximum reimbursement price (TFR) for Cimetidine (Tagamet) and Ranitidine (Zantac and Raniplex)
January 2006	Introduction of TFR on Famotidine (Pepcidine)
Panel B. Regulatory changes affecting the supply side	
January 2006	Price cut of all drugs in a class if generics entered or have been available for 24 months—Omeprazole (Losec) and Lansoprazole (Takepron, Lanzor)
January 2008	Price cut for branded drugs if enough sales of generics of the same or close substitute molecules—Esomeprazole (Nexium)
January 2009	Revision of the price cut rule (18 months instead of 24) for Omeprazole, Lansoprazole, and Pantoprazole (Pantozol)
January 2012	Revision of the price cut rule at generic entry for Omeprazole, Lansoprazole, Pantoprazole, and Rabeprazole (Pariet)

Note: Price cuts in 2006, 2009, 2012 are of different percentages.

substitutes for these drugs (hospitalization and surgery target different conditions) make the market easily identifiable in the A02B class, without having to include drugs from other therapeutic classes among competitors (Crawford and Shum 2005). The market comprises three subclasses that can be regarded as three different generations of drugs treating ulcer and ulcer-related conditions. The subclass of histamine antagonists (H2) includes anti-ulcer treatments of the first generation, introduced in the 1970s and 1980s, which treat ulcer symptoms by blocking the action of histamine in the stomach. H2 drugs are based on a number of molecules, the most common of which are Cimetidine (brand name: Tagamet), Famotidine (brand name: Pepcidine), Ranitidine (brand names: Zantac and Raniplex), and Nizatidine (brand name: Panaxid). H2 had considerable success in many countries, driven by SmithKline's Tagamet (Cimetidine) and Glaxo's Zantac (Ranitidine); they remained top sellers until the late 1980s, when a new generation of ulcer treatments was introduced, the proton-pump inhibitors (PPI). These drugs, instead of blocking the reception of histamine, act at the source of acid secretion, inhibiting it for a longer time, and are considered superior to H2 and other existing drugs. This subclass includes several derivatives of benzimidazole: Omeprazole (brand name: Losec, the world's top-selling drug for several years), Esomeprazole (brand name: Nexium), Lansoprazole (brand names: Lanzor and Takepron), Pantoprazole (brand name: Pantozol), and Rabeprazole (brand name: Pariet). Finally, the third subclass is a residual category, which includes Prostaglandins, which are used primarily for the prevention and treatment of peptic ulcer in the elderly (Misoprostol, brand name: Cytotec).

The anti-ulcer market has long been one of the top-selling therapeutic classes worldwide (being the leader from 1990 to 2003). This was driven by the presence of blockbusters and competition based on subsequent innovations. Anti-ulcer drugs are manufactured by several of the most important pharmaceutical players: AstraZeneca (Losec and Nexium), GlaxoSmithKline (Zantac), Takeda (Takepron and Pantozol), Pfizer (Cytotec), Sanofi (Lanzor), Johnson & Johnson (Pariet), Merck (Pepcidine), Abbott (Raniplex), Aptalis (Tagamet), Norgine (Panaxid), and Forest (Pylera).

In addition, the market experienced patent expiration for major drugs in the early 2000s, and several entry waves of generics started populating the French market.

C. *Data and Descriptive Statistics*

We use data from IMS Health covering all wholesale transactions in the retail and hospital sector (revenues and quantities sold for each drug in a country-year) for the period 2003–2013. We also use advertising data from IMS Health Global Promotional Track for France, Germany, and the United States (IMS Health–Base Global Promo Track 2001–2014). We have data on advertising expenditures for each drug by media at the country level for France, Germany, and the United States. Descriptive statistics on advertising by market are presented in Appendix Table A1 and report the yearly average of total advertising expenditures for branded drugs or generics by country and the part of this advertising that corresponds to detailing expenses. In France, most expenses are in the form of detailing, with the rest being in journal publications, meetings, and other. Advertising of generics is also much lower than for branded drugs, and this is also true in the United States but not in Germany, where the ratio of advertising expenses over total revenue is much higher for generics than in France or the United States. We also observe the number of detailing units,[2] which will be useful for computing an average price per detailing unit in each year and country. In the quantity sales data, a drug-country-year triplet observation is uniquely identified by the name of the drug, its manufacturer, its molecule, its therapeutic form, and its brand type (originator, licensed or generic drug). We compute an average wholesale price per standard unit from the figures on quantities (where standard units are defined as the smallest unit of the drug standardized across dosage and therapeutic form) and revenues per year (in constant US$). The data were aggregated at the therapeutic form level to avoid distinguishing the different methods of administration of exactly the same drug (tablet and effervescent capsules, for instance). We use these IMS data for both quantities and revenues for France, Germany, and the United States, but we also use the average wholesale prices in Italy, Spain, and the United Kingdom as instrumental variables (see Section IV). We also use data from the French regulatory agency HAS (available at www.theriaque.org) to gather additional information on the indications and side effects of each drug, the medical benefit indices (SMR and ASMR[3]) for each indication (a rating used recently by Kyle and Williams 2017), and the date of introduction and level of TFR.

Between 2003 and 2013, a total of 103 different drugs were sold in France by 29 different companies: among them, 13 are branded firms, and the remaining 16 are generic manufacturers. The majority of the drugs (77) belong to the PPI subclass

[2] Detailing corresponds to promotional activity by pharmaceutical sales representatives to physicians. They are defined in the data as a direct contact between physicians and the pharmaceutical company, whether a visit or telephone call from a sales representative, e-details or live videoconferencing. Detailing units are defined as the number of brand presentations to a physician over the period, aggregated at the country level, and the detailing cost corresponds to how much it would cost for a sales representative to visit (in person or via phone) a physician, including not only her salary and benefits but also travel cost, gas, and maintenance by the minute.

[3] SMR (service médical rendu/absolute medical benefit) is an absolute rating of drug importance, and ASMR (amélioration du service médical rendu/improvement in medical benefit) is a relative rating of therapeutic value compared to existing treatments.

(A02B-C), which represents the bulk of sales, followed by H2 (A02B-A), with 24 products; Prostaglandins (A02B-B) are present with only one drug (Pfizer's Cytotec); and a combination of an anti-ulcer and antibiotic drug completes the list. French anti-ulcer drugs in this period are based on 11 active ingredients: 5 PPI (Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole, and Rabeprazole), 4 H2 (Cimetidine, Famotidine, Nizatidine, and Ranitidine), 1 Prostaglandin (Misoprostol), and 1 combination (Bismuth and antibiotic). For eight of these, generics were or became available during the sample period: Misoprostol, Nizatidine, and the combination drug were sold only as brand names. In Germany and the United States, the number of drugs is higher than in France, and all drugs sold in France are always sold in these two other countries.

The therapeutic benefit of these drugs was classified as important by the CEPS for most of the years in the sample, granting a 65 percent reimbursement rate, except for some older H2 drugs, the reimbursement for which has been reduced to 35 percent since 2007. The therapeutic improvement vis-à-vis existing drugs was considered insufficient (ASMR level 5 on a 1–5 scale), except for AstraZeneca's Losec (Omeprazole) and Nexium (Esomeprazole). Additional measures of drug quality, beyond ASMR, are the number of therapeutic forms (between 1 and 4 in the data), indications, and side effects. A higher number of therapeutic forms makes it possible to better suit the needs of heterogeneous patients. Generic drugs offer at most two different forms. The number of indications and side effects differs significantly across drugs, from a minimum of two to a maximum of nine indications (Losec and Nexium) and eight side effects (Nexium's peculiarity).

Table 2 shows that there is a steady and significant increase in the number of drugs marketed, from 25 in 2003 to 94 in 2013, due to the entry of generics, the market share of which rose significantly during the period. In the early 2000s, several Ranitidine- and Cimetidine-equivalents entered the market (Zantac and Tagamet lost patent protection in the 1990s), but generics still represented a residual category in terms of volumes and revenues. In 2004, a second entry wave took place in the form of generics of the world's top-selling drug, Losec (AstraZeneca's Omeprazole), followed by many others at the patent expiration of other PPI molecules during the later years of the sample period. By 2011, generic sales constituted more than half of the class volume, representing the vast majority at the end of the sample period. These figures are similar in Germany and the United States, with the former reaching even higher levels of generic penetration (see Appendix Tables A2 and A3). Interestingly, in France, the market for anti-ulcer drugs expanded at the same time as generic penetration, meaning that the sales of branded versions did not decline dramatically. Actually, aggregate quantity increased by approximately 50 percent during the period. However, revenues also declined, leading to a decreasing average price per standard unit, in line with generics being cheaper (the price of generics is capped at a fixed percentage of the price of their brand-name counterpart) and to the increased pressure imposed by the reform on the regulated prices of brand-name drugs.

D. *Difference-in-Differences Evidence of the Effect of Regulation on Prices*

As reported in Table 1, there are several regulatory changes that may affect demand or supply for anti-ulcer drugs in France during the period of study. In specific, the

Table 2—Summary Statistics for France

Year	Number of drugs			Quantity	Market share (%)		Wholesale Price/std unit		Firm revenue
	All	Branded	Generics	(1,000 std units)	Branded	Generics	(US$)	(€)	(1,000 US$)
2003	25	12	13	1,131,140	98	2	0.75	0.55	1,414,127
2004	39	12	27	1,233,735	86	14	0.78	0.57	1,455,683
2005	40	12	28	1,334,331	77	23	0.70	0.51	1,423,278
2006	42	12	30	1,444,926	73	27	0.63	0.46	1,404,320
2007	51	12	39	1,508,936	70	30	0.60	0.44	1,364,369
2008	49	12	37	1,535,426	61	39	0.56	0.41	1,240,799
2009	59	12	47	1,596,513	55	45	0.52	0.38	1,183,251
2010	62	12	50	1,669,252	50	50	0.46	0.33	1,069,219
2011	74	12	62	1,732,595	39	61	0.43	0.31	974,594
2012	86	12	74	1,820,351	29	71	0.39	0.28	853,985
2013	94	11	83	1,890,575	18	82	0.32	0.23	619,035

Notes: Price is the average price per standard unit in US$ or in € (constant exchange rate for 2014:II: €/US$ = 1.3772). Expenses is the total manufacturer-level revenue of the class. Wholesale prices are at the manufacturer level. Here, the market shares are relative to the total sales of anti-ulcer drugs (no outside good as in the model).

regulator introduced price cuts on branded drugs since 2006. Furthermore, reimbursement rules changed over time and affected some drugs with a maximum reimbursement price through the TFR rule explained above. Before showing how one can structurally identify and estimate the impact of these regulations on prices, demand, and expenditures, we provide difference-in-differences evidence on the effects of these events on prices. The main focus of our structural model will be to quantify the effects of price regulation and in particular the price cuts imposed since 2006. These cuts affect the price of the brand-name drugs after generic entry or when generics have been on the market for at least 24 months, whether they are based on the same molecule or on different ones considered close substitutes. The drugs subject to these cuts belong to the PPI category and include Losec (Omeprazole), Lanzor and Takepron (Lansoprazole) since late 2006, Nexium (Esomeprazole) since 2008, Pantozol (Pantoprazole) since 2009, and Pariet (Rabeprazole) since 2012. Moreover, H2 anti-ulcer drugs were affected by the introduction of the TFR. This rule, which imposes a maximum reimbursement price, was introduced at the end of 2003 and caps the reimbursement level of branded drugs and their generics. In 2004 and 2005, three anti-ulcer drugs were subject to this rule: Tagamet (Cimetidine), Zantac, and Raniplex (Ranitidine); a fourth was added in 2006, Pepcidine (Famotidine). Although TFR is not the main object of our analysis, as it is a policy affecting demand and not supply directly, our structural model will address the role of the TFR rule on demand. Previous studies have shown that policies that impose additional copayments on patients demanding high-priced branded drugs (similar to the French TFR rule) may result in lower drug prices (see Brekke, Grasdal, and Holmås 2009 and Brekke, Holmås, and Straume 2011, 2013 on Norway). For this reason, we believe that it is important to control for TFR in the difference-in-differences analysis, to rule out the possibility that the drugs subject to TFR are different from other drugs within the anti-ulcer market.

Using the data from France, Germany, and the United States, we test the effects of both price cuts and TFR on the prices of drugs using triple difference regressions within this class and across markets. To do this, we define the group of drugs denoted

"TFR" as those drugs that have been subject to the maximum reimbursement price rule in France since 2004, and we denote by "Price Cut" the dummy variable for the group of drugs subject to that rule in France (the two rules are mutually exclusive). Of course, these two rules are supposed to have affected the price of drugs in France only and not in Germany and the United States, but these drugs could also be different from other drugs within the anti-ulcer market, hence the use of interaction with country dummies.

Table 3 reports the results of the regression of the log price of drugs on drug characteristics, on the drug group dummies TFR and Price Cut, on the interaction between these group dummies and the dummy for whether the time period is after the regulatory event (i.e., when the TFR or price cut was introduced for each affected drug), and on the interaction between the dummy variable for France after the start of the regulatory event and these group dummies. The coefficients of these last interactions can be interpreted as the effects of the regulatory event in France on prices. In column 1, by adding country fixed effects, molecule fixed effects, and year fixed effects, we find that the drugs in the Price Cut and TFR groups are slightly more expensive (although the effect is not significant) and that their prices have increased slightly (albeit not significantly). However, the interaction of each group dummy with the regulatory period dummy "After" and the interaction with the French dummy shows that in France these drugs became cheaper when each of these regulations was implemented. The effect is significant for both Price Cut and TFR (except for the last two specifications for Price Cut). When using different country and year fixed effects or country and molecule fixed effects in columns 2, 3, and 4, the results are similar, but the significance is weaker in the fourth specification. Note that in column 4, we have country-molecule-year fixed effects, meaning that the effects of drug characteristics and regulation are identified from variations within a molecule-country-year triplet. Table 3 also shows that branded drugs and those with an indication for the eradication of *helicobacter pylori* are more expensive, whereas drugs with more side effects are cheaper (the results are similar with price as the dependent variable).

This difference-in-differences evidence seems to confirm that these regulatory events did reduce prices; however, this is conditional on counterfactual prices having been similar. It is indeed possible that demand changed during these years due to country-specific changes, leading to lower prices, or that specific cost shocks also affected the equilibrium pricing. A structural estimation will allow us to interpret those results and test whether regulation actually constrained prices or whether observed price changes are simply due to demand or supply conditions. Moreover, our structural approach will allow us to perform simulations of counterfactual policies.

II. Supply Model and Identification of Margins

Assuming that the shape of demand for pharmaceuticals is known, we first present our model of the effect of regulation on the supply side and defer the modeling and estimation of demand to the next section.

We focus on pricing with an exogenously given market structure, taking entry decisions as exogenous. Pharmaceutical innovation involves long R&D delays,

Table 3—Triple Difference Regression of log Prices

Variables	log price (1)	log price (2)	log price (3)	log price (4)
Drug characteristics				
Branded	1.648	1.667	1.824	2.023
	(0.484)	(0.507)	(0.501)	(0.597)
Nb. side effects	−0.352	−0.349	−0.341	−0.285
	(0.0957)	(0.103)	(0.0855)	(0.0350)
Formats	0.131	0.123	0.0345	0.0172
	(0.166)	(0.174)	(0.175)	(0.199)
Helicobacter indication	3.199	3.192	2.821	1.790
	(0.960)	(1.062)	(0.197)	(0.679)
NSAID indication	−0.642	−0.477	1.227	−3.531
	(0.440)	(0.483)	(0.356)	(0.645)
Drug group dummies				
Group TFR	0.158	0.198	−0.183	−0.0559
	(0.364)	(0.421)	(0.444)	(0.425)
Group Price Cut	0.166	0.0600	−0.299	−0.750
	(0.280)	(0.290)	(0.295)	(0.321)
Drug group dummies after				
TFR × after	0.341	0.324	0.639	0.468
	(0.558)	(0.622)	(0.690)	(0.724)
Price Cut × after	0.232	0.290	0.113	0.659
	(0.233)	(0.188)	(0.186)	(0.354)
Reimbursement rule change in France				
TFR × after × France	−0.770	−0.814	−1.656	−1.627
	(0.541)	(0.542)	(0.694)	(0.772)
Price regulation in France				
Price Cut × after × France	−0.773	−0.737	−0.293	−0.328
	(0.353)	(0.338)	(0.291)	(0.384)
Country fixed effects	Yes			
Molecule fixed effects	Yes	Yes		
Year fixed effects	Yes			
Country year fixed effects		Yes	Yes	
Country-molecule fixed effects			Yes	
Country-molecule-year fixed effects				Yes
Observations	2,614	2,614	2,614	2,614
R^2	0.507	0.525	0.599	0.670

Notes: Standard errors in parentheses under each coefficient. Dependent variable is price in US$. Data for France, Germany, and the United States from 2003 to 2013.

decided many years in advance, and generic entry is constrained by patent protection. Danzon, Wang, and Wang (2005), Kyle (2007), and Danzon and Epstein (2008) have shown that delays in entry can be strategic, but we leave to future research the modeling of pricing and regulation in a fully dynamic setting. Moreover, all but one entry in our data are due to generics, and thus, they will not be affected by anticipation in the pricing decisions for branded drugs.

In France, the prices of drugs must be agreed upon by the regulator (CEPS) and are not determined under fully binding regulatory rules. Thus, it is possible that pharmaceutical companies obtain prices that maximize profits. Indeed, lobbying and

negotiations between the regulator and companies may lead to a price equilibrium not far from profit maximization equilibria (Grandfils 2008): it is known that the price approved by the regulator is often that proposed by the manufacturer in the first place through a procedure called "dépôt de prix" (Grandfils and Sermet 2006). This seems to signal that, despite regulation, the price remains a decision made primarily by the company.

We first present the notations and the standard case of price competition without price regulation, and then our model with price constraints is introduced with a brief discussion of the analogy with Nash bargaining models.

A. *Equilibrium without Price Regulation*

In the case of free price setting, which is the most relevant model for the United States and Germany but could also be the equilibrium outcome for France, it is well known how profit-maximizing prices should be set and how marginal costs can be identified if the shape of demand is known and a model of firm behavior is assumed (Berry, Levinsohn, and Pakes (BLP) 1995; Nevo 2001).

Denote by Π_{ft} the variable profit of multiproduct firm f in market t, where a market will be defined as a country-year. As fixed costs and other R&D costs are not affecting pricing decisions, a firm f selling all of the products in set F_f will maximize

$$\Pi_{ft} = \sum_{j \in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t, \mathbf{a}_t) - a_{jt}\,, \tag{1}$$

where p_{jt} is the price of drug j, a_{jt} is the detailing expense for drug j, c_{jt} is the constant marginal cost of product j, and $q_{jt}(\mathbf{p}_t, \mathbf{a}_t)$ is the quantity of drug j demanded given the vector $\mathbf{p}_t$ of all drug prices and the vector of detailing expenditures $\mathbf{a}_t$ for all J products.

As assumptions on firms' detailing choices are not necessary to identify marginal costs, we only consider the firms' profit-maximizing conditions in prices and assume that they compete in price à la Bertrand. Assuming that a pure-strategy Bertrand-Nash equilibrium in prices exists, the price of any product j sold by firm f must satisfy the first-order condition

$$q_{jt} + \sum_{k \in F_f} (p_{kt} - c_{kt}) \frac{\partial q_{kt}(\mathbf{p}_t, \mathbf{a}_t)}{\partial p_{jt}} = 0. \tag{2}$$

Then, with $\mathbf{1}_{\{j \in F_f\}} = 1$ if $j \in F_f$ and 0 otherwise, denoting by D_f the $J \times J$ diagonal matrix whose row ith element is $\mathbf{1}_{\{i \in F_f\}}$, by Q_{p_t} the $J \times J$ matrix whose row i column j element is $\partial q_{jt}(\mathbf{p}_t, \mathbf{a}_t)/\partial p_{it}$ and $\mathbf{q}_t = (q_{1t}, \ldots, q_{Jt})'$, $\mathbf{c}_t = (c_{1t}, \ldots, c_{Jt})'$, we obtain the usual formula valid for all firms f:

$$D_f(\mathbf{p}_t - \mathbf{c}_t) = -\left[D_f Q_{p_t} D_f\right]^{-1} D_f \mathbf{q}_t. \tag{3}$$

Thus, given demand estimates and the observation of prices, one can obtain price-cost margins per product and per year by solving the system of first-order conditions obtained above. This is the usual identification result of price-cost margins.[4]

An alternative strategy to identify the marginal costs of drugs is to use the long-term price equilibrium of drugs after the entry of generics under the assumption that margins are almost zero for those drugs. In this case, the marginal cost of a molecule can be thought of as the lowest price of its generic version (Grabowski and Vernon 1992). This approach is very robust in cases in which marginal costs are "constant" over time, as it does not rely on any demand specification, and when the lowest price of generics by molecule has converged, which does not seem to be the case for anti-ulcer molecules, where some generics have entered only recently.

B. *Price-Constrained Equilibrium*

Let us now consider the effects of price regulation on the pricing equilibrium. In France, regulation amounts to imposing some price ceiling on branded or generic drugs, either because of explicit constraints on prices (as in the case of the price cut rules in place after 2006) or because of implicit constraints imposed by the regulator to the industry. For simplicity, we consider a market t (which can represent a country and year) in which firms are potentially price constrained such that each price p_{jt} must belong to a set $\mathbf{\Omega}_{jt}$.

For branded drugs in France, some price ceiling $\overline{p}_{jt}$ for drug j may be imposed by the regulator when the drug is first authorized and revised over time, in which case $\mathbf{\Omega}_{jt} = [0, \overline{p}_{jt}]$. For generic drugs, French regulation also imposes a price ceiling that is a specific proportion of the price of the branded version. If for a generic drug j we denote by $b(j)$ the index of the branded version of the same molecule, the price constraint can then be written as $p_{jt} \leq \tau_{b(j)t} p_{b(j)t}$, where $\tau_{b(j)t}$ is a year-specific (and sometimes molecule-specific) factor set by the regulator; then, $\mathbf{\Omega}_{jt} = [0, \tau_{b(j)t} p_{b(j)t}]$. Until 2005, it was 55 percent at the time of generic entry, then reduced to 50 percent in 2006, 45 percent in 2009, and 40 percent in 2012. This percentage may be higher in exceptional cases approved by the regulator (high production costs, late entry for generic manufacturers, low price of the branded drug) but reducing to less than 10 percent the difference between the brand-name and the generic price.

Then, removing detailing arguments ($\mathbf{a}_t$) from demand to simplify notation, firm f's constrained price maximization, given other firms' pricing strategies, is

$$\max_{\{p_{jt}\}_{j \in F_f}} \Pi_{ft} = \sum_{j \in F_f} \left(p_{jt} - c_{jt}\right) q_{jt}(\mathbf{p}_t) \quad \text{subject to} \quad p_{jt} \in \mathbf{\Omega}_{jt}. \tag{4}$$

[4] Remark that if advertising is optimally chosen jointly with prices, first-order conditions in advertising lead to a full set of constraints between the matrix of advertising elasticities of demand, that of the price elasticity of demand and the ratio of advertising expenditures to revenue. However, using only the optimal pricing strategy allows us to identify marginal costs and is robust to the modeling of the supply side determination of advertising.

Assuming that a pure-strategy Bertrand-Nash equilibrium in prices exists, the necessary first-order conditions of the problem above are[5]

$$q_{jt} + \sum_{k \in F_f} (p_{kt} - c_{kt}) \frac{\partial q_{kt}(\mathbf{p}_t)}{\partial p_{jt}} = \lambda_{jt} \quad \forall j \in F_f, \forall f. \tag{5}$$

In the current regulatory framework in France, denoting by $\tilde{\lambda}_{jt}$ the Lagrange multiplier of the price cap constraint that may implicitly or explicitly be imposed by the regulator on branded drugs ($p_{jt} \leq \overline{p}_{jt}$) and on generic drugs ($p_{jt} \leq \tau_{b(j)t} p_{b(j)t}$), λ_{jt} is equal to the "true" Lagrange multiplier $\tilde{\lambda}_{jt}$, except in the case in which the manufacturer owns both the branded and generic drug version, in which case for the branded drug j, $\lambda_{jt} = \tilde{\lambda}_{jt} - \tau_{jt} \tilde{\lambda}_{g(j)}$, where $g(j)$ denotes the generic version of j.[6]

Before studying under which conditions one can identify marginal costs in this model of Bertrand-Nash competition with price constraints, it is interesting to compare this modeling to Nash bargaining. Our modeling reflects the French regulatory system, where firms propose prices through a procedure called "dépôt de prix" that the regulator accepts or rejects. However, our constrained Bertrand-Nash equilibrium can be identical to a Nash-in-Nash bargaining equilibrium in some cases. For example, if the regulatory objective is a function $W_t(\mathbf{p}_t)$ of prices (for example a consumer welfare measure), and if θ_{jt} is the bargaining parameter of the firm for drug j at t, assuming simple drug-by-drug bargaining for each firm, a Nash-in-Nash bargaining equilibrium in price would imply the following first-order condition (see Horn and Wolinsky 1988, Collard-Wexler, Gowrisankaran, and Lee forthcoming):

$$\frac{\partial \Pi_{ft}(\mathbf{p}_t)}{\partial p_{jt}} = q_{jt}(\mathbf{p}_t) + \sum_{k \in F_f} (p_{kt} - c_{kt}) \frac{\partial q_{kt}(\mathbf{p}_t)}{\partial p_{jt}} = \frac{1 - \theta_{jt}}{\theta_{jt}} \frac{\partial \ln \Delta_f W_t(\mathbf{p}_t)}{\partial p_{jt}} \Pi_{ft}(\mathbf{p}_t), \tag{6}$$

where $\Delta_f W_t(p_t)$ is the change in consumer welfare obtained by agreeing on the price p_{jt} with firm f. This first-order condition shows that there is always a bargaining parameter $\theta_{jt} \in [0, 1]$ such that $\frac{1 - \theta_{jt}}{\theta_{jt}} \Pi_{ft}(p_t) \frac{\partial \ln \Delta_f W_t(\mathbf{p}_t)}{\partial p_{jt}} = \lambda_{jt}$ since $\lambda_{jt} \geq 0$, implying that the constrained Bertrand-Nash equilibrium can be seen as the solution of a Nash-in-Nash bargaining model. If we impose constraints on the bargaining parameters θ_{jt}, for example to be identical across the products of a given firm, the bargaining model then imposes restrictions on the equilibrium prices. These restrictions will be more or less desirable depending on whether the bargaining model is a good approximation of the real world. One interesting difference is that a Bertrand-Nash equilibrium with price caps allows $\partial \Pi_{ft}(\mathbf{p}_t)/\partial p_{jt}$ to be zero when p_{jt} is lower than the price cap, while a Nash bargaining model with a firm-level bargaining parameter $\theta_{jt} = \theta_{ft} \in]0, 1[$ implies that it is always strictly positive.

[5] This is always possible provided that there exist N_j functions Ψ^n_{jt} such that $p_{jt} \in \Omega_{jt} \Leftrightarrow \Psi^n_{jt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t) \leq 0$ for $n = 1, \ldots, N_j$. Then, the first-order conditions are valid, and we have $\lambda_{jt} = \sum_{k \in F_f} \sum_{n=1}^{N_j} \Lambda^n_{kt} \partial \Psi^n_{kt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t)/\partial p_{jt}$, where Λ^n_{kt} is the Lagrange multiplier of the price constraint $\Psi^n_{jt}(\mathbf{p}_t, \mathbf{c}_t, \mathbf{q}_t) \leq 0$.

[6] This is the case only for the manufacturer (Sanofi) owning the branded drug Lanzor and several generic versions.

C. *Identification of Marginal Costs under Constrained Equilibrium in Prices*

In the case of a Bertrand-Nash equilibrium in prices, the first-order conditions of firm f can be written in matrix form as

$$D_f(\mathbf{p}_t - \mathbf{c}_t) = -\left[D_f Q_p(\mathbf{p}_t) D_f\right]^{-1} D_f(\mathbf{q}_t - \lambda_t), \tag{7}$$

where the elements of $\boldsymbol{\lambda}_t = (\lambda_{1t}, \ldots, \lambda_{Jt})$ are unknown (J_t allows the total number of products to vary with t).

Thus, with $\boldsymbol{\lambda}_t$ being unknown, even with known demand and prices, one cannot identify price-cost margins without further assumptions. Theoretically, the net effects of regulation on prices are ambiguous and will depend on all own- and cross-price elasticities of demand. A price reduction for one drug can affect other drugs that are not constrained because of cross-price elasticities of demand. Using first-order conditions, for each vector $\boldsymbol{\lambda}_t$, we have price-cost margins or marginal cost $c_{jt}(\boldsymbol{\lambda}_t)$ as a known function of $\boldsymbol{\lambda}_t$ (depending on demand and prices). Using the superscript f for the vector in which the elements corresponding to products not belonging to firm f are replaced by zeros, the first-order conditions can also be written as

$$\mathbf{c}_t^f(\boldsymbol{\lambda}_t^f) = \mathbf{p}_t^f + Q_p^f(\mathbf{p}_t)^{-1}(\mathbf{q}_t^f - \boldsymbol{\lambda}_t^f). \tag{8}$$

Thus, we cannot identify marginal costs without restrictions on $\boldsymbol{\lambda}_t^f$. Moreover, price constraints have spillover effects across drugs because the marginal cost of product i of firm f depends on the constraint of price j of firm f through $\boldsymbol{\lambda}_{jt}^f$ according to

$$\frac{\partial c_{it}^f(\boldsymbol{\lambda}_t^f)}{\partial \boldsymbol{\lambda}_{jt}^f} = -\left[Q_p^f(\mathbf{p}_t)^{-1}\right]_{i,j} \quad \text{for } i,j \in F_f, \tag{9}$$

where $[\,\cdot\,]_{i,j}$ stands for the row i, column j term of the matrix in the brackets.

However, adding some cost restrictions may allow identification. Our approach is similar to that of Goldberg (1995), who uses observations not subject to quotas in the car market to identify the effect of quantity constraints on exports.

Let us first assume that some unconstrained markets S are observed, such that

$$\boldsymbol{\lambda}_t = 0 \quad \text{for any } t \in S. \tag{10}$$

If we add the very simple cost restriction that the marginal costs of drugs should be the same across markets, whether price constrained or not, then we can easily identify the costs of drugs using only observations from unconstrained markets, provided that the drugs in constrained markets are also present and observed in other markets in which prices are freely chosen by firms. Assuming such cost equality across markets is of course too strong, but a similar idea can be applied and used for identification with more flexible cost restrictions across markets. We thus assume

that for any $t \in S$, there exists a vector of observed variables $\mathbf{z}$ such that, for all $t_0 \notin S$, the marginal costs satisfy for all j:

$$c_{jt} - c_{jt_0} = \left(\mathbf{z}_{jt} - \mathbf{z}_{jt_0}\right)'\delta + \omega_{jt} \quad \text{with} \quad E\left(\omega_{jt} \left| \mathbf{z}_{jt} - \mathbf{z}_{jt_0}\right.\right) = 0. \tag{11}$$

This assumption means that cost differences between markets in S and other markets satisfy the cost restriction above, such that the difference in costs across markets depends linearly on a set of observable differences $\mathbf{z}_{jt} - \mathbf{z}_{jt_0}$ and on unobserved, market-specific, additive, mean-independent shocks ω_{jt}.

Then, we can state the following proposition that allows us to identify the marginal costs for potentially constrained markets (see the proof in Appendix A).

PROPOSITION 1: *With Assumptions* (10) *and* (11) *and a market* $t_0 \notin S$, *marginal costs* $\mathbf{c}_{t_0}$ *are*

$$\mathbf{c}_{t_0} = \mathbf{p}_{t_0} + Q_p^f(\mathbf{p}_{t_0})^{-1}(\mathbf{q}_{t_0} - \boldsymbol{\lambda}_{t_0}), \tag{12}$$

where $\boldsymbol{\lambda}_{t_0}$ *is identified using the following moment condition*:

$$E\left(\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right)\right) = 0 \tag{13}$$

with vector $\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right)$ *defined by*

$$\begin{aligned}\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right) = {} & \left[\mathbf{p}_t - \mathbf{p}_{t_0} + Q_p(\mathbf{p}_t)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0}\right] \\ & + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} - \left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)'\delta\end{aligned} \tag{14}$$

provided that the matrix $E\left[\left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)', Q_p\left(\mathbf{p}_{t_0}\right)^{-1}\right]$ *has full rank.*

The proposition shows that identification is obtained when all prices are potentially constrained in market t_0, provided that the rank condition is satisfied: this intuitively means that there are enough goods markets that are unconstrained ($\sum_{t \in S} J_t$ is sufficiently large) and that the observable factors $\mathbf{z}$ that explain marginal cost differences are not collinear with the columns of the inverse of the price derivatives of demand or, equivalently, with the columns of the transpose of the matrix of cofactors of the price derivatives of demand. In a two-product case, this would mean that observable factors $\mathbf{z}$ are not in the space spanned by the vectors of the absolute values of own- and cross-price elasticities of the other product.[7]

Assumption (11) makes use of restrictions on marginal costs across markets. The identification power in our application will come from the fact that there can be relevant and robust cost restrictions across markets and products with constrained and unconstrained prices. As all drugs in France are potentially price constrained, our identification will come from restrictions on the marginal costs of the same drug across countries, some regulated (France) and others not price constrained (the

[7] In the 2×2 matrix case, the vectors $\mathbf{z}$ must not be in the space spanned by vectors $(q_2(1-q_2), q_1 q_2)'$ and $(q_1 q_2, q_1(1-q_1))'$.

United States or Germany). Restrictions across drugs within countries can also be used if one can identify years and products where prices should not be constrained, as in Lasio (2015), who exploits the removal from coverage and price regulation that happened in a different drug class in France.

In Appendix B, we provide further details on the empirical estimation counterparts of the moment condition (13) used for the estimation of parameters $\boldsymbol{\lambda}_t$ and thus of the marginal costs. In our application, we use a log-cost restriction based on drug-specific effects and costs in the United States and Germany. This is justified by the fact that the marginal costs are likely to have some market-specific component because they include packaging costs and transportation costs for each country. Denoting in the vector $\mathbf{z}_t$ the set of all these explanatory variables, we obtain estimates of the vector $\boldsymbol{\lambda}_t$ as the solution of a nonlinear least squares problem:

$$\boldsymbol{\lambda}_t = \underset{\boldsymbol{\lambda} \geq \mathbf{0}}{\arg\min} \left\| \left[I - \mathbf{z}_t (\mathbf{z}_t' \mathbf{z}_t)^{-1} \mathbf{z}_t' \right] \ln(\mathbf{c}_t(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t)) \right\|. \tag{15}$$

Appendix B shows that this problem has a closed-form solution when the cost restriction is in levels instead of logs.

III. Demand Model

To identify the shape of demand for pharmaceuticals in each market, we estimate a random utility discrete choice model, which has the advantage of being flexible enough to capture rich substitution patterns among differentiated products. The model we use explicitly accounts for heterogeneity in price sensitivity and preferences for certain drug characteristics, as in the study on demand for painkillers in Sweden by Björnerstedt and Verboven (2016). We assume that demand is static, hence we are not allowing for consumer learning as in Ching (2010a, b). Although we think that learning is important when we consider the choice of treatment for individual patients (Crawford and Shum 2005), it seems to be much less of a first-order concern when considering aggregate demand at the year level. Moreover, we believe that the uncertainty over drug quality for this market in this period is small, as all branded drugs entered before 2003 and the diffusion of generics was already quite high (different from Ching 2010a, b). For this reason, we use a static model and leave for future research a dynamic structural model.

A. *Random Utility Model*

Anti-ulcer drugs can be partitioned into three subclasses, which refer to different generations of products. Older H2 drugs are still widely used, even if PPI are considered superior products, while Prostaglandins are mainly prescribed for elderly patients. Differences also exist across molecules within a subclass. For instance, H2 anti-ulcer drugs are easily substitutable among one another, but there exist differences between, say, Cimetidine and Ranitidine, as a drug may be more appropriate to treat one condition or more suitable for one type of patient. Given a molecule, there is also product differentiation between branded and generic drugs. Even if almost therapeutically equivalent and (nearly) perfect substitutes (other than potential differences in the inert components, shape, and color of the drug that do not

compromise efficacy or curative effects for most patients), patients have historically perceived vertical differentiation.

The demand for drugs is driven by the prescription of physicians, the ministry recommendations, the preferences of patients, and by the role of pharmacists in the substitution toward generics. Our modeling approach does not disentangle the prescription and purchase process whereby the patient, the physician, and the pharmacist interact. With aggregate-level data such as those on sales that we use, we have no ability to identify each actor's preferences in our demand specification. This means that the preferences revealed by our demand model have to be interpreted with caution in terms of welfare. In particular, the price sensitivities may be the result not only of patients' out-of-pocket costs but also of the incentives for pharmacists and physicians to choose one product versus another.

With these caveats in mind, we specify a random utility for each drug $j \in \{1, \ldots, J_t\}$ for patient i in period t as

$$u_{ijt} = \sum_k \alpha_i^k x_{jt}^k - \beta_i^0 p_{jt} \mathbf{1}_{\{p_{jt} \leq \overline{p}_{jt}^{tfr}\}} - \beta_i^1 p_{jt} \mathbf{1}_{\{p_{jt} > \overline{p}_{jt}^{tfr}\}} + \zeta_{jt} + \varepsilon_{ijt}, \tag{16}$$

where x_{jt}^k are k drug characteristics including detailing a_{jt}, p_{jt} is the price of the drug, $\overline{p}_{jt}^{tfr}$ is the maximum reimbursement price of the drug (coming from the TFR rule), which by convention will be equal to $+\infty$ for drugs that are not subject to TFR reimbursement rules, ζ_{jt} are drug-period-specific effects, and ε_{ijt} is consumer i's deviation from the mean utility of taking drug j in period t. The preference parameters α_i^k, β_i^0, β_i^1 are allowed to vary across users i. Note that β_i^0 can be interpreted as the price sensitivity for all drugs not subject to the maximum reimbursement price or with prices below the maximum reimbursed level $\overline{p}_{jt}^{tfr}$, while β_i^1 is the price sensitivity of drugs subject to the TFR reimbursement rules when the price is above $\overline{p}_{jt}^{tfr}$, meaning that the reimbursement rate is lower for patients who have to pay the difference out of pocket.

The model is completed by the inclusion of an outside good, which corresponds to not taking any drug or using milder over-the-counter heartburn medications, with a normalized indirect utility $u_{i0t} = \varepsilon_{i0t}$.

We assume that each user chooses an element in the choice set $\{0, 1, \ldots, J_t\}$ according to maximum utility (16). This modeling of choices can be seen as a reduced form of a more complex mechanism by which patients, prescribers, and pharmacists interact. It is thus important that the preference parameters be heterogeneous across users i, because of unobserved variation in price-sensitivity that may be driven by the patient's choices and their reimbursement scheme; by the prescriber's choice, which may follow the insurance system's recommendation to prescribe cheaper drugs; and by the pharmacist, who also influences the choice of brand-name versus generic drugs. In particular, in France, the pharmacist's margins are regulated such that pharmacists have a preference for generic drugs. Indeed, pharmacists' margins decrease stepwise in the price of the drug (26.1 percent of the retail price if below 22.9€, 10 percent between 22.9€ and 150€, and 6 percent above 150€) and are larger in relative terms for generic than branded drugs (because the absolute margins of generics are equal to those of the branded drug), which may influence

their effort in generic substitution when facing the purchaser.[8] Heterogeneity in the preference parameters $(\alpha_i^k, \beta_i^0, \beta_i^1)$ across decision makers in this demand model is thus crucial to capture the aggregate shape of demand resulting from these heterogeneous situations.

We specify random coefficients $\left(\alpha_i^k, \beta_i^0, \beta_i^1\right) = (\alpha^k + \sigma_\alpha^k \nu_i^k, \beta^0 + \sigma_{\beta^0} \nu_i^{\beta_0}, \beta^1 + \sigma_{\beta^1} \nu_i^{\beta_1})$, where $\boldsymbol{\nu}_i = (\nu_i^k, \nu_i^{\beta_0}, \nu_i^{\beta_1})$ is distributed with PDF φ and summarize all the unobserved consumer characteristics, and $(\sigma_\alpha^k, \sigma_{\beta^0}, \sigma_{\beta^1})$ characterize how consumer tastes vary according to these unobserved characteristics. Indirect utility can then be redefined as $u_{ijt} = \delta_{jt} + \mu_{ijt} + \varepsilon_{ijt}$ with mean utility $\delta_{jt} = \sum_k \alpha^k x_{jt}^k - \beta_i^0 p_{jt} \mathbf{1}_{\{p_{jt} \leq \overline{p}_{jt}\}} - \beta_i^1 p_{jt} \mathbf{1}_{\{p_{jt} > \overline{p}_{jt}\}} + \zeta_{jt}$ and deviation $\mu_{ijt} = \sum_k \sigma_\alpha^k x_{jt}^k \nu_i^k - \sigma_\beta p_{jt} \nu_i^p$.

Under the assumption that ε_{ijt} is i.i.d. Gumbel (extreme value type I) distributed, the choice probability of alternative j by i is

$$s_{ijt}(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t) = \frac{\exp\left(\delta_{jt} + \mu_{ijt}\right)}{1 + \sum_k \exp\left(\delta_{kt} + \mu_{ikt}\right)}. \tag{17}$$

Then, the market share of product j, s_{jt}, is given by

$$s_{jt}(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t) = \int s_{ijt}(\mathbf{x}_t, \mathbf{p}_t, \boldsymbol{\zeta}_t)\, \varphi(\boldsymbol{\nu}_i)\, d\boldsymbol{\nu}_i \tag{18}$$

and own- and cross-price elasticities follow the classical formulas in a random coefficient logit.

As the data allow us to observe quantities and not market shares, we approximate the aggregate yearly market size denoted by M_t using a fixed coefficient logit version of this model with a nonlinear least squares calibration procedure similar to that in Huang and Rojas (2013, 2014). The method estimates the market size as the solution to the maximization of the fit of the model that does not specify the outside option but uses market shares relative to one inside good instead. Despite being based on a "misspecified" model (as it cannot be used in a logit model with random coefficients), we believe that this method provides a good approximation of the market size, which avoids making more ad hoc assumptions. In a market where total sales grow over time, it is particularly difficult to guess the potential market size, as we do not know if it is stable over time or grows like total sales or at what rate. The details are provided in Appendix C. The market sizes are such that the outside good's market share declines from 38 percent in 2003 to 17 percent in 2010 and then remains stable until 2013.

B. *Identification and Estimation*

Identification of this random coefficient logit model can be obtained with aggregate data using moment conditions between constructed demand shock variables ζ_{jt} and some instrumental variables (Berry 1994; BLP 1995). As in simple logit

[8] In France, pharmacists are independent and need to pay for their stocks. The regulated margins imply that the return to their capital stock is higher for generics because the ratio of margin to price of the drug is higher for generics.

demand models, one has to take into account the problem of endogeneity of prices correlated with unobserved demand factors ζ_{jt}. Previous estimation of demand models in pharmaceuticals has used instrumental variables regularly proposed in empirical IO, such as measures of the degree of competition (Stern 1996), of costs (Azoulay 2002), or prices for different markets or segments (Hausman instrumental variables, used for example in Azoulay 2002; and Berndt, Kyle, and Ling 2003). Other approaches use the characteristics of competing products (BLP 1995). Then, the estimation can be performed on aggregate data with generalized method of moments using the moment condition

$$E\left[\zeta_{jt}(\theta) \,|\, \mathbf{x}_t, \mathbf{w}_t\right], \tag{19}$$

where $\theta = (\alpha^k, \beta^0, \beta^1, \sigma_\alpha^k, \sigma_{\beta^0}, \sigma_{\beta^1})$ is the vector of parameters, and $\mathbf{w}_t$ are instrumental variables, for example cost shifters as in Nevo (2000). Instruments are crucial for the consistency and robustness of the estimates (Knittel and Metaxoglou 2014).

Using data from the hospital segment and from other countries, we define Hausman-style instrumental variables to instrument prices in the retail sector. For France, we use prices of anti-ulcer drugs sold in French and foreign hospitals (Germany, Italy, Spain, the United Kingdom, and the United States). However, the validity of such instruments relies on the fact that prices across markets are correlated because of common cost shocks and not because of common unobserved demand shifters (such as changes in scientific knowledge). Thus, we regress those prices on molecule dummies and country and year fixed effects and use the residuals as instrumental variables for the price in France. Controlling for country and time effects, we isolate the quality of each drug proxied by molecule dummies, which is the part of the price more likely to be correlated with demand unobservables: what remains should be correlated with the marginal cost of each drug. As additional instruments, meant to control for transport costs, we use the predictions from a regression of prices on interactions between firm dummies and exchange rates between US$ and, separately, euros, UK pounds, and Swiss francs (which are the currencies of most drug-producing countries). Finally, we include industry price indices and wages in each country.[9]

Our demand specification includes detailing expenses at the drug-year level. By doing so, we need to control for the potential endogeneity of this form of advertising, which is likely to be positively correlated with the price and may thus lead to biased coefficients. The instruments we use for prices can also be assumed to instrument for detailing expenses, as detailing benefits will clearly depend on the marginal cost of drugs. However, we also add instruments that should affect detailing independent of the costs of drugs: we use the average price of detailing per drug and its square. We obtain this average price using the detailing dataset that reports detailing expenses and the quantity of detailing "units" measured at the brand level in each country. Detailing units are defined as a direct contact in promotional activity by the pharmaceutical company with a physician. The detailing cost corresponds

[9] Data are from the French National Statistical Institute INSEE for France, the US Bureau of Labor Statistics for the United States, and Eurostat for Germany. We use the producer price index for all pharmaceuticals and wages in the manufacturing industry for France, the price index for anti-secretory/antispasmodics and wages in the pharmaceutical manufacturing industry for the US, and the price index for pharmaceutical preparations and wages in the manufacturing of basic pharmaceutical products and preparations for Germany.

to how much it would cost for a sales representative to visit a physician (details on these measures are in Section IC).

Following BLP (1999) and Reynaert and Verboven (2014), we use approximations of optimal instrumental variables (Chamberlain 1987), which are $E\left[\frac{\partial \zeta_{jt}(\theta)}{\partial \theta'} | \mathbf{x}_t, \mathbf{w}_t\right]$, to improve the efficiency of our estimation. Reynaert and Verboven (2014) show that in the case in which price equals marginal cost (perfect competition), we can approximate these optimal instrumental variables by using the predicted price $\hat{p}_{jt}$ from the regression $p_{jt} = \mathbf{x}_{jt}\gamma_x + \mathbf{w}_{jt}\gamma_w + \varepsilon_{jt}$ (where $\mathbf{w}_{jt}$ are country-specific cost shifters) and derivatives of the mean utility with respect to variance coefficients $\partial \delta_{jt}/\partial \sigma_\alpha^k$, $\partial \delta_{jt}/\partial \sigma_\beta$ (approximated by taking derivatives at the mean instead of the mean of derivatives). These nonlinear functions of exogenous variables and cost shifters are only approximations of optimal instruments in the case of perfect competition but prove to be quite informative even in the case of imperfect competition (Reynaert and Verboven 2014).

IV. Estimation Results

A. *Demand Estimation Results*

The results of the demand model are reported in Table 4.[10] The variables used in the demand specification are the brand type (branded or generic), molecule dummies, the number of side effects, and the number of formats. We also include a dummy for each of the main indications of anti-ulcer drugs: one for the eradication of *helicobacter pylori* (the major bacterial cause of ulcer), one for GERD (gastroesophageal reflux disease), and one for co-prescription with non-steroidal anti-inflammatory drugs (NSAID). Interactions between the branded dummy and the number of formats and the number of side effects are also included. These variables capture the most important product characteristics that influence demand and are the result of a specification search allowing for more interactions. We also control for detailing expenses for each drug-market, as previous research has documented the importance of advertising in affecting demand for pharmaceuticals, by complementing scientific information (Ching and Ishihara 2010; Ching et al. 2016), directing sales toward certain brands (business stealing), or even increasing sales for the whole market (Leffler 1981; Ching and Ishihara 2012; Anderson, Ciliberto, and Liaukonyte 2013; Anderson et al. 2016; Shapiro 2018). Detailing was found to be the advertising strategy most effective at increasing sales (Berndt et al. 1995, 1996; Berndt, Pindyck, and Azoulay 2003; Azoulay 2002; Arcidiacono et al. 2013 for anti-ulcer drugs) and at decreasing price elasticity (Rizzo 1999; Donohue and Berndt 2004).

Our results show that some molecules are preferred over others (as captured by molecule dummies not reported in Table 4 along with year dummies), reflecting perceived quality, which is higher for PPIs and lower for drugs based on older

[10] Coefficients are estimated through the simulated method of moments. We use 500 normalized Halton draws for the simulations used to compute the aggregated market shares. As Knittel and Metaxoglou (2014) and Dubé, Fox, and Su (2012) emphasize, we checked the robustness of the estimates across different sets of starting values, tight convergence criteria, and minimization algorithms. Our estimates are very robust to starting values and simulation draws once we use the optimal instrumental variables approximation.

Table 4—Estimation Results of Random Coefficient Logit Model

	France		Germany		US	
	Mean	Sigma	Mean	Sigma	Mean	Sigma
Price			−5.50	3.00	−4.06	2.97
			(1.50)	(1.87)	(1.36)	(1.52)
Price below TFR ($p_{jt} \times \mathbf{1}_{\{p_{jt} \leq \overline{p}_{jt}^{tfr}\}}$)	−6.95	6.62				
	(2.70)	(3.25)				
Price above TFR ($p_{jt} \times \mathbf{1}_{\{p_{jt} > \overline{p}_{jt}^{tfr}\}}$)	−18.73	6.83				
	(6.24)	(1.38)				
Detailing	0.27		0.17		0.05	
	(0.11)		(0.04)		(0.14)	
Branded	2.44	1.07	2.81	0.27	6.31	3.10
	(1.37)	(3.17)	(1.39)	(0.80)	(4.91)	(1.55)
Nb. formats	0.49		0.38		1.40	
	(0.30)		(0.25)		(0.55)	
Generic × nb. formats	1.90		1.48		0.02	
	(0.48)		(0.29)		(0.99)	
Nb. side effects	−0.25		0.02		−0.39	
	(0.07)		(0.19)		(0.14)	
Generic × nb. side effects	−0.05		−0.22		0.57	
	(0.19)		(0.19)		(0.79)	
Helicobacter indication	1.36		1.73		3.58	
	(0.26)		(0.42)		(0.78)	
NSAID indication	0.61		0.46		0.18	
	(0.29)		(0.16)		(0.35)	
GERD indication	−1.44		−1.52		−1.58	
	(0.35)		(0.25)		(0.42)	
Year fixed effects	Yes		Yes		Yes	
Molecule fixed effects	Yes		Yes		Yes	

Notes: Standard errors in parentheses under each coefficient. The Mean columns report the mean of random coefficients and the estimates of fixed coefficients. The Sigma columns report the estimates of the standard deviation of random coefficients.

molecules. Branded drugs are preferred over generics in all three countries, although the effect is not significant in the United States. As expected, in line with findings in the literature (Berndt et al. 1995, 1996, 2003; Azoulay 2002; and Arcidiacono et al. 2013), detailing positively affects demand, although not significantly for the United States. Having an indication for the eradication of *helicobacter pylori* (the major bacterial cause of ulcer) or for co-prescription with non-steroidal anti-inflammatory drugs (NSAID) is more valuable (except for Germany), while being indicated to treat gastroesophageal reflux (GERD) is less. The other measures of quality, namely the number of available therapeutic forms (formats) and the number of side effects, have the expected sign when they are significant.

We allow random coefficients for the price and for the branded dummy. Consumers are heterogeneous in their price sensitivity in the three countries (although the variance estimate is not very precise in the case of Germany) but less so in their preference for branded drugs, except in the United States where there is substantial and significant heterogeneity. In France, the price sensitivity is much larger when the price is above the reimbursement price (denoted $\overline{p}_{jt}^{tfr}$): in this case, the out-of-pocket

TABLE 5—OWN- AND CROSS-PRICE ELASTICITIES FOR MAIN DRUGS, 2009 (*France*)

	Branded						Generic	
Subclass	H2	H2	PPI	PPI	PPI	Prost.	H2	PPI
Company	Aptalis	Glaxo	AstraZ	AstraZ	Takeda	Pfizer	Mylan	Mylan
Molecule	Cimet.	Ranit.	Omep.	Esom.	Lanso.	Miso.	Ranit.	Omep.
Drug name	Tagamet	Zantac	Losec	Nexium	Takepron	Cytotec		
Tagamet	−6.96	2.84	0.003	0.23	0.05	0.01	0.02	0.14
Zantac	0.71	−5.62	0.002	0.19	0.04	0.01	0.02	0.13
Losec	0.00	0.00	−5.48	1.64	0.16	0.00	0.003	0.05
Nexium	0.00	0.00	0.19	−3.90	0.25	0.005	0.01	0.14
Takepron	0.00	0.00	0.13	1.73	−5.24	0.01	0.01	0.16
Cytotec	0.002	0.01	0.01	0.81	0.17	−2.45	0.02	0.16
Ranit. Mylan	0.001	0.003	0.02	0.68	0.13	0.01	−3.00	0.23
Omep. Mylan	0.001	0.002	0.04	0.91	0.16	0.01	0.03	−3.68

Notes: Each column is the price elasticity of demand for the drug in the first row with respect to the drug named in the first column. Company names: Glaxo is GlaxoSmithKline. AstraZ is AstraZeneca. Molecules: Ranit. is Ranitidine; Omep. is Omeprazole; Esom. is Esomeprazole; Lanso. is Lansoprazole; Miso. is Misoprostol.

cost of the drug for the patient is increased by the difference between p_{jt} and $\overline{p}_{jt}^{tfr}$; thus, it is understandable that patients are much more price sensitive. The heterogeneity in price sensitivity is however similar across the different reimbursement regimes as suggested by the similar magnitude of the sigmas associated with the two price coefficients.

From this estimated demand model, the mean own-price elasticity across products and years for France is −3.6 and ranges from −13 to −1 across products. Overall, generics show lower own-price elasticities than branded drugs (−2.9 versus −5.7): this can be interpreted as a consequence of the incentive for generic substitution for pharmacists as explained before. Indeed, the pharmacists' margins on each drug are regulated as a percentage of the price of the branded drug, and the margin is required to be the same in absolute terms for the generic and branded versions. As a consequence, pharmacists earn a higher ratio of margin to price on generics, and the difference increases with the price of the drug. This may explain why the own-price elasticity of branded drugs can be larger in absolute value than the own-price elasticity of the generic. Table 5 reports own- and cross-price elasticities for the main drugs in France in 2009. Price elasticity tends to be higher for drugs subject to the TFR rule with a price above the maximum reimbursement price (Tagamet, Zantac, and Pepcidine after 2006), which comes from the additional copayments for patients in this case. Consistent with medical evidence, anti-ulcer drugs are highly differentiated (low cross-price elasticities) and are mostly substitutable within subclasses (H2, PPI, Prostaglandins). This is clear from the magnitude of the sales gained by drugs in each class if same-class competitors raise prices (Zantac-Tagamet, Nexium-Losec-Takepron). PPI branded drugs are those that usually have the largest cross-price elasticities with other drugs, showing that the branded and even generic PPI drugs are close substitutes, but they also have quite significant cross-price elasticities with H2 drugs. However, the substitutability relationships go beyond ATC subclass or molecule: patients are willing to switch to the best-seller Nexium if the price of Zantac increases, instead of buying the closest alternative, i.e., one of its generics, such as Mylan's Ranitidine.

Online Appendix Table B1 shows that elasticities for higher quality and more recent branded drugs (in the PPI subclass) tend to decrease gradually over time. Older drugs (H2 and Prostaglandins) display increasing or fairly stable own-price elasticities.

B. *Structural Estimation of Margins and Costs*

As reported in Table 1, several regulatory rules may have imposed price cuts on both branded and generic drugs since 2006. Table 1 lists the drugs that were potentially affected by these constraints. Moreover, even before 2006, prices were subject to regulation, as they were set by the regulator (CEPS). However, a potential price cap may not be binding, as the counterfactual price decision of a firm not subject to such a constraint could have led to the same choice. Our identification method allows us to determine whether constraints are binding. Once demand is estimated, we use our supply-side model to obtain price-cost margins and marginal costs and test whether price constraints are actually binding.

Using the structural supply models, we can estimate price-cost margins ignoring price regulation and assuming that firms can freely set their prices (Section IIA) and under price-constrained profit maximization (Section IIB). We assume that firms' pricing is not constrained in the United States or in Germany. In France, we allow prices to be possibly constrained at any time, but several regulatory events likely increased the constraints on the price setting of drugs in certain years. For example, the anti-ulcer drugs Losec, Lanzor, and Takepron fall under the potential price cut rule after 2006, either because of generic entry in the corresponding subclass (Lansoprazole for Lanzor and Takepron) or because generics had been on the market for long enough (Omeprazole generics for Losec). Given these regulatory rules, it is interesting to check whether estimates of constraints show that the prices of these drugs were indeed more downward constrained after 2006. As explained in Section IIB, we assume that the log marginal cost of drugs in France is the sum of a time-invariant drug effect and a drug-specific additive linear function of the log costs in the United States and Germany, plus an uncorrelated additive deviation. Formally, we implement a nonlinear least squares estimator of $\boldsymbol{\lambda}_t$ as shown in equation (15) as

$$\boldsymbol{\lambda}_t \;=\; \underset{\boldsymbol{\lambda}\geq \mathbf{0}}{\arg\min} \sum_{j=1}^{J} \omega_{jt}(\boldsymbol{\lambda})^2, \tag{20}$$

where $\omega_{jt}(\boldsymbol{\lambda}_t)$ is the residual of the linear regression

$$\ln c_{jt}(\boldsymbol{\lambda}_t) \;=\; \rho_j + \rho_{US} \ln c_{jt}^{US} + \rho_{GR} \ln c_{jt}^{GR} + \omega_{jt}(\boldsymbol{\lambda}_t). \tag{21}$$

As our estimation method is a constrained nonlinear least squares (NLLS) one, the asymptotic distribution of $\boldsymbol{\lambda}_t$ is nonstandard. We use the method of Wang (1996) to compute the asymptotic distribution and use the asymptotic law of $\boldsymbol{\lambda}$ to test $\lambda_{jt} > 0$

TABLE 6—NLLS ESTIMATES OF λ_{jt} (*Normalized by Market Size*)

	All products		Products with λ_{jt} significantly positive				
	Number of products		Number of products		λ_{jt}	s_{jt}	$\sum_j s_{jt}$
Year	Branded	Generics	Branded	Generics	Mean	Mean	Mean
2003	12	11	1	5	0.00026	0.00105	0.00628
2004	12	27	1	9	0.00029	0.00183	0.01826
2005	12	28	1	3	0.00027	0.00084	0.00334
2006	12	30	2	5	0.00023	0.01168	0.08176
2007	12	37	3	10	0.00033	0.00904	0.11756
2008	12	36	1	6	0.00030	0.00127	0.00891
2009	12	47	0	11	0.00031	0.00138	0.01519
2010	12	50	1	11	0.00083	0.00318	0.03816
2011	12	62	2	26	0.00152	0.00634	0.17764
2012	12	74	4	36	0.00210	0.00626	0.25034
2013	11	83	3	47	0.00288	0.00858	0.42907

for each product.[11] Table 6 reports the constrained nonlinear least squares estimates of the λ_{jt} parameters for all products j in France from 2003 to 2013 after normalization by the market size. With some abuse of notation, we replace $q_{jt} - \lambda_{jt}$ with $M_t(s_{jt} - \lambda_{jt})$ in equation (8) such that the scale of parameters λ_{jt} is the same as that of market shares s_{jt}. In Table 6, we have the total number of branded and generic products in France, the corresponding number of products with λ_{jt} significantly different from zero and their mean. The last two columns report the mean and the sum of market shares of products with a corresponding λ_{jt} that is significantly different from zero.

The results show that not all products are significantly constrained by regulation and in particular that many more products have a significant λ_{jt} estimate starting in 2011. There are more products with a significant λ_{jt} in more recent years, and they represent a larger total market share, due to more generic products having entered the market and potentially because more molecules became subject to price cuts, following the entry of generics in the PPI subclass. Note that products that have a λ_{jt} not significantly different from zero are still directly constrained by regulation if one product owned by the same firm has a λ_{jt} that is significantly positive. Furthermore, even if none of the λ_{jt} values of a firm is significantly different from zero, the prices chosen by this firm are affected indirectly by the regulatory constraints on other products through the equilibrium conditions. The magnitude of the λ_{jt} estimates is between one-fourth and one-half of the market share of the corresponding product, suggesting that they should have an economically significant impact on equilibrium prices. Counterfactuals will confirm that the regulatory constraints on prices are economically significant.

[11] Denoting by $\boldsymbol{\lambda}_t^0$ the true parameters, Wang (1996) shows that $\boldsymbol{\lambda}_t - \boldsymbol{\lambda}_t^0$ converges in distribution to the optimal solution of the problem

$$\min_{\boldsymbol{\lambda}} \left\{ (\boldsymbol{\lambda} - \boldsymbol{\lambda}^0)' \boldsymbol{\Omega} (\boldsymbol{\lambda} - \boldsymbol{\lambda}^0) - 2 (\boldsymbol{\lambda} - \boldsymbol{\lambda}^0)' \xi \right\} \quad \text{subject to} \quad \boldsymbol{\lambda} - \boldsymbol{\lambda}^0 \geq 0,$$

where ξ is an $N(0, \boldsymbol{\Omega})$ random vector, and where $\boldsymbol{\Omega}$ is the asymptotic limit of the variance covariance matrix

$$\boldsymbol{\Omega} = \hat{\sigma}^2 \left[\frac{\partial \omega_t(\boldsymbol{\lambda})'}{\partial \boldsymbol{\lambda}} \frac{\partial \omega_t(\boldsymbol{\lambda})}{\partial \boldsymbol{\lambda}} \right]^{-1} \quad \text{with} \quad \hat{\sigma}^2 = \frac{1}{J} \sum_{j=1}^{J} \omega_{jt}(\boldsymbol{\lambda})^2.$$

We thus use the asymptotic law of $\boldsymbol{\lambda}$ to test $\lambda_{jt} > 0$ for each product.

Table 7—Average Price-Cost Margins by Molecule (*France*)

		Not accounting for price regulation (%)			Accounting for price regulation (%)		
Subclass	Molecule	All drugs	Branded	Generic	All drugs	Branded	Generic
H2	Cimetidine	52	15	62	41	14	47
	Ranitidine	30	24	32	23	19	24
	Famotidine	28	10	36	20	9	26
	Nizatidine	18	18		14	14	
PPI	Omeprazole	29	22	30	22	14	23
	Esomeprazole	43	24	50	31	15	37
	Lansoprazole	39	20	45	29	14	34
	Pantoprazole	43	20	47	33	14	36
	Rabeprazole	45	18	60	33	13	43
Prost.	Misoprostol	47	47		37	37	
Combi.	Bismuth/ Antibiotic	27	27		21	21	

Notes: Margins as a percentage of price. Empty cells indicate that there is no generic version of the molecule named in the corresponding row. When not taking into account price regulation, we infer price cost margins as if firms were free to choose prices.

We now turn to the corresponding marginal cost estimates $c_{jt}(\boldsymbol{\lambda}_t)$ using equation (8). First, the linear regression (21) of $\ln c_{jt}(\hat{\lambda}_t)$ on the fixed effects ρ_j, $\ln c_{jt}^{US}$ and $\ln c_{jt}^{GR}$ shows that $\rho_{US} = 0.05$ and $\rho_{GR} = 0.71$ and are both statistically significant at the 1 percent level, while fixed effects are also statistically significant, and the R^2 of the regression is 0.88.

As a means of comparison, we also estimate the marginal costs denoted $c_{jt}(\mathbf{0})$ that we would obtain under the assumption that prices are not constrained (Section IIA). Table 7 reports average price-cost margins by molecule. It shows the estimated margins ignoring or accounting for price regulation. The margins are between 9 percent and 37 percent for branded drugs and 23 percent to 47 percent for generics when accounting for price regulation. Some generics show much higher margins than their corresponding branded versions. This is not surprising: it is common wisdom in the industry that generic firms display lower marginal costs than branded manufacturers, and this is especially true for older molecules (Arcidiacono et al. 2013). Markups also vary substantially across molecules. Examining margins drug by drug also uncovers interesting variation across drugs: the difference is important for some PPI drugs for the full period, while for others, it is small initially but grows over time, showing that constraints mattered more over time, and this is consistent with the explicit price cuts in the period 2006–2012 for these molecules.

Unsurprisingly, the estimates of λ_{jt} were often larger and (more) significant in the years when the price cuts were introduced for each molecule. This translates into larger differences between constrained and unconstrained margins. This effect persists for certain PPI drugs, while it fades out for others, meaning that the regulated prices in later years are closer to what the unregulated prices for these drugs would have been, presumably due to stronger competition from other drugs. Some significant differences in the markups under the two models shed light on the spillover effects of regulation on drugs not directly subject to price cuts, showing how the prices chosen by manufacturers are affected by the regulatory constraints on close PPI substitutes through the equilibrium conditions. The effect on drugs in

the H2 subclass seems to prevail in the beginning of the period, when Cimetidine and Ranitidine became subject to TFR, which determines the maximum reimbursement that a patient can obtain. Our demand estimates show that the TFR regulation affected the shape of demand, and these results suggest that the CEPS may have placed additional pressure on prices for these drugs when introducing the maximum reimbursement price with the TFR rule.

Table B2 in the online Appendix displays the annual averages of the estimated price-cost margins (as a percentage of price) for the constrained model and the free pricing model. The average price-cost margin is 6 to 8 percentage points lower when taking into account the price constraints until 2009 and 10 to 15 percentage points lower from 2010 to 2013. This difference is larger for generics than for branded drugs. The average margins for branded drugs are smaller as a percentage of the price than for generics.

These comparisons show how much one would overestimate margins, or underestimate costs, if not taking into account price constraints. However, they do not show what the counterfactual price difference would be if there were no pricing regulation. It is certainly possible that margins under the two models are not estimated to be very different given the observed equilibrium prices, while the counterfactual free pricing margins would be very different because the prices of substitute drugs would change. We turn to the counterfactual analysis in the next section.

V. Counterfactuals

In this section, we analyze counterfactual scenarios in which we change the regulatory environment of drug price setting in France. Holding the shape of demand unchanged, we first study the case in which drug prices would no longer be constrained by the regulator but freely chosen by firms. We expect prices to increase, as we found that price constraints are sometimes binding, but the magnitude of the effect on prices, demand, and expenses is unknown. Then, we investigate another counterfactual in which the regulator would set price caps through an external reference pricing policy. In both counterfactuals, not only can we evaluate the changes in prices, demand, and expenses, but we can also compute the consumer surplus evaluated by the preferences revealed by our demand model. Of course, as patients' revealed preferences are affected by the health insurance system, this measured surplus may not represent the true benefit for society, whose willingness to pay for drugs is mismeasured by the prescriber/patient's price sensitivity.

To evaluate the variance due to the estimation of demand parameters and marginal costs in the counterfactuals, we simulate confidence intervals drawing in the distribution of the estimated demand parameters and then simulate all counterfactuals for each bootstrap sample. This allows us to construct 95 percent confidence intervals (which are not always centered around the counterfactual simulations at the mean parameter estimates).

A. *Counterfactuals of Free Pricing in France*

Using marginal costs estimated while taking into account constraints on prices, we assess the impact of the constraints by simulating the counterfactual market

equilibrium under free pricing. Specifically, we estimate the price equilibrium with free pricing for branded drugs and maintain the current regulatory rules for generics that cap the price of generics as a fixed proportion of the price of the corresponding branded drug (which, on average across drugs and years, results in generics having approximately one-half the price of their branded version).[12] We thus solve the following Bertrand-Nash price equilibrium in which all firms f choose prices such that

$$\max_{\{p_{jt}\}_{j\in F_f}} \Pi_{ft} = \sum_{j\in F_f} \left(p_{jt} - c_{jt}\right) q_{jt}(\mathbf{p}_t) \tag{22}$$

subject to

$$p_{jt} \leq \tau_{b(j)t} p_{b(j)t} \quad \text{only if } j \text{ is a generic}$$

while imposing that prices cannot be smaller than marginal costs ($p_{jt} \geq c_{jt}$). Then, the simulated confidence intervals on the counterfactual results tell us how statistically significant the counterfactual results are compared to the observed values. The results on the confidence intervals on price changes are reported in online Appendix Tables B3 and B4.

Our results show that the observed prices for branded drugs under the current regulation tend to be lower than prices in the counterfactual scenario in which price regulation is removed (percentage changes are reported in Table B3, where negative numbers mean that observed prices are lower than counterfactual prices). Observed and counterfactual prices begin to diverge more in the years when the price cuts were introduced. This is true for all PPI drugs (those directly affected by the price cuts since 2006), which show fairly close observed and counterfactual prices in the early years of the sample but larger and significant differences subsequently. For example, the gap is already significant in 2005 for Losec and tends to increase once its closest PPI competitors also become subject to the price cuts. A closer examination of the effects by drug shows how some drugs are almost unaffected, while others are and strongly so, even though they are not directly subject to the price cuts. The price decline due to regulation for generics (displayed in Table B4) is always smaller than for branded drugs, in relative terms and even more in absolute terms, although the magnitude of the effect is heterogeneous across molecules.

Comparing those counterfactual effects on price with the triple difference effects estimated in Table 3, we see that the difference-in-differences estimates of price cuts on the prices of drugs in France would strongly overestimate the impact of this regulation on prices, as we find estimates of -33 percent (column 4 of Table 3, coefficient of "price cut" $\times$ After $\times$ France). Evaluating the average counterfactual price change due to regulation on the set of drugs subject to the "price cut" rule (Losec, Lanzor, and Takepron since 2006; Nexium since 2008; Pantozol since 2009; and Pariet since 2012), we find instead a 6 percent lower price due to the price

[12] This percentage evolved over time: until 2005, at entry, the generic price could not exceed 55 percent of the branded regulated price. The share was reduced in later years: 50 percent in 2006, 45 percent in 2009, and 40 percent in 2012.

constraints, ranging from a 1 percent decline in 2006 up to a 17 percent decline in 2013, when all PPI molecules became subject to the regulation.

The regulatory constraints on prices entail an overall positive albeit relatively modest effect on quantities consumed (these results are not reported to save space). The effect arises primarily from an increase in branded drug consumption compared to generic consumption. Price effects are thus not encouraging generic use (and even reduce it at the end of the period) but are instead increasing the sales of branded drugs. Price cuts are also steering consumption toward certain drugs. The higher counterfactual free prices would result in lower sales for most PPI drugs in later years, in favor of cheaper, older, and less effective H2 drugs. However, the blockbuster Losec, despite a higher counterfactual price, would benefit from the higher prices of its closest competitors (Nexium and Takepron) and sell even more than under the regulated lower price. In terms of total expenses, the price regulation has small effects until 2010, and then leads to a 5 to 6 percent decrease in 2011 and 2012 and up to 10 percent in 2013, when the large price-reducing effect of regulatory constraints made it possible to reduce total expenditures on anti-ulcer drugs.

Hence, while reducing prices on high-quality PPI drugs encourages their consumption at the expense of older and less-effective H2 drugs, it is doing so at the expense of their generic versions, which also see their prices reduced but by less in absolute and percentage terms. Generic manufacturers are substantially harmed by price cuts, as profits would be 23 percent higher in a free pricing scenario, compared to an increase of only 15 percent for branded firms. The regulation of prices thus reduces one layer of differentiation between branded and generic drugs, the difference in price. Without this wedge, the preference for the branded drugs prevails (as captured by our demand estimates), and generics lose sales in favor of the now cheaper, yet still more expensive, branded versions. The mechanism is similar to the segmentation identified in previous research (Frank and Salkever 1997; Ching 2010b), with the price difference between the branded and the generic drug acting as a differentiation device that regulation reduces.

Table 8 shows the savings due to price regulation compared to the counterfactual situation of free pricing. Overall, the current regulatory rules generated savings of $150 million for the anti-ulcer market in France over the period 2003–2013, i.e., approximately 2 percent of total expenditures for this market. The savings materialize mostly at the end of the period, driven by lower expenditures on PPI drugs, which more than compensate for the slightly higher expenses on H2 drugs. Without additional policy changes in the regulation of prices, the free pricing of drugs would lead to an increase in drug expenditures. We also find that consumer surplus is higher under the constrained price equilibrium than under free pricing. Table 8 shows that the increase is 1.1 percent in 2003, 1.3 percent in 2006, 2.6 percent in 2009, and 10.2 percent in 2012, primarily and unsurprisingly due to greater utilization of sometimes cheaper drugs and of branded drugs preferred by consumers. However, these results must be taken with caution both because of the interpretation of consumer welfare, as measured by the revealed preferences of our demand models, and because the confidence intervals on overall consumer surplus are quite wide and, for example, range from 4.2 percent to 20.4 percent around the point estimate of 15.4 percent.

It is interesting to compare the previous results to those from a fully free pricing equilibrium, in which generics are no longer subject to a cap on their price in the

Table 8—Counterfactual Savings and Surplus from Free Pricing

		2003	2006	2009	2012	2003–2013
Subclass	Molecule					
H2	Cimetidine	−913	−239	−28	−83	−2,120
	Ranitidine	−894	−578	−384	1133	−4,007
	Famotidine	−37	8	18	42	134
	Nizatidine	−4	1	3	6	5
PPI	Omeprazole	−469	1,916	2,111	13,091	59,149
	Lansoprazole	666	616	−468	3,853	9,973
	Pantoprazole	82	333	1,710	1,203	17,495
	Esomeprazole	1,672	−1,067	1,095	4,488	44,213
	Rabeprazole	407	389	−832	28,273	27,918
Prost.	Misoprostol	−277	−239	−181	−145	−2,375
Combi.	Bismuth/ Antibiotic					53
Total		234	1,140	3,044	51,860	150,439
Subtotal	Branded	382	1,903	4,107	30,389	88,242
	Generics	−148	−763	−1,064	21,471	62,197
Consumer surplus change		+1.1%	+1.3%	+2.6%	+10.2%	+15.4%

Notes: Savings are in 1,000 US$. Negative numbers indicate increased expenditures compared to observed. Surplus change is as a percentage of the surplus under the current regulation.

form of a percentage of the branded price (not reported). As expected, all generics increase their prices in this counterfactual scenario. More interesting, branded manufacturers respond by setting prices only slightly higher than those observed under the current price regulation. This branded behavior reflects a relatively lower and highly heterogeneous brand preference in France than in other countries, presumably driven by the strong incentives for pharmacists to substitute branded drugs with generics despite the likely preference of patients for branded drugs. As a consequence of the smaller price difference between the branded and the generic, demand shifts from generic to branded drugs, while the aggregate effects on expenditures are similar to those obtained under the cap on generics. Ultimately, allowing generics to freely set their prices seems to lead to a larger shift in sales to branded drugs.

B. *Counterfactuals of External Reference Pricing in France*

External reference pricing was introduced in France in 2004 as one criterion used by the CEPS in setting the price of new drugs. It only applies to drugs that entered the French market after this date and to none in the anti-ulcer market until 2013. The rationale behind this policy is to reward innovative drugs (i.e., those with a significant therapeutic improvement, measured by ASMR values of 1, 2, or 3 on a 1–5 scale) by guaranteeing a 5-year price at the same level as observed in other European countries. In specific, the price of innovative drugs cannot be lower than the lowest price observed in the reference countries, which are Germany, Italy, Spain, and the United Kingdom. For non-innovative drugs (i.e., with ASMR values of 4 or 5), the goal in price setting is to generate savings vis-à-vis an existing comparator drug. For these drugs, external reference pricing may also be used by the CEPS, as long as it is able to restrict prices.

We thus perform counterfactual simulations with an explicit cap on prices $\overline{p}_{jt}^{ref}$ for drug j in year t that is defined as the lowest price among the prices in year $t-1$ in France, Germany, Italy, Spain, and the United Kingdom (provided that it is above the marginal cost). For the two innovative drugs in our sample, Losec and Nexium (ASMR values of 2 and 3), the cap is the average price across the four reference countries in 2003 for the years 2004–2008 and in 2008 for the years 2009–2013. This definition of external reference prices implies that observed prices tend to be, on average, higher than these hypothetical external reference prices from 2003 to 2005 but lower after 2006, which is when the French regulator introduced price cut rules. For generics, we maintain the current regulation that caps their price as a percentage of the branded drug (as described in Section VA). We thus solve the following external reference pricing equilibrium in which all firms f choose prices such that

$$\max_{\{p_{jt}\}_{j\in F_f}} \Pi_{ft} = \sum_{j\in F_f} (p_{jt} - c_{jt})\, q_{jt}(\mathbf{p}_t) \tag{23}$$

subject to

$$p_{jt} \leq \overline{p}_{jt}^{ref} \quad \text{if } j \text{ is a branded drug (Reference Pricing);}$$

$$p_{jt} \leq \tau_{b(j)t} p_{b(j)t} \quad \text{if } j \text{ is a generic.}$$

We also require all prices to exceed marginal costs ($p_{jt} \geq c_{jt}$), and we solve for the Bertrand-Nash equilibrium.

Online Appendix Tables B5 and B6 report the confidence intervals on price changes from the current observed prices to the equilibrium prices under the external reference pricing caps, as a percentage of counterfactual prices. Overall, the counterfactual prices under the external reference pricing rule are lower (and in some years significantly so) than the observed prices under the current regulation. Hence, despite the introduction of price cuts in France, which lower prices with respect to a free pricing scenario, external reference prices as defined above would further reduce prices. However, the differences across drugs are substantial. Old H2 and Prostaglandin drugs, which enjoy lower prices in the reference countries, would be forced to set a lower price in all years. Of the innovative drugs, only Nexium (with a price cap significantly higher than the observed price), would set a consistently higher price than the observed one (but usually lower than the reference cap) except in 2013; the difference for Losec is less sizable. Other PPI drugs would benefit from the higher prices for the two closest competitors, also being able to increase their prices, although not always. The downward effect on the prices of generic drugs under this counterfactual regulation (reported in Table B6) is consistent across all molecules and years and often very strong, with observed prices sometimes being more than twice the counterfactual prices. Demand would on average increase, driven by higher sales of now much cheaper H2 drugs at the expense of more innovative and more effective PPI drugs, with only Nexium and Losec limiting their losses despite their higher prices thanks to their recognized superior quality. Unsurprisingly, given their much lower price, the big winners from external

Table 9—Counterfactual Savings and Surplus with External Reference Caps

		2004	2006	2009	2012	2004–2013
Subclass	Molecule					
H2	Cimetidine	−608	−365	−103	675	−652
	Ranitidine	−339	−1,323	−951	4,534	2,525
	Famotidine	83	−114	−78	95	−61
	Nizatidine	−4	−15	21	31	38
Subtotal H2						
PPI	Omeprazole	−6,241	−17,175	−6,751	43,880	34,593
	Lansoprazole	−292	4,997	−2,596	25,622	81,427
	Pantoprazole	4,985	8,565	4,663	20,743	109,294
	Esomeprazole	1,210	851	5,180	9,162	68,689
	Rabeprazole	1,531	4,340	3,995	21,829	99,573
Subtotal PPI						
Prost.	Misoprostol	45	−363	−153	637	−113
Combi.	Bismuth/ Antibiotic					382
Total		371	−601	3,226	127,209	395,695
Subtotal	Branded	7,594	20,025	24,687	27,216	267,745
	Generics	−7,222	−20,626	−21,462	99,993	127,950
Consumer surplus change		+6%	+9%	+24%	+30%	+39%

Notes: Savings are in 1,000 US$. Negative numbers indicate increased expenditures relative to observed. Surplus change is as a percentage of the counterfactual estimated surplus.

reference pricing are generics, the sales of which increase significantly. Then, despite the much lower price level, on average, expenditures under external reference pricing regulation would not differ substantially from those observed under the current regulatory rules in the early years, as reported in Table 9: the increased demand would slightly outweigh the effect of lower prices until 2009. After 2009, however, external reference pricing would lead to savings, with total expenditures declining by up to 50 percent at the end of the period. Moreover, in this counterfactual scenario, expenditures on generics are higher, except in 2012–2013, when demand increases but the price is so low that it generates savings relative to current price regulation. As a result, Table 9 shows that the counterfactual consumer surplus would be much larger than the observed one (+39 percent with confidence interval [+37 percent, +47 percent]) and would increase over time.

These counterfactual simulations suggest that different regulatory rules may lead to different equilibrium levels of demand and prices but that they may also determine winners and losers. Branded PPI drugs, which can generally set a higher price, sell less, to the benefit of H2 drugs and to their generics, when they become available. Thus, this rule seems to encourage generic sales, but it imposes strong pressure on their margins (for some, the price is estimated to decrease to the marginal cost). Therefore, it would fulfill one of the objectives of the French regulator, to increase generic penetration, but it is unclear what the long-run effects might be if generics were priced at the level of marginal costs. To assess these long-run effects on the entry and exit of drugs, however, we would need a dynamic model, something which is outside the scope of our paper.

We also simulate the counterfactual in which generics are also subject to external reference pricing, with caps based on generic prices in other countries. Our simulations suggest that this rule would lead to generic prices very close to and sometimes

higher than the observed values. Branded prices would be similar to those estimated in the previous counterfactual, except for a downward pressure that these more expensive generics seem to be placing on some PPI branded drugs at their entry on the market. Thus, in this scenario, generics would enjoy a larger markup but to the detriment of their sales. However, the effect does not seem to simply be a transfer from generics to branded, as total demand declines, expenditures increase, and consumer surplus is estimated to be lower than the observed value, especially later in the period.

VI. Conclusion

We develop a structural model of demand and supply to study the impact of the price regulation of anti-ulcer drugs in France. Using IMS Health data on retail sales of anti-ulcer drugs for the period 2003-2013, we first estimate demand for France, the United States, and Germany, using a flexible model that accommodates the consumer heterogeneity prevalent in this market. The results confirm that anti-ulcer drugs are strongly differentiated and that consumers are highly heterogeneous in their price sensitivity. Consistent with the previous literature, brand-name drugs are preferred to their generic versions, and detailing increases demand. We use these demand estimates to investigate the effect of price regulations on firms' pricing behavior. We model the pricing decisions of firms as being potentially constrained by these regulatory rules in the form of price caps. Identification relies on observing the same products in a regulated market (France) and in markets under free pricing (the United States and Germany) and uses cost restrictions for the same drugs across markets. The results show that not all products are significantly constrained by regulation and that, unsurprisingly, this is more common in the years when the French regulator (CEPS) introduced price cuts for branded drugs based on the availability of generics, which directly affected six anti-ulcer drugs in our sample after 2006.

To quantify the effects of regulation, we perform a counterfactual simulation of the equilibrium without any price regulation for branded drugs, with generics still subject to the cap based on the price of their branded versions. We find that recent regulation was effective in reducing prices, especially for high-quality drugs, and this encouraged their consumption. However, it did so at the expense of their generic versions, which also experienced a decline in price but one that is lower in both absolute and percentage terms. With a smaller wedge between the branded and generic prices, the preference for the branded drugs captured by our demand estimates shifts demand from generics to the now cheaper, yet still more expensive, branded versions. Nevertheless, price constraints generate some modest savings, on average 2 percent of total expenses for the full 11-year period. Counterfactuals also show that consumer surplus increases thanks to regulation, due to greater utilization of cheaper and preferred branded drugs.

We simulate a second counterfactual equilibrium under an external reference pricing policy (similar to that introduced in France but never used for the drugs in our sample), which caps the price in France with a reference depending on the price of the same drug in Italy, Germany, the United Kingdom, and Spain. We find that prices would decline even more and demand would increase but less than proportionally, leading to additional savings. Furthermore, generic penetration would

increase (one of the objectives of the French regulator), driven by very small generic margins. While this short-run effect would increase consumer surplus, it is unclear what the long-run effects on the entry and exit of generics could be.

Our work demonstrates the importance of accounting for regulation in estimating market power or welfare and raises concerns about the ability of regulators to predict ex ante the equilibrium effects generated by different regulatory rules. While we believe that this may be a general message and not something that is induced by the specific setting that we study, we are aware of some limitations of our work. For example, the results produced by our static model do not take into account dynamics in demand, such as learning effects, or dynamics in supply, and only provide a short-term evaluation of the effects of the policy. An evaluation of the long-run effects of a regulation should take into account its effects on research and development and the entry of drugs, both branded and generic, topics that we leave for future research.

Appendix

A. *Proof of Proposition 1*

With Assumptions (10) and (11), c_t is identified using price-cost margins solutions (3) in all unconstrained markets S. Then, using (8) and

$$\mathbf{c}_{t_0} = \mathbf{p}_{t_0} + Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0} - Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0},$$

we have

$$\begin{aligned}\mathbf{c}_t - \mathbf{c}_{t_0} &= \mathbf{p}_t - \mathbf{p}_{t_0} + Q_p(\mathbf{p}_t)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0} + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} \\ &= \left(z_t - z_{t_0}\right)'\delta + \boldsymbol{\omega}_t.\end{aligned}$$

Denoting

$$\begin{aligned}\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right) &= \left[\mathbf{p}_t - \mathbf{p}_{t_0} + Q_p(\mathbf{p}_t)^{-1}\mathbf{q}_t - Q_p(\mathbf{p}_{t_0})^{-1}\mathbf{q}_{t_0}\right] \\ &\quad + Q_p(\mathbf{p}_{t_0})^{-1}\boldsymbol{\lambda}_{t_0} - \left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)'\delta\end{aligned}$$

using (11), the true $\boldsymbol{\lambda}_{t_0}$ should satisfy the moment condition for all $t \in S$:

$$E\left(\boldsymbol{\omega}_t\left(\delta, \boldsymbol{\lambda}_{t_0}\right)\right) = 0.$$

The identification rank condition is that the matrix $E\left[\frac{\partial \boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})}{\partial \delta}, \frac{\partial \boldsymbol{\omega}_t(\delta, \boldsymbol{\lambda}_{t_0})}{\partial \boldsymbol{\lambda}_{t_0}}\right] = \left[\left(\mathbf{z}_t - \mathbf{z}_{t_0}\right)', Q_p^{-1}(\mathbf{p}_{t_0})\right]$ has full rank $J_{t_0} + \dim(\delta)$. As J_t is the number of goods in market t, and the expectation of the moment condition is over goods and markets $t \in S$, we also need that $J_{t_0} + \dim(\delta) \leq \sum_{t \in S} J_t$ which will be often the case. ∎

B. *Estimation of Constrained Marginal Costs*

Given the demand estimates that determine the demand shape $Q_p(\mathbf{p}_t)$, given a vector λ_t, the marginal cost vector is

$$\mathbf{c}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t) \;=\; \mathbf{p}_t + A(\mathbf{p}_t)\,(\mathbf{q}_t - \boldsymbol{\lambda}_t),$$

where $A(\mathbf{p}_t) \;=\; \sum_f Q_p^f(\mathbf{p}_t)^{-1}$ is composed of block of the inverse demand derivatives by firm $Q_p^f(\mathbf{p}_t)$ ($Q_p^f(\mathbf{p}_t)$ is the matrix on demand derivatives $Q_p(\mathbf{p}_t)$ where all rows and columns not corresponding to firm f products are replaced by zeros). Remark that the cost vector $c_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t)$ implicitly depends on demand estimates through the estimated $A(\mathbf{p}_t)$.

We impose a cost restriction that can be written with a given vector of observable variables $\mathbf{z}_t$, with a known transformation $f(\cdot)$, as

$$f(\mathbf{c}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t)) \;=\; \mathbf{z}_t\gamma + \boldsymbol{\omega}_t$$

with

$$E[\boldsymbol{\omega}_t \,|\, \mathbf{z}_t] \;=\; 0.$$

We thus look for (λ_t, γ) that satisfy this moment condition whose empirical counterpart leads us to the following minimization problem:

$$\min_{(\boldsymbol{\lambda}_t, \gamma)} \left\| f(\mathbf{c}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t)) \;-\; \mathbf{z}_t\gamma \right\|,$$

using the usual L_2 norm, which leads to the following solution:

$$\boldsymbol{\lambda}_t \;=\; \arg\min_{\boldsymbol{\lambda}} \left\| \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right] f(\mathbf{c}_t(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t)) \right\|,$$

where we replaced γ by the ordinary least squares (OLS) estimates of the projection of $f(\mathbf{c}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t\ \mathbf{q}_t))$ on $\mathbf{z}_t$. The vector $\boldsymbol{\lambda}_t$ will be the solution of the same problem with a minimization over $\lambda \;\geq\; 0$ if the constraint is known to be of the form $p_{jt} \;\leq\; \overline{p}_{jt}$.

In the particular case where $f(\cdot)$ is the identity, we obtain a closed-form solution for $\boldsymbol{\lambda}_t$ as is shown below.

As the residual $\boldsymbol{\omega}_t$ of the orthogonal projection of $\mathbf{c}_t$ on $\mathbf{z}_t$ is

$$\begin{aligned}
\boldsymbol{\omega}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t) \;&=\; \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right] \mathbf{c}_t(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{q}_t) \\
&=\; \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right] \left(\mathbf{p}_t + A(\mathbf{p}_t)\,\mathbf{q}_t\right) - \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right] A(\mathbf{p}_t)\,\boldsymbol{\lambda}_t \\
&=\; \tilde{\boldsymbol{\omega}}_t(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t) - B(\mathbf{p}_t, \mathbf{z}_t)\,\boldsymbol{\lambda}_t\ ,
\end{aligned}$$

where $\tilde{\omega}_t$ is the residual of the orthogonal projection of $\left(\mathbf{p}_t + A\left(\mathbf{p}_t\right)\mathbf{q}_t\right)$ on z_t and $B\left(\mathbf{p}_t, \mathbf{z}_t\right)$ the residual of the orthogonal projection of $A\left(\mathbf{p}_t\right)$ on z_t:

$$\tilde{\omega}_t\left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right) = \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right]\left(\mathbf{p}_t + A\left(\mathbf{p}_t\right)\mathbf{q}_t\right),$$

$$B\left(\mathbf{p}_t, \mathbf{z}_t\right) = \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right]A\left(\mathbf{p}_t\right).$$

The problem is thus

$$\min_{\boldsymbol{\lambda}_t} \boldsymbol{\omega}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right)'\boldsymbol{\omega}_t\left(\boldsymbol{\lambda}_t, \mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right)$$

whose first-order condition leads to

$$-\tilde{\boldsymbol{\omega}}_t'\left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right)B\left(\mathbf{p}_t, \mathbf{z}_t\right) + \boldsymbol{\lambda}_t'B\left(\mathbf{p}_t, \mathbf{z}_t\right)'B\left(\mathbf{p}_t, \mathbf{z}_t\right) = 0$$

and thus the following solution:

$$\boldsymbol{\lambda}_t = \left[B\left(\mathbf{p}_t, \mathbf{z}_t\right)'B\left(\mathbf{p}_t, \mathbf{z}_t\right)\right]^{-1}B\left(\mathbf{p}_t, \mathbf{z}_t\right)_t'\tilde{\boldsymbol{\omega}}\left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right),$$

which exists and is unique if $B\left(\mathbf{p}_t, \mathbf{z}_t\right)'B\left(\mathbf{p}_t, \mathbf{z}_t\right)$ is invertible. Thus, $\boldsymbol{\lambda}_t$ is the OLS coefficient of the projection of $\tilde{\omega}\left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right)$ on $B\left(\mathbf{p}_t, \mathbf{z}_t\right)$.

Remark also that if the price constraint is known to be a price ceiling as $p_{jt} \leq \overline{p}_{jt}$ then we know that λ_{jt} is the Lagrange multiplier associated with this constraint and should be nonnegative. In this case $\boldsymbol{\lambda}_t = \arg\min_{\boldsymbol{\lambda}\geq\mathbf{0}}\left\| \left[I - \mathbf{z}_t\left(\mathbf{z}_t'\mathbf{z}_t\right)^{-1}\mathbf{z}_t'\right] \times f(\mathbf{c}_t(\boldsymbol{\lambda}, \mathbf{p}_t, \mathbf{q}_t))\right\|$ which has also a closed-form solution if $f(\cdot)$ is linear. Actually when $f(\cdot)$ is the identity,

$$\boldsymbol{\lambda}_t = \left[\left[B\left(\mathbf{p}_t, \mathbf{z}_t\right)'B\left(\mathbf{p}_t, \mathbf{z}_t\right)\right]^{-1}B\left(\mathbf{p}_t, \mathbf{z}_t\right)_t'\tilde{\boldsymbol{\omega}}\left(\mathbf{p}_t, \mathbf{z}_t, \mathbf{q}_t\right)\right]_+$$

where $\left[\cdot\right]_+$ means that each nonpositive element of the vector is replaced by zero.

C. *Market Size Approximation*

In our demand model we normalize the utility of the outside good and model the aggregate market share of each drug as a function of different characteristics. As usual, one needs to take a stand on the potential market size, in order to use observed sales quantities q_{jt} and market size M_t to obtain measures of market shares as $s_{jt} = q_{jt}/M_t$. As the market size is not observed and we do not have an obvious definition of the potential market for anti-ulcer drugs, we approximate market size per year using the insights of Huang and Rojas (2013, 2014) in the simple case of the fixed coefficient logit version of our model. In the logit case, we can simply use the market share equations of the logit to obtain, by difference between two goods j and j',

$$\ln q_{jt} - \ln q_{j't} = \sum_k \alpha^k\left(x_{jt}^k - x_{j't}^k\right) - \beta\left(p_{jt} - p_{j't}\right) + \zeta_{jt} - \zeta_{j't}$$

which does not depend on any market size assumption and allows to identify α^k, β, by two stage least squares with the usual instrumental variables. In a second stage we estimate the market sizes M_t that minimize

$$\min_{M_t} \sum_t \left(\sum_k \left[\hat{\alpha}^k(M_t) - \hat{\alpha}^k \right]^2 + \left[\hat{\beta}(M_t) - \hat{\beta} \right]^2 \right)$$

where $\hat{\alpha}^k(M_t)$ and $\hat{\beta}(M_t)$ are the 2SLS coefficient estimates of the following equation:

$$\ln q_{jt} - \ln \left(M_t - \sum_{k=1}^{J} q_{kt} \right) = \sum_k \alpha^k x_{jt}^k + \beta p_{jt} + \zeta_{jt}.$$

D. *Additional Tables*

TABLE A1—DESCRIPTIVE STATISTICS ON PROMOTIONAL EXPENSES PER YEAR (*France*)

		Promotional activity		Sales		
Country	Drugs	Detailing expenses	Other expenses	Total std. units	Total revenue	Mean number of molecules
France	Generics	23	30	661,180	261,695	7.7
	Branded	78,650	88,735	468,729	510,157	11.5
Germany	Generics	30,787	33,127	1,183,946	451,724	10.7
	Branded	75,382	77,203	228,744	258,760	15.1
United States	Generics	58	742	872,036	297,256	12.0
	Branded	572,960	933,106	665,647	2,166,961	16.0

Notes: All expenses are in 1,000 US$ per year. Other expenses include meetings, journal advertising, clinical trials, mails. Direct To Consumer Advertising is forbidden in France.

TABLE A2—SUMMARY STATISTICS FOR THE UNITED STATES

	Number of drugs			Quantity	Market share (%)		Price	Revenue
Year	All	Branded	Generics	(1,000 std units)	Branded	Generics	(US$/std unit)	(1,000 US$)
2003	66	15	51	2,025,452	67	33	0.88	4,034,679
2004	70	17	53	1,875,573	64	36	1.10	4,091,029
2005	71	17	54	1,795,266	63	33	1.14	4,113,685
2006	72	16	56	1,894,541	62	38	0.97	4,329,421
2007	73	17	56	1,925,183	59	41	1.08	4,437,844
2008	76	16	60	1,845,887	51	49	1.01	4,264,548
2009	84	17	67	1,919,050	45	55	1.12	4,116,476
2010	88	16	72	1,956,464	35	65	1.40	3,841,758
2011	95	16	79	2,013,497	29	71	1.31	3,414,379
2012	100	17	83	1,788,713	28	72	1.34	3,111,634
2013	112	16	96	1,757,347	25	75	1.67	3,014,056

Notes: Price is the average price per standard unit in US$ across all drugs. Revenue is total revenue of the class.

Table A3— Summary Statistics for Germany

Year	Number of drugs			Quantity	Market share (%)		Price	Revenue
	All	Branded	Generics	(1,000 std units)	Branded	Generics	(US$/std unit)	(1,000 US$)
2003	90	18	72	922,774	40	60	1.63	1,024,096
2004	83	15	68	963,578	44	56	1.75	1,153,481
2005	90	15	75	1,118,165	49	51	1.65	1,225,519
2006	92	15	77	1,222,855	43	57	1.56	1,087,547
2007	86	15	71	1,413,689	32	68	1.56	1,040,938
2008	90	13	77	1,611,532	29	71	1.49	1,079,989
2009	113	12	101	1,791,422	17	83	1.25	953,712
2010	116	12	104	1,979,180	10	90	1.26	800,048
2011	109	13	96	2,176,575	5	95	2.02	662,924
2012	111	13	98	2,377,741	4	96	1.97	643,147
2013	106	13	93	2,541,186	3	97	2.01	591,608

Notes: Price is the average price per standard unit in US$ across all drugs. Revenue is total revenue of the class.

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