CROSS-NATIONAL EVIDENCE ON GENERIC PHARMACEUTICALS:
PHARMACY VS. PHYSICIAN-DRIVEN MARKETS

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ABSTRACT

This paper examines the role of regulation and competition in generic markets. Generics offer large potential savings to payers and consumers of pharmaceuticals. Whether the potential savings are realized depends on the extent of generic entry and uptake and the level of generic prices. In the U.S., the regulatory, legal and incentive structures encourage prompt entry, aggressive price competition and patient switching to generics. Key features are that pharmacists are authorized and incentivized to switch patients to cheap generics. By contrast, in many other high and middle income countries, generics traditionally competed on brand rather than price because physicians rather than pharmacies are the decision-makers. Physician-driven generic markets tend to have higher generic prices and may have lower generic uptake, depending on regulations and incentives.

Using IMS data to analyze generic markets in the U.S., Canada, France, Germany, U.K., Italy, Spain, Japan, Australia, Mexico, Chile, Brazil over the period 1998-2009, we estimate a three-equation model for number of generic entrants, generic prices and generic volume shares. We find little effect of originator defense strategies, significant differences between unbranded and unbranded generics, variation across countries in volume response to prices. Policy changes adopted to stimulate generic uptake and reduce generic prices have been successful in some E.U. countries.

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I. Introduction

Pharmaceutical markets in the U.S. are characterized by relatively high prices while drugs are on patent, followed by rapid generic entry and low generic prices once patents expire. In 2009, generics accounted for 74.5 percent of prescriptions (Berndt and Aitken, 2010) but only about 20 percent of sales, because generic erosion is rapid and generic prices are low, relative to originator prices in the U.S. By contrast, generic penetration is slower and generic prices are higher, both absolutely and relative to originator prices, in many other countries, implying only modest savings from generics for payers and patients. These modest generic savings are prima facie surprising. Post-patent entry should in theory be profitable for generic producers and appealing for customers, because generics can largely free-ride on the R&D and informational investments made by originator firms, thereby realizing much lower cost structures. Expiry of patent barriers to entry also makes generic markets potentially more competitive than originator markets.

This paper argues that these cross-national differences in generic shares and prices reflect differences in regulatory and reimbursement policies that drive countries to have either pharmacy-driven or physician-driven generic markets. The U.S. is a prototypical pharmacy-driven generic market. Pharmacists are the key decision-maker for generics, because they are legally authorized to substitute any substitutable (AB-rated) generic unless the physician explicitly requires the brand, which is rare. U.S. pharmacies have financial incentives to prefer cheaper generics and brand is irrelevant for substitutable generics that by regulation are certified to be bioequivalent to the originator. Generics are therefore unbranded and compete on price for the business of highly-price conscious pharmacies. Centralized purchasing by large chain pharmacies has intensified generic competition in the U.S. Tiered co-payment structures have encouraged patients to accept generics. However, pharmacies decide which generic to dispense and patients, payers/PBMs and physicians usually play no role in choosing one generic manufacturer over another (except for drugs dispensed through the mail, for which the PBMs operate their own pharmacies). The U.K. and Canada resemble the U.S. pharmacy-driven generic model in some respects, but with important differences, notably in Canada which regulates generic prices rather than relying on competition.

By contrast, the regulation/reimbursement structure for generics in many other countries has traditionally given less authority and fewer or even perverse incentives to pharmacies. In

particular, substitution was only permitted if the physician prescribed by chemical name (which is uncommon except in the U.K.), and pharmacy dispensing fees that increased with the price of the drug discouraged substitution of cheaper products, even if permitted. In markets where pharmacists are either not authorized or incentivized to substitute, physicians prescribe generics and originators by brand name and have little incentive to be price-sensitive (unless they are personally at risk for drug costs). Generic companies therefore market "branded generics" that compete on brand rather than price. Among major E.U. markets, France, Spain, Italy and Germany were traditionally physician-driven, branded generic markets. Latin America also has physician-driven, branded generic markets, with the added feature that many of these branded generics are "similar" (have not met bioequivalence standards to the originator) and are therefore of uncertain quality. Our basic hypothesis is that branded generics in physician-driven generic markets will tend to be higher priced and have lower market shares than unbranded generics in pharmacy-driven generic markets.

During the 2000's, all the major E.U. countries adopted policy changes to reduce prices and/or increase generic uptake and thereby realize generic savings. In 1989, Germany adopted generic reference pricing to encourage competition in off-patent products and expanded the system to include on-patent products in 2005. France, Italy and Spain adopted variants of generic reference pricing in the early 2000's.[1] Although such RP systems usually induce originators to cut prices to the RP, whether they create strong incentives for generic competition below the initial RP depends critically on rules and incentives for pharmacy substitution. Most of these countries have also expanded authorization for pharmacy substitution and modified dispensing fees to incentivize generic use. Since 2007, German sickness funds have contracted directly with generic companies, using competitive bidding to drive price competition and capture the resulting savings for payers.

Latin American markets were also traditionally physician-driven, branded generic markets, but with many "similares" or copy products that were launched prior to originator patent expiry and were not required to meet bioequivalence standards. Brazil and Mexico have established regulatory frameworks to authorize true, bioequivalent generics, but many similares remain on the market. Pharmacy substitution is usually not legally authorized in countries where

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[1] Under generic reference pricing, the payer sets a single reference price (RP) as a maximum reimbursement for all generically equivalent products, leaving the patient to pay any excess of the manufacturer's price over the RP.

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generics are not required to be bioequivalent. In practice, patients often purchase drugs without a prescription, in which case pharmacists may advise on substitution. Because generic quality is uncertain, brand plays an important role in generic choice. Thus although patients generally pay out-of-pocket for outpatient drugs and are presumably price sensitive, quality uncertainty leads to competition on brand and undermines competition on price.

In Japan, physicians and hospitals traditionally dispensed the drugs that they prescribed and captured any margin between a drug's reimbursement price and its market price (or acquisition cost). Branded generics were the norm. Their incentive was to maintain the reimbursement price as high as possible, to enable discounting of the market price below the reimbursement price, to increase the margin realized by the dispensing providers. Savings accrued to payers only with a lag, as reimbursement prices were adjusted based on market prices every two years. Unbranded generics had little presence in Japan until recent reforms.

This paper examines the performance of generic markets in 10 countries (the U.S., the U.K., Germany, France and Spain, Italy, Japan, Canada, Brazil and Mexico) over the period 1998-2009. Our analysis draws on data from IMS Health Inc. on the universe of drug sales in these countries. Our data permit both between-country comparison of branded vs. unbranded generic markets and within-country comparison over time, to estimate effects of the policy changes. We estimate a model for three dimensions of generic markets: any entry and number of generic manufacturers; generic prices, relative to baseline originator prices; and generic volume share. We examine how each of these dimensions of generic markets changed over time in response to policy changes.

We also examine the effects on generic markets of originator defense strategies, specifically, launch of new licensed brand products (co-branding) or new formulations prior to patent expiry. Theory and prior evidence suggest that co-branding may be effective in physician-driven, branded generic markets (for Italy, see Pammoli et al. 2002; for Germany, see Appelt, 2009); however, such strategies are less likely to be effective in pharmacy-driven, unbranded generics market. Launching new formulations prior to patent expiry on older formulations may be a rational strategy in both market types, depending on reimbursement rules. Originator strategies to deter generic entry have been the focus of the E.U. Generics Inquiry.

Our empirical evidence confirms that generic price competition is greater in pharmacy-driven markets than in physician-driven markets, provided that pharmacies face financial

incentives to prefer cheaper products. Branded generics, which predominate in physician-driven markets, are less price competitive than unbranded generics that predominate in pharmacy-driven markets, as predicted. Our results confirm previous evidence that generic entry is related to market size; however, differences across countries in number of generic competitors is not explained by overall market size, plausibly because the extent of price competition, cost structures and profit margins also differ. We find little evidence that originator defense strategies are successful on average, except that launch of delayed release formulations does deter generic penetration in the U.S. Recent changes in generic regimes in four previously physician-driven, branded generic markets of the E.U. (Spain, France, Italy and Germany) have had significant effects, with unbranded generics gaining share. However, these countries still lag the U.S. and U.K. in speed and extent of generic penetration.

II. Generic Regulation and Reimbursement

Generic entry is constrained in all countries that are members of the World Trade Organization (WTO) by patents and regulatory protections of innovator products. Although all WTO countries must recognize a 20-year product patent term, effective patent life for pharmaceuticals is typically shorter but differs across countries (Grabowski and Kyle, 2007). Most countries provide for some patent term restoration to compensate for time lost during R&D, and a data exclusivity period during which generics may not reference the originator data for regulatory approval. Patents may also be challenged prior to expiry, and this is increasingly common in the U.S. The originator's effective patent life post launch is the net result of all these factors.

Patents may be challenged in any country, but the U.S. is unique in rewarding successful challenges, by granting 180-day market exclusivity to the first generic to successfully challenge the originator patents (a paragraph IV certification).[2] During this 180 days, the originator may market an authorized generic (licensed under the originator's NDA), but no other ANDA-approved generics can enter. These paragraph IV and associated 180-day exclusivities have reportedly become increasingly common since the late 1990's, which is expected to result in

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[2] The 1984 Waxman-Hatch Act's Abbreviated New Drug Application (ANDA) process permits generic approval with evidence of bioequivalence, once the originator's patents and other exclusivities have expired or been successfully challenged.

higher generic prices during the first two quarters post launch in the U.S. Greater use of paragraph IV may also result in earlier generic entry over time in the U.S., unless it is offset by increased originator use of mechanisms for patent and exclusivity extensions.

In addition to patent and data exclusivity provisions, the incentives for generic entry and generic price competition depend on regulatory rules affecting generic competition and reimbursement, including rules government pharmacists' authority to substitute generics; reimbursement incentives for substitution; whether generic prices are regulated or competitively set; and patients' incentives to accept generics, through co-payment structures. The tiered co-payment structure in the US offers patients a larger financial incentive to accept generics than in any other country.

Table 1 summarizes regulatory and reimbursement characteristics of our sample countries. This is an oversimplification of the complex regimes and changes over time in each country.[3] As a rough characterization, we assume that the U.S., the U.K., and Canada are primarily pharmacy-driven generics markets, and physician-driven markets include France, Germany, Italy, and Spain at the start of our period, plus Japan, Brazil, and Mexico.

Most countries implemented changes in the 2000's. France, Germany, Italy, and Spain implemented multiple policy changes to stimulate generic uptake and/or reduce prices. The U.K. changed its rules for setting generic reimbursement in 2005. Brazil and Mexico encouraged bioequivalence testing and the growth of unbranded generics. The U.S. experienced some growth in paragraph IV challenges, and the 2003 Medicare Modernization Act reduced the incentives for originators to list late patents by permitting only one 30-month stay per molecule.[4] Some Canadian provinces reduced the regulated prices on generics, and other changes were adopted in 2010, after our observation period. Our empirical analysis tests for effects of these changes in each country.

III.   Previous Literature

Early studies of generic entry and price competition focused on the U.S. Models of number of entrants have consistently found that generic entry is related to market size (for example, Scott Morton, 1999; Saha et al., 2006) and that generic prices are inversely related to

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[3] More detail is reported in an Appendix available upon request from the corresponding author.
[4] When a generic company challenges an originator patent, the originator may obtain an injunction for up to 30 months or the resolution of the litigation, whichever occurs first.

number of generic competitors in the U.S. (Grabowski and Vernon, 1992; Saha et al., 2006). Most previous studies do not address the role of pharmacies as key decision-makers in U.S. generic markets and the effects of pharmacy-driven markets on the nature of competition. Several papers (for example, Scott Morton, 2000) hypothesize that originator firms may use promotion to deter generic penetration but find no effects. This is unsurprising in the context where pharmacy substitution is the norm, such that detailing to persuade physicians to choose a particular brand does not assure that the originator product is dispensed. In such markets, originator advertising generally declines and ultimately ceases as patent expiration approaches.[5] Reiffen and Ward (2005) estimate a structural model of generic entry and prices using data from the early 1990s.

Several recent papers have examined generic uptake in other countries. Hollis (2003) reports on anti-competitive effects of strategic licensing of brand-controlled "pseudo-generics" in Canada, which are found to deter generic entry. Magazzini et al. (2004) examine generic entry in the U.S., the U.K., Germany and France using sales data from July 1987-December 1998 on major molecules with patent expiry 1986-1996. Using a Tobit estimator applied to pooled panel data for the four countries, they conclude that market share of licensed products (defined as products launched within 3 years of patent expiry) is negatively related to unbranded generic market share whereas number of different brand names has a positive effect. Possible reasons for these apparently contradictory findings are not explored.[6] Appelt (2009) provides evidence of originator licensing strategies prior to patent expiry and branded generics' use of trade marks to enhance brand competition in Germany's branded generic market. Hudson (2000) examines generic entry and erosion of brand shares in four markets (U.S., U.K., Germany and Japan) using data from the early 1990's which predates the more recent growth in generic erosion in the U.S. and pro-generic policy changes in other countries. Moreno-Torres et al. (2009) provide detailed evidence on generic entry in Spain. Ghislandi et al. (2005) and Garattini and Ghislandi (2006) discuss recent changes in Italy. Kanavos et al. (2008) and Puig-Junoy (2010) discuss European price regulation and its impact on generic competition.

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[5] Ellison and Ellison (2011) find weak evidence for pre-patent expiry use of promotion to deter generic entry by medium-sized incumbents, using data from 1986-1992, which predate the growth of payer strategies to encourage pharmacy substitution and generic uptake by patients.
[6] They regress market share of unbranded drugs on lagged market share of licensed products in an uncensored Tobit model that includes markets with no generics. The negative coefficient on licensed products may be dominated by the observations with zero generic share (for which the relationship is necessarily negative), and it is unclear whether it would hold in the subset of market with generic entry.

Our paper adds to these previous studies by providing a consistent analysis and comparison across 10 different countries and over a more recent time period that includes experience after the recent reforms in several countries. Our approach is also the first to focus on the importance of pharmacy substitution and pharmacy incentives in creating pharmacy-driven rather than physician-driven generic markets, and the resulting distinction between competition focused on price vs. brand.

IV.   Data

The data for this study are from the IMS MIDAS database of quarterly sales of all drugs over the period 1998-2009 in 10 countries, including the major E.U. markets, two major Latin American markets, the U.S., Canada and Japan. Within this universe of products, we define the sample of molecules potentially subject to generic entry as molecules with global age (years since first global launch of the molecule) between 8 and 20 years. This age window was selected based on the assumption that product patents are filed at roughly the same date in all countries, that R&D (discovery, preclinical and clinical trials, and regulatory review) typically absorbs at least 8 of the 20 year patent term, and that most countries offer patent extensions or supplementary protection certificates for up to 5 years to compensate for this loss.[7] This age range encompasses the ages with greatest generic entry, although entry in most countries spans a longer age range. We define the lag in generic entry of product i in country j as months from first originator launch of that product in country j, recognizing that this lag may reflect legal barriers as well as economic factors.[8]

Our analysis focuses on single molecule prescription drugs in the retail pharmacy channel. We exclude combination products, for which global age and hence generic eligibility are ambiguous. We exclude biologics because they are ineligible for the standard abbreviated generic approval procedures in the U.S. and most other countries.[9] We also excluded miscellaneous therapeutic categories (hospital solutions, diagnostic agents, various) and unusual forms (non-human use, use unknown). IMS assigns each product into one of five license

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[7] Defining products eligible for generic entry by expiry date of all listed patents is not appropriate, even if we had the data, because generic companies increasingly challenge listed patents prior to their expiry.

[8] Major differences across countries in regulatory and reimbursement barriers to generic entry are described in an Appendix, which is available upon request from the corresponding author.

[9] Abbreviated approval procedures for biosimilars have been outlined in the E.U. and U.S. in the late 2000's. Although a few biosimilars have been launched, their higher regulatory costs and lower substitutability make them very different from chemical generics analyzed here.

categories: originator brand, licensee, branded generic, unbranded generic, or "Patent not assigned".[10] Our analysis is at the level of the presentation (molecule-form-strength) because pharmacy substitution is authorized only within presentation. All price and sales data are adjusted to 2009 values using country-specific general producer price indexes (PPIs) as the best available measure of input costs. Most analysis is in local currency units, but where prices are converted to U.S. dollars we use 2009 exchange rates.

Although this IMS database is more comprehensive and more detailed than the data used in previous studies, certain limitations must be noted. First, the IMS categorization of generics as branded or unbranded is the best available but may nevertheless be an imperfect indicator for whether products compete primarily on brand or price. Second, the products designated as generics in some countries, notably Brazil and Mexico, include copy products (similares), some of which entered early in the originator life, due to lack -- or weak enforcement -- of product patent regimes, and are not necessarily bioequivalent to the originator drug.[11] Third, the IMS data do not designate which generics have met bioequivalence tests and hence are more likely to be considered substitutes by physicians, pharmacists and patients than those that lack a bioequivalence certification. Fourth, when a merger occurs between two firms, IMS consolidates their separate data retroactively. Our data may therefore potentially undercount the number of generic competitors, particularly in the earlier years.

V.   Empirical Framework and Methods

Our descriptive and regression analyses focus on the main determinants of overall generic savings to payers: whether and when generic entry occurs; number of branded and unbranded generic competitors; generic and originator prices; and generic volume shares. The analysis is at the level of the presentation-country-quarter, defined by molecule, four-digit anatomical therapeutic class, formulation and strength, because pharmacy substitution of generics is authorized only between presentations with the same molecule, formulation and strength. We

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[10] We used the corporation and molecule age to reassign products with Patent Not Assigned into branded generic or unbranded generic status.

[11] We excluded from these calculations the small number of generic launches that reportedly occurred within 5 years of the originator launch, except in countries where such early launch dates are plausible due to late adoption of patent regimes (Brazil, Mexico, Italy, and Spain). For other countries, we reassigned the license status of these implausibly early generics from branded generic to licensed brand and included them as licensees in all other analysis. We also exclude generics for which no originator is present in any year of our data.

estimate a four equation model for: any generic entry for the ith presentation in country j in year t; number of generic firms, conditional on entry; generic or originator price (relative to baseline originator price); and generic volume share:

$$G_{ijt} = f_1 (R_{ijt-2}; D_{ijt-2}; F_{ij}; M_{ij}; Z_t; u_{1ijt}) \qquad (1)$$

$$N_{ijt} = f_2 (R_{ijt-2}; D_{ijt-2}; F_{ij}; M_{ij}; Z_t; u_{2ijt}) \qquad (2)$$

$$P_{ijt} = g (N_{ijt}^b; N_{ijt}^u; F_{ij}; M_{ij}; Z_t; u_{3ijt}) \qquad (3)$$

$$S_{ijt} = h (P_{ijt}; N_{ijt}^b; N_{ijt}^u; F_{ij}; M_{ij}; Z_t; u_{4ijt}) \qquad (4)$$

where G_{ijt} is an indicator for Any Generic entrant in the presentation-country-year, N_{ijt} is number of generic manufacturers (branded and unbranded), conditional on entry, P_{ijt} is normalized price (generic or originator, defined below), S_{ijt} is generic volume share; R_{ijt-2} is molecule sales in the presentation-country lagged 2 quarters; D_{ijt-2} is a vector of (lagged) originator defense strategies; F_{ij} is a vector of indicators for non-oral forms; and M_{ij} is molecule-specific characteristics. Z_t is a vector of indicators for two time periods, 2002-05 and 2006-09, that test for changes in the dependent variable, relative to the referent period, 1998-2001.

We estimate separate regressions for each country, to permit all coefficients to vary by country. Other details of the estimation approach are reported in Section VI.B., with reporting of regression results. We now discuss the rationale for included variables and their measurement:

1. Any Generic (G) and Number of Generics (N)

Sales (R): We postulate the same model for entry of Any Generic and Number of Generics, conditional on entry, but allow parameter estimates to differ. Following Bresnahan and Reiss (1991), Scott Morton (1999, 2000) and others, equations (1) and (2) hypothesize that any generic entry and number of generic competitors in a presentation-market depend on the market size (R, gross sales), assuming certain fixed entry cost per firm, due to regulatory and other entry requirements that may differ across countries. Market size is measured by annual sales at manufacturer prices in the retail and hospital channels combined, lagged two quarters.[12] Costs of entry differ by formulation (F), with higher manufacturing and regulatory costs for intravenous, topical, and other complex forms compared to simple oral solids (tablets and capsules).

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[12] The appropriate lag for the Originator sales variable depends on when generic firms make entry decisions. If potential entrants accurately project market sales at the time they are likely to enter, our two quarter lagged revenue measure should reasonably characterize the expected relative market size that was relevant to generic decisions to undertake entry.

Originator Defense Strategies (D): We test for effects of three potential originator defense strategies: Number of Licensees, Number of New Originator Formulations launched just prior to patent expiry, and OTC share, all lagged two quarters. Originators may have incentives to launch co-branded licensees to steel share and pre-empt generic competitors in physician-driven generic markets with brand competition. Such incentives are not expected in price-competitive, pharmacy-driven markets such as the U.S., except for authorized generics launched during the Paragraph IV exclusivity period.[13] Incentives to launch improved formulations, such as extended release forms, may exist in both pharmacy and physician-driven markets, because generic substitution is only permitted within a formulation. The originator's incentive to launch new formulations close to patent expiry of older forms is increased if the new forms receive some additional patent or regulatory exclusivity and can be reimbursed at prices above the price of generic versions of the older formulations. Such conditions exist in the U.S., where aggressive marketing can successfully switch physicians/patients to the new, protected forms and away from the patent-expiring form which faces generic entry. However, launching new formulations is less likely to be profitable in countries where reference pricing or similar reimbursement rules limit reimbursement for all formulations of a molecule to the lowest price per daily dose for that molecule, which is likely to be a generic once the patent expires on any formulation in the molecule. Finally, for molecules that meet regulatory requirements for patient self-medication, originators may launch an over-the-counter (OTC) formulation to preempt generic competition in the Rx formulation after patent expiry.

Molecule Global Age, Launch Lag and Diffusion (M) and Form (F): Molecule Global Age (months since first launch of the molecule in any of our sample countries, hereafter "global launch") is included as a proxy for unobserved patent term. The greater Molecule Global Age, the more likely that unobserved patents and other exclusivity barriers to entry have expired. Country-specific Molecule Launch Lag (months from global launch to first launch in country j) is a proxy for country-specific data exclusivities that usually run from the originator's country-specific launch. It is also expected to be positively associated with generic entry. Global

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[13] In the U.S., several originator firms in the early 1990's launched their own generic products to compete with true generics; however this strategy simply accelerated the downward pressure on generic prices and was abandoned. Originator launch of generics in the U.S. is now confined to "authorized generics" launched during the 180-day exclusivity period awarded to paragraph IV challengers, when prices remain high because only one ANDA-approved generic competitor is present..

Diffusion, measured as the number of countries in our sample in which the molecule is launched, is an indicator for availability of foreign supply sources and possible economies of scale for generic suppliers; it is expected to be positively associated with entry. A vector of Formulation indicators (F) controls for formulations (extended release, intravenous, topical, other complex forms) that have higher manufacturing and/or regulatory costs than the referent oral solid forms, and are therefore expected to attract less generic entry.

Regulatory Changes (Z): Entry incentives depend on regulatory and reimbursement provisions, which differ by country and over time within country. Because regulatory and reimbursement policies affecting generics differ significantly across countries and several countries changed multiple policies over our time period, we use two indicator variables for years 2002-2005 and 2006-2009 to measure the combined effects of country-specific policy changes. The referent period is 1998-2001.

2. Normalized Generic Price

Our measure of generic price P_{ijt}^G for presentation i in country j in period t is the volume-weighted average generic price for all generic versions of presentation ijt, normalized (divided) by the earliest originator price for presentation i in country j in our dataset. This normalization yields a unit-free measure of price that permits comparison of trends over time and across molecules and countries, for products with very different absolute price levels. It is independent of exchange rates and country-specific changes in the originator price.[14]

Number of Generic Competitors (N): Under standard models of competition, normalized generic price is expected to be inversely related to number of generic competitors, with a greater effect for unbranded generic competitors (N^u) than for branded generic competitors (N^b). The effect of generic competitors on price is expected to be greater in countries with pharmacy-driven vs. physician-driven markets.[15]

Regulatory Changes (Z), Formulation (F), and Molecule Characteristics (M): Time period indicators are included to capture effects of regulatory and reimbursement changes that affected generic prices directly, such as the change in reimbursement rules in the U.K., reference

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[14] Several previous papers use the contemporaneous generic/brand price ratio, which may confound changes in generic prices in the denominator with changes in originator prices in the numerator.
[15] N can be treated as predetermined in the price equation due to the regulatory lag in getting market authorization. In the U.S., this takes at least a couple of years.

pricing in France, or sickness fund contracting in Germany. Formulation indicators and Global Diffusion control for cost differences.

3. Normalized Originator Price

We estimate a similar model of normalized originator price P_{ijt}^{O}, also normalized to the earliest originator price for the same presentation in the dataset. Frank and Salkever (1992, 1997) and Regan (2008) have argued that originators pursue a segmentation strategy that leads to increased originator price in response to generic competition. Although this may have been an optimal strategy in the 1990's in the U.S., this may no longer be true in the 2000's, given the growth of insurance plans that require patients to pay the difference between the generic co-pay and the originator price or third-tier co-payment.. In most countries other than the US, including the U.K., price regulatory systems disallow post-launch originator price increases and, more generally, may make segmentation pricing strategies infeasible and/or non-optimal. In countries with generic reference pricing, such as Germany and France, although pricing above the reference price is permitted in theory, in practice originators usually cut price to the reference price because patient demand is very elastic above the reference price (see Stargardt, 2010, for recent evidence from Germany). Thus normalized originator prices are expected to be flat or declining after generic entry in most countries. It is an empirical question whether increasing price in response to generic entry remains an optimal strategy in the US and possibly Mexico, where price regulation is weakly enforced.

4. Generic Volume Share

Generic volume share is expected to be inversely related to generic price in pharmacy-driven markets. In physician-driven markets, price sensitivity is expected to be weaker, especially for branded generics and before reforms to stimulate price sensitivity. Simultaneous determination of price and volume is expected in countries where generic prices are competitively determined (U.S., U.K.). We therefore estimate eq. (4) with both OLS and two-stage least squares (2SLS), in which generic price is treated as endogenous using the hospital price and an indicator for chronic medications as instruments. For other countries where generic prices are set by regulation or constrained through RP reimbursement, generic prices may be less responsive to market conditions, in which case OLS estimation may be appropriate. The Generic

Volume Share equations also include as control variables: number of branded and unbranded competitors (treated as predetermined), generic age (months since first generic launch of presentation i in country j), formulation and molecule effects, as well as time dummies to capture regulatory changes.

VI.   Results

A. Descriptive Analysis

We first characterize the cross-national differences in generic markets using graphic analysis to compare generic entry, generics prices and shares across countries. For some variables, we compare starting (1998-2001) and ending (2006-2009) values, hereafter referred to as 2001 and 2009. For other variables, we show average values over the entire period to conserve space, but note that this masks the changes over time, which are discussed later. Descriptive statistics are reported in Appendix Table 1.

1.   Any Generic and Number of Generics

Almost all countries experienced an increase in the percent of molecules in the 8-20 year cohort with generic entry over the 2000's decade (Figure 1). France had the largest percentage increase from 7 to 25 percent. Brazil has the highest generic presence, with 41 percent of molecules age 8-20 years having a generic, plausibly reflecting similares that entered before patent protection.

Figure 2 shows the effective patent life or mean age of the originator at first generic entry for the molecule (Generic launch lag).[16] The low initial values in 2001 for Spain (8.1 years) and Italy (8.7 years) may reflect originator-initiated ("authorized") generics that do not represent a true generic challenge to effective patent life. Over time, generic launch lags decline in some countries, including France, Germany and the U.K., reflecting more rapid entry possibly in response to pro-generic policies. Generic launch lags increased in Italy, Spain, Brazil and Mexico, possibly reflecting fewer copy products as enforcement of IP improved. In the U.S. the mean generic lag increased minimally, from 11.2 in 2001 to 11.4 in 2009. This suggests that any

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[16] A small number of generic launches reportedly occurred within 5 years of the originator launch. We treated such early launch dates as implausible and excluded them from these calculations in all countries except Brazil, Chile, Mexico, Italy, and Spain, which had late or weak patent enforcement.

increase in Paragraph IV patent challenges was on average offset by increased use of exclusivity extensions, such as for pediatric trials. Effective patent life is almost two years longer in the US (11.3 years) than in Canada (9.4 years).

Once generic entry occurs, in most countries the number of generic manufacturers increases initially and reaches a plateau roughly two years from first generic entry (Figure 3). Germany has the most generic manufacturers per presentation, averaging 9 by quarter 5, followed by France and Japan at 5-6, all traditionally branded generic markets. By contrast, the U.S. averages 4-5 generic manufacturers per presentation. Although Brazil and Mexico have a high proportion of molecules with generic presence, they have relatively few (1-2) generics per presentation.

This evidence of more generics per presentation in countries other than the U.S. is *prima facie* surprising because the U.S. has much larger sales, by value or volume, than other countries (Table 2-3). Country-specific studies (e.g. Scott Morton, 1999) have consistently found a strong relationship between number of generic entrants and sales, consistent with standard entry models with fixed costs (Bresnahan and Reiss, 1991). This cross-national evidence of more manufacturers per presentation in much smaller markets than the US implies that the gross sales value necessary to attract generic entry is lower in other countries, plausibly due to higher expected generic prices and less price-competitive generic markets in other countries.

To provide evidence on this, Table 3 shows median annual sales per generic manufacturer and price per dose at 2 years since generic entry, overall and by number of generics per presentation. All other countries (except Japan) have lower overall average gross sales per generic manufacturer and higher average price per dose than the U.S., followed by the U.K.[17] Price per dose is relatively high ($0.88) in the U.S. for presentations with only one generic, which would primarily reflect paragraph IV exclusive markets. However, for the typical presentation with at least 4 generics, the U.S. average price ($0.23) is lower than all other countries except the U.K. ($0.22). Conversely, Canada has the highest generic prices and lowest sales per manufacturer, plausibly due to regulatory barriers to price competition. The decline in average generic price with number of manufacturers is greater in the U.S. and the U.K. than in other countries – indeed, the relationship is positive or flat in Canada, Italy, Japan and Mexico.

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[17] Japanese price are lower on a per dose basis because average grams of active ingredient per dose are consistently lower in Japan than in most other countries (Danzon and Furukawa, 2008).

This evidence is consistent with the branded and/or price-regulated generic markets being less price competitive than the U.S. and U.K., enabling generics firms to survive on lower gross sales per presentation than is feasible in the more price competitive U.S. or U.K. markets.[18]

Figure 4 shows the life-cycle of normalized generic prices by quarter since first generic entry.[19] In the U.S., generic prices are initially 75 percent of baseline originator price, consistent with limited competition during the paragraph IV exclusivity period. Thereafter, generic prices drop rapidly to 36 percent of baseline originator price after two years. The U.K., Germany and Mexico also have declining generic prices after generic entry but at higher levels – declining after two years to 60 percent of the originator price in the U.K., 50 percent in Germany and 72 percent in Mexico. In all other countries, generic prices are relatively flat over time, at 50-70 percent of baseline originator prices, despite entry of more competitors shown in Figure 3. This evidence of relatively high normalized price levels that are flat over time despite competitive entry is consistent with the hypothesis of weak price competition in physician-driven, branded generic markets, despite multiple generic competitors per presentation.

Figure 5 shows that normalized originator prices are generally stable in response to generic entry, but at different levels reflecting different regulatory regimes. In the U.S., the mean normalized originator price is 1.24 at generic entry, reflecting the increase in real originator prices over time prior to patent expiration that is common in the U.S.[20] However, whereas some earlier studies found that originator prices increase in response to generic entry (Frank and Salkever, 1997; Regan, 2008), our results show a modest decline in originator prices after generic entry in the U.S. from 1.24 to 1.13, possibly reflecting the smaller size of the brand loyal market in recent years compared to the time of these earlier studies. In Germany and France, originator prices decline by 21 and 12 percent, respectively, in the 2 years post generic entry, plausibly reflecting the incentive of originators to cut prices to the reference price in these countries. In most other countries originator prices are stable over the two years following

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[18] These IMS prices may be upward biased for true transactions prices in countries where off-invoice discounts to pharmacies are common. These discounts average over 30 percent in the U.S. (CBO, 2005). The fact that gross sales per generic are smaller in other countries than in the U.S. makes it unlikely that any unobserved discounts are greater in other countries than the U.S.

[19] Recall that normalization is to the earliest originator price available in our dataset ("baseline originator price"), which is invariant over time for each presentation. Although these baseline originator prices are observed at different originator ages, including some that occur after generic entry, given the stability of originator prices (see Figure 5) this should not matter. Moreover the normalization is invariant over time for a given presentation, so measures of generic price change over time are unaffected by differences across molecules in the baseline originator age.

[20] Recall that we deflate all nominal prices by the country-specific general Producer Price Index.

generic entry, between 70-90 percent of baseline prices (except 60 percent for Italy), consistent with regulatory constraints on price increases and possibly some mandatory cuts. .

Conditional on generic entry, generic penetration is most rapid and reaches the highest peak in the U.S. (89 percent of unit volume in two years), followed by Canada (74 percent) (Figure 6). High generic penetration in Canada, despite its high regulated generic prices, is consistent with the hypothesis of extensive off-invoice discounting to pharmacies that is not captured by payers or in the IMS data. Ontario has recently taken steps to change this system.[21] The U.K. also has relatively rapid generic adoption due to strong pharmacy substitution incentives. In Germany the rapid generic adoption presumably reflect both drug budgets for physicians and requirements for generic substitution adopted during the 2000s. Japan and Italy have the lowest generic shares (under 40 percent).

Over the 2000's, most countries experienced growth in generic uptake, primarily due to growth in unbranded generics (Figure 7). Of the four E.U. countries that adopted significant pro-generic policy changes (France, Germany, Italy and Spain) all started with relatively high branded generic shares in 2000 but achieved growth in unbranded and total generic penetration over time, except Italy, where growth in unbranded share is more than offset by decline in branded generic share. Although at the start of the period only the U.S., Canada and the U.K. had predominantly unbranded generics, by the end this was also true for France, Germany, and Spain. By contrast, Brazil and Mexico remain predominantly branded, and Japan is roughly evenly split, but with a very low generic share.

B. Multivariate Regressions

Appendix Tables 2-5 report the full regression analysis of determinants of generic entry, generic and originator prices and generic market shares, for branded and unbranded generics combined, to conserve space. Summary Tables 4-7 report key coefficients, including coefficients with branded and unbranded generics measured separately. We estimate separate equations for each country, to permit all coefficients to vary across countries. The unit of observation is the country-quarter-presentation (molecule-formulation-strength). We report marginal effects with robust standard errors and clustering by molecule to address unobserved molecule-specific effects. Some explanatory variables that are treated as pre-determined are lagged two quarters.

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[21] See http://www.mercer.ca/referencecontent.htm?idContent=1377645&siteLanguage=1007, accessed 6/24/2011.

We report probit estimates for the Any Generic equation and use a negative binomial estimator for the Number of Generics equation. Results are robust to alternative estimation methods, including OLS and zero-inflated negative binomial models. [22] To address the potential endogeneity of price in the volume share equations for countries where generic prices are determined by market competition (especially the U.S. and U.K.), we estimated both OLS and two-stage least squares (2SLS) via generalized method of moments (GMM). Instrumental variables are generic price in the hospital channel and an indicator for therapeutic classes that treat chronic conditions. These results are reported below the OLS estimates in Table 4.

1. Any Generic and Number of Generics

The probability of Any Generic and Number of Generic manufacturers conditional on entry are both positively related to lagged log sales in almost all countries (Table 4), consistent with standard theories of entry in markets with fixed costs and evidence from previous studies. The exception is that Any Generic is not significantly related to sales in the U.S., suggesting that even small markets attract generic entry. In the traditionally physician-driven, branded generic markets of France, Germany, Spain and Italy, the responsiveness of entry to sales is higher for unbranded generics than for branded generics, as expected if unbranded generics are typically lower priced and therefore need larger sales volume to break even.

The evidence in Appendix Tables 2-3 suggests that proliferation of licensee brands by the originator does deter entry of any generic in Italy, consistent with Magazzini et al. (2004), but not in other countries.[23] There is no support for the hypothesis that licensees reduce the Number of Generics, conditional on entry, in any country. Thus, this more recent evidence conflicts with earlier findings for Canada (Hollis, 2003) and Germany (Appelt, 2009), possibly because a brand saturation strategy becomes ineffective as a generic entry deterrent as generic markets become more unbranded and pharmacy-driven, as competition shifts to price rather than brand.[24]

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[22] We do not estimate a hazard model for generic launch because defining the starting point is conceptually and empirically problematic, given that patents can be challenged, and we lack data on expected expiry dates for patents and data exclusivities.

[23] The marginally significant negative coefficient on licensees in the Any Generic equation for the U.S. is probably spurious. Licensee proliferation is irrational in a market dominated by pharmacy substitution, and co-branding is extremely rare in the US. The mean number of licensees in the U.S. (0.42) compared to Italy (0.76) and Germany (0.86) is consistent with the hypothesis that licensing co-branded pseudo-competitors is a less common strategy for originators in the U.S. than in physician-driven, branded generic markets.

[24] The significantly positive licensee coefficients for Number of Generics in Spain and Brazil may reflect coding error, because licensees in these countries may be local branded generics manufacturers.

The originator defense strategy of launching alternative formulations shortly prior to patent expiry does deter any generic entry in the U.S. and also reduces number of generic entrants in the U.S. and Canada, but not in other countries. This evidence that launching new formulations is uniquely effective in the U.S. (and partially effective in Canada) is consistent with the hypothesis that U.S. reimbursement systems facilitate both switching patients and maintaining high prices for these new forms, compared to price-regulated markets which often reimburse new formulations at the same price as older versions of the same molecule under reference pricing.

Extended release, intravenous, topical and other complex formulations are much less likely to attract generic entry than oral solids in multiple countries, plausibly due to higher manufacturing and possibly regulatory costs. OTC market share of the presentation does not deter Any Generic entry but does reduce number of generic entrants in the U.S., plausibly because OTC prices are relatively cheap in the U.S. and hence offer consumers a popular alternative to generic Rx versions, although the OTC forms are not covered by insurance. OTC effects are also negative for France. Hospital share of sales is negatively related to Any Generic and Number of Generics in most countries.[25] This suggests that hospitals markets are less attractive to generics than retail pharmacy sales, possibly because originators give large price discounts to hospitals in most countries, including in countries that regulate retail prices.[26]

Molecule Global Age is positively related to Any Generic and Number of Generics, confirming that this variable is a rough proxy for unobserved patent terms. Delay in originator launch is negatively related to Any Generic and Number of Generics in the U.S., with less consistent effects in other countries, suggesting that data exclusivities that run from country-specific molecule launch are a more binding barrier to generic entry in the U.S. Global Diffusion of a molecule is positively associated with Number of Generics in Canada, Germany, Spain, Brazil and Mexico, suggesting that availability of foreign supplies of active ingredients and/or finished product facilitates generic entry in these countries, because local generic firms rely on foreign suppliers.

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[25] The IMS data do not report hospital sales for the Latin American countries.
[26] Scott-Morton (1999) found a positive relation between hospital share and generic entry. Magazzini et al. (2004) found a negative relation between hospital share and unbranded generic share in a regression that pooled 4 countries, including the U.S.

2. Prices

Normalized Generic Prices: Previous studies of U.S. generic markets have consistently shown that generic prices decline with number of generic competitors. Whether price competition works as effectively for physician-driven, branded generics markets and how this has changed over time are important empirical questions addressed in Appendix Table 4, summarized in Table 5.

Normalized generic prices are negatively related to number of unbranded generics in most countries, and unbranded generics are more effective at reducing prices than branded generics in Germany, Italy, Spain, Brazil and Mexico, as predicted. Prices are unrelated to number of competitors in France, suggesting that the reference price system and other regulations may have blunted price competition. In Japan, generic prices are negatively related only to branded generics, possibly because unbranded generics are still uncommon. Unbranded and branded generics have similar and large negative effects on price (0.076 and 0.097 percent, respectively) in the U.K., where aggressive pharmacy substitution plausibly forces both branded and unbranded generics to compete on price. In Canada an additional branded or unbranded generic reduces generic price by only 0.01 percent, plausibly due to regulation of generic prices that applies to both unbranded and branded generics. In Mexico generic prices are positively related to number of branded suppliers.

Normalized Originator Prices: Consistent with our graphical analysis, multivariate regression analysis shows no evidence that originator prices increase with number of generics in the U.S. (Table 5), contrary to segmentation theory and previous evidence (Frank and Salkever, 1997; Regan 2008). The measured effect for number of unbranded generics is negative but very small (0.006) and only marginally significant in the U.S. By contrast, originator prices are negatively related to the number of unbranded generics but number of branded generics has no effect in France, Italy and Spain. This suggests that the reference pricing systems in these countries have brought down originator prices and, together with other measures, have encouraged the entry of unbranded generics that compete on price.

3. Generic Volume Shares

Table 6 reports effects of generic prices on generic volume shares for OLS and 2SLS-GMM estimators. Endogeneity of generic prices is plausible in the U.S. and the U.K., where generic prices are unregulated and generics compete on price to gain market share. The 2SLS

estimates pass tests for instrument validity and overidentification in all countries. For other countries where generic prices are either regulated or constrained by reference pricing, and competition focused on brand rather than price at least initially, prices are less endogenous to share, and OLS results may be plausible. For most countries the OLS and 2SLS results are similar, with 2SLS showing slightly more negative share elasticities than OLS, especially in Canada.[27]

Generic volume shares are significantly negatively related to generic prices in the U.S., the U.K. and Canada, the three countries with pharmacy-driven generic markets throughout the period, and also in France and Germany, which adopted measures to stimulate switching to cheaper generics over the 2000's. The estimated elasticity of volume with respect to price for Canada is much more negative using 2SLS (-1.114) than OLS (-0.382), which suggests that the hospital generic price we use as an instrument is a more accurate indicator of the true ex-manufacturer price to pharmacists, net of unobserved discounts, than the official retail price reported in the IMS retail data.

Generic price has no significant effect on generic share in Italy, Spain and Japan. The lack of price sensitivity is unsurprising in Japan, because physicians' absolute dispensing margins tend to increase with drug price. Lack of price sensitivity in Italy and Spain may reflect reference price reimbursement systems that encourage originators to drop their price to the reference price (Garratini and Ghislandi, 2006), thereby eliminating financial incentive for physicians/patients/pharmacists to prefer generics. The estimated OLS effect of generic price on share is positive in Mexico, despite its predominantly self-pay market. This is consistent with the hypothesis that consumers purchase on brand rather than price when quality is uncertain due to lack bioequivalence requirements (Danzon, Mulcahy and Towse, 2011).

Generic shares are also positively related to Generic Age (years since generic entry), consistent with standard diffusion models. Controlling for price, generic shares are positively related to number of generic manufacturers in most countries; however, we treat this primarily as a control variable due to the possibility of endogeneity.

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[27] For Brazil and Mexico, 2SLS cannot be estimated due to lack of data on hospital price which is used as an instrument.

4. Effects of Policy Changes

To provide a rough measure of the effects on generic entry, prices and shares due to policy changes and other factors over our time period, the regressions include two indicator variables, for years 2002-2005 and years 2006-2009, with the initial period 1998-2001 as the referent. Table 7 reports the coefficients on the 2006-2009 indicators, with tests for significance of change relative to the initial period.

The probability of Any Generic has increased significantly in the U.S.,[28] the U.K., France and Germany, all of which have adopted measures to promote generic entry. Number of generic manufacturers per presentation, conditional on entry, has increased significantly in France, Germany, Italy and Brazil, with positive but less significant effects in Spain and Mexico. Interestingly, the number of branded generic manufacturers has declined significantly in the U.K., Germany, Italy, Spain and Japan, while the number of unbranded generic manufacturers has increased significantly in all countries except the U.S., U.K. and Canada, which had strong unbranded generic presence and pharmacy-driven markets initially, and Mexico. Thus, the policy changes have clearly had some success in promoting entry of unbranded generics.

Normalized generic prices have declined in all countries except in the U.S., which already had very low generic prices. The large decline in U.K. generic prices plausibly reflects the changes in generic reimbursement adopted in 2005. Normalized originator prices declined in all countries except the U.S. and Mexico, where they increased, and Canada with no change.

Generic share of volume, conditional on generic presence, has increased significantly in the U.S., U.K., France, (Japan) and Brazil. With the exception of Brazil, this generic share growth is due almost entirely to unbranded generics, which have also had very modest share growth in Japan. Thus, the policy changes in the E.U. countries appear to have increased the number of generics and their market share, with greatest growth (18.8 percent) in France. The U.S. and the U.K. have also seen 18.2 and 15.5 percent, respectively, increase in generic market shares. The largest decline in generic prices was in the U.K. (33 percent), followed by France, Italy, Spain and Brazil (25-29 percent).

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[28] The U.S. 2003 MMA limited originator incentives to use patent proliferation to deter generic entry, by permitting only one 30 month stay per product.

VII. Savings from Generics

Payer savings from generics depends on the generic-originator price difference and on the share of prescriptions that are dispensed generically.[29] We calculate the percent savings from generic price, generic unit volume and generic savings as a percent of total drug spending in 1998-2001 and 2006-2009, calculated as follows (where Q denotes units, P denotes price, superscripts O and G denote originator and generic, respectively): Percent savings in price, $[(P^O - P^G)*Q^G] / (P^{G*}Q^G)$, measures the counterfactual percent increase in cost if all generically-dispensed units were sold as originators; Percent savings in volume, $(P^G*Q^G) / (P^G*Q^G + P^O*Q^O)$, is the generic share of unit volume for molecules in our 8-20 year cohort, weighted by their respective prices; Total percent savings for the 8-20 age cohort , $[(P^O - P^G)*Q^G] / (P^O*Q^G + P^O*Q^O)$, measures how much higher expenditure would be if there were no generics for drugs in the 8-20 year cohort. An alternative Total savings measure calculates the generic savings for the 8-20 year cohort as a percent of total expenditure on all drugs. The estimates for each time period and country are in Table 8, which also reports the change in savings between the early and later periods.

Savings from low generic prices are far greater in the U.S. than in any other country in 2001, but by 2009 the U.K. prices yield similar savings and the U.K. therefore has the greatest increase in price savings over the period. Of course, these estimates are sensitive to the originator prices, which are relatively high in the U.S., but the U.S. generic prices are also absolutely low relative to other countries (Table 3).

The savings from generic share of unit volume increased most in France, from 7 percent in 2001 to 55 percent in 2009. As of 2009, generic shares of the 8-20 year cohort total volume are higher in Canada, the U.K., France and Germany than in the U.S., because although the U.S. has the highest generic penetration conditional on generic entry, Canada, France and Germany on average have earlier generic entry, presumably due to fewer patent extensions for originators. Thus although Paragraph IV challenges have shortened expected patent life for some drugs,

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[29] Our savings calculations ignore any change in total (originator plus generics) unit volume of the molecule following generic entry. In theory lower generic prices might induce increased utilization of molecules with generics, including therapeutic substitution away from similar, on-patent molecules. In practice, U.S. evidence generally indicates no increase in utilization at the molecule level following generic entry, plausibly because any positive response to lower prices is offset by the decline in originator promotion that occurs in markets with pharmacy substitution, unless payers aggressively encourage therapeutic substitution, as some payers did when generic simvastatin became available in the statin class.

originators in the U.S. on average lose less volume share to generics than originators in these other countries in the 8-20 year phase of originator life. Relatively high originator prices in the denominator also reduce our measure of volume savings for the U.S.

The total generic savings on the 8-20 year cohort are highest in the U.K. and the U.S., which would have spent 272 percent and 238 percent more, respectively, on these drugs, in the absence of generics. Canada, France and Germany would have spent 43-55 percent more, in the absence of generics. Among the E.U. countries which made major changes, only France has significant increase in savings (39.3 percentage points) from 1998-2009. In Germany savings on price and total savings appear to have declined, even though volume share increased; however, price savings in Germany may be understated if the discounts granted directly to sickness funds are not reflect in IMS price data. Spain has modest declines in price and volume savings from generics, possibly because reference pricing has reduced prices but increased volume share for originators. And such savings, due to the effect of generics on originator prices, are not reflected in our estimates of savings due to generics.

Generic savings as a share of total drug spending is under 10 percent in all countries except the U.S. and U.K. However, this measure is heavily influenced by on-patent originator prices in the denominator, which reflect policies to encourage R&D and other factors. This Total savings measure is therefore less relevant as a measure of savings achieved by policies to encourage generics than the measures which report savings relative to total sales for the 8-20 year cohort.

VIII. Conclusions

Cross-national differences in policies towards generics have resulted in major differences in generic entry, generic prices and generic market shares, and in whether generic markets are pharmacy-driven with unbranded generics, as in the U.S. and U.K., or physician driven with branded generics, as has traditionally been the norm in most other countries. Over the last decade, policies adopted in France, Spain, Italy and Germany to increase generic uptake and price-competitiveness have resulted in some growth in the share of unbranded generics in these countries. Reference pricing policies may have stunted the growth of generic shares and price competition, although to the extent that they also reduce originator prices, they yield savings without generic adoption. As of 2009, the policy changes appear to have been most effective in

France, which experienced a large increase in generic penetration and some reduction in generic prices, whereas incremental savings were at most modest in Italy, Spain and Germany. The U.K.'s policies to reduce generic reimbursement prices have also achieved very significant price savings and increased generic penetration. Although the data do not permit precise measurement of individual policy effects, these results are consistent with the hypothesis that policies to shift generic markets from physician-driven, branded generics towards pharmacy driven, unbranded generics, can potentially yield significant savings to payers, provided that these policies are appropriately designed such that payers rather than pharmacies capture most of the savings.

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Table 1: Regulatory and Reimbursement Rules, by Country

	Pharmacy Generic Subst.	Pharmacy reimb based on price	Discounts to pharmacies	Generic RP	Regulated Generic Price	Patient co-pay incentive, other than RP	Physician Incentive
US	Yes	No	Yes	Yes	No	Yes	No
UK	Yes [1]	No	Yes	Yes	No	No	Yes
Canada	Yes	No	Yes	Yes	Yes	No	No
France	1999	Pre 2002	Yes	2003	Yes	No	2000 [2]
Germany	2002	Pre 2007	Banned in 2006	1989	No	No	Yes
Italy	2001	Yes	No	2001	Yes	No	No
Spain	Yes	No	Yes	2000	No	No	No
Japan	No	Yes	Yes	No	Yes	Yes	No
Australia	1994	Yes	Yes	Yes	Yes	No	No
Mexico	No [3]	No	No	No	No	Yes	No
Chile	No	No	No	No	No	Yes	No
Brazil	Yes	No	No	No	2004	Yes	No

[1] INN Rx only for outpatient Rx; also substitution for originator Rx in hospitals.

[2] From 2000, French physicians were required to prescribe at least a specified percent generic, which has increased over time.

[3] Substitution permitted only with interchangeable generics, which were a small share of total volume until 2005, and if the prescription is generically written. Since over 60% of Rx-bound medicines are dispensed without an Rx, substitution restrictions may be moot.

Figure 1: Percent of Molecules with Any Generic

Y-axis: Percent of Molecules with Any Geneirc

Data labels (Years 1998-2001 [count], Years 2006-2009 [count]):
- U.S.: 0.22 [192], 0.34 [250]
- U.K.: 0.18 [182], 0.29 [222]
- Canada: 0.29 [150], 0.35 [196]
- France: 0.07 [174], 0.25 [207]
- Germany: 0.21 [227], 0.33 [244]
- Italy: 0.25 [212], 0.28 [209]
- Spain: 0.36 [187], 0.34 [213]
- Japan: 0.30 [309], 0.36 [302]
- Brazil: 0.38 [169], 0.41 [182]
- Mexico: 0.22 [184], 0.31 [216]

Note: Sample includes molecules with global age 8-20 years
No.of molecules in sample reported in brackets

■ Years 1998-2001   ■ Years 2006-2009

Figure 2: Mean Molecule Age at Generic Entry (Generic Launch Lag)

Y-axis: Originator Age at First Generic Launch

Data labels (Years 1998-2001, Years 2006-2009):
- U.S.: 11.2, 11.3
- U.K.: 12.0, 11.4
- Canada: 10.5, 9.4
- France: 12.5, 10.8
- Germany: 11.3, 10.1
- Italy: 8.7, 11.0
- Spain: 8.1, 9.9
- Japan: 11.9, 12.1
- Brazil: 5.9, 8.3
- Mexico: 9.4, 9.7

Note: Sample includes molecules with global age 8-20 years

■ Years 1998-2001   ■ Years 2006-2009

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Figure 3: Generic Manufacturers, By Time Since First Generic Entry

Note: Sample includes molecules with global age 8-20 years

◆ U.S.   ■ U.K.   ▲ Canada   ■ France   ✳ Germany   ● Italy   ■ Spain   — Japan   ◆ Brazil   ▲ Mexico
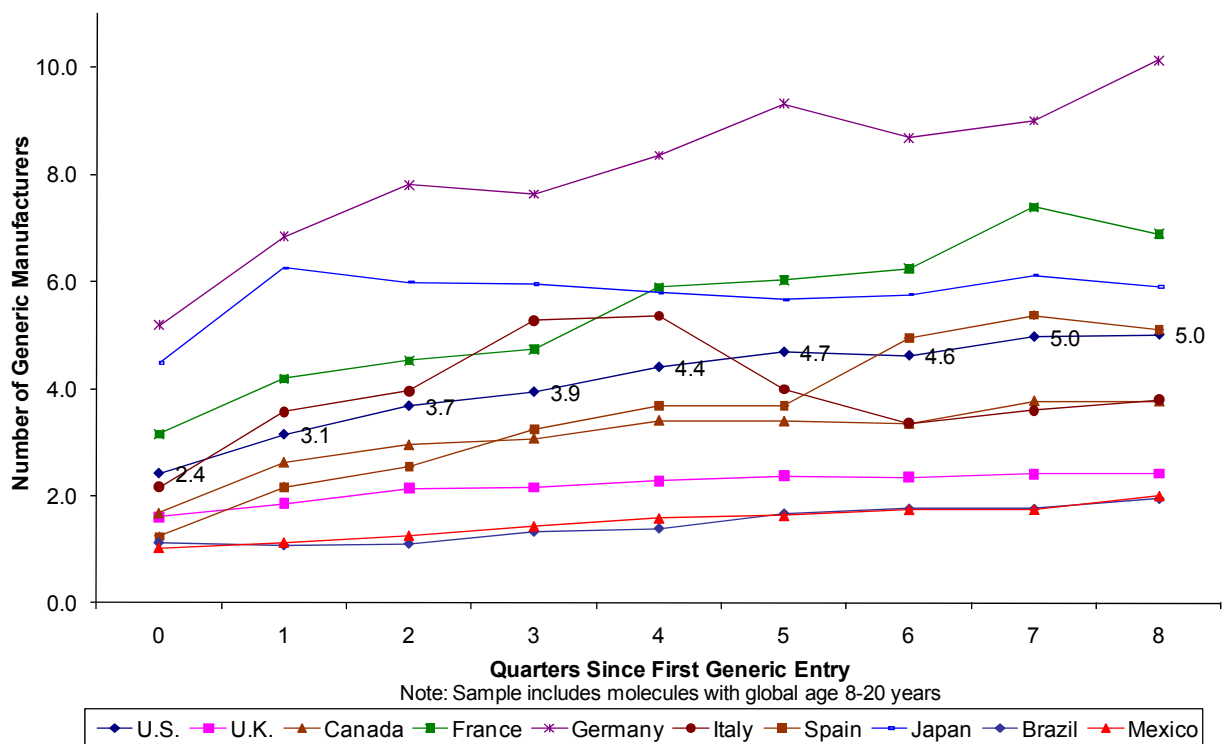
Figure 4: Normalized Generic Price, By Time Since First Generic Entry

Note: Sample includes molecules with global age 8-20 years

◆ U.S.   ■ U.K.   ▲ Canada   ✕ France   ✳ Germany   ● Italy   + Spain   — Japan   ◆ Brazil   ▲ Mexico

30
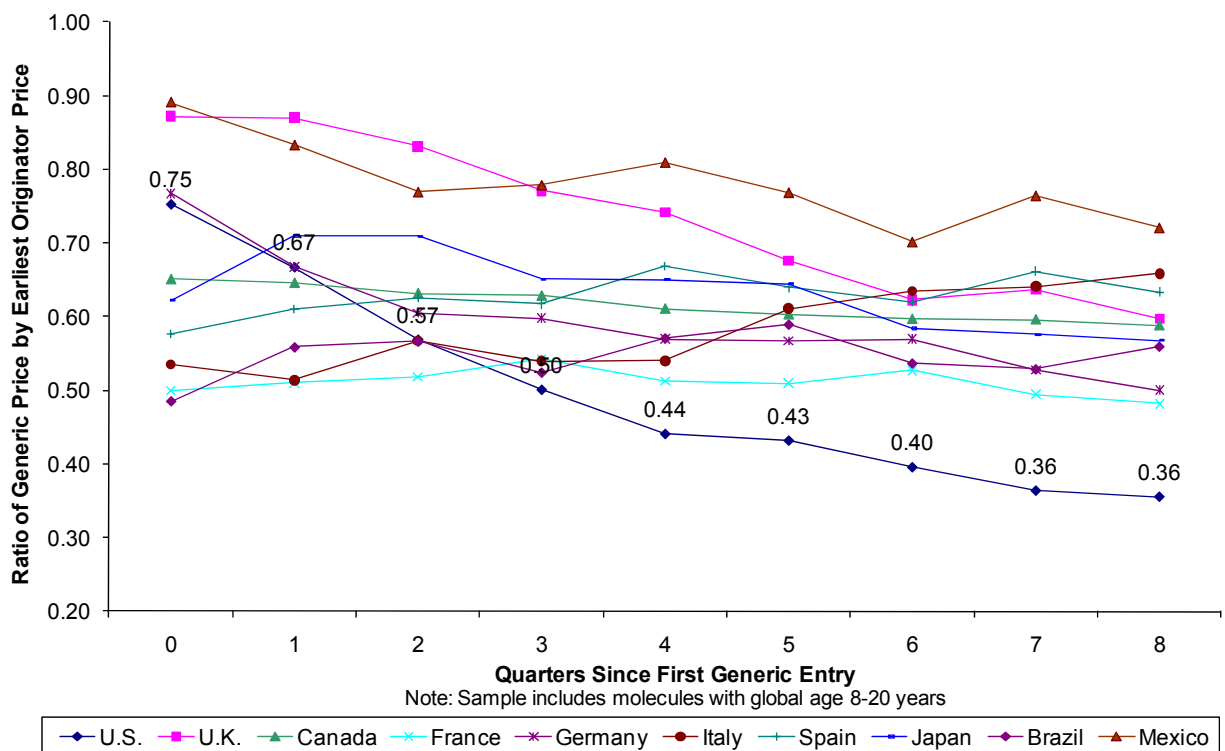
Figure 5: Normalized Originator Price, By Time Since First Generic Entry

Note: Sample includes molecules with global age 8-20 years

◆ U.S. ■ U.K. ▲ Canada ✕ France ✳ Germany ● Italy ✦ Spain — Japan ◆ Brazil ▲ Mexico
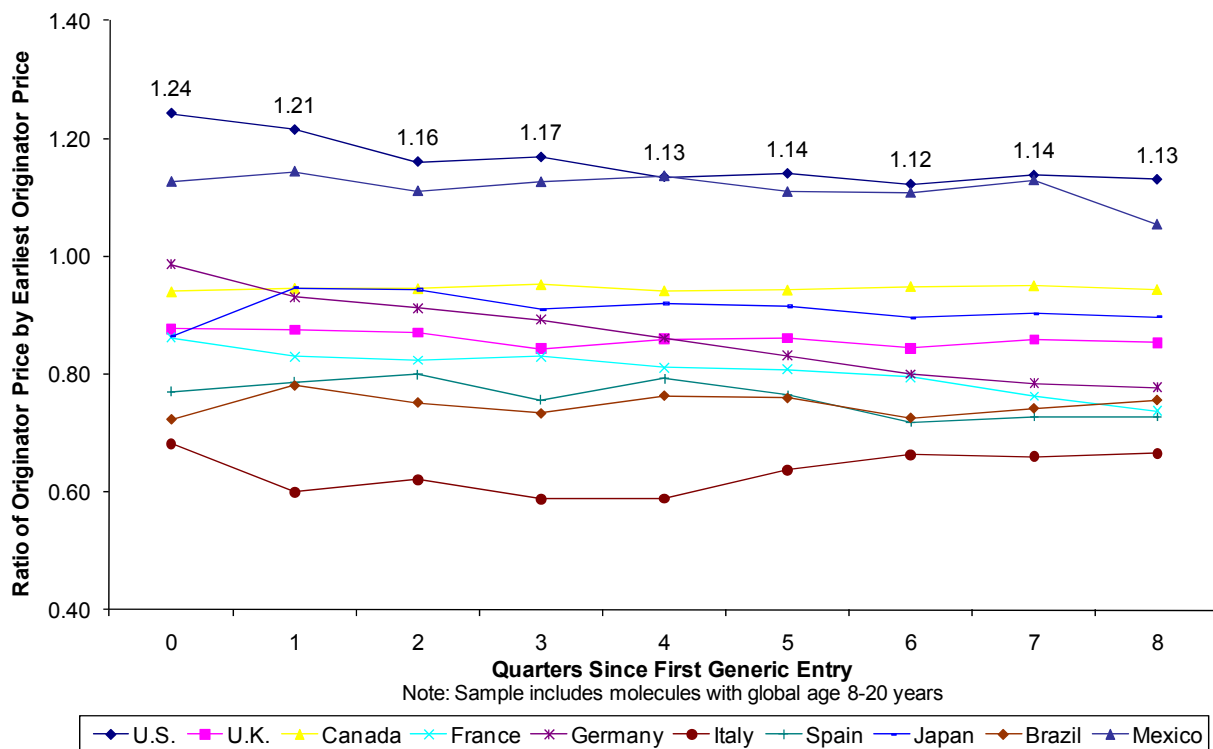
Figure 6: Generic Share of Volume, By Time Since First Generic Entry

Note: Sample includes molecules with global age 8-20 years

◆ U.S. ■ U.K. ▲ Canada ■ France ✕ Germany ● Italy ✦ Spain — Japan ◆ Brazil ▲ Mexico

31
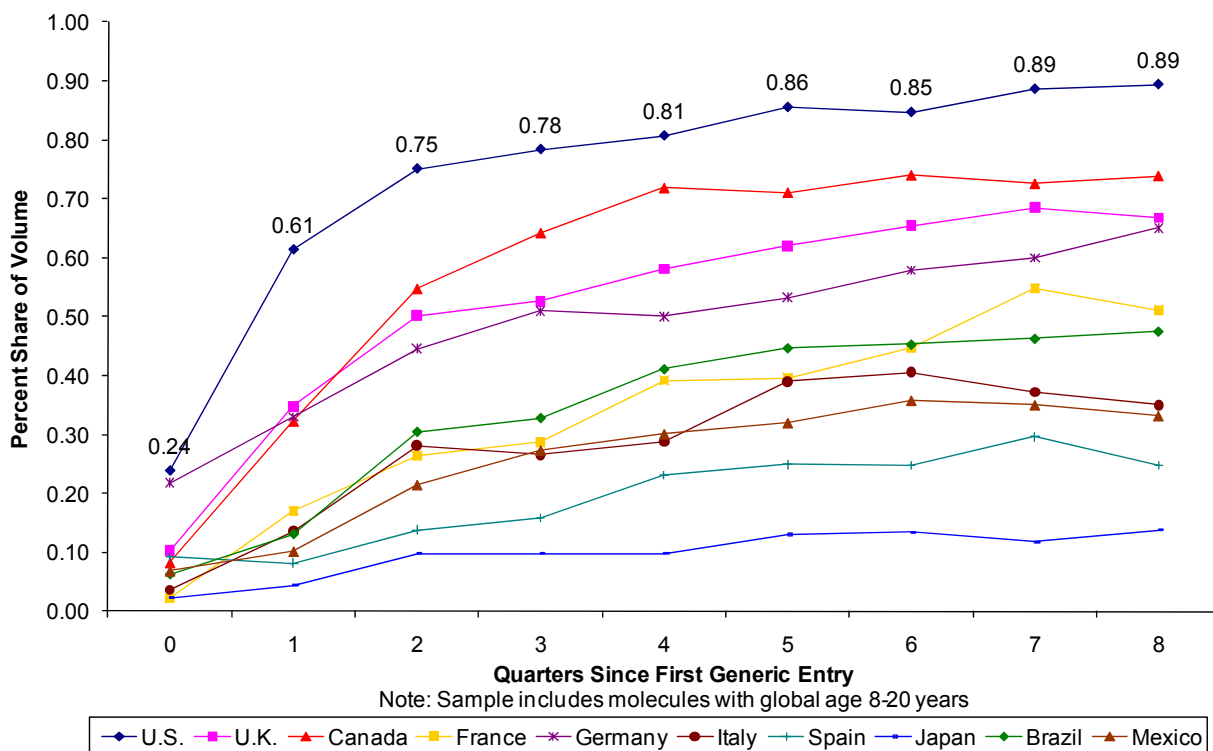
Figure 7: Generic Share of Volume, 24 Months Since First Generic Entry

Note: Sample includes molecules with global age 8-20 years

Legend: ■ Branded generic ■ Unbranded generic
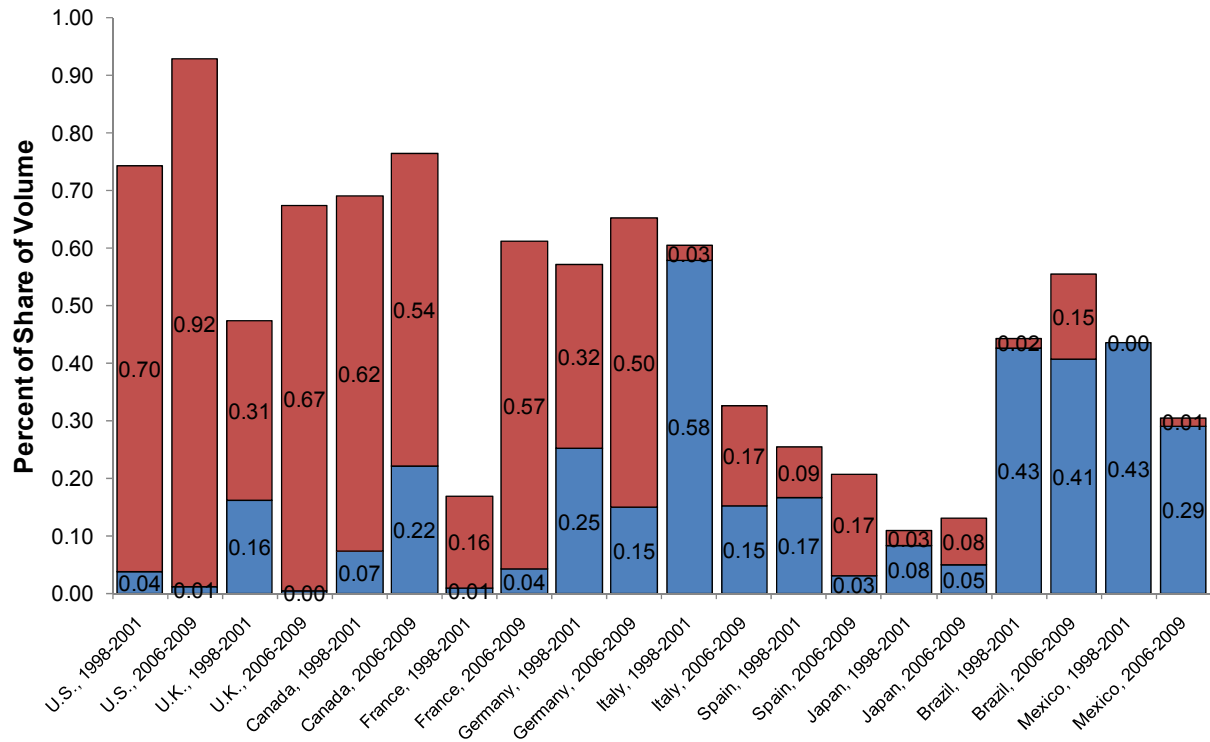
Table 2: Pharmaceutical Sales and Unit Volume

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Sales										
Total market	$326,438	$24,001	$21,564	$51,742	$52,615	$31,731	$26,375	$111,732	$21,731	$13,992
Retail market[1]	160,840	12,165	11,701	16,672	16,218	10,135	13,410	38,239	5,877	4,260
Generic market	40,459	4,662	5,307	4,228	6,845	2,875	3,734	9,510	3,562	1,843
Sample cohort[2]	83,333	3,852	3,966	5,101	4,515	2,841	3,219	14,923	797	763
Generic market	6,324	615	953	654	1,126	264	414	354	354	88
Unit volume										
Total market	505,325	114,274	79,097	147,957	158,167	66,998	71,519	339,007	124,123	62,118
Retail market[1]	170,899	45,738	31,764	39,630	39,317	28,335	35,026	135,878	20,394	7,649
Generic market	128,555	31,540	25,500	19,264	30,357	13,125	17,246	76,733	14,424	4,627
Sample cohort[2]	41,574	9,107	5,234	9,219	9,898	7,461	7,689	28,563	2,258	750
Generic market	18,215	5,150	1,991	2,260	6,313	1,212	2,223	1,545	1,331	178
Generic % sales										
Retail market[1]	25.2	38.3	45.4	25.4	42.2	28.4	27.8	24.9	60.6	43.3
Sample cohort[2]	7.6	16.0	24.0	12.8	24.9	9.3	12.9	2.4	44.4	11.6
Generic % volume										
Retail market[1]	75.2	69.0	80.3	48.6	77.2	46.3	49.2	56.5	70.7	60.5
Sample cohort[2]	43.8	56.5	38.0	24.5	63.8	16.2	28.9	5.4	58.9	23.8

Sales ($USD) and unit volume are reported in millions for the 12 months ending June 2009. [1]Retail market excludes combination products, biologics, OTC, and hospital channel. [2]Sample cohort includes molecules with global age 8-20 years.

Table 3: Market Size and Generic Entry

Median annual sales ($USD, M, 2009 exchange rates) and mean generic price per dose ($USD) at 24-27 months since generic entry

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Per generic manufacturer										
Annual sales	3.99	2.88	1.11	2.00	1.02	2.66	1.96	4.03	1.87	1.16
Price per dose	0.36	0.37	0.57	0.39	0.38	0.49	0.43	0.30	0.49	1.00
1 generic manufacturer										
Annual sales	2.41	2.06	1.58	2.50	5.40	5.49	3.67	1.59	2.30	1.09
Price per dose	0.88	0.44	0.51	0.67	0.93	0.56	0.60	0.27	0.49	0.92
2 or 3 generic manufacturers										
Annual sales	11.02	5.22	3.25	3.94	1.76	2.24	5.72	8.27	8.39	3.01
Price per dose	0.47	0.47	0.59	0.30	0.40	0.24	0.44	0.31	0.47	1.32
4+ generic manufacturers										
Annual sales	34.0	18.0	6.11	20.4	11.37	13.4	16.66	50.3	5.30	6.88
Price per dose	0.23	0.22	0.57	0.40	0.32	0.52	0.37	0.32	0.45	1.03

n/a, no cases in sample. Sample includes oral-solid presentations only.

Table 4: Effects of Market Size on Any Generic Entry and No. of Generic Manufacturers

Dependent variable: Any generic entry

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
lnSales	0.003	0.028***	0.024***	0.020***	0.043***	0.033***	0.036***	0.039***	0.055***	0.008

Dependent variable: No. of generic manufacturers, conditional on generic entry

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
lnSales	0.715***	0.340***	0.566***	1.588***	2.581***	0.663***	0.981***	1.825***	1.115***	0.421***

Dependent variable: No. of branded generic manufacturers, conditional on generic entry

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
lnSales	0.003	0.017	0.211***	0.223**	0.904***	0.279***	0.210**	1.392***	0.937***	0.397***

Dependent variable: No. of unbranded generic manufacturers, conditional on generic entry

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
lnSales	0.712***	0.312***	0.352***	1.437***	1.804***	1.124**	1.196***	0.501***	0.338***	0.083**

Marginal effects from Probit and Negative-Binomial regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10

Table 5: Effects of No. of Generic Manufacturers on Normalized Generic and Originator Price

Dependent variable: Normalized generic price

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
GenMfrBrand	0.029	-0.097***	-0.014**	-0.014	-0.009**	0.002	-0.006	-0.010***	-0.006**	0.038*
GenMfrUnbr	-0.043***	-0.076***	-0.011**	-0.006	-0.015***	-0.043***	-0.013***	0.001	-0.012**	-0.080**

Dependent variable: Normalized originator price

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
GenMfrBrand	0.107	-0.024	-0.020**	-0.001	-0.017*	0.000	-0.002	-0.004***	-0.010***	0.005
GenMfrUnbr	-0.006*	-0.004	-0.001	-0.013***	-0.006	-0.031***	-0.017***	-0.003***	-0.010*	-0.010

Marginal effects from OLS regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05,

Table 6: Effects of Normalized Generic Price on Generic Share of Volume

Dependent variable: Generic share of volume

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
GenPrice[1]	-0.144***	-0.228***	-0.382***	-0.262*	-0.202**	0.039	-0.068	0.050	-0.346***	0.140**
GenPrice[2]	-0.207***	-0.224***	-1.111***	-0.425**	-0.371***	0.002	-0.019	0.038	n/a	n/a

Marginal effects from [1]OLS and [2]2SLS-GMM regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10. n/a, instrumental variables not available.

Table 7: Summary Effects of Policy Changes for Years 2007-2009, Relative to Years 1998-2001										
Dependent variable: Any generic entry										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.147***	0.091***	-0.008	0.097***	0.071**	-0.046	-0.133***	0.046	-0.043	-0.012
Dependent variable: No. of generic manufacturers, conditional on generic entry										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.385	-0.199	0.497	3.803***	2.612**	1.867**	1.739*	-0.347	1.479***	0.570*
Dependent variable: No. of branded generic manufacturers, conditional on generic entry										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.039	-0.237***	0.652*	-0.497	-1.125**	-0.785***	-1.448***	-2.325***	0.034	0.601*
Dependent variable: No. of unbranded generic manufacturers, conditional on generic entry										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.352	0.183	-0.023	4.472***	3.855***	8.680***	7.618***	2.738***	4.434***	0.057
Dependent variable: Normalized generic price										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.011	-0.331***	-0.092***	-0.250***	-0.151***	-0.298***	-0.277***	-0.128***	-0.273***	-0.129**
Dependent variable: Normalized originator price										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.044**	-0.139***	-0.007	-0.149***	-0.156***	-0.279***	-0.221***	-0.169***	-0.176***	0.047**
Dependent variable: Generic share of volume										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.182***	0.155***	0.010	0.188***	0.001	-0.046	-0.021	0.033*	0.181***	0.070
Dependent variable: Branded generic share of volume										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.008	0.014	0.046	0.036**	-0.018	-0.033	0.049	0.014	0.090*	0.032
Dependent variable: Unbranded generic share of volume										
	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
Years 2006-2009	0.174***	0.141**	-0.035	0.152***	0.019	-0.014	-0.070**	0.019***	0.090**	0.038***
Period dummies for years 1998-2001 (omitted), 2002-2006, 2007-2009. Significant at ***p<0.01, **p<0.05, *p<0.10										

Table 8: Savings from Generics

Percent savings in prices

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
P1: Years 1998-2001	4.439	0.556	1.358	0.578	1.109	0.085	0.375	0.750	0.490	0.222
P2: Years 2002-2005	3.051	0.798	0.718	0.648	0.710	0.135	0.326	0.658	0.927	0.355
P3: Years 2006-2009	4.554	4.091	0.796	0.790	0.807	0.148	0.192	0.664	1.353	1.194
% diff. P3-P1	0.115	3.535	-0.562	0.212	-0.302	0.063	-0.183	-0.085	0.863	0.973

Percent share of unit volume

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
P1: Years 1998-2001	0.372	0.430	0.463	0.070	0.562	0.234	0.440	0.033	0.364	0.254
P2: Years 2002-2005	0.542	0.635	0.659	0.302	0.662	0.231	0.408	0.044	0.608	0.291
P3: Years 2006-2009	0.521	0.664	0.691	0.549	0.621	0.240	0.393	0.064	0.719	0.285
% diff. P3-P1	0.150	0.234	0.228	0.479	0.059	0.007	-0.047	0.031	0.355	0.031

Total percent savings from generics, for the 8-20 year cohort

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
P1: Years 1998-2001	1.651	0.239	0.629	0.041	0.623	0.020	0.165	0.025	0.178	0.056
P2: Years 2002-2005	1.655	0.507	0.473	0.196	0.470	0.031	0.133	0.029	0.564	0.103
P3: Years 2006-2009	2.375	2.715	0.550	0.433	0.501	0.036	0.076	0.043	0.972	0.340
% diff. P3-P1	0.724	2.476	-0.079	0.393	-0.122	0.016	-0.090	0.018	0.794	0.284

Total percent savings from generics, relative to total market

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
P1: Years 1998-2001	0.025	0.008	0.048	0.001	0.052	0.002	0.032	0.002	0.028	0.004
P2: Years 2002-2005	0.065	0.061	0.035	0.010	0.062	0.003	0.018	0.003	0.079	0.007
P3: Years 2006-2009	0.201	0.235	0.053	0.029	0.049	0.003	0.007	0.005	0.063	0.020
% diff. P3-P1	0.176	0.227	0.005	0.028	-0.003	0.001	-0.026	0.003	0.035	0.016

Appendix Table 1: Descriptive Statistics

U.S.	N	Mean	STD	Min	Max
GenMfr	24,595	1.05	2.67	0	23
GenMfrBrand	24,595	0.02	0.13	0	1
GenMfrUnbr.	24,595	1.04	2.65	0	23
GenPrice	354	0.77	0.43	0.08	1.88
OrigPrice	4,751	1.14	0.34	0.02	2.47
GenShare	5,665	0.84	0.24	0.0000003	1.00
Sales	24,595	137,524,067	359,636,059	128	5,301,822,792
Licensees	24,595	0.42	0.50	0	2
OrigForms	24,595	0.58	0.85	0	4
OTC share	24,595	0.80	8.85	0	100.00
Hosp. share	24,595	22.37	32.57	0	99.98
Ext. release	24,595	0.06	0.24	0	1
IV form	24,595	0.20	0.40	0	1
Topical form	24,595	0.04	0.19	0	1
Other form	24,595	0.15	0.36	0	1
Global age	24,595	163.82	41.41	96	240
Molecule lag	24,572	24.72	32.18	0	204
GenAge	5,665	39.93	31.47	0	169
Global avail.	24,595	0.45	0.50	0	1

U.K.	N	Mean	STD	Min	Max
GenMfr	19,554	0.40	1.00	0	7
GenMfrBrand	19,554	0.04	0.24	0	3
GenMfrUnbr.	19,554	0.36	0.89	0	6
GenPrice	661	0.54	0.32	0.01	1.00
OrigPrice	3,207	0.84	0.15	0.16	1.18
GenShare	3,580	0.62	0.32	0.000004	1.00
Sales	19,554	11,488,867	28,129,153	5	383,365,491
Licensees	19,554	0.29	0.48	0	2
OrigForms	19,554	0.86	1.03	0	4
OTC share	19,554	0.80	8.44	0	100.00
Hosp. share	19,554	26.40	36.91	0	100.00
Ext. release	19,554	0.04	0.20	0	1
IV form	19,554	0.12	0.33	0	1
Topical form	19,554	0.04	0.19	0	1
Other form	19,554	0.16	0.37	0	1
Global age	19,554	163.65	40.64	96	240
Molecule lag	19,554	19.23	31.78	0	213
GenAge	3,579	36.38	26.82	0	152
Global avail.	19,554	0.52	0.50	0	1

Appendix Table 1: Descriptive Statistics (Continued)

Canada	N	Mean	STD	Min	Max
GenMfr	15,723	0.97	2.16	0	12
GenMfrBrand	15,723	0.33	0.99	0	6
GenMfrUnbr.	15,723	0.65	1.53	0	9
GenPrice	2,227	0.58	0.13	0.18	1.19
OrigPrice	3,524	0.91	0.15	0.03	2.10
GenShare	4,137	0.71	0.30	0.000007	1.00
Sales	15,723	11,220,881	29,250,230	13	360,446,191
Licensees	15,723	0.28	0.46	0	2
OrigForms	15,723	0.43	0.76	0	4
OTC share	15,723	0.06	2.52	0	100.00
Hosp. share	15,723	16.94	29.19	0	100.00
Ext. release	15,723	0.06	0.23	0	1
IV form	15,723	0.10	0.30	0	1
Topical form	15,723	0.05	0.21	0	1
Other form	15,723	0.17	0.37	0	1
Global age	15,723	162.85	40.80	96	240
Molecule lag	15,723	31.79	30.56	0	224
GenAge	3,997	52.37	37.43	0	158
Global avail.	15,723	0.56	0.50	0	1

France	N	Mean	STD	Min	Max
GenMfr	14,510	0.66	2.40	0	16
GenMfrBrand	14,510	0.07	0.38	0	4
GenMfrUnbr.	14,510	0.59	2.22	0	16
GenPrice	506	0.65	0.34	0.18	2.37
OrigPrice	1,460	0.78	0.16	0.35	1.05
GenShare	1,590	0.41	0.33	0.0000004	1.00
Sales	13,296	20,115,626	48,705,099	33	726,745,404
Licensees	14,510	0.42	0.56	0	2
OrigForms	14,510	0.38	0.72	0	3
OTC share	14,510	0.48	6.74	0	100.00
Hosp. share	14,510	10.55	21.19	0	100.00
Ext. release	14,510	0.04	0.19	0	1
IV form	14,510	0.04	0.19	0	1
Topical form	14,510	0.06	0.23	0	1
Other form	14,510	0.18	0.38	0	1
Global age	14,510	167.34	40.79	96	240
Molecule lag	14,510	32.39	36.29	0	210
GenAge	1,574	25.42	17.85	0	101
Global avail.	14,510	0.47	0.50	0	1

Appendix Table 1: Descriptive Statistics (Continued)

Germany	N	Mean	STD	Min	Max
GenMfr	24,390	2.02	5.52	0	41
GenMfrBrand	24,390	0.70	2.21	0	30
GenMfrUnbr.	24,390	1.34	3.82	0	34
GenPrice	4,092	0.54	0.29	0.01	1.25
OrigPrice	4,379	0.78	0.28	0.07	1.82
GenShare	5,203	0.65	0.32	0.000003	1.00
Sales	24,390	11,731,786	27,256,808	10	534,265,566
Licensees	24,390	0.86	1.67	0	13
OrigForms	24,390	0.92	1.05	0	5
OTC share	24,390	1.90	13.55	0	100.00
Hosp. share	24,390	17.19	30.46	0	99.99
Ext. release	24,390	0.04	0.20	0	1
IV form	24,390	0.18	0.38	0	1
Topical form	24,390	0.05	0.22	0	1
Other form	24,390	0.16	0.37	0	1
Global age	24,390	166.55	41.33	96	240
Molecule lag	24,390	22.87	29.40	0	225
GenAge	4,994	45.41	34.06	0	169
Global avail.	24,390	0.41	0.49	0	1

Italy	N	Mean	STD	Min	Max
GenMfr	19,881	0.55	2.58	0	41
GenMfrBrand	19,881	0.29	1.48	0	32
GenMfrUnbr.	19,881	0.26	1.49	0	17
GenPrice	2,552	0.83	0.27	0.13	1.60
OrigPrice	2,722	0.80	0.27	0.13	1.44
GenShare	3,290	0.41	0.35	0.000002	1.00
Sales	19,881	11,712,076	25,519,945	6	244,190,237
Licensees	19,881	0.76	0.87	0	4
OrigForms	19,881	0.40	0.72	0	3
OTC share	19,881	3.07	16.86	0	100.00
Hosp. share	19,881	8.15	19.51	0	99.99
Ext. release	19,881	0.04	0.19	0	1
IV form	19,881	0.08	0.27	0	1
Topical form	19,881	0.06	0.24	0	1
Other form	19,881	0.24	0.43	0	1
Global age	19,881	170.00	40.61	96	240
Molecule lag	19,881	31.31	33.07	0	179
GenAge	3,290	110.32	63.35	0	239
Global avail.	19,881	0.41	0.49	0	1

Appendix Table 1: Descriptive Statistics (Continued)

Spain	N	Mean	STD	Min	Max
GenMfr	19,481	1.50	4.50	0	52
GenMfrBrand	19,481	0.56	1.81	0	19
GenMfrUnbr.	19,481	0.97	3.41	0	38
GenPrice	4,319	0.72	0.23	0.05	1.12
OrigPrice	4,988	0.75	0.21	0.06	1.05
GenShare	5,775	0.45	0.34	0.000005	1.00
Sales	19,481	9,847,623	20,464,211	5	286,687,223
Licensees	19,481	0.66	0.78	0	4
OrigForms	19,481	0.43	0.75	0	3
OTC share	19,481	0.35	5.56	0	100.00
Hosp. share	19,481	9.62	25.04	0	100.00
Ext. release	19,481	0.04	0.19	0	1
IV form	19,481	0.08	0.26	0	1
Topical form	19,481	0.07	0.26	0	1
Other form	19,481	0.21	0.41	0	1
Global age	19,481	166.81	40.66	96	240
Molecule lag	19,481	37.69	34.16	0	202
GenAge	5,775	108.80	59.05	0	239
Global avail.	19,481	0.48	0.50	0	1

Japan	N	Mean	STD	Min	Max
GenMfr	24,692	1.31	3.71	0	36
GenMfrBrand	24,692	1.00	2.92	0	28
GenMfrUnbr.	24,692	0.33	1.70	0	36
GenPrice	5,061	0.56	0.19	0.08	1.05
OrigPrice	5,526	0.91	0.11	0.60	1.12
GenShare	5,963	0.15	0.26	0.000004	1.00
Sales	24,690	36,489,426	89,855,117	34	1,429,952,122
Licensees	24,692	0.55	0.69	0	6
OrigForms	24,692	0.45	0.83	0	5
OTC share	24,692	0.63	7.34	0	100.00
Hosp. share	24,692	41.77	29.06	0	99.96
Ext. release	24,692	0.03	0.16	0	1
IV form	24,692	0.20	0.40	0	1
Topical form	24,692	0.05	0.23	0	1
Other form	24,692	0.09	0.28	0	1
Global age	24,692	171.69	40.91	96	240
Molecule lag	24,692	24.13	37.52	0	211
GenAge	5,666	52.09	37.40	0	177
Global avail.	24,692	0.27	0.44	0	1

Appendix Table 1: Descriptive Statistics (Continued)

Brazil	N	Mean	STD	Min	Max
GenMfr	15,826	1.47	3.53	0	38
GenMfrBrand	15,826	1.10	2.80	0	33
GenMfrUnbr.	15,826	0.47	1.46	0	15
GenPrice	4,076	0.48	0.23	0.03	1.15
OrigPrice	4,239	0.68	0.19	0.14	1.23
GenShare	6,115	0.67	0.35	0.0003	1.00
Sales	15,826	3,518,583	7,132,281	409	78,588,090
Licensees	15,826	0.29	0.50	0	2
OrigForms	15,826	0.24	0.51	0	3
OTC share	15,826	0.42	6.21	0	100.00
Hosp. share	n/a	n/a	n/a	n/a	n/a
Ext. release	15,826	0.05	0.21	0	1
IV form	15,826	0.15	0.36	0	1
Topical form	15,826	0.05	0.21	0	1
Other form	15,826	0.17	0.38	0	1
Global age	15,826	165.97	40.70	96	240
Molecule lag	15,804	46.04	37.10	0	189
GenAge	6,115	89.02	47.69	0	214
Global avail.	15,826	0.49	0.50	0	1

Mexico	N	Mean	STD	Min	Max
GenMfr	16,437	0.66	1.98	0	28
GenMfrBrand	16,437	0.60	1.76	0	23
GenMfrUnbr.	16,437	0.10	0.53	0	10
GenPrice	2,738	0.82	0.36	0.11	3.70
OrigPrice	2,568	1.07	0.27	0.32	1.96
GenShare	3,726	0.50	0.40	0.000009	1.00
Sales	16,437	2,392,473	4,593,691	3	43,338,891
Licensees	16,437	0.32	0.51	0	4
OrigForms	16,437	0.40	0.78	0	4
OTC share	16,437	0.55	6.87	0	100.00
Hosp. share	n/a	n/a	n/a	n/a	n/a
Ext. release	16,437	0.03	0.18	0	1
IV form	16,437	0.14	0.35	0	1
Topical form	16,437	0.06	0.24	0	1
Other form	16,437	0.20	0.40	0	1
Global age	16,437	166.74	40.82	96	240
Molecule lag	16,437	39.69	39.63	0	231
GenAge	3,726	89.26	56.57	0	222
Global avail.	16,437	0.44	0.50	0	1

Appendix Table 2: Regressions of Probability of Any Generic Entry on Market Size and Controls

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
lnSales	0.003	0.028***	0.024***	0.020***	0.043***	0.033***	0.036***	0.039***	0.055***	0.008
	[0.005]	[0.005]	[0.008]	[0.004]	[0.005]	[0.008]	[0.007]	[0.005]	[0.009]	[0.007]
Licensees	-0.061*	-0.004	-0.017	-0.031	0.002	-0.040**	0.032	0.022	0.020	0.022
	[0.031]	[0.027]	[0.041]	[0.019]	[0.006]	[0.018]	[0.031]	[0.019]	[0.040]	[0.037]
Orig. forms	-0.036**	0.010	-0.011	0.027**	0.029**	-0.015	0.029	0.071***	0.000	0.019
	[0.018]	[0.013]	[0.032]	[0.013]	[0.014]	[0.023]	[0.033]	[0.017]	[0.036]	[0.019]
OTC share	0.001**	0.001**			0.001	0.000	0.000	0.000	-0.002**	0.001	0.003***
	[0.000]	[0.000]		[0.001]	[0.001]	[0.002]	[0.001]	[0.001]	[0.001]	[0.001]
Hosp. share	-0.001	-0.002***	-0.004***	-0.001*	-0.001	-0.003***	-0.003**	-0.001*		
	[0.001]	[0.000]	[0.001]	[0.001]	[0.001]	[0.001]	[0.001]	[0.001]		
Ext. release	-0.149***	-0.123***	-0.219***	-0.088***	-0.134***	-0.102*	-0.146**	-0.053	-0.183**	-0.177***
	[0.029]	[0.032]	[0.035]	[0.024]	[0.039]	[0.052]	[0.065]	[0.073]	[0.076]	[0.040]
IV form	-0.031	-0.001	0.203*	-0.025	-0.035	0.078	0.075	-0.112***	0.230***	0.000
	[0.070]	[0.051]	[0.120]	[0.046]	[0.061]	[0.091]	[0.113]	[0.038]	[0.058]	[0.052]
Topical form	-0.183***	-0.180***	-0.259***	-0.085**	-0.197***	-0.037	-0.133*	-0.011	-0.215***	-0.144***
	[0.029]	[0.018]	[0.027]	[0.035]	[0.022]	[0.080]	[0.070]	[0.078]	[0.058]	[0.042]
Other form	-0.161***	-0.178***	-0.183***	-0.113***	-0.139***	-0.014	-0.036	-0.083**	0.017	-0.044
	[0.028]	[0.021]	[0.036]	[0.021]	[0.029]	[0.031]	[0.051]	[0.033]	[0.069]	[0.037]
lnGlobalAge	0.813***	0.640***	0.624***	0.443***	0.604***	0.362***	0.540***	0.617***	0.612***	0.434***
	[0.054]	[0.044]	[0.071]	[0.061]	[0.050]	[0.061]	[0.069]	[0.057]	[0.089]	[0.064]
lnMolLag	-0.034***	-0.002	-0.023	0.002	-0.003	-0.006	-0.041*	-0.015*	-0.066**	-0.053***
	[0.010]	[0.008]	[0.021]	[0.007]	[0.010]	[0.012]	[0.022]	[0.009]	[0.028]	[0.018]
Global avail.	-0.002	0.017	-0.034	0.034	0.050	0.016	0.147***	-0.121***	0.141***	0.163***
	[0.035]	[0.029]	[0.048]	[0.028]	[0.037]	[0.037]	[0.049]	[0.035]	[0.053]	[0.036]
Years 2002-2005	0.114***	0.059**	-0.017	0.029	0.050**	-0.056***	-0.062***	0.014	0.045	-0.010
	[0.031]	[0.025]	[0.028]	[0.025]	[0.022]	[0.020]	[0.023]	[0.023]	[0.033]	[0.024]
Years 2006-2009	0.147***	0.091***	-0.008	0.097***	0.071***	-0.046	-0.133***	0.046	-0.043	-0.012
	[0.038]	[0.032]	[0.040]	[0.033]	[0.030]	[0.030]	[0.034]	[0.028]	[0.047]	[0.035]
N	24,572	19,554	15,713	13,296	24,390	19,881	19,481	24,690	15,804	16,437
Pseudo R2	0.28	0.38	0.22	0.30	0.28	0.11	0.17	0.25	0.15	0.18

Marginal effects from Probit regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10

Appendix Table 3: Regressions of No. of Generic Manufacturers on Market Size and Controls

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
InSales	0.715***	0.340***	0.566***	1.588***	2.581***	0.663***	0.981***	1.825***	1.115***	0.421***
	[0.086]	[0.043]	[0.100]	[0.188]	[0.263]	[0.196]	[0.189]	[0.181]	[0.156]	[0.079]
Licensees	0.468	-0.192	-0.246	-0.600	0.059	0.267	1.321**	-0.148	0.903*	0.217
	[0.503]	[0.135]	[0.368]	[0.503]	[0.163]	[0.487]	[0.593]	[0.403]	[0.486]	[0.287]
Orig. forms	-0.548***	0.148	-0.583***	0.636	0.663	0.778	0.784	0.164	0.412	0.343*
	[0.205]	[0.115]	[0.221]	[0.414]	[0.420]	[0.495]	[0.657]	[0.359]	[0.411]	[0.196]
OTC share	-0.013*	-0.001		-0.025**	0.026***	-0.002	0.040***	0.012	0.023	0.009
	[0.008]	[0.002]		[0.010]	[0.007]	[0.013]	[0.010]	[0.022]	[0.016]	[0.012]
Hosp. share	-0.016*	-0.008**	-0.045***	-0.054	-0.150***	-0.031	-0.027	-0.042**		
	[0.009]	[0.004]	[0.013]	[0.036]	[0.038]	[0.020]	[0.028]	[0.017]		
Ext. release	-3.291***	-0.188	-1.761***	-0.704	-1.009	2.432**	-2.710***	-0.640	-2.354***	-1.317***
	[0.289]	[0.365]	[0.396]	[1.329]	[1.484]	[1.142]	[0.865]	[2.306]	[0.316]	[0.185]
IV form	-2.145***	-0.637**	-0.123	-3.149*	1.365	2.586	-1.151	-0.540	1.076	0.015
	[0.556]	[0.248]	[0.961]	[1.623]	[2.830]	[1.729]	[1.467]	[1.539]	[0.980]	[0.522]
Topical form	-2.269***	-0.559***	-1.606***	1.647	-8.072***	-0.966**	-2.417***	-1.964**	-1.010	-1.360***
	[0.655]	[0.149]	[0.293]	[2.218]	[0.481]	[0.464]	[0.900]	[0.998]	[1.086]	[0.338]
Other form	-1.420***	-0.324	-1.630***	-2.122*	-5.745***	-0.723	-2.143**	-1.530**	-0.643	-1.264***
	[0.474]	[0.262]	[0.418]	[0.991]	[0.702]	[0.455]	[0.967]	[0.616]	[0.691]	[0.243]
InGlobalAge	4.695***	1.582**	3.218***	5.587	11.097***	4.587***	7.204***	2.382*	2.721***	2.459***
	[0.999]	[0.615]	[0.887]	[3.711]	[2.913]	[1.395]	[1.757]	[1.395]	[1.048]	[0.822]
InMolLag	-0.327**	0.036	-0.759***	-0.359	-0.207	-0.357	-1.221*	0.031	-0.965***	-0.489***
	[0.149]	[0.058]	[0.215]	[0.222]	[0.336]	[0.273]	[0.687]	[0.226]	[0.317]	[0.159]
Global avail.	0.759	0.180	0.885**	0.903	2.594***	-0.427	2.177**	0.184	1.168***	1.064***
	[0.546]	[0.270]	[0.391]	[0.801]	[0.957]	[0.716]	[0.917]	[0.769]	[0.426]	[0.319]
Years 2002-2005	-0.622	-0.175	0.493	1.138	0.825	-0.172	0.355	-1.082***	1.332***	0.375*
	[0.524]	[0.345]	[0.371]	[1.782]	[0.977]	[0.354]	[0.542]	[0.358]	[0.313]	[0.223]
Years 2006-2009	0.385	-0.199	0.497	3.803***	2.612**	1.867**	1.739*	-0.347	1.479***	0.570*
	[0.528]	[0.389]	[0.468]	[1.295]	[1.292]	[0.826]	[0.925]	[0.528]	[0.500]	[0.318]
N	5,665	3,580	4,137	1,544	5,203	3,290	5,775	5,962	6,115	3,726

Marginal effects from Negative-Binomial regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10

Appendix Table 4: Regressions of Normalized Generic Prices on No. of Generic Manufacturers and Controls

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
GenMfrBrand	0.029	-0.097***	-0.014**	-0.014	-0.009**	0.002	-0.006	-0.010***	-0.006**	0.038*
	[0.043]	[0.033]	[0.005]	[0.009]	[0.004]	[0.004]	[0.004]	[0.002]	[0.002]	[0.020]
GenMfrUnbr.	-0.043***	-0.076***	-0.011**	-0.006	-0.015***	-0.043***	-0.013***	0.001	-0.012**	-0.080**
	[0.005]	[0.014]	[0.005]	[0.004]	[0.003]	[0.006]	[0.002]	[0.002]	[0.005]	[0.037]
Ext. release	0.084	0.224***	0.074**	-0.019	0.031	0.036	0.142***	-0.047	0.041	0.383***
	[0.067]	[0.074]	[0.029]	[0.020]	[0.033]	[0.043]	[0.033]	[0.034]	[0.051]	[0.087]
IV form	-0.099	0.140***	0.027	-0.138**	0.240***	-0.074	-0.028	0.126***	0.052*	-0.094*
	[0.070]	[0.048]	[0.042]	[0.057]	[0.043]	[0.073]	[0.040]	[0.033]	[0.029]	[0.055]
Topical form	0.200**	0.278***	0.016	0.343***	0.115**	-0.069	0.069***	0.112**	0.222**	0.061
	[0.089]	[0.040]	[0.038]	[0.039]	[0.050]	[0.051]	[0.025]	[0.049]	[0.094]	[0.086]
Other form	0.076	0.178**	-0.060	-0.061**	0.198***	0.063*	0.058	0.165***	0.071**	0.070
	[0.072]	[0.068]	[0.040]	[0.027]	[0.075]	[0.034]	[0.035]	[0.034]	[0.030]	[0.079]
InGlobalAge	-0.156	-0.542***	0.060	0.026	-0.385***	-0.003	-0.200***	-0.353***	-0.059	-0.215*
	[0.109]	[0.115]	[0.057]	[0.046]	[0.066]	[0.074]	[0.052]	[0.064]	[0.050]	[0.117]
InMolLag	0.013	0.029*	-0.013	-0.002	0.021	-0.014	0.016	0.001	0.016	-0.028
	[0.015]	[0.015]	[0.011]	[0.008]	[0.013]	[0.014]	[0.012]	[0.006]	[0.014]	[0.026]
Global avail.	0.015	-0.079	0.033	0.000	0.005	0.009	-0.056***	0.068***	-0.084***	-0.016
	[0.042]	[0.048]	[0.028]	[0.033]	[0.040]	[0.044]	[0.021]	[0.024]	[0.025]	[0.055]
Years 2002-2005	0.011	-0.097***	-0.055**	-0.040*	-0.026	-0.126***	-0.114***	-0.049***	-0.246***	-0.058
	[0.036]	[0.031]	[0.027]	[0.023]	[0.029]	[0.023]	[0.018]	[0.017]	[0.017]	[0.041]
Years 2006-2009	0.011	-0.331***	-0.092***	-0.250***	-0.151***	-0.298***	-0.277***	-0.128***	-0.273***	-0.129**
	[0.043]	[0.045]	[0.031]	[0.034]	[0.042]	[0.032]	[0.023]	[0.023]	[0.027]	[0.056]
N	5,097	3,369	3,820	1,522	4,768	2,922	5,236	5,672	4,671	2,814
R-squared	0.32	0.44	0.10	0.55	0.54	0.62	0.67	0.35	0.54	0.15

Marginal effects from OLS regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10

Appendix Table 5: Regressions of Generic Share of Volume on Normalized Generic Price, No. of Generic Manufacturers and Controls

	U.S.	U.K.	Canada	France	Germany	Italy	Spain	Japan	Brazil	Mexico
GenPrice	-0.144***	-0.228***	-0.382***	-0.262*	-0.202**	0.039	-0.068	0.050	-0.346***	0.140**
	[0.039]	[0.053]	[0.115]	[0.135]	[0.083]	[0.165]	[0.124]	[0.093]	[0.102]	[0.068]
GenMfrBrand	0.022	0.063*	0.031***	0.017	0.010*	-0.004	0.030***	0.005**	0.011***	0.026***
	[0.023]	[0.033]	[0.010]	[0.016]	[0.006]	[0.009]	[0.007]	[0.002]	[0.004]	[0.009]
GenMfrUnbr.	0.009***	0.095***	0.036***	0.035***	0.019***	0.021	0.007**	0.003*	0.023***	0.008
	[0.003]	[0.020]	[0.010]	[0.007]	[0.003]	[0.014]	[0.003]	[0.002]	[0.007]	[0.020]
Ext. release	-0.087*	-0.070	0.109*	0.052	-0.043	0.183	-0.086	0.131	-0.093	-0.051
	[0.044]	[0.069]	[0.061]	[0.047]	[0.092]	[0.136]	[0.115]	[0.138]	[0.099]	[0.066]
IV form	-0.174***	-0.279***	0.040	-0.161	0.079	0.153	0.001	0.148***	-0.086	-0.048
	[0.034]	[0.105]	[0.068]	[0.169]	[0.084]	[0.100]	[0.097]	[0.040]	[0.056]	[0.078]
Topical form	0.017	-0.156***	0.023		-0.151***	0.091	-0.003	0.019	-0.211***	0.068
	[0.032]	[0.041]	[0.076]		[0.046]	[0.084]	[0.218]	[0.022]	[0.057]	[0.083]
Other form	-0.046	-0.239***	0.056	-0.187***	0.075	0.088	0.001	0.131***	-0.048	-0.006
	[0.037]	[0.041]	[0.055]	[0.062]	[0.057]	[0.077]	[0.060]	[0.048]	[0.063]	[0.070]
lnGlobalAge	0.056	0.142	0.099	0.040	-0.076	0.137	-0.006	-0.149	-0.237**	0.116
	[0.060]	[0.114]	[0.069]	[0.102]	[0.101]	[0.152]	[0.110]	[0.104]	[0.100]	[0.110]
lnMolLag	0.012*	-0.014	-0.024	-0.003	0.021*	0.012	-0.011	0.000	0.099**	0.010
	[0.007]	[0.015]	[0.015]	[0.018]	[0.011]	[0.023]	[0.034]	[0.005]	[0.038]	[0.026]
lnGenAge	0.091***	0.092***	0.077***	0.102***	0.115***	0.041	0.099***	0.042***	0.140***	0.090***
	[0.011]	[0.016]	[0.020]	[0.013]	[0.015]	[0.030]	[0.016]	[0.014]	[0.021]	[0.024]
Global avail.	-0.037*	0.000	0.047	-0.039	0.018	-0.101	-0.040	0.038	0.015	-0.004
	[0.021]	[0.048]	[0.044]	[0.033]	[0.032]	[0.064]	[0.048]	[0.027]	[0.049]	[0.060]
Years 2002-2005	0.136***	0.177***	0.032	0.039	0.036	0.030	0.002	0.028*	0.065*	0.051
	[0.027]	[0.056]	[0.031]	[0.041]	[0.033]	[0.056]	[0.035]	[0.015]	[0.036]	[0.038]
Years 2006-2009	0.182***	0.155***	0.010	0.188***	0.001	-0.046	-0.021	0.033*	0.181***	0.070
	[0.027]	[0.059]	[0.033]	[0.044]	[0.049]	[0.078]	[0.050]	[0.019]	[0.052]	[0.050]
N	5,097	3,369	3,680	1,514	4,566	2,922	5,236	5,385	4,671	2,814
R-squared	0.47	0.57	0.35	0.68	0.52	0.15	0.31	0.13	0.45	0.25

Marginal effects from OLS regressions, clustered by molecule; robust standard errors in brackets, significant at ***p<0.01, **p<0.05, *p<0.10