

Online Appendix
for
Reference Pricing as a Deterrent to Entry:
Evidence from the European Pharmaceutical Market

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A Dataset Construction

In this section I describe the IMS MIDAS database, the variables it contains, its missing data, and how the missing data is imputed. I also provide a brief description of additional data sources.

A.1 Dataset Characteristics

Coverage

We have data for 27 European countries, giving us almost complete coverage of the European Economic Area.¹ The data usually covers sales through the retail channel (i.e. pharmacies) and the hospital channel for 48 quarters, starting in 2001 (either Q2 or Q3) and ending in 2013 (either Q1 or Q2). Several countries have partial data. The most common data issues concern missing years, missing hospital sales data, and having sales data in Euro instead of local currency (for countries where the Euro is not the local currency). The problem with having data in Euros instead of the local currency is that IMS converted the data using a fixed exchange rate (for the entire 12-year sample) instead of a quarter-specific exchange rate. This affects makes the sales figures unreliable in countries that do not have a fixed exchange rate with the Euro. Table E.2 describes our data coverage by country.

Since the problem that we study concerns spillover effects across countries, it is imperative that we try to include in our sample as many countries as possible. Ultimately, we end up discarding 2 of the 27 countries in our sample due to unresolvable data problems: Czech Republic and Slovakia. These two countries had non-Euro currencies with fluctuating exchange rates during our sample period, which means that their sales data is unreliable. We include them in the reduced form results that do not involve prices, but drop them from the structural analysis.

Twelve of the remaining 25 countries have some data issue: Denmark, Estonia, Greece, Ireland, Latvia, Lithuania, Luxembourg, Netherlands, Portugal, Romania, Slovenia, and Sweden. Some of these have are minor data issues that do not affect the analysis. Denmark and Slovenia report retail and hospital sales jointly, which limits our ability to separate retail and hospital products in some robustness checks, but leaves our main specification unaffected. Denmark and Estonia only have sales in Euros, but their currency was tightly pegged to Euro throughout the duration of our sample period, so the conversion leaves the sales figures unaffected. Slovenia also only reports sales in Euros, and for the first 3 years of our sample data its currency was not pegged to the Euro. However, the Slovenian Tolar fluctuated considerably less than the Czech and Slovak currencies, so we ultimately decided to keep the data in the sample (without additional corrections).

The remaining data issues concern the lack of hospital sales data in 9 countries, and missing years for Netherlands and Sweden. We address these problem by performing a series of imputation steps that allow us to keep all these countries in the sample. These steps are detailed in section A.3.

¹We are missing data for Cyprus, Iceland, Lichtenstein, and Malta. Croatia is also a current member of the EEA, but only entered in 2015, which is outside our sample.

Variables

In its raw form, the data is stored as excel files, one for each country. The variables contained in each file are described in Table E.1. Each product is identified by a combination of active ingredient (molecule), marketing firm, therapeutic class (defined by the ATC4 classification), product name (both international and country-specific), form, strength, and package.² Besides revenue and quantity sales, the data provides a few additional characteristics: whether the product is a prescription or an over-the-counter medication, the launch date, the estimated patent expiration date, the product type (brand or generic), protection status, and licensing information.

Main Sample Identification

Our main sample of drugs includes products that satisfy the following requirements:

- First launched on or after January 1st, 1995
- Patent expiration occurred on or after January 1st, 2003 (giving at least one full year of potential observations)
- At least one launch in a country on or after January 1st, 2002
- The firm selling the product is classified as the originator firm (i.e. the first recorded launch date of the molecule is associated to that firm)
- At least 50% of the launches occurred prior to patent expiration (this condition eliminates a handful of products that did not receive EU-wide approval)
- The product satisfies at least one of these three conditions:
 - It received approval from the EMA
 - It received at least one approval using the Mutual Recognition Procedure
 - It is sold in at least 11 countries as of December 31st, 2012

This gives us a sample of 481 products.

A.2 Construction of Therapeutic Classes

Broadly speaking, our therapeutic classes are defined at the ATC3 level, which corresponds to a therapeutic-pharmacological subgroup within one of the 14 main systems (Table E.3). In addition, we aggregate classes that contain classes of products that share the same molecules (e.g. D7A&D7B|CORTICOSTEROID, TOPICAL, PLAIN & COMBO is a therapeutic class that combines both plain and combination corticosteroids), and classes of products that have broad applications (e.g. oncologics, which are separated in three large classes: cytotoxics, hormonals, and

²For more details on the ATC classification, please see <http://www.ephmra.org/classification>.

targeted therapies). We also separate classes of products that have similar pharmacological profile, but are used to combat different diseases (e.g. J5B, which includes non-HIV antivirals, is separated in J5B1, Viral Hepatitis; J5B3, Herpes Antivirals; J5B4, Flu Antivirals; and J5B5,9, Other Respiratory Antivirals). Finally, we make a few adjustments for complex diseases with therapies that come from a broad spectrum of therapeutic areas (e.g. Multiple Sclerosis includes Beta interferons (the L3B2 ATC4 code), plus a handful of drugs from other classes, mainly monoclonal antibodies).

A.3 Imputation of Missing Data

There are three types of missing data instances that we need to account for. First, some products are missing some years of data, or have negative sales recorded in a small number of instances. Second, a handful of countries are partially or completely missing data for the hospital channel. Third, the Netherlands and Sweden have missing data for a few years in the initial part of the sample.

Imputation of Missing Years of Data for Individual Products

Occasionally, we see some years of missing data or negative sales for some drugs. We treat negative sales as missing when we do this imputation.

There are three instances in which this can happen. First, we may see sales recorded in non-consecutive years (e.g. 2003 and 2005), but not in years in between (e.g. 2004). Second, in some cases we observe a launch date, but no sales (e.g. a product is recorded as having being launched in 2002 but first sale is recorded in 2004). Finally, in other cases we see a product disappear.

In the first instance, we use simple linear interpolation to fill in the missing years. In the second instance, we adjust the launch date instead of the sales variable, and replace it with the date when sales are first recorded. In the last instance we apply no adjustment and simply assume that the product exited exogenously (i.e. the firm did not choose to withdraw the product). We manually checked all these cases, and they all fall in one of two categories. Either the product had been declining in sales for a few years, until it disappeared; or the product was subject to a forced withdrawal by the EMA (we note these instances in Table E.5).

Imputation of Hospital Missing data

Ireland, Lithuania, Portugal, and Romania are missing hospital sales for a few years at the beginning of the sample, but all have at least a few years of hospital sales available. Estonia, Greece, Latvia, Luxembourg, and the Netherlands are missing hospital sales entirely. We impute hospital sales using information contained in other years and other countries.

Wherever possible, we calculate drug-country specific share of sales through the hospital channels, and use it to project sales for missing years. This strategy is only available for countries that

have partially missing hospital sales. For countries that are missing hospital sales entirely, we use the drug-specific share of hospital sales.

The imputation works in two steps. First, we calculate the share of hospital sales s_{ij}^h (or s_i^h , for the drug-specific share) using data from other years and countries. Then, hospital sales are equal to

$$S_{ijt}^{\text{Hospital}} = S_{ijt}^{\text{Retail}} \cdot \frac{s_{ij}^h}{1 - s_{ij}^h}$$

We do the same imputation for quantity sold and revenue sales.

For countries that are missing hospital sales in all years, we cannot impute sales of products that are sold exclusively through the hospital channel. This is a shortcoming of the data, but unfortunately, not one that we can address in any way.

Imputation of Missing Years of Data for Countries

The only information we have on the fully missing years for Sweden and the Netherlands is what products are sold during those years, which we can deduct using the launch date.³ To impute quantity sold we use the demand primitives implied by our structural demand system. To impute prices, we simply use the first available price.

A.4 Additional Data Sources

Additional data sources are reported in Table E.4. We use approval dates from the EMA and the Heads of Medicines Agencies to calculate launch delays. We use data from the Global Burden of Disease study to calculate market size for the demand system. We use exchange rates to transform sales reported in local currencies to Euros. Finally, we use data on GDP and population to run some simple reduced-form checks.

All these additional data sources are publicly available (see the links in Table E.4, which are accurate as of November 20th, 2017).

B Institutional Details

In this section we present some evidence on the impact that the introduction of the EMA had on delays. We also include the reference pricing matrices that we constructed for each year.

B.1 The Effect of the European Medicines Agency on Delays

Prior to 1995, pharmaceutical companies seeking to sell prescription drugs in Europe needed to separately apply for marketing approval in each country. The EMA was founded in 1995 in an effort to reduce the administrative burden faced by companies.

³If a product that was available in a missing year disappeared before it could be recorded in our data we will not be able to observe it. However, product withdrawals are rare.

Figure E.1 plots the number of new molecular entities approved each year since 1995. We distinguish between approvals obtained directly from the EMA, through the centralized procedure, approvals obtained through the Mutual Recognition Procedure (which was also installed after the EMA was introduced), and other approvals. We can see that within a few years virtually every drug is using one of the two main procedures introduced by the EMA. In recent years, drugs are also increasingly reliant on the centralized procedure, rather than the Mutual Recognition Procedure.

In the data, we observe a market decrease in the average launch delay before and after the founding of the EMA (Figure E.2). A variety of factors likely contribute to this decrease. First, the new centralized approval procedure should reduce the fixed cost of entry in each country. This should be especially helpful for small low-income countries. Second, it should reduce the time necessary to receive approval. Third, it may reduce the protectionist tendency of member states to prevent entry from firms whose drugs compete with drugs produced by domestic manufacturers.

The clear discontinuity in delays between the pre-1995 sample, and the post-1995 sample is what motivated our choice to restrict the analysis to drugs that were first launched after January 1st, 1995.

B.2 External Reference Pricing Functions, 2002-2012

Even though external reference pricing functions differ significantly across countries, only a few changes occurred to these functions over the period between 2002 and 2012, We list them in Table E.6. For completeness, we also report reference pricing functions for all countries and years in Figure E.3.

C Additional Reduced-Form Evidence

In this section we present some additional reduced-form evidence on the correlation between market outcomes and delays. Part of this analysis motivated our choice of functional forms for the demand and price system.

We also discuss some additional evidence of heterogeneous delays across drugs and countries by looking at delays for innovative products, and across therapeutic classes.

C.1 Delays Across Countries

Figure E.4 contains a series of maps that display the fraction of drugs launched in each country within the first 6 years of the marketing approval date. We select a balanced subsample of 142 drugs that received approval through the centralized procedure on or before December 31st, 2006 (out of the 481 in our main sample) to ensure that we can observe the first 6 years of their life-cycle in our data.

Several interesting patterns emerge. First, Eastern Europe is lagging behind the rest of the continent. 6 years after the original approval of a product, Bulgaria, Estonia, Latvia, and Lithuania

are the nations with the lowest diffusion rates, followed by Romania and Hungary.⁴ Second, even though the remaining European countries achieve similar diffusion rates by year 4, entry patterns differ considerably even between countries with similar market size and income level. For example, the UK has market size and prices similar to France and Italy, but almost all drugs are available in the UK within 12 months, whereas France and Italy only achieve a comparable diffusion rate after 3 years. The same comparison can be made between Austria and Belgium, or Sweden and Switzerland.

C.2 Correlation between Quantity, Prices, and Delays

In the reduced-form section of the paper we show that price levels and market size appear to be inversely correlated with delays across countries. In this section we present some additional evidence of the correlation between delays and market outcomes (quantity sold and price). We look for evidence that products with relatively higher price (or quantity) are launched earlier.

We test this hypothesis by first isolating within-country variation in demand and price. We do this by regressing quantity sold and price on drug and country fixed-effects:

$$\begin{aligned}\ln(q_{ijt}) &= \theta_i^q + \gamma_j^q + \varepsilon_{ijt}^q \\ \ln(p_{ijt}) &= \theta_i^p + \gamma_j^p + \varepsilon_{ijt}^p\end{aligned}$$

In these regressions i indexes products, j indexes country, and t indexes periods. The residuals ε_{ijt}^q and ε_{ijt}^p reflect both a fully stochastic component (reflecting uncertainty that the firm cannot observe in advance), as well as information that is not reflected in the drug and country fixed effect, but that the firm sees in advance. For example, if Italy had a disproportionately large number of diabetes patients, we would expect ε_{iITAt}^q to be large for insulin and other diabetes medication.

To check whether within-country variation in market outcomes is correlated with firm behavior, we check whether the residual is correlated with delays and order of entry, by running the following linear regressions:

$$\begin{aligned}y_{ij} &= \gamma_j^y + \beta_q \varepsilon_{ijt^0}^q + \varepsilon_{ij}^y \\ y_{ij} &= \gamma_j^y + \beta_p \varepsilon_{ijt^0}^p + \varepsilon_{ij}^y\end{aligned}$$

As independent variables y_{ijt} we use both the entry delay in months, and the order of launch (i.e. the rank of the country j in the launch sequence of drug i). As dependent variable we use the

⁴The Netherlands also appear to have very low diffusion rates. Rather than reflecting a real empirical phenomenon, this result is caused by missing data. Our coverage for the Netherlands starts in 2007 and includes only retail sales (and not sales through the hospital channel), which means that many products never appear in the data because they are only available in hospitals or they had already exited the market in 2007. Unfortunately, the sample selected to draw this figure draw heavily on this earlier cohort of drugs, exacerbating the problem. In reality, the Netherlands have one of the highest (and fastest) diffusion rates, comparable to those of Germany or Sweden.

value of the residual in the launch year t^0 .⁵

We report our results in Table E.7. We find that $\varepsilon_{ijt^0}^q$ is negatively correlated with both months of delay as well as order of launch, meaning that within each country, products with low demand tend to enter later.

Surprisingly, we do not find the same result for $\varepsilon_{ijt^0}^p$. There are two possible reasons to explain this phenomenon. First, it could be that $\varepsilon_{ijt^0}^p$ only contains information that the firm does not observe in advance. In this case, we would not expect the firm's actions to reflect anything that is unknown about price prior to entry. Second, it is possible that there is not enough within-country, cross-drug variation in price. In the data, we note that a price regression on drug and country fixed effects achieves a coefficient of variation of 0.98, meaning that these two variables soak up a lot of variation. The equivalent regression on sales has a much lower coefficient (around 0.77), which suggests that there may be more variation in quantity that the firm can act upon.

These regressions also serve to motivate our choice of demand and price functions. In our demand functions we include drug-country fixed effects, since our regressions suggest that using a separate set of fixed effects may fail to capture important variation that is known to the firm. In our price functions however, we include drug and country fixed effects separately. The regression results in this section suggest that this is enough to capture the variation in price that is relevant for firms' actions.

C.3 Delays for Innovative Drugs

We also look at whether innovative drugs experience fewer delays. To classify drugs according to their innovative status we rely on work by Lanthier et al. (2013), who classify drugs approved by the FDA in three categories: first-in-class, advance-in-class, and addition-to-class. First-in-class drugs are the first to be approved within their respective class. Advance-in-class are not the first to be approved within the class, but received a priority review designation, which usually means that the drug has the potential to represent a major advance in treatment. All other drugs are considered to be addition-to-class drugs.

We apply this classification to our drugs and calculate average delays for all matched drugs by country.⁶ Figure E.5 shows our results. We find some evidence that innovative drugs tend to experience fewer delays, although the difference is only a couple of months. Interestingly, the effect is much smaller in Eastern European countries.

C.4 Delays across therapeutic classes

To check whether there are significant differences in delays across therapeutic classes, we run a regression of delays on country fixed effects and class fixed effects. Since most classes only have

⁵When we do not observe sales in the launch year (because launch occurred before 2002), we use the residual from the first available year.

⁶We are able to match 285 out of the 481 drugs in our sample. The difference is due to the fact that the FDA and the EMA sometimes approve different drugs, the different time-span our paper and Lanthier's paper cover, and the fact that our merge on molecule string may be imperfect.

a handful of products, we aggregate them at the ATC1 level, which indicates the main system for which drugs are used (see Table E.3).

We plot the coefficient from this regression in Figure E.6. We find virtually no evidence of meaningful differences across therapeutic classes. With a single exception, all the coefficients from the regression indicate that differences across these classes are within 6 months. While some of the coefficients indicate that the difference in delays is significant, this difference is very small. The exception is ATC code 1, which indicates antiparasitic products. Specifically, all products in this group belong to the therapeutic class of Antimalarial medications. Given that malaria is virtually non-existent in Europe, this result is unsurprising.⁷

D Moment Inequality Extensions

In this section we describe extensions of the moment inequality approach used in the paper, which, subject to additional assumptions, can be used to improve the bounds obtained in the estimation.

D.1 Moment Inequalities with Entry and Approval Data

To derive a lower bound using entry data we calculate the overall probability of a delay across all drugs in the sample. The assumption we use in the estimation is that the probability of a delay is country-specific, but homogeneous across all drugs. Under this assumption, the overall probability of a delay in any given subsample of drugs should be higher than the probability of an idiosyncratic delay (as long as the subsample was not selected based on entry data). This suggests that we could obtain a tighter upper bound by simply looking at moment inequalities based on subsamples of the data instead of only looking at the full sample.

Formally, let G be a partition of our set of drugs. For each set $g \in G$, let $(1 - \bar{\psi}_{gj})$ be the probability that product $i \in g$ will enter in country j in a given year. Since by assumption ψ_j is constant across drugs, it follows that $\bar{\psi}_{gj} \geq \psi_j$ for all g , and therefore

$$\psi_j \leq \psi_{Gj}^{\min} = \min_{g \in G} \{\bar{\psi}_{gj}\}$$

Figure E.7 plots the values and confidence intervals for ψ_{gEU10} for the partition of the sample generated by the therapeutic class variable. Since we may be concerned about false positives (the partition includes around 100 sets), we use 99% confidence intervals around the point estimates. We find that in three instances the parameter estimate for $\bar{\psi}_{gj}$ is lower and significantly different from the estimate obtained from the full sample. The three classes are erectile dysfunction, cytotoxics (i.e. drugs for chemotherapy), and nasal corticosteroids without anti-infectives. The point estimates for the first two classes fall within the confidence interval for ψ_{EU10} that we calculated in the paper (curiously, the point estimate for erectile dysfunction drugs almost exactly coincides

⁷Malaria was officially eradicated in Europe in 2016 (<http://www.euro.who.int/en/media-centre/sections/press-releases/2016/04/from-over-90-000-cases-to-zero-in-two-decades-the-european-region-is-malaria-free>).

with our estimate for the lower bound). The latter category only contains one drug, fluticasone furoate (Avamys, by Glaxosmithkline), which entered with no delay in all Eastern European countries.

The main downside of this approach is that it relies heavily on the assumption that ψ_{EU10} is constant across drugs. This may not be true if, for example, the government has accelerated procedures for drugs that are considered important. This may be the case with oncologics (though it is unclear why the same distinction would apply to the other two categories), and suggests that further work on heterogeneity across drugs may be warranted.

D.2 Moment Inequalities with Expected Profits Data

In the empirical implementation of the revenue-based moment inequalities we were able to generate a lower bound on the probability of an idiosyncratic delay, but not an upper bound. This is a result of certain features of the model and the data. In particular, we find that the expected profits of the firm are decreasing in the probability of an idiosyncratic delay. This implies that the inequalities will generate a one-directional bound on the parameter (for details, see Section 6.2 of the paper).

In this section we discuss an extension of the moment inequalities which can be helpful in generating an upper bound in these situations. The idea of this extension is to prove that for a given value of the idiosyncratic delay parameter no strategy will ever yield expected profits as high as what the firm obtained in the data.

Suppose that in the data we can observe $V(\mathcal{A}^*(\psi^0); \psi^0, \cdot)$ (i.e. the expected profits of the firm when playing the optimal strategy and for the true value of the parameter). Further suppose that we can find a function

$$F^{ub}(\psi, \cdot)$$

such that

$$F^{ub}(\psi, \cdot) \geq V(\mathcal{A}^*(\psi); \psi, \cdot)$$

for all ψ . Then, if there exists ψ' such that

$$F^{ub}(\psi', \cdot) < V(\mathcal{A}^*(\psi^0); \psi^0, \cdot)$$

ψ' is rejected from the identified set for \cdot .⁸

As long as $V(\mathcal{A}^*(\psi^0); \psi^0, \cdot)$ is bounded, finding candidates for $F^{ub}(\cdot)$ will not be hard. However, it may be challenging to find a function whose value is low enough to obtain meaningful inference from the data. Here we propose a possible strategy to come up with a family of such

⁸To see why, suppose ψ' is the true value of ψ , i.e. $\psi' = \psi^0$. Then

$$V(\mathcal{A}^*(\psi^0); \psi^0, \cdot) > F^{ub}(\psi^0, \cdot) \geq V(\mathcal{A}^*(\psi^0); \psi^0, \cdot)$$

Hence, $V(\mathcal{A}^*(\psi^0); \psi^0, \cdot) > V(\mathcal{A}^*(\psi^0); \psi^0, \cdot)$, which is a contradiction.

functions that could prove useful in this regard.

The basic idea is to use the expected profit of the firm when facing a simplified environment that is tweaked to be more favorable to the firm (relative to the true environment). For example, one obvious candidate for $F^{ub}(\cdot)$ in the empirical application we consider is the expected profits of the firm when ERP is eliminated. In this scenario, the firm always earns more money, since the externality of ERP is eliminated. Moreover, with this structure, the model has a clear, unique solution: applying for entry everywhere right away.

This function satisfies two main criteria: it is easy to compute, and it is always an upper bound for $V(\mathcal{A}^*(\psi); \psi, \cdot)$. Unfortunately this function also does not deliver a meaningful bound when tested empirically: it was unable to reject any value of the parameters that had not already been rejected using our original moment inequalities. Nonetheless, this approach could provide a promising avenue for future research.

References

Lanthier, Michael, Kathleen L Miller, Clark Nardinelli, and Janet Woodcock, "An improved approach to measuring drug innovation finds steady rates of first-in-class pharmaceuticals, 1987-2011.," *Health affairs (Project Hope)*, aug 2013, 32 (8), 1433–9.

E Tables and Figures

Table E.1: VARIABLES IN THE IMS MIDAS DATABASE

Variable Name	Description	Variable Type
country	Country	
distributionchannel	Distribution Channel	Hospital/Retail
mlist	Active Ingredient	Product definition
crp	Marketing Firm	Product definition
atc4	ATC4	Product definition
internationalproduct	International Product Name	Product definition
prd	Local Product Name	Product definition
productform	Product Form	Product definition
productinternationalstrength	Strength	Product definition
internationpack	International Package Identifier	Product definition
localpack	Local Package Identifier	Product definition
rxorotc	Rx or OTC	Product characteristics
localproductlaunchdate	Local Product Launch date	Product characteristics
estpatentexpirydate	Estimated Patent Expiration Date	Product characteristics
protection	Protection Status	Product characteristics
producttype	Product Type	Product characteristics
licensinginformation	Licensing Information	Product characteristics
sales_mnf_qtr_'qrt'_'yr'_local_curr	Sales in local currency	Sales information
sales_mnf_qtr_'qrt'_'yr'_lceuro	Sales in Euro	Sales information
standard_units_qtr_'qrt'_'yr'	Quantity sold	Sales information

Table E.2: DATA AVAILABILITY BY COUNTRY

Country	Years	Hospital Sales Data	Currency
Austria	2001Q2-2013Q1	Available	Euro
Belgium	2001Q2-2013Q1	Available	Euro
Bulgaria	2001Q3-2013Q2	Available	Local
Czech Republic	2001Q2-2013Q1	Available	Euro ^a
Denmark	2001Q2-2013Q1	Not distinguished separately	Euro ^b
Estonia	2001Q3-2013Q2	Not available	Euro ^c
Finland	2001Q2-2013Q1	Available	Euro
France	2001Q2-2013Q1	Available	Euro
Germany	2001Q2-2013Q1	Available	Euro
Greece	2001Q2-2013Q1	Not available	Euro
Hungary	2001Q3-2013Q2	Available	Local
Ireland	2001Q2-2013Q1	Available starting 2006Q1	Euro
Italy	2001Q2-2013Q1	Available	Euro
Latvia	2001Q3-2013Q2	Not available	Local ^d
Lithuania	2001Q3-2013Q2	Available starting 2002Q3	Local ^d
Luxembourg	2001Q2-2013Q1	Not available	Euro
Netherlands	2007Q2-2013Q1	Not available	Euro
Norway	2001Q3-2013Q2	Available	Local
Poland	2001Q3-2013Q2	Available	Local
Portugal	2001Q2-2013Q1	Available starting 2010Q1	Euro
Romania	2001Q3-2013Q2	Available starting 2005Q1	Local
Slovakia	2001Q3-2013Q2	Available	Euro ^e
Slovenia	2001Q3-2013Q2	Not distinguished separately	Euro ^f
Spain	2001Q2-2013Q1	Available	Euro
Sweden	2004Q1-2013Q2	Available	Local
Switzerland	2001Q3-2013Q2	Available	Local
UK	2001Q3-2013Q2	Available	Local

^a The Czech koruna appreciated substantially against the Euro between 2001 and 2012. The average rate fell from 34.021 Ck for 1 Euro in 2002Q1, to 25.167 Ck for 1 Euro in 2012Q4.

^b The value of a Danish Krona oscillated between 0.13398 and 0.13468 Euros in the period from 2001 to 2012.

^c The Estonian kroon was pegged to the Euro (at a rate of 15.6466 krooni per Euro) until adoption of the Euro in 2011.

^d Latvia and Lithuania adopted the Euro after the end of our data (in 2014 and 2015 respectively).

^e The Slovak koruna appreciated substantially against the Euro until its adoption in 2009. The average rate fell from 42.234 Sk for 1 Euro in 2002Q1, to 30.35 Sk for 1 Euro in 2008Q4.

^f The value of the Slovenian tolar depreciated from 219.3683 to 239.9533 SIT for 1 Euro between 2001Q3 and 2004Q3. After that, the exchange rate remained constant until the country adopted the Euro in 2007.

Table E.3: ATC MAIN SYSTEMS

Code	Contents
A	Alimentary tract and metabolism
B	Blood and blood forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genito-urinary system and sex hormones
H	Systemic hormonal preparations, excluding sex hormones and insulins
J	Antiinfectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculo-skeletal system
N	Nervous system
P	Antiparasitic products, insecticides and repellents
R	Respiratory system
S	Sensory organs
V	Various

This table describes the classification of the first digit of the ATC code (or ATC1). Each letter roughly corresponds to an organ system. For more details on the ATC classification system, see <http://www.ephmra.org/classification>

Table E.4: ADDITIONAL DATA SOURCES

Data	Use	Source	Source Link
Drug Approval Date (EMA)	Calculate launch delays	European Medicines Agency	http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp
Drug Approval Date (Mutual Recognition Procedure)	Calculate launch delays	Heads of Medicines Agencies	http://mri.cts-mrp.eu/Human/about
Incidence of Disease	Calculate market size for each market (therapeutic area and country)	Global Burden of Disease Study	http://ghdx.healthdata.org/gbd-results-tool
Exchange Rates	Adjust sales to Euros	European Central Bank	https://www.ecb.europa.eu/stats/policy_and_exchange_rates/euro_reference_exchange_rates/html/index.en.html
GDP and Population	Regression controls and market size construction	Eurostat	http://ec.europa.eu/eurostat/web/national-accounts/data/database

Table E.5: WITHDRAWN PRODUCTS

Molecule Name	Approval Date	Withdrawal Year
DROTRECOGIN ALFA (ACTIVATED)	22aug2002	2011
EPOETIN DELTA	01jan2007	2009
GLIMEPIRIDE#ROSIGLITAZONE	01nov2006	2010
LUMIRACOXIB	01jan2005	2007
METFORMIN#ROSIGLITAZONE	20oct2003	2010
RIMONABANT	19jun2006	2009
ROSIGLITAZONE	11jul2000	2010
SIBUTRAMINE	01apr2001	2010
SITAXENTAN	10aug200	2010
VALDECOXIB	27mar2003	2008

This table lists all molecule that received approval by the EMA and later had that approval rescinded for safety reasons. An exact withdrawal data is not available since recalls generally take place over at least a few months.

Table E.6: CHANGES TO REFERENCE PRICING FUNCTIONS

Year	Country	Implemented change
2005	AUSTRIA	Added new EU member states (CZ EE HU LT LV PL SL SK).
2008	AUSTRIA	Added new EU member states (BG RO).
2005	BELGIUM	Added new EU member states (CZ EE HU LT LV PL SL SK).
2008	BELGIUM	Added new EU member states (BG RO).
2011	BELGIUM	Changed formula to average.
2005	FINLAND	Added new EU member states (CZ EE HU LT LV PL SL SK).
2008	FINLAND	Added new EU member states (BG RO).
2010	GREECE	Removed DK, EE, and SE. Changed formula to average of 3 lowest prices.
2011	HUNGARY	Added BG, CH, DK, EE, LT, LU, LV, NL, NO, RO, SE, UK.
2005	ITALY	Added new EU member states (CZ EE HU LT LV PL SL SK).
2008	ITALY	Added new EU member states (BG RO).
2012	POLAND	Added AT, BG, EE, FI, LV, NO, RO, SL, SK.
2007	PORTUGAL	Added Greece.
2012	PORTUGAL	Changed basket to Italy, Spain, Slovenia.
2008	SPAIN	Added Slovenia (new EURO member).
2009	SPAIN	Added Cyprus and Malta (new EURO members).
2010	SPAIN	Added Slovakia (new EURO member).
2012	SPAIN	Added Estonia, Latvia, and Lithuania (new EURO members).

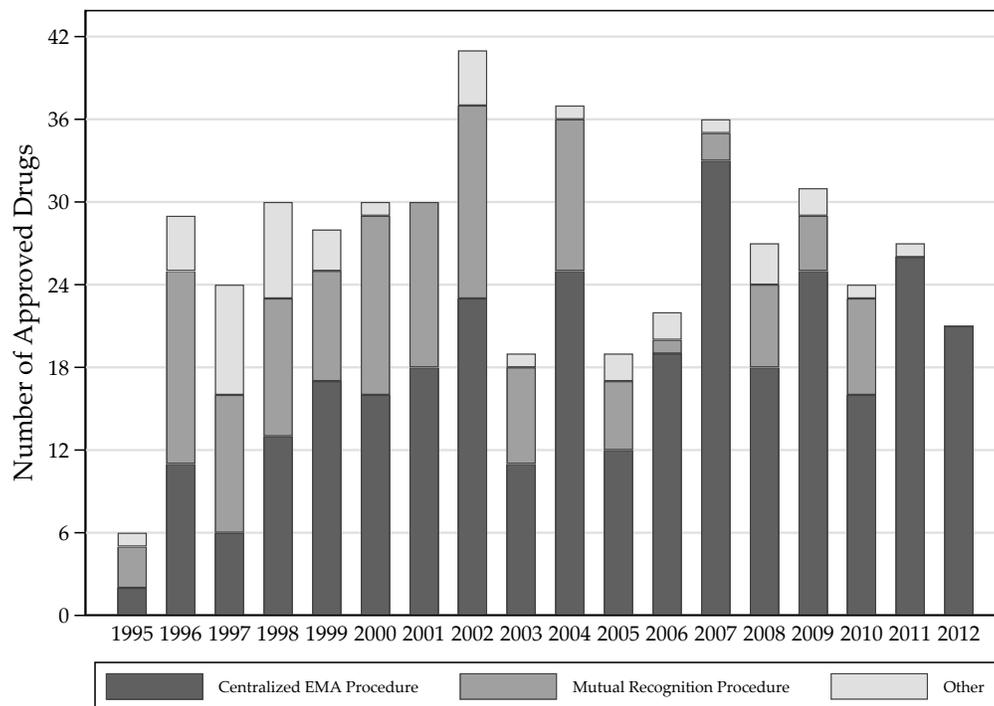
This table lists all the changes that were made to reference pricing functions, sorted by country and year. Most changes involved the addition of new EU/EURO Member States. Figure E.3 also plots the full reference pricing matrices for all countries and years. Please refer to it for more details.

Table E.7: CORRELATION OF WITHIN-COUNTRY VARIATION AND FIRM BEHAVIOR

	Launch Order		Delay	
ε_{ijt}^q	-0.435***		-1.546***	
	[-0.487,-0.383]		[-1.759,-1.333]	
ε_{ijt}^p		0.068		0.068
		[-0.116,0.252]		[-0.686,0.821]
Country FE	Y	Y	Y	Y
N	8,894	8,894	8,894	8,894
R^2	0.50	0.48	0.23	0.22

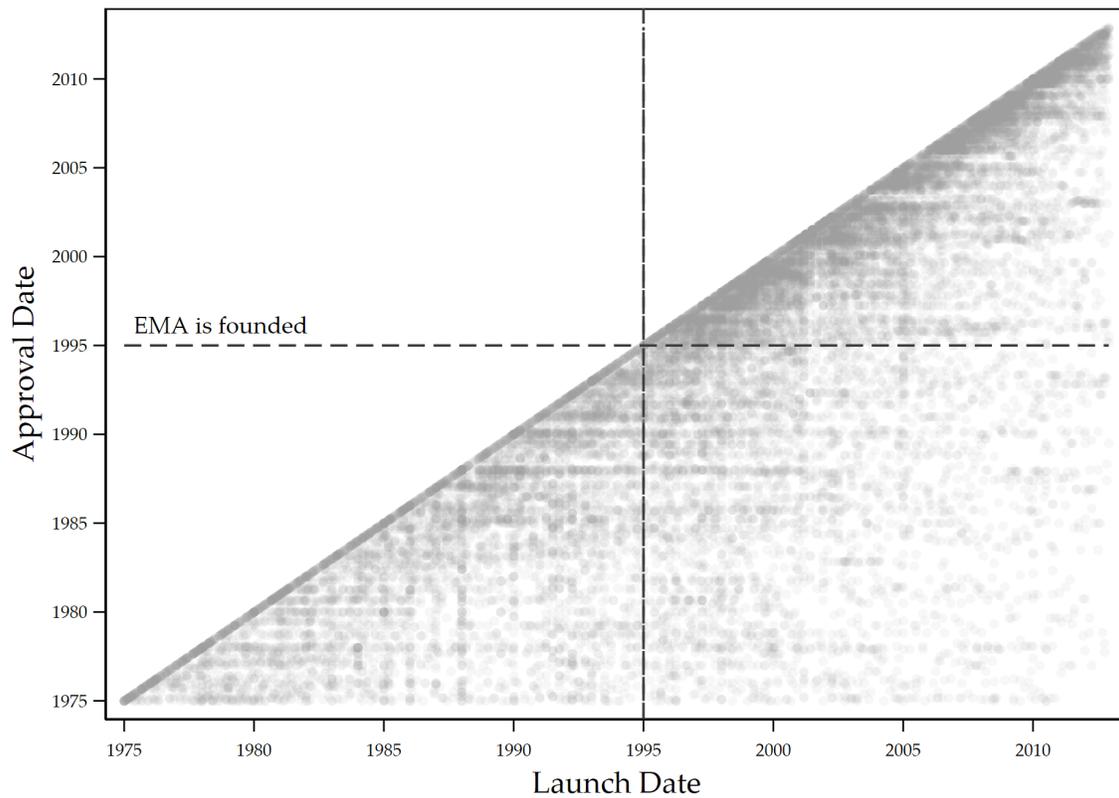
This table show the results of a regression of launch order (or delay) on country fixed effects plus a residual from a regression of log quantity (or price) on country and drug fixed effects (see Section C.2 for more details on the specification).

Figure E.1: NUMBER OF DRUG APPROVALS BY YEAR



This stacked bar chart shows the number of new molecular entities approved in Europe by year, starting in 1995 (the year the EMA was founded). Approvals are divided according to the procedure used by the firm (for more details on each procedure, please consult Section 2.1 of the paper).

Figure E.2: DELAY PATTERNS BEFORE AND AFTER THE EMA



This scatter-plot shows the distribution of the launch of new drugs. Each launch in each country is recorded separately, and is defined by two coordinates: the date in which the product was approved, and the date in which it was launched. If there were no delays, then all points should lie on the 45-degree line. It's very clear from the plot that drugs approved after 1995 experienced fewer delays (this is clear from the increased concentration of dots close to the 45-degree line), which suggests that the EMA had a large negative effect on delays. This result is what motivated our choice to focus only on the post-1995 sample.

Figure E.3: EXTERNAL REFERENCE PRICING MATRICES

(a) 2002

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT	■	■				■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Belgium	BE	■	■																										Lowest
Bulgaria	BG				■																			■	■	■			Avg. of 3 lowest
Switzerland	CH				■	■																							Average
Czech Republic	CZ				■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE												■				■	■	■										Lowest
Greece	EL	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Finland	FI	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
France	FR	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Hungary	HU	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Ireland	IE	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Italy	IT	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Lithuania	LT				■								■										■					Average - 5%	
Luxembourg	LU																												
Latvia	LV																■											Lowest	
Netherlands	NL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Norway	NO	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Avg. of 3 lowest
Poland	PL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Portugal	PT	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Romania	RO	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Sweden	SE																												
Slovenia	SL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average - 5%
Slovakia	SK	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

(b) 2003

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT	■	■				■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Belgium	BE	■	■																										Lowest
Bulgaria	BG				■																			■	■	■			Avg. of 3 lowest
Switzerland	CH				■	■																							Average
Czech Republic	CZ				■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE												■				■	■	■										Lowest
Greece	EL	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Finland	FI	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
France	FR	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Hungary	HU	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Ireland	IE	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Italy	IT	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Lithuania	LT				■								■										■					Average - 5%	
Luxembourg	LU																												
Latvia	LV																■											Lowest	
Netherlands	NL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Norway	NO	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Avg. of 3 lowest
Poland	PL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Portugal	PT	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
Romania	RO	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Lowest
Sweden	SE																												
Slovenia	SL	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average - 5%
Slovakia	SK	■	■			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

Figure E.3: EXTERNAL REFERENCE PRICING MATRICES

(c) 2004

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT																												Average
Belgium	BE																												Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
Czech Republic	CZ																												Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE																												Lowest
Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

(d) 2005

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT																												Average
Belgium	BE																												Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
Czech Republic	CZ																												Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE																												Lowest
Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

Figure E.3: EXTERNAL REFERENCE PRICING MATRICES

(e) 2006

Country	Country Code	Basket																											Formula
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK	UK	
Austria	AT	■	■																										Average
Belgium	BE	■	■																										Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
Czech Republic	CZ																												Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE																												Lowest
Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

(f) 2007

Country	Country Code	Basket																											Formula
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK	UK	
Austria	AT	■	■																										Average
Belgium	BE	■	■																										Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
Czech Republic	CZ																												Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE																												Lowest
Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

Figure E.3: EXTERNAL REFERENCE PRICING MATRICES

(g) 2008

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT																												Average
Belgium	BE																												Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
Czech Republic	CZ																												Avg. of 4 lowest plus 3%
Germany	DE																												
Denmark	DK																												
Estonia	EE																												Lowest
Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

(h) 2009

Country	Country Code	Basket																										Formula	
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT	LU	LV	NL	NO	PL	PT	RO	SE	SL	SK		UK
Austria	AT																												Average
Belgium	BE																												Lowest
Bulgaria	BG																												Avg. of 3 lowest
Switzerland	CH																												Average
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Germany	DE																												
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Greece	EL																												Mean of (EU10 mean) + 2*(EU15 + CH mean)
Spain	ES																												Average
Finland	FI																												Average
France	FR																												Average
Hungary	HU																												Lowest
Ireland	IE																												Average
Italy	IT																												Average
Lithuania	LT																												Average - 5%
Luxembourg	LU																												
Latvia	LV																												Lowest
Netherlands	NL																												Average
Norway	NO																												Avg. of 3 lowest
Poland	PL																												Lowest
Portugal	PT																												Average
Romania	RO																												Lowest
Sweden	SE																												
Slovenia	SL																												Average - 5%
Slovakia	SK																												Average
United Kingdom	UK																												

* Luxembourg only references the drug's country of origin.

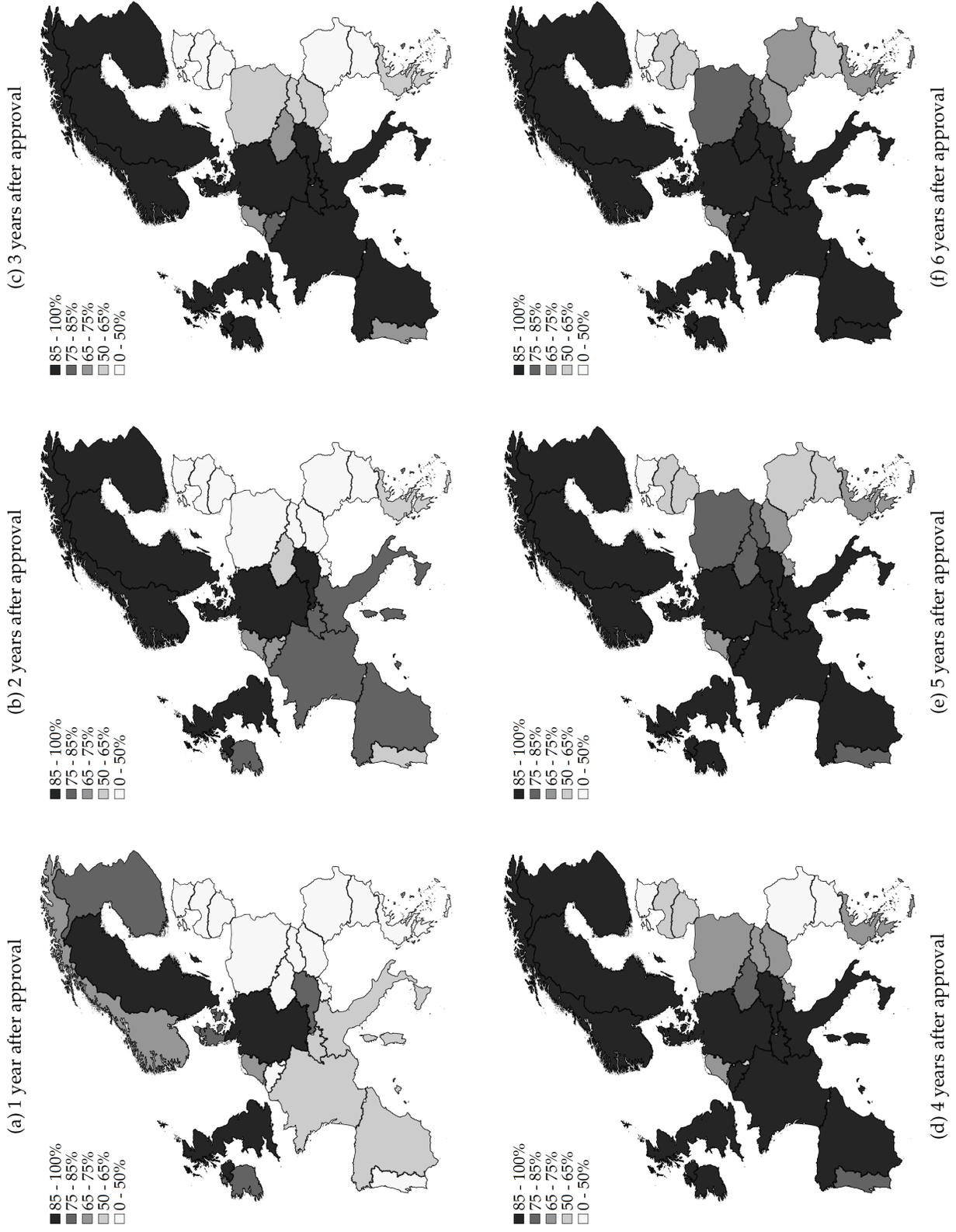
Figure E.3: EXTERNAL REFERENCE PRICING MATRICES

(k) 2012

Country	Country Code	Basket																Formula												
		AT	BE	BG	CH	CZ	DE	DK	EE	EL	ES	FI	FR	HU	IE	IT	LT		LU	LV	NL	NO	PL	PT	RO	SE	SL	SK	UK	
Austria	AT																													Average
Belgium	BE																													Average
Bulgaria	BG																												Avg. of 3 lowest	
Switzerland	CH																												Average	
Czech Republic	CZ																												Avg. of 4 lowest plus 3%	
Germany	DE																													
Denmark	DK																													
Estonia	EE																												Lowest	
Greece	EL																												Avg. of 3 lowest	
Spain	ES																												Average	
Finland	FI																												Average	
France	FR																												Average	
Hungary	HU																												Lowest	
Ireland	IE																												Average	
Italy	IT																												Average	
Lithuania	LT																												Average - 5%	
Luxembourg	LU																													
Latvia	LV																												Lowest	
Netherlands	NL																												Average	
Norway	NO																												Avg. of 3 lowest	
Poland	PL																												Lowest	
Portugal	PT																												Average	
Romania	RO																												Lowest	
Sweden	SE																													
Slovenia	SL																												Average - 5%	
Slovakia	SK																												Average	
United Kingdom	UK																													

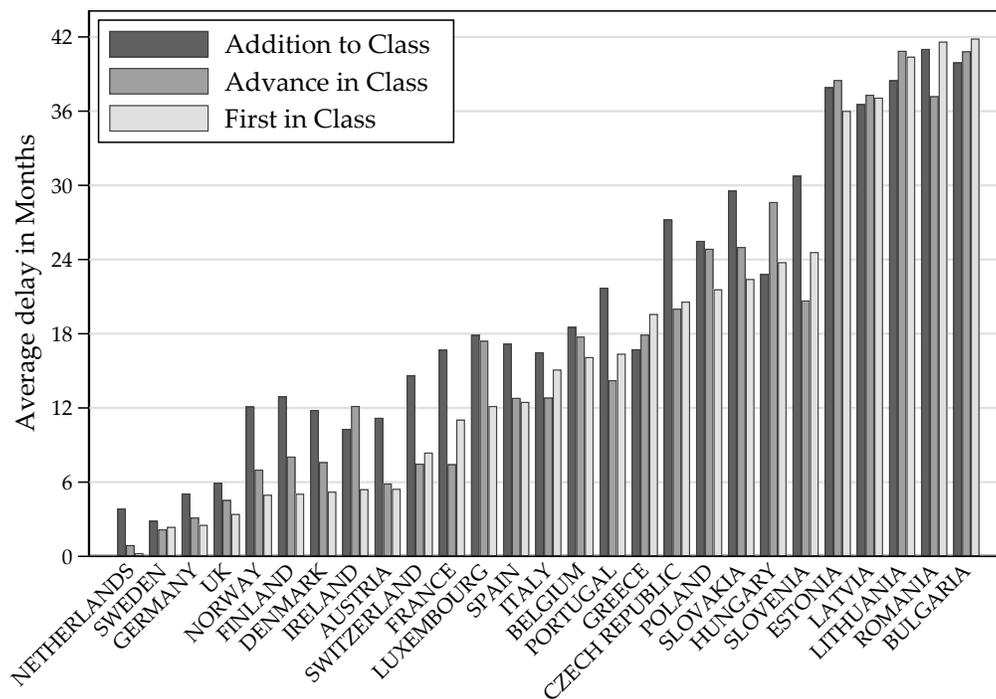
* Luxembourg only references the drug's country of origin.

Figure E.4: DIFFUSION OF EMA-APPROVED DRUGS IN EUROPEAN COUNTRIES



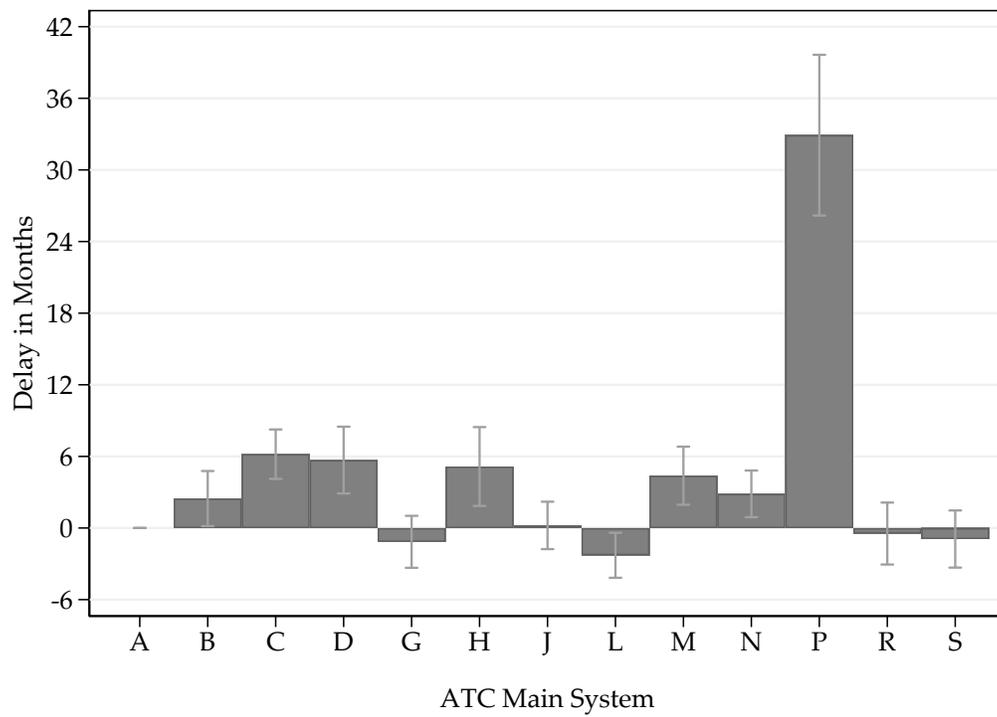
This figure shows the diffusion rate of prescription drugs across European countries at 1 year intervals, for 6 years. We use a balanced sample of 142 drugs that were approved by the EMA on or before December 31st, 2006.

Figure E.5: DELAYS BY INNOVATIVE STATUS



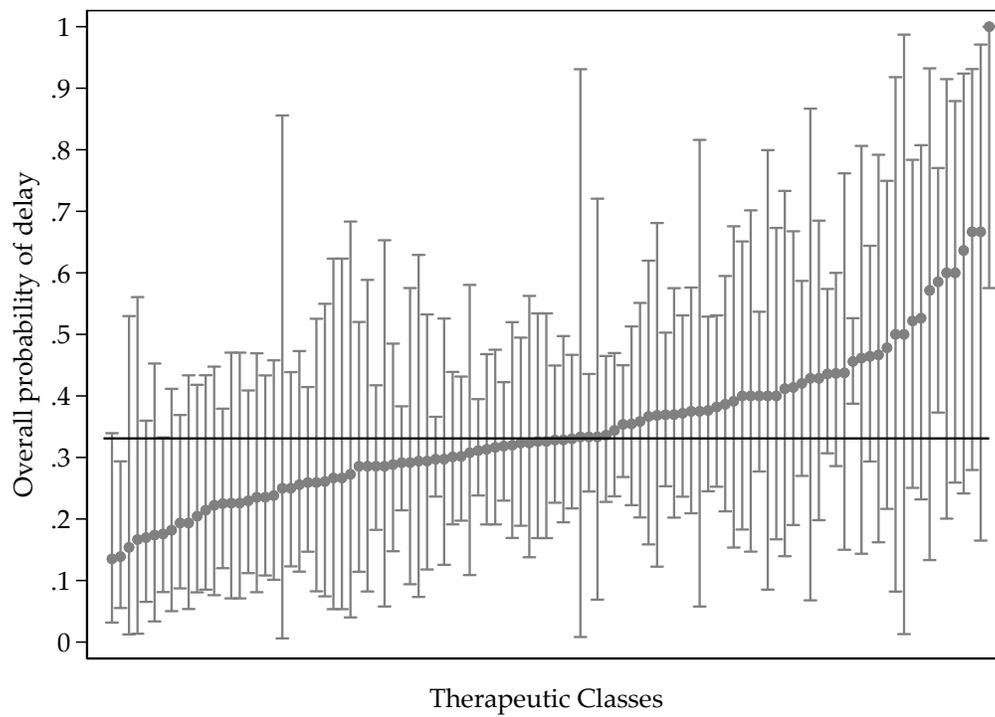
This chart plots the average delays of drugs separated according to their innovative status. First-in-class drugs (i.e. drugs who are the first to treat a certain disease or to exploit a specific treatment path) and drugs that represent and advance-in-class tend to experience fewer delays, but only in Western Europe (see Section C.3 for details on the classification).

Figure E.6: Delays by ATC Main System



This chart plots the average delays of drugs separated according to their ATC1 classification (see Table E.3 for a description of what each letter stands for). We do not find large differences across therapeutic classes, with the exception of Antiparasitic drugs (P). The only products from our sample that belong to this class are antimalarial treatments.

Figure E.7: Probability of Delay in Eastern Europe by Therapeutic Class



This graph plots the overall probability of delay in Eastern European countries for drugs separated according to their therapeutic class. Vertical bars represent the 99% confidence interval, while the black horizontal line is the estimate for ψ_{EU10} obtained from the overall sample.