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Patents and the Global Diffusion of New Drugs

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Abstract
This paper studies how patent rights and price regulation affect how fast new drugs are launched in different countries, using newly constructed data on launches of 642 new drugs in 76 countries for the period 1983-2002, and information on the duration and content of patent and price control regimes. Price regulation strongly delays launch, while longer and more extensive patent protection accelerates it. Health policy institutions, and economic and demographic factors that make markets more profitable, also speed up diffusion. The effects are robust to using instruments to control for endogeneity of policy regimes. The results point to an important role for patents and other policy choices in driving the diffusion of new innovations.

This project was initiated by Jean (Jenny) Lanjouw. Tragically, Jenny died in late 2005, but had asked us to complete the project. This took much longer than expected because it involved complete reconstruction of the data set and empirical work. It is essentially a new paper in its current form, but it remains an important part of Jenny's legacy and a topic to which she devoted much of her intellectual and policy efforts. We hope she would be satisfied with our work which, for us, was a labor of love.

Key words: Patents, pharmaceuticals, diffusion, drug launches, price regulation
JEL: O31; O33; O34; O38; I15; I18; K19; L65

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1 Introduction

In 1999 lovastatin, a blockbuster cholesterol drug with peak sales of more than $1 billion in the U.S., became commercially available in Egypt—twelve years after it was first approved for sale by the U.S. Food and Drug Administration. As we will show, this is not exceptional—long launch lags are common and nearly 40 percent of all new drugs are only launched in ten or fewer countries. Since delayed launch means foregone health benefits, it is important to understand how public policy affects the diffusion of new drug innovations. In this paper we demonstrate that the patent and price regulation policies governments adopt have a powerful impact on the speed at which new drugs become available in different countries.

Promoting affordable access to new drugs is a central objective of government policy. There are two distinct challenges in achieving this: how to provide adequate incentives for the development of new drugs, and how to ensure affordable prices of drugs once they are developed. Governments use two main instruments to achieve these goals: patents and price regulation. It is well known that there is a tension between these objectives. The innovation literature emphasizes the basic tradeoff between the dynamic gains from stronger incentives to develop new technology provided by patents and the static welfare loss created by the resulting higher prices.[1] Much of the policy debate around patents and "access" to new medicines has focused on pricing—the potential for patent-protected products to leave large numbers of patients priced out the market in countries with limited private health insurance and poorly funded public health systems. As many poorer countries have been required to provide patent protection for pharmaceutical products under the 1994 TRIPS Agreement, patent policy has largely been evaluated in terms of the static welfare loss associated with higher prices in emerging markets (Chaudhuri, Goldberg and Gia, 2006; Duggan and Goyal, 2012; Kyle and Qian, 2013).[2]

In the debates over the TRIPS Agreement (and more recently, the proposed Transpacific Partnership trade agreement), developing countries and public health advocacy groups argued that harmonization of patent policy was both unnecessary and harmful when viewed

[1] The classic statement of the tradeoff is Arrow (1962), which spawned a huge literature. Empirical studies of the impact of patent rights on the rate and direction of innovation are more recent, and include Branstetter and Sakakibara (2001), Moser (2005), Qian (2007), Kyle and McGahan (2012), Williams (2013), Galasso and Schankerman (2013), and Budish, Roin and Williams (2014).

[2] TRIPS is the acronym for the Agreement on Trade-Related Aspects of Intellectual Property Rights, which is administered by the World Trade Organization. For discussion of the political economy of TRIPS and other international trade-related agreements, see Sell (2006). Grossman and Lai (2004) provide a theoretical analysis of patent regimes in a trading world economy with different market sizes and capacity for innovation; also see related work by Scotchmer (2004) There have also been studies of how price discrimination in pharmaceuticals can help improve global welfare while also preserving innovation incentives (e.g., Jack and Lanjouw, 2005).

from the perspective of this tradeoff.[3] For low income countries, the welfare loss from patents involves not just the traditional static efficiency cost from prices above marginal cost, but also the worrying prospect that large segments of the population may have no affordable access to new drug therapies. This has led economists to recommend alternative ways for governments to provide innovation incentives while maintaining low prices in developing countries, especially for vaccines.[4] Moreover, the increase in innovation incentives from having patent rights in low income countries is likely to be small for many kinds of drugs because these countries do not account for a large part of the global market.[5]

However, this debate misses a critical element: the impact patent rights and other policies have on the diffusion of new drugs. The public health benefits of new drugs depend, first, on how quickly drugs are launched in the 'local' markets in different countries and, second, on how widely they are adopted within a country, once they have been launched. Once a drug has been discovered, the sunk R&D costs are not relevant to the decision to launch in different countries. However, the decision to launch in a country, and to develop the marketing and distribution infrastructure required to promote within-country adoption, will be sensitive to drug manufacturers' assessment of anticipated profits relative to these country-specific costs. Of course, if these costs were negligible, both aspects of diffusion would be driven by demand side factors—i.e., heterogeneity in the profitability of adoption in different countries. This is the perspective that has been most emphasized in the economics literature on diffusion, beginning with the seminal work of Griliches (1957). But diffusion also has a supply side—sunk investments required to enter new markets, set up distribution channels and inform potential customers about new products. If launch costs are sufficiently large, the diffusion of new technologies will be significantly influenced by policies that affect profitability in different markets. This supply-side perspective is at the heart of economic models of entry (e.g., Bresnahan and Reiss, 1988; Holmes, 2011; Collard-Wexler, 2013), and has been under-appreciated as a factor limiting diffusion of innovations across different markets.

Of course, the potential importance of patent rights in promoting global diffusion of innovation is not limited to pharmaceuticals. However, drugs are a good example to study both

[3] For example, see "USTR's proposal for the Intellectual Property Chapter of the Trans-Pacific Partnership (TPP) will endanger access to medicines for all," Public Citizen et al. (February 12, 2014), available at http://www.citizen.org/statements-of-support

[4] These include auctions (Kremer, 1998) and bulk purchasing with free distribution (Kremer, 2002; Kremer and Glennester, 2004). For a good discussion of non-patent incentive mechanisms, see Scotchmer (2004).

[5] An important exception to this are drugs for "neglected diseases" whose burden falls disproportionately on the population of low-income countries. With little or no market for these drugs in high-income countries, the strength of intellectual property rights in emerging markets could play a larger role in innovation incentives (Cockburn and Lanjouw, 2005). Again, patents are not the only way to provide incentives to do R&D in these areas, see e.g. Ridley, Grabowski and Moe (2006) who proposed the transferable Priority Review Voucher mechanism now implemented in the USA.

because of their economic importance and because there are significant, country-specific costs of launching new drugs.[6] These include the costs of conducting additional clinical trials to meet local requirements, obtaining regulatory approval, setting up local distribution and marketing networks, and educating healthcare providers. These fixed costs must be incurred in every country in which a drug is launched: outside tightly integrated trading blocs such as the European Union, there are few international protocols that recognize regulatory approval of drugs across borders, and limited economies of geographic scope in marketing and distribution. Moreover, the bulk of these entry costs apply whether or not the first entrant in a country is the original innovator of the drug, its licensee or a generic imitator.

Existing studies on the relationship between intellectual property rights and the spread of new technologies have focused on two main channels, international trade and technology transfer by multinational companies. In particular, two recent papers identify these impacts by exploiting the strengthening of IP rights, mostly associated with the TRIPS Agreement. Delgado, Kyle and McGahan (2013) show that the timing of implementation of TRIPS (the compliance date varied across countries) is associated with increased trade flows in sectors that are IP-intensive relative to a control group. They find that the impact varies substantially across sectors, and notably was larger in the information and communication technology sector than in biopharmaceuticals, where compliance was subject to more exceptions and complementary resources in distribution play a large role. Branstetter, Fishman and Foley (2006) use firm-level data to show that royalty payments and R&D expenditures by multinational affiliates increase after IP reforms were adopted in sixteen countries (some before TRIPS) and that this effect is concentrated among affiliates of parent companies that use U.S. patents extensively prior to the reforms. In both of these papers, the patent reforms are treated as exogenous events.

There are two main related studies of cross-country diffusion of pharmaceuticals. Kyle (2007) uses a large data set on new molecules launched in OECD countries from 1980-2000, and shows that price regulation significantly retards launches and, interestingly, that firms are less likely to follow launch in a low-price country with launch in a high-price country (possibly due to 'reference pricing' policies by drug price regulators). However, the paper does not examine the impact of patent rights on drug launch dates, as there is not much variation among OECD countries. In related research, Kyle (2006) analyzes a similar sample of drug launches in the smaller set of G7 countries, focusing on how firm

[6] A launch decision in one country may depend on policy regimes in other countries. Such 'policy externalities' can arise from benchmark pricing formulas (Bloom and van Reneen, 1998; Jacobzone, 2000; Brekke, Grasdal and Holmas, 2009), and parallel trade that erodes price differences across country borders (Kanavos et. al., 2004; Ganslandt and Maskus, 2004). In this paper we focus on how domestic policies affect launch lags, but do not incorporate these policy externalities. A full treatment of dynamic entry decisions across markets with spillover effects remains an important topic for future research.

characteristics affect launch timing (possibly because they are correlated with unobserved entry costs).[7]

In this paper we study how both patent regimes and price regulation, as well as economic factors such as market size and demographics, affect the speed and geographic extent of diffusion of new pharmaceutical products across countries. The empirical analysis is based on a large data set that covers launches of 642 new drugs in up to 76 countries during the period 1983-2002, together with information on the nature and evolution of patent and price regulation regimes in these countries. Importantly, the countries in the data set span all levels of economic development, exhibit a wide variety of patent regimes, and changed important aspects of patent policy with respect to pharmaceuticals over time.

In the analysis we distinguish between two types of patent rights: those that protect of methods of manufacture ('process patents') and those that protect pharmaceutical products ('product patents'). Process patents are considered relatively weak, as they do not prevent cost-based competitive entry by entrants with superior manufacturing processes. Indeed, some countries (such as India) purposefully adopted a "process-only" patent regime for pharmaceutical innovations in order to foster a domestic industry based on inventing around originators' manufacturing processes. Product patents are typically considered stronger rights, blocking entry by competitive (or generic) products and allowing for more effective appropriation of rents. However, there is a wide variation across countries (and over time within countries) in both the duration and content of both process and product patents, which provides the potential for identifying the effects of regime choice on diffusion.

There are four main empirical findings in the paper. First, we show that new drugs become available in many countries only after long lags (often more than 10 years) between the date when a product in first launched commercially anywhere in the world (typically in the US, Europe, or Japan) and its launch in other countries. Many new drugs are never launched outside a handful of wealthier countries. Second, we demonstrate that the patent policies governments adopt strongly affect how quickly new drug therapies are launched in their countries. Longer duration, and stronger, patent rights substantially speed up diffusion. These impacts are large and robust to a variety of empirical specifications. For example, controlling for economic and demographic factors, moving from a regime of no product patents to a long product patent term increases the per-period hazard of launch by about 23 percent. Allowing for endogeneity of policy regimes using instrumental variables increases the magnitude of estimated effect to between 64 percent and 72 percent, depending on the choice of instruments. This is equivalent to reducing launch lags by about 100 percent. Short product patents have no effect. Process patents also promote faster launch,

[7] Other studies that use much smaller samples of drugs/countries include Danzon, Wang and Wang (2005), and Berndt, Blalock and Cockburn (2011).

but the impact is not as large as for product patents. Importantly, we find that these effects hold equally for low and middle income countries as for high income countries.

Third, we show that countries that adopt strong pharmaceutical price regulation experience significantly longer launch lags for new drugs. We estimate that introducing price regulation decreases the per-period hazard of launch by about 15 percent, which is equivalent to increasing launch lags by about 25 percent (when instrumented, 49 to 60 percent reduction in the hazard rate, equivalent to about a 80 percent to 100 percent increase in launch lags.) Fourth, we find that new drugs are launched much faster in countries that have health policy institutions that promote availability and distribution of drugs—in particular, adopting the Essential Drug List of the World Health Organization and having a National Formulary—and these institutions do not appear to be simply a proxy for unobserved institutional quality.

Finally, we find that local market size, as captured by population, per capita income, health expenditures, and demographic factors influencing drug use) has a big impact on the speed of drug launches. These results are consistent with earlier studies of U.S. data showing that market size is related to both higher levels of pharmaceutical innovation and non-generic entry (e.g., Scott-Morton, 1999; Acemoglu and Linn, 2004; Dubois, Mouzon, Scott Morton and Seabright, 2011).

All of these key findings are robust to using a variety of instrumental variables, based primarily on a country's political and legal institutions, to address potential concern about endogeneity of policy regimes. In fact, the estimated impacts of price regulation and patent policy using instruments (in a full information maximum likelihood framework) are, as indicated above, higher than those in the baseline specifications of the hazard model.

The paper is organized as follows. Section 2 develops a simple dynamic model of drug launches, as a framework for interpreting our empirical results. In Section 3 we describe the data set (details are provided in the Data Appendix). Section 4 presents non-parametric evidence on the geographic and temporal diffusion of new drugs, and how it varies with the economic development and patent and price regulation regimes. We describe the specification of the hazard model of drug launches in Section 5.1 and the main econometric results in Section 5.2. In Section 6 we present robustness analysis. In Section 7 we show that the results are robust to using instruments to address the endogeneity of policy regimes. Section 8 uses our parameter estimates to simulate the impact of counterfactual policy regimes on drug diffusion. In the conclusion we summarize the key findings and directions for future research.

2 A Model of Drug Launch

Consider a firm that has developed a new drug i which can be launched in a set of countries, denoted by $j = 1, ..., J$. The firm obtains a product patent on the drug in each country at time $t = 0$.[8] Patent protection lasts for T_j periods in country j. After the patent expires, we assume that generic competition drives the price to marginal cost.

If the firm launches the drug in country j, it incurs a sunk entry cost of σ_{ij}.[9] During patent protection, the firm earns flow profit in period t equal to $\pi(x_{ij})\omega_{ijt}$, where x_{ij} denotes a vector of variables that capture market size, regulation and health institutions, and demographic characteristics of the country. In our analysis, we use three variables to capture market size, population, GDP per capita, and health expenditures per GDP. Regulatory variables include measures of the duration and strength of patent policies (both for pharmaceutical products and processes, as explained later) and price controls. Demographic variables include the fraction of the population over 65 and a measure of income inequality. The variable ω_{ijt} denotes a profitability shock that reflects unobservable factors affecting demand and productivity. For simplicity, in the model (though not in the empirical work), we treat x_{ij} as constant over time.

We assume ω_{ijt} evolves as a first-order Markov process

$$\omega_{ijt} = \lambda\omega_{ij,t-1} + \eta_i + \mu_j + \upsilon_{ijt} \tag{1}$$

where $\lambda \in (0, 1)$, η_i and μ_j denote drug and country-specific random effects, respectively, which we assume the firm knows, and ν_{ijt} is an *iid* disturbance. The random effects allow the profitability shock ω_{ijt} to be correlated across countries for a given drug, and across drugs for a given country.[10] The Markov specification implies that $\Pr(\omega_{ijt} \mid \omega_{ij,t-1})$ is stochastically increasing in $\omega_{ij,t-1}$.

The present value of launch at time t, conditional on available information, is

$$E(V_{ijt} \mid \omega_{ijt}, \eta_i, \mu_j) = \sum_{k=0}^{T_j - t} \beta^k \{\pi(x_{ij}) E(\omega_{ij,t+k} \mid \omega_{ijt}, \eta_i, \mu_j)\} - \sigma_{ij}$$

[8] The first country in which a patent is applied for sets the global priority date. International patent protocols require that the inventor apply for protection in other countries within 18 months of the priority date, after which the right expires. As an empirical matter, the launch of new drugs often occurs much later than the patent application date. Our assumption that the drug is patented in all countries is made for simplicity only.

[9] The entry cost includes the cost of obtaining regulatory approval in the target country (there is no mechanism for multi-country regulatory review), investment in physical distribution channels, information provision to doctors and pharmacies, and securing registration on the national drug formulary. These costs can vary substantially both with the type of drug and the country of launch.

[10] The random effects specification implies that $E(\omega_{ijt}\omega_{i'jt}) = \sigma_\mu^2$ and $E(\omega_{ijt}\omega_{ij't}) = \sigma_\eta^2$ for $i \neq i'$ and $j \neq j'$.

where $\beta \in (0,1)$ is the discount rate. The firm launches the drug in country j when $E(V_{ijt} \mid \omega_{ijt}, \eta_i, \mu_j) \geq 0$. Given the Markov assumption on ω, the optimal entry rule is to launch the drug when the profit shock ω_{ijt} exceeds a threshold level, ω^*_{ijt} (Ericson and Pakes, 1995). Essentially, this rule applies because the value function $E(V_{ijt} \mid \omega_{ijt}, \eta_i, \mu_j)$ is increasing in ω_{ijt}.

The first-order Markov assumption delivers a simple closed-form solution for ω^*_{ijt}. From equation (1),

$$\omega_{ij,t+k} = \lambda^k \omega_{ijt} + (\eta_i + \mu_j) \sum_{m=0}^{k-1} \lambda^m + \sum_{m=0}^{k-1} \lambda^m \upsilon_{ij,t+k-m} \qquad k > 0$$

which implies

$$E(\omega_{ij,t+k} \mid \omega_{ijt}, \eta_i, \mu_j) = \lambda^k \omega_{ijt} + (\eta_i + \mu_j) \sum_{m=0}^{k-1} \lambda^m$$

since $E(\upsilon_{ij,t'} \mid \omega_{ijt}, \eta_i, \mu_j) = 0$ for $t' > t$. Thus

$$E(V_{ijt} \mid \omega_{ijt}, \eta_i, \mu_j) = \omega_{ijt} \pi(x_{ij}) \sum_{k=t}^{T_j - t} \phi^k + \theta(T_j - t)(\eta_i + \mu_j) - \sigma_{ij} \tag{2}$$

where $\phi = \beta\lambda \in (0,1)$ and $\theta(T_j - t) = 1 + \sum_{k=1}^{T_j - t} \beta^k \sum_{m=0}^{k-1} \lambda^m$. Setting $E(V_{ijt} \mid \omega_{ijt}, \eta_i, \mu_j) = 0$, the entry condition is

$$\omega_{ijt} \geq \omega^*_{ijt} = \frac{\sigma_{ij} - \theta(T_j - t)(\eta_i + \mu_j)}{\pi(x_{ij}) \frac{1 - \phi^{T_j - t + 1}}{1 - \phi}} \tag{3}$$

The entry threshold ω^*_{ijt} is determined by $Z_{ijt} = (x_{ij}, T_j, t, \eta_i, \mu_j)$ which we assume the firm observes. The threshold is declining in patent duration T_j and variables that increase flow profit $\pi(x_{ij})$, including the duration and strength of patent rights, and rising in the sunk entry cost σ_{ij}, elapsed time since first worldwide launch t, and price regulation which reduces flow profit. The threshold increases with time since first worldwide launch t because, when the remaining patent period $T_j - t$ is smaller, the profit shock must be larger to generate sufficient expected flow profits to cover the entry cost.

The probability that the drug is launched in country j at time t, given that it has not been launched before (the hazard rate), is

$$\begin{aligned} h(t \quad | \quad Z_{ijt}) &= \Pr(\omega_{ijt} \geq \omega^*_{ijt} \mid \omega_{ij1} < \omega^*_{ij1}, ..., \omega_{ij,t-1} < \omega^*_{ij,t-1}) \\ &= \Pr(\omega_{ijt} \geq \omega^*_{ijt} \mid \omega_{ij,t-1} < \omega^*_{ij,t-1}) \end{aligned} \tag{4}$$

where the second equality follows from the first-order Markov assumption on ω. This implies that the hazard rate is a decreasing function of factors that raise the threshold ω^*_{ijt}.This is summarized in the following proposition:

Proposition: The hazard rate of drug launch in a country is increasing in factors that increase flow profit, including the duration and strength of patent protection, population, GDP per capita, health expenditures per GDP and the fraction of population over 65. The hazard rate of drug launch is declining in price regulation which reduces flow profit, and in the time elapsed since first launch and the sunk cost of entry.

In the empirical analysis we estimate a hazard model of drug launch to examine some of these predictions..

3 Data and Measurement

In this section we briefly describe the construction of the data set. Details of the procedures and sources are provided in the Data Appendix.

Identifying drug launches

A launch is defined as the first appearance of the identified molecule (new chemical entity) in a given country, whether in proprietary or generic form. Determining if, and when, a new drug becomes available in a given country is not straightforward. Since almost all countries require formal approval from a health and safety regulator before a drug can be marketed, administrative records could potentially be used for this purpose. But poor record keeping in some countries, lack of easily accessible public records, and language barriers make it infeasible to track regulatory approvals for large numbers of drugs across many countries, particularly for historical data. Regulatory approvals also do not directly track commercial availability (formal approval is not the same as de facto launch of a product).

We rely on a compilation of product launches obtained from a commercial market research company, IMS Health Inc. This database tracks product launches in all therapeutic classes in up to 76 different countries from 1983-2002. Product launches were identified by IMS from a variety of sources, including regulatory approvals, announcements by manufacturers, local media reports, and IMS' active surveillance of distribution channels as part of other data gathering efforts. Because India was not covered by IMS during this period, we supplement this data source with information from an Indian market research company, ORG/MARG, that tracked product launches in a limited set of therapeutic over the same period.

To track launches accurately, drugs must be unambiguously identified across countries. Unfortunately there is considerable variation across time and over countries in how a given

chemical entity is named.[11] Failing to recognize equivalent chemical entities will result in over-counting of new products, under-counting of the number of countries in which a given drug is launched, and inaccurate dating of launches. As detailed in the Data Appendix, it took considerable effort to track the history of drug launches in these data due to changes in country coverage, and difficulties in consistently identifying drugs due to variations in product names. The source dataset contains more than 180,000 observations on product-country launches. These products contained approximately 9,600 distinct active drug ingredients in use around the world during the sample period, for which we compiled more than 250,000 synonyms from a variety of reference sources. Of these 9,600 distinct active ingredients we focus on 642 clearly identifiable chemical entities that were first introduced anywhere in the world during this period, and then identify the date when they first appear in any product launched in each country. Several important choices were made in creating this dataset to minimize under-counting of launches. We excluded products in a variety of therapeutic classes where it was particularly difficult to identify active ingredients unambiguously.[12] We also used a relatively broad definition of what constitutes an equivalent chemical entity by grouping together all of the salts and esters of a given 'active moiety'. This procedure may ignore clinically important differences among variants that would lead a pharmacologist to distinguish between different products, but it makes our results conservative in the sense that we may be over-counting launches of equivalent products. Because the country coverage of the source data expanded over time (and 'new' countries appeared, such as the Czech Republic and Slovakia) we were careful to account for left-censoring of launches (i.e. drugs were excluded from being 'at risk' of launch in a country if their first worldwide launch occurred prior to entry of the country into the dataset.)

Patent and price control regimes

For each country in our sample, we characterize the domestic patent regime along four dimensions: duration of patent term, coverage of pharmaceutical products, coverage of chemical manufacturing processes, and an index of the strength of patent protection that reflects the degree to which patent law provisions favor patent holders versus potential infringers (*Pro-patent Index,* which varies from zero to one). The variables are constructed using data from Ginarte and Park (1997), Park (2008) and other reference sources cited in the Data Appendix. These variables change slowly over time, and while there is considerable convergence towards the "TRIPS standard" (e.g., 20 year term, no exceptions for pharmaceutical products) by the end of the sample period, there was considerable variation

[11] For example, the drug known as acetominophen in North America is known as paracetamol in most other countries, and is sold under more than 50 different brand names around the world.

[12] These include product classes such as dermatologicals, where the boundary between prescription drugs, over-the-counter medicines and personal care products is particularly blurred, and vaccines and biologics where nomenclature was not well standardized during this period.

among countries during the 1980's and 1990's.

We have no reason to believe that the relationship between patent term and the hazard of drug launch is linear. Rather than impose a functional form, we use three mutually exclusive dummy variables to capture patent term duration: *Short* = 0 < duration ≤ 12 years (from application date); *Medium* = 13 ≤ duration ≤ 17 and *Long* = duration ≥ 18 (the reference category is no patent protection).[13] Note that since the average period between patent application and marketing approval on a product is about 10 years (Grabowski and Kyle, 2007), a *Short* patent conveys essentially no effective coverage to the patentee. We use two separate sets of these dummy variables, one for product patents (*Short_Product, Medium_Product* and *Long_Product*) and another for process patents (*Short_Process*, *Medium_Process* and *Long_Process*). In terms of country/year observations, short, medium and long process patents account for 10.8, 22.3 and 60.0 percent of the sample; for product patents the figures are 6.4, 16.5 and 58.2 percent, respectively. We experimented with different definitions of the cutoffs for these patent duration categories: *Short* 0-10, 0-11 and 0-13; *Medium* 11-16, 12-16, 13-16, 13-17 and 14-16; and *Long* ≥ 17, ≥ 18 and ≥ 19. As we discuss later, the econometric results presented in Section 5 are generally robust to these alternatives.

Countries approach the control of pharmaceutical prices in a bewildering variety of ways. We consider systems of explicit price regulation and summarize the variation across countries with two dummy variables—one for the existence of "some" price regulation and the second for "extensive" price control. A price regime is labeled as "extensive" if all drugs are regulated, rather than just a subset of the market, or if a country's price regulation is identified by commentators as being particularly rigorous. The set of reports and legal texts consulted in making this determination are given in Lanjouw (2005). In the sample, 22 percent of country/year observations are coded as having no price controls, 31 percent with some price regulation and 47 percent with extensive controls.[14]

Pharmaceutical policy institutions

The observed timing of market entry reflects both the decisions of firms and the efficiency of a country's regulatory process. We capture government policies that promote access to pharmaceuticals by coding three dummy variables for each country-year. The first is whether a country had adopted a national formulary, where listed drugs would be eligible for distribution through a publicly funded health system, typically more widely prescribed,

[13] Where the patent term runs from date of grant rather than date of application, as was the case in e.g. the U.S. prior to 1995, we added two years to make the term roughly equivalent to one running from date of application. Results were not sensitive to changing this assumption about the pendency period to three years.

[14] Appendix Table 1 provides information, for each country in the sample, on the number of years of coverage, number of drugs launched, average percentage of drugs launched within 5 years of their initial launch date anywhere, and the product patent, process patent, and price regulation regimes and their changes over time.

and with payment mechanisms in place. The second is whether a country had adopted the Essential Drug List (EDL) promulgated by the World Health Organization, which indicates that a country's health institutions are oriented towards promoting access to basic drugs. The third is whether a country has a formal "national drug policy," i.e. an effort to coordinate industrial policy and domestic regulation to promote access to safe and effective pharmaceuticals. At the start of our sample period, 65 percent of countries had a national formulary, 41 percent had adopted the EDL and 63 percent had issued a national drug policy; by 1997 all countries had adopted all three.

Demographic and Income Variables

We use a set of income and demographic variables to control for variations in the potential demand for pharmaceuticals. These include: population size and the fraction of population over 65 years old, real GDP per capita in purchasing power parity terms, income inequality measured by the Gini coefficient, and health care expenditures as a percent of GDP. We also include measures of the quality of regulatory bureaucracy and the rule of law, both taken from the World Bank.

Many of the explanatory variables are available annually, but others only in one or several cross-sections (details in the Data Appendix). Table 1 presents summary statistics for the variables used in the econometric analysis.

4 Drug Diffusion: Non-parametric Evidence

We begin with some non-parametric evidence on the pattern of global drug diffusion. Table 2 presents information on the geographic span of drug launches, and shows the distribution of the number of countries for which a launch was observed for each drug in the sample. Recognizing that this tabulation does not account for right-censoring (some drugs may have launched in some countries after the sample period ends), these statistics illustrate the dominant, and striking, feature of this measure of diffusion: how limited it is. In the entire sample of new drugs, 39 percent were launched in ten or fewer countries, and only 41 percent were launched in more than 25 countries. The mean number of countries in which a drug was launched is 22.4 (median of 18) out of a possible 76. The fact that drugs are not launched more widely can be due to various factors: the limited size and demographic features of markets, and the availability of substitutes, may limit anticipated demand to a level that does not justify the cost of entry; differences in disease patterns across countries; and rejection by some local regulatory authorities. Even among the wealthier countries with most developed health care systems, not all of these drugs became available during the sample period: the USA, Germany, and the UK, for example, saw launches of only about 60 percent of the sample of drugs. The limited availability of new drugs (at least by this

measure) suggests a substantial welfare loss. The good news from a welfare perspective is that the geographic diffusion is substantially wider for the (arguably) higher quality drugs—as proxied by those obtaining approval from the U.S. Food and Drug Administration, which is among the most stringent regulatory agencies in the world (column 3), and the subset of FDA-approved drugs that pass a priority review screening (column 4).[15] For these drugs, more than half are eventually launched in more than 25 countries (though with long lags, as we will see later). But even among these high quality new drugs, 13 percent were only launched in three or less countries within the sample period.

Because launch lags (the time elapsed between first worldwide launch and launch in a given country) can be long and the sample is truncated at 2002, Table 2 likely underrepresents the true extent of diffusion. To examine the temporal aspects of diffusion, and to address this potential undercounting of launches, in Table 3 and Figures 1 through 4 we present results from nonparametric analyses of time-until-launch that estimate the distribution of launch lags allowing for right-censoring. Figures plot the Kaplan-Meier 'failure' function (i.e., $1 - \hat{S}_t$ where $\hat{S}_t$ is the estimated survival function) while the table reports only the time corresponding to the 25th percentile of launch lags. A number of findings stand out. First, as shown in Figure 1, even after 10 years, only 41 percent of drug-country opportunities for a launch were taken up. Even after 20 years or more, less than 50 percent of possible launches had taken place, and as practical matter, many of these drugs may never be launched in large numbers of countries. While not all of the country-years in which a drug was not launched necessarily represent welfare losses (some drugs may have become obsoleted by advances in technology, may have no value in contexts where important complementary technologies or resources for health care are not available, or may only be useful for treating diseases with very low incidence in a country), this evidence of limited diffusion is nonetheless very disappointing from a welfare perspective. Even in the subsample of FDA-approved drugs, only 54 percent were launched in the average country within 10 years. (Diffusion of non-FDA-approved drugs was much slower and less extensive, with 19 percent of drug-country launch opportunities filled within 10 years.)

Second, delays in launching drugs are strongly related to per capita income. Measured in terms of the estimated time for 25 percent of possible drug-country launches to take place, the first panel of Table 3 shows that the diffusion pattern is strongly related to market size, as proxied by the level of GDP per capita. (In the regressions that follow, we will also control for population size). As shown in the first column, it takes nine years for 25 percent of drugs to be launched in the average low income country, but only two years in high income countries. This income-related disparity persists when we focus only on

[15] Of the 642 drugs in the sample, 66% were approved by the FDA, and 41% of which (27% of the full sample) were priority-reviewed by the FDA. While we focus on diffusion lags, there is also evidence that FDA approval times are shorter for more important drugs (Dranove and Meltzer, 1994).

the higher quality drugs (second and third columns of Table 3). The full distribution of estimated launch lags broken out by countries' income level is given in Figure 2. (Medium income includes both the lower middle and upper middle income categories of the World Bank.)

Third, the pace and extent of diffusion is strongly associated with a country's patent and price regulation regimes. In the second panel of Table 3 and in Figure 3 we show results broken out by a summary measure of each country's patent regime. The duration of patent rights is categorized as None, Short, Medium and Long (recall that we define Short as a patent term of 10 years or less, Medium as 11 to 16 years and Long as 17 years or longer) and a country/year observation is assigned to that category if it had either process and/or product patents in that group. With no patents, the estimated time for 25 percent of drug-country launch opportunities to be filled is eight years, falling to less than 2.6 years with long-duration patents. In the third panel of Table 3 and in Figure 4 we group observations where there was either no or weak price regulation versus strong.[16] In countries with no or weak price regulation, the equivalent statistic is three years, rising to five where price regulation is strong. The estimated 'failure' functions plotted in Figures 3 and 4 are very different across categories, and the log-rank test for homogeneity strongly rejects the null of no difference across categories: $\chi^2(3) = 750$ for patent regimes, and $\chi^2(2) = 267$ for price controls.

5 Empirical Model and Results

5.1 Econometric Specification

To analyze the timing of drug launches more formally, and control for other covariates, we use a parametric hazard model. A launch is defined as the first appearance of the identified molecule (new chemical entity) in a given country, whether in proprietary or generic form. The launch lag in a country is dated relative to the first global launch of the molecule (measured in days). We adopt the proportional hazard model with the Weibull distribution. The hazard of launch for drug i in country j at time t can be expressed as

$$h(t \mid x_{ij}(t)) = \alpha t^{\alpha-1} e^{x_{ij}(t)'\beta} \tag{5}$$

where $x_{ij}(t)$ is a set of time-varying covariates and the scalar $\alpha > 0$ and vector β are parameters to be estimated. This specification imposes a monotone hazard rate, but it can be either increasing ($\alpha > 1$) or decreasing ($\alpha < 1$) over time. The model of drug launch in

[16] In regressions of the type discussed below we found no statistically discernible distinction between weak price controls and no price controls.

Section 2 predicts that the hazard rate declines with t : since the remaining patent duration falls with t, the threshold profitability shock required for launch must be larger to generate rents to cover the entry cost. The parameter estimates of α presented below confirm this prediction.[17] For continuous covariates, the parameter β_l reported in the tables correspond to the percentage change in the per period conditional probability (hazard) of launch due to a unit change in x_l (for discrete covariates, e.g., patent and price regulation regimes, β_l is the percentage change in moving from the reference category to the focal regime).[18] Equivalently, we can interpret the negative of the parameters (scaled by the estimate of α) as the log change in the predicted time to launch.

For any given drug the hazard of launch is likely to differ across countries for reasons other than a country's economic and demographic characteristics and policy regime, for example if the incidence of the relevant disease varies across countries. We address this in three ways. First, we include a set of 14 therapeutic class dummies (the 'first level' ATC code assigned by the World Health Organization) in all regressions. This allows the baseline hazard rate to be different for each group of drugs. Second, in all regressions we use standard errors clustered at the drug-country level. Finally, as one of the robustness checks, we allow for unobserved heterogeneity across drugs by including a random drug effect.

5.2 Baseline Results

Table 4 presents the maximum likelihood parameter estimates for various specifications of the hazard model. In column (1) the control variables include elapsed time since first global launch, the set of patent and price control policy dummies, population and per capita income to control for market size, a dummy variable for whether the drug was approved by the FDA (as an indicator of drug quality), and a set of therapeutic class dummies. Note first that the estimate of the Weibull ancillary parameter, α, is 0.614, which is statistically different from one and confirms a declining hazard of launch, consistent with the theoretical model. This estimate is stable across specifications.

Second, as expected, we find that a larger population and higher GDP per capita in-

[17] We also experimented with a log-logistic model that is more flexible in that it can generate a distribution with a non-monotonic hazard rate. The parameter estimates from that specification indicated that the hazard declines over time after a few weeks. This is interesting because it suggests that, unlike in most of the literature on the diffusion of innovations, learning about the potential profitability of markets does not appear to be an important factor for the global diffusion of drugs – if this were the case then we should see an a hazard rate that increases with time since first worldwide launch.

[18] With time varying covariates, the hazard function at time t must be defined conditional on the entire sequence of covariates up to t, call it $\mathbf{X}_{ij}(t) = \{x_{ij}(s) : \ s \leq t\}$. Thus the marginal impact of a covariate on the survival probability and hence the launch lag will depend on the sequence $\mathbf{X}_{ij}(t)$. In our later discussion of how covariates affect predicted launch lags, we focus on the coefficients β. One can also use the estimated coefficients to compute the marginal effect of covariates on the launch lag for each drug-country pair, and then average these marginal effects over pairs using their specific sequence $\mathbf{X}_{ij}(t)$. We do not do that here.

crease the hazard of launch. This finding that market size is an important determinant of drug diffusion is consistent with previous studies that document the role of market size on pharmaceutical innovation and entry (see the Introduction for relevant citations). The elasticities of the per period hazard of launch with respect to population and per capita income are 0.074 and 0.247. In terms of their effect on launch lags, these are equivalent to elasticities of about -0.12 and -0.40, respectively. Third, the coefficient on the dummy for FDA-approved drugs confirms that these high quality drugs are launched much faster—their per period hazard of launch is more than double that of low quality drugs, and their predicted time to launch is less than one half of the lag for low quality drugs**.** Finally, there are significant differences in the speed of drug diffusion across therapeutic classes. Coefficients on the therapeutic class dummies (not reported in the table) range from -0.81 to 0.26, equivalent to launch lags over 130 percent faster or almost 60 percent slower than the reference category, and we strongly reject the hypothesis that the coefficients on therapeutic class dummies are jointly zero (p-value < 0.001). This holds for all specifications.

Turning to the key policy variables, the first important finding is that extensive price controls significantly delay drug diffusion.[19] Having strong price regulation reduces the hazard of launch by 15 percent, equivalent to 25 percent increase in the predicted launch lag.[20] In addition, both process and product patents have a large effect on launch lags. In interpreting these coefficients, it is important to recognize that these dummies are mutually exclusive within process and within product, but not across product and process. Thus while the estimated coefficient on *Short_Process* implies that relative to having no patent protection, a short process patent regime—such as that used by India between 1971 and 2005—reduces launch lags by 19 percent, moving to *Medium_Process* gives an incremental gain of 13 percent. The coefficient on *Long_Process* is smaller (and not significant), suggesting that long process patents may undermine vibrant process-related innovation as an avenue for entry by indigenous firms (but caution is warranted, as we later show that *Long_Process* is significant when we use instrumental variables to account for endogeneity of policy regimes). It should also be noted that the coefficient on *Short_Process* is identified off a relatively small number of observations: only a handful of countries in the sample had this type of patent regime, and some for only limited periods of time, and it is possible that the estimated effect is confounded with other (unobserved) aspects of their internal

[19] Of course, firms can adopt strategies to forestall price regulation or mitigate its effects. An interesting example of this is the study by Ellison and Wolfram (2004), which shows that drug firms acted to limit price increases during a period of intensive political discussion of health care reform in the U.S.

[20] We also tried using two separate dummy variables for weak and strong price regulation in a variety of specifications not reported here. We consistently found that weak controls have no statistically significant effect on launch lags. Therefore, in all specifications reported in the paper we use only one dummy variable for strong regulation, and combine country/year observations with weak and no controls as the reference group.

market. One of these countries was India, which may be a special case in terms of the size of its internal market and success in developing a highly competitive export-oriented generic sector during this period.

The parameters also show that long product patents have a powerful effect on diffusion. Short product patents, *Short_Product* ($\leq$ 10 years), and medium product patents, *Medium_Product*, do not have strongly significant effects relative to no patent protection, which is what would be expected given the long development and regulatory lags (and the fact that patents are taken out very early in the R&D process to ensure priority). However, long product patents (*Long_Product*) reduce launch lags by 55 percent.[21] In addition to patent term, the content of patent protection also matters for diffusion. The point estimate of the *Pro-patent Index* is statistically significant and implies that a one standard deviation increase in the index reduces predicted launch lags by about 11.3 percent.[22]

It is also worth pointing out that patent rights can affect the direction, as well as the speed, of drug diffusion. Strong patent rights may be particularly important for inducing launch of drugs that are only useful for treating smaller patient populations. Non-patent advantages over competitors (e.g., market frictions, first mover advantages etc.) may be sufficient for first entrants to recover fixed costs of entry for blockbuster drugs, but this will typically not be the case for other types of drugs.

In column (2) we examine how health expenditures, in addition to the overall level of purchasing power, affect the incentives to launch in a country. To do this, we include both the logs of GDP per capita and the percentage of GDP that is devoted to health expenditures. This sharply reduces the impact of GDP per capita (the implied elasticity on launch lags falls from -0.40 to -0.04), but the effect is picked up by health expenditures (elasticity on launch lags of -0.51). Adding the two coefficients, the implied elasticity of the time to launch with respect to health expenditures per capita is -0.55. The coefficients on the process and product patent regimes are generally robust, except for the *Pro-patent Index* where the coefficient declines by half, and the coefficients on *Short_Product* and *Medium_Product*, where *Short_Product* becomes much smaller and statistically insignificant and *Medium_Product* increases to about one half the magnitude of *Long_Product* and

[21] Taken at face value, this regression specification would also imply that the product and process effects are additive: e.g., a country with *Medium_Process* and *Long_Product* would have 32.4 + 54.5 =95% lower launch lags. In fact, since the patent terms likely overlap substantial, the actual period of market exclusivity for the patent holder will be close to the longer of the patent terms, and the impact on launch lags is better estimated by the largest of the two coefficients rather than their sum.

[22] As indicated in Section 3, we tried using different definitions of the patent term for both process and product patents. The parameter estimates are similar to those reported in Table 4. The only notable differences occur when we define long patents as $\geq$ 17 years (rather than the baseline definition $\geq$ 18). In that case, the point estimates of the coefficients on *Medium_Process* and *Long_Product* decline by about a third (though the differences are not statistically significant), and the coefficient on *Long_Process* is now positive and statistically significant.

becomes strongly significant. (These coefficients are stable across the all the specifications that control for health expenditures.)

Column (3) expands the set of control variables to include the Gini index of income inequality, the fraction of elderly in the population (another dimension of effective market size), and three health policy 'institutions'. The first, and most important, observation is that the estimated coefficients on the price regulation and patent regime variables are robust to adding these new controls. Second, drugs are launched faster in countries with more elderly in the population, and the implied impact is large—a standard deviation increase in the fraction of population over age 65 reduces launch lags by 21 percent. Third, we find that, for a given level of GDP per capita, the distribution of income is a significant determinant of market entry. Greater income *inequality* (higher Gini) increases the speed of diffusion significantly—the coefficient implies that a standard deviation rise in the Gini index reduces launch lags by 23 percent. The likely reason is that greater inequality makes it more likely that there are at least some elements in the population (the 'wealthy elite') that can afford to buy the drugs.[23]

Next we use dummy controls for three health policy institutions—whether the country has a national formulary, an essential drug list, and a national drug policy. The essential drug list and national formulary play two roles. They facilitate the distribution of drugs to the population, which should increase effective market size and thus promote earlier drug launches. At the same time, they signal more effective institutions for implementing any price control regimes that may be in place, which would reduce incentives to launch. Their impact is thus an empirical question. We find that these health institutions have a large and statistically significant impact on the speed of drug diffusion. The point estimates imply that the predicted time to launch is 31 percent lower in countries that have adopted the Essential Drug List,[24] and an additional 16 percent lower if they have a national formulary in place. We find no significant effect of having a formal national drug policy which may not be surprising since, while it signals policy intent, it is a less concrete manifestation than the other two institutions.[25] Unfortunately, it is not possible with the available data to unbundle

[23] While this may be true in countries with relatively low levels of per capita income, one might think that inequality could have a smaller, or perhaps even an opposite, effect in higher income countries (where less inequality might empower more consumers to be able to afford new drugs). When we drop high income countries from the sample and re-estimate the model (reported later), we still find that inequality reduces launch lags, but the coefficient is only half as large. This is consistent with the idea that there is a threshold level of income that makes an individual a potential consumer of new drugs, and the effect of inequality on the demand for drugs depends on the distribution of income around that threshold.

[24] This is *not* the effect on launch times for drugs which are listed on the EDL. While it would be interesting to look at the diffusion rate specifically for EDL-listed drugs, there were too few additions to the EDL during the sample period to do this reliably.

[25] Of course, these variables may also serve as proxies for broader institutional quality in the country, though we also include an index of the rule of law (from the World Bank) in this, and all subsequent, regressions. Its estimated coefficient is never statistically significant, however.

these institutions and identify the specific features that make entry more attractive. This is an important challenge but it requires more detail about the how these institutions actually function in different countries.

Finally, it may be important to recognize that the quality of regulatory agencies varies across countries. If this is correlated with the choice of policy regimes, we might misattribute the impact of such policies on the timing of drug launches. To address this concern, in column (4) we include a measure of bureaucratic quality for each country/year observation, taken from the World Bank. We expect countries with higher quality regulators to screen more carefully, and this should generate longer launch lags on average. However, the impact of better screening should depend on the quality of the drug—more effective regulators are more likely to block, or delay, low quality drugs. To test this idea, we interact the measure of bureaucratic quality with dummy variables for whether the drug was approved by the FDA (BQ_FDA and BQ_nonFDA). When we do this, the estimated coefficients on the demographic and policy variables remain stable. The new finding is that higher quality bureaucracy is associated with longer launch lags for all drugs but, as expected, the effect is an order of magnitude larger for low quality drugs than for those approved by the FDA, and both are statistically significant. The parameter estimates imply that a standard deviation increase in bureaucratic quality increases launch lags by three percent for FDA-approved drugs, but by almost 50 percent for low quality drugs.

6 Robustness Analysis

In this section we check the robustness of the main results to a variety of different specifications. In each case, we introduce the changes relative to the baseline specification given in column (4) of Table 4.

First, in column (1) of Table 5 we introduce random drug effects, to allow for unobserved drug-specific variation such as a drug's potential market size (i.e., difference in the incidence of the targeted diseases or conditions) or differences in the difficulty and cost of obtaining regulatory approval. These random effects enter as a multiplicative factor in the model for the hazard function, and are assumed to follow a Gamma distribution (this standard formulation yields a convenient analytical expression for the likelihood function). Overall, the results are similar to (and not statistically different from) the estimates of the baseline specification.

Second, we re-estimated the baseline regression using a more disaggregated classification of therapeutic categories. This uses 61 rather than 14 therapeutic classes, based on the second level of the World Health Organization ATC classification (for example, 'anti-hypertensives' as opposed to 'cardiovascular system'). The results, given in column (2), are

very close to the baseline specification.

Third, we examine whether our previous results for the pooled sample of drugs also hold when the model is estimated using data only for (arguably) higher quality drugs, as represented by those that were approved by the FDA in the U.S. Since high quality drugs are especially important for public health, it is critical to know how policy choices affect their diffusion. In addition, idiosyncratic regulatory requirements on safety and efficacy may make it possible for drugs to be approved in one country but then fail to reach other markets because they do not meet the local regulatory standards. As a consequence, an observed failure to launch may be driven by variation in the regulatory environment, rather than by the profitability calculations as modeled in Section 2. Focusing on drugs approved by the FDA, one of the world's most stringent regulatory authorities, helps rule this out—albeit without addressing problems such as a drug failing to launch because a country requires that clinical trials be conducted on its own residents before approving a drug and these are too costly relative to anticipated profits. The results are presented in column (3). All of our main findings hold up, and the point estimates are very close to the estimates from the baseline specification for both price regulation and patent policy regimes, as well as the other covariates.

Fourth, we consider differences between high income and developing countries. Historically there has been much less variation in patent regimes in high-income countries than in developing economies and there was (and remains) serious opposition to harmonization of patent policies under the TRIPS Agreement. Opponents of harmonization on a relatively long-duration and broad-based patent standard asserted then (and now) that the effects of patent protection are likely to be more damaging for developing countries, both because their capacity to innovate in drugs was lower (reducing any positive incentive effects from patents) and because the deleterious price effects of patent protection could fatally undermine the market for drugs in poorer countries. However, the important question of impact of patent rights on the *diffusion* of drugs (as opposed to their pricing) has received little attention in these debates. We examine this question in column (4) of Table 5, where we drop high income countries from the sample. It is striking that the qualitative results, and most of the point estimates—including the coefficients on the policy regimes—are very similar to the baseline specification where we use all countries. The main differences are that the impact of population is smaller among lower/middle income countries, the pro-patent index is no longer significant, and the relative magnitudes of the impact of EDL and national formularies are reversed.

Fifth, we extend the baseline specification to allow for interactions between price regulation and patent policy regimes. There are reasons to expect the effect of patent regimes to depend on whether there is strong price regulation in place. In the extreme case where

price controls bring prices down to unit cost, patent protection would not provide any incentive for launch. In less extreme cases, we would expect the incentives from patent rights to be reduced. To investigate this, we interact the dummy for price regulation with the two extreme patent regimes, *Short_Process* and *Long_Product*.[26] The results in column (5) provide some evidence that price controls strongly dilute the incentive effects of patent protection. In the absence of price regulation, the point estimates of *Short_Process* and *Long_Product* on the launch hazard are both about 0.33 and highly significant. When there is strong price regulation, the impact of *Short_Process* falls essentially to zero (the estimate is -0.04, and the test on the sum of coefficients does not reject the null of zero, p-value=0.63), while for *Long_Product* it declines by about 40 percent to 0.204 but is still strongly significant (p-value <0.001). These results highlight the importance of taking the interactions between policy instruments into account in designing overall policy strategy for pharmaceuticals.

Finally, we investigate how indigenous innovative capacity affects the timing of drug launches. A drug can be launched by the firm that developed it, its licensee, or a domestic competitor (often, a generic drug company) in cases where the new molecule is not protected by a product patent. To cover launch costs, the most common avenue for competitive entry by indigenous firms is to innovate on the drug manufacturing process—typically involving chemical engineering—and protect it with a process patent. Our data do not unambiguously identify whether products are launched in a country by the product innovator, its licensee, or a competitor, so we cannot directly examine the role of competitive entry. Instead, we construct a proxy to capture local technical capacity to do process innovation, using the stock of patents in fields related to chemical engineering and manufacturing in each country/year, and test how this innovative capacity affect the timing of launches.[27] When we add this control (column 6), the estimated parameters on the patent and price regulation (and other) variables are robust. This shows that the observed policy regimes are not simply proxies for having a strong local R&D capability (which might in turn influence which policies are adopted). The point estimate on the stock of chemical patents is positive and statistically significant, indicating that countries with greater local capacity for chemical

[26] We also tried interacting price regulation with *Medium_Process* and *Medium_Product*, but these two patent regimes are highly correlated in the sample (very few countries have long product patents without long process patents), and the results were not clear-cut. We do not interact price regulation with *Short_Product* or *Long_Process* as neither of these variables entered significantly in the baseline regression.

[27] The measure is is a count of patents by application date (measured in 1000's of patents) in any of the international patent classes (IPC) corresponding to chemical engineering and manufacturing, as indexed by the American Chemical Society (Data Appendix for details). The count is constructed for each country/year, based on the country of the inventor and cumulated into a stock using a 15 percent depreciation rate and an assumed pre-sample growth of 10 percent to initialize the stock. If a patent has multiple inventors listed, we count the patent in each of the listed countries. Results are very similar if we just use the patent flow. We do not use logs because nearly 40 percent of the country/year observations are zero.

process innovation (and, presumably, therefore, local pharmaceutical manufacturing capacity) have somewhat faster drug launches. This points to a potentially important role for indigenous entry, and highlights the need for process patent protection in countries with local technical capacity (especially where product patent rights are absent or ineffective).

7 Endogenous Policy Regimes

Patent and price control regimes are outcomes of a political process, which raises a concern about endogeneity. The most likely source is unobserved heterogeneity across countries in political institutions that affects both the choice of policy regime and the timing of new drug launches—e.g., variation across countries in the profitability of markets, institutional quality and policy enforcement.[28] For example, firms have greater incentives to lobby for strong patent rights where entry is more profitable, which would cause us to over-estimate the effect of patent rights on the timing of drug launches. But the bias can also go the other way—countries with weak enforcement may be more willing to adopt the appearance of strong patent rights, inducing negative covariance of patent rights with the disturbance and thus a downward bias. However, patent reform is often forced as a condition of entry into new political groups (e.g., joining the European Union), bilateral trade negotiations, and international trade agreements such as TRIPS (Sell, 2003), all of which may limit the scope for endogenous patent regimes. Price regulation is more likely to suffer from endogeneity, since governments have greater flexibility in setting price controls, even if in more recent years the U.S. has pushed for limitations in the context of bilateral trade agreements (there are examples in our sample of countries reversing price regulation reforms within a few years).

To address concerns over endogeneity, we need instrumental variables that are correlated with policy choices but do not directly affect the timing of drug launches (and uncorrelated with unobserved country level heterogeneity). We use a set of five instruments based on political, legal and demographic characteristics of a country (details of the variables and sources are provided in the Data Appendix). The first is *Political_Constraints* which measures the degree to which voting rights within the political (legislative and executive) structure constrains policy change (this is used in the political science literature as a proxy for credible policy commitment). The second is *Executive_Orientation* which codes whether the executive comes from a right, left or center party with respect to its orientation on economic policy (the reference category is no executive). The third instrument is

[28] Reverse causality is hard to rationalize in our context, at least contemporaneously. Regime choice might be negatively correlated with *past* launch lags – long delays might induce governments to introduce more attractive policy regimes – but whether this induces endogeneity bias depends heavily on the assumed structure of errors in the launch and regime choice equations.

Ethnolinguistic_ diversity which is a measure of population diversity that has been used in the economics and political science literature as an indicator of difficulty in reaching and committing to political decisions. These three instruments vary across countries and over time. The fourth instrument, *Legal_ Origin*, codes whether the legal system is based on common law (U.K.), French law, or German law, with Socialist or other legal origins as the reference category; this measure is time invariant. The last instrument is *RTA* which is the cumulative number of regional trade agreements that the country has entered into, which varies across countries and over time.

There is no compelling reason to think that the first three instruments either directly affect launch decisions or are correlated with unobserved institutional quality or profitability of local markets, conditional on the policy regimes and other controls. However, one might be concerned that the number of *RTA*'s reflects unobserved trade openness of an economy, which could affect launch decisions. For this reason, and more generally to examine the robustness of the parameter estimates to the choice of instruments, we use four alternative subsets of instruments. The narrowest set includes only *Political_ Constraints* and *Executive_ Orientation*. The second set adds *Ethnolinguistic_ diversity*, the third includes *Legal_ Origin* and the most expansive set also adds *RTA*.

We begin by testing the exogeneity of price controls and patent policy regimes using the Rivers-Vuong (1988) approach. To do this, we estimate 'first stage' regressions for the choice of policy regimes—specifically, a Probit for price regulation and Ordered Probits for the process and product patent regimes. In these regressions, we use all controls from the baseline specification of the hazard model plus the various sets of instruments described above. While the instruments are not derived from a structural model of policy regime choice, the instruments have statistically significant explanatory power in these regressions.[29] Likelihood ratio tests decisively reject the null hypothesis that the instruments have no effect on the choice of price regulation and patent regimes (p-values <0.001 for all four sets of instruments).[30] Using the first stage regressions, we compute the generalized

[29] Given the importance of political economy considerations on the choice of intellectual property regimes, constructing such a model remains a difficult, and open, research challenge. As indicated in the introduction, existing studies that exploit patent reforms for identification have treated the policy changes as exogenous.

[30] Details of the first stage parameter estimates are available on request. A brief summary of the qualitative results for the instruments (based on statistically significant coefficients) is as follows. Greater *Political_ Constraints* (stronger policy commitment) are associated with the absence of price controls and shorter process and product patents. *Executive_ Orientation* from a Center party makes price controls less likely (more likely with a Left party) and is associated with longer process and product patent protection. Higher *Ethnolinguistic_ diversity* (weaker policy commitment) makes price controls less likely, process patents shorter, and product patents longer. Turning to *Legal_ Origin*, we find that price controls are most strongly associated with French legal origins, followed by U.K. and German legal systems. The German and U.K. legal origins are also associated with longer process and product patents. Finally, higher *RTA* (more trade openness) is correlated with longer process and product patents as well as the presence of price controls.

residuals and add them as regressors in the hazard model. Exogeneity of individual policy regimes is tested by the statistical significance of the coefficient on the associated generalized residuals, and by joint tests for groups of regimes—e.g., process and/or product patents. We strongly reject the hypothesis that price controls are exogenous, using each of four instrument sets (p-values: <0.001 for the first three sets, and 0.004 for the fourth). However, the tests for patent regimes are mixed: we reject the hypothesis that *Short_Process* and *Medium_Product* patent regimes are exogenous, but do not reject the hypothesis for the other four patent regimes (using three of the four instrument sets). However, we strongly reject the joint hypothesis test that the process patent and/or patent regimes are exogenous (p-values<0.001) using each of the instrument sets.

In view of these mixed findings, we proceed to estimate the hazard model allowing for endogenous policy regimes. To do this, we follow the approach of Lillard (1993) and formulate the model as a system of four simultaneous equations: the hazard launch equation and the three policy regime equations (probit for price regulation, ordered probits for process and product patent regimes). Each of the regime equations includes all country-level variables from the hazard model plus the instruments described above. This model is estimated by full information maximum likelihood.[31]

In Table 6 we summarize the FIML parameter estimates for the patent and price regulation variables in the hazard equation (For brevity, we suppress coefficients for the other controls and the 'ancillary' policy regime equations. Details are available on request). These estimates were obtained using a piece-wise linear spline for the duration-dependent component of the log-hazard, which is capable of approximating a variety of parametric models, so the parameters are not strictly comparable to the Weibull estimates in Tables 4 and 5. For reference, columns (1) and (2) present the parameters obtained from estimating the baseline specification of the hazard model as a single equation, and it is worth noting that the estimates in columns (1) and (2) are very similar to those from the Weibull specification.[32] Column (2) includes a normally distributed country random effect, with little impact on the estimated coefficients in column (1).[33]

[31] Two points should be noted. First, we introduce correlation between the disturbances in the launch and regime equations by adding a common random country effect to each (its coefficient is normalized in the process patent equation). In the absence of such correlation, the regimes would not be endogenous in the launch equation (which the Rivers-Vuong test rejected). Efforts to estimate the launch equation by non-linear GMM as a less restrictive alternative to the FIML procedure used did not succeed in obtaining convergence. With time-varying covariates, the data form a large unbalanced panel in which each observation in the GMM objective function (observed launch status minus predicted in the final period) is conditional on the entire history of each drug-country up to the last period observed, making the selection of valid instruments very challenging.

[32] The duration-dependent part of the hazard function is modeled using year dummies for $t \in [0, 9]$ and $t > 9$. Estimated coefficients on these time dummies imply a pattern of duration dependence consistent with a Weibull distribution with slope parameter of about 0.6, through to about 12 years.

[33] Not surprisingly, estimated coefficients on some of the other country-specific variables that change

Columns (3)-(6) present the FIML estimates for the policy regime variables using alternative sets of instruments with a country random effect common across equations. Three main conclusions stand out. First, endogeneity of policy regimes leads us to under-estimate their impacts on the timing of drug launches in an uninstrumented single-equation model: the estimated impact of price regulation and the patent regimes here are generally larger than those obtained when the policy regimes as treated as exogenous. Note that if endogeneity were driven by unobserved heterogeneity in the profitability of markets, we would expect an upward bias in the magnitude of the coefficients. To the contrary, our findings suggest that the endogeneity bias is more consistent with negative correlation between the adoption of strong policy regimes and unmeasured aspects of political and legal institutions, such as enforcement of patent rights. Second, the overall pattern of policy impacts is similar to what we found in the earlier regressions. Process patents raise the hazard of launch (i.e., reduce launch lags), and the impact increases with the duration of such patents, though the differences are not all statistically significant. (Note that in the earlier results for the baseline specification we found no significant impact for long process patents, but when we use instruments we do). Again, as before, we find that *Medium_Product* and *Long_Product* have large impacts on launch lags, while short product patents have little effect. Third, the pattern of estimated parameters is fairly robust across the different instrument sets.[34]

8 Policy Simulations

In this section we simulate how different policy choices affect the speed of new drug diffusion. The metric we adopt is the predicted time it takes for 25 percent of drugs to be launched ($LAG25$) under different counterfactual policy regimes. Using our estimated parameters, we solve for the value of the 25th percentile of the estimated 'failure' function for each drug/country observation, conditional on covariates, and then examine the median value across observations.[35] We begin with a benchmark computation of $LAG25$ for a regime with no patent protection or price regulation, and then introduce three counterfactual policy regimes: short process patents, long product patents, and price controls. Table (7) shows results for both for all drugs and for subset of FDA-approved drugs, and then for low, middle and high income countries.

relatively little over time (such as health expenditures/GDP) are sensitive to including a country random effect.

[34] There are some exceptions: the impacts of *Medium_Product* and *Long_Product* are notably larger in columns (4), (5) and (6), and in column (5) the coefficient on *Short_Process* is not significant while the coefficient on *Short_Product* is significant at the 5 percent level.

[35] To do this, we set the values of the time-varying covariates at their sample means (over time) for each drug/country observation. We focus on the median value of $LAG25$ because many drugs are never launched in a number of countries, so the distribution of $LAG25$ is sharply skewed, rendering the mean (or median) of the predicted survival function a somewhat misleading summary statistic.

Panel A of Table 7 is based on the baseline Weibull regression estimates from column (4) of Table 4 which, as discussed in the previous section, likely under-estimate the impact of policy choices on launch lags. The results further confirm our descriptive findings that diffusion of new drugs is slow, and varies across drug and income categories.[36] In the benchmark case with no patents or price controls, it takes 4.63 years for 25 percent of drugs to be launched in the pooled sample. This falls to 3.01 years for FDA-approved drugs, which is good news from a welfare perspective. But there is substantial variation across income categories—the median lags are more than three times longer in low income countries (8.85 years) as compared to high income countries (2.60 years). Setting the patent regime to short process patents only (i.e., *Short_Process* = 1 and price controls and all other patent variables = 0) reduces predicted launch lags by about 25 percent. Slightly shorter launch lags are estimated for a regime with no process patents but long product patents (and no price controls). Introducing price controls in a regime with no patents increases lag times by 29 percent above the benchmark. Recall that given the functional form of the baseline empirical model, the percentage effects of these policy regimes are additive: thus introducing both price controls and *Long_Product* generates a predicted median value of *LAG25* of 4.09 years. In other words, price regulation removes most of accelerated diffusion induced by long product patents.

Panel B presents the median predicted launch lags when we use the FIML parameter estimates on the policy variables, which take into account the endogeneity of policy regimes.[37] Using these coefficients, product patents emerge as much more effective than process patents (69 percent reduction in launch lags compared to 29 percent), and price regulation has a very large impact, more than doubling launch lags.

In both panels, the same pattern of results holds for the subset of FDA-approved drugs, and for low, middle, and high income countries. In low income countries, *LAG25* is depressingly high in the benchmark case, at almost nine years. Notice that, based on these results, a policy regime directed solely at lowering prices on drugs that have been already been launched (no patents, and strong price controls) would increase launch lags very substantially to over three times longer than in a 'pro-innovator' regime with no price controls and long product patents.

Some qualifications should be kept in mind. First, these calculations are not a welfare assessment of different regimes—that would require, at a minimum, consideration of how these policies they affect drug prices. This is extremely difficult unless one can model both

[36] Although similar to the numbers in Table 3, note that these figures are not directly comparable since they control for economic and demographic variables, drug therapeutic class, and set the patent and price controls policy variables to counterfactual values.

[37] Specifically we recompute the predicted launch lags from the Weibull model after substituting the coefficients on the patent and price controls variables with values from the FIML estimates in column (3) of Table 6 (which has a minimal, conservative instrument list).

the demand side—as a practical matter, this requires restricting the analysis to specific classes of drugs (e.g., Chaudry, Goldberg and Gia, 2006)—and the supply side, i.e., the investment required for launch. Second, because our empirical model is not structural, counterfactual assessment of policies is subject to the Lucas critique, among other issues. A third, and related, point is that countries develop institutions, and invest in human capital, over long time periods, and in ways that both influence, and in turn are influenced by, the policy regimes they adopt. Thus there may be important, and unmodeled, path dependencies driving observed outcomes—and the estimated policy impacts shown here may take many years to unfold. Any assessment of a new policy regime needs to take into account the capacity of the country to adapt and the costs of doing so.

9 Concluding Remarks

This paper studies how patent rights and price regulation affect launch lags for new drugs. Using new data on launches of 642 new molecules in 76 countries during 1983-2002, we show that, all else equal, longer and more extensive patent protection accelerated diffusion, while price regulation strongly delayed it. Health policy institutions, and economic factors that make markets more profitable, also sped up diffusion. These results hold both for developing countries and high income countries, and the results are robust to using instrumental variables to address the endogeneity of policy regimes. Our findings also raise the broader point, not limited to pharmaceuticals, that patent rights can have an important impact on the *diffusion* of new innovations as well as on the rate at which new innovations are created.

Of course, the same policies that promote faster launch—stronger patent rights and the absence of price regulation—are also those that raise prices. This highlights the basic tradeoff countries face between making new drug therapies available and making them affordable. Finding ways to best mitigate the adverse effects of this tradeoff is a major challenge.

There are two main directions for future research. One is to study how severe the tradeoff between faster diffusion and higher prices actually is—i.e., how much prices are raised by stronger process or product patent protection—by using data on sales and prices within countries with different patent regimes. A second interesting direction for research is to develop a structural model of drug launches which could be used to back out unobserved launch costs in each country and then to conduct important counterfactual policy experiments. One question of particular interest is the effects on global drug diffusion of introducing multilateral recognition of drug trials and regulatory approval.

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Data Appendix

New Drug Launches

The phenomenon of interest here is the dating of the launch of each new drug in each country. This was derived from the dating of launches of drug products, which contain the new drug, in combination with inactive ingredients and potentially other active ingredients. The distinction between 'drug' and 'drug product' is significant. Not all new drugs are launched as exactly the same product in all countries. A given 'active moiety' may be approved as different salts or esters in different countries (as sulfate, hydrochloride, maleate etc.) or in different galenical forms (tablet, injectable, topical cream etc.), or may be sold in combination with different sets of other active ingredients.

Drug launches were identified from two sources of data, in which the unit of observation is a drug product. The first is the December 2002 version of the "LifeCycle: Drug Launches" database obtained from IMS Health, Inc. This file contained 187,725 observations on retail drug product launches for the period 1982-2002. The unit of observation is product-country-year, with each observation recording: (1) the trade name (proprietary product name, or brand name); (2) a listing of active ingredients using non-proprietary generic chemical name; (3) the composition, listing the formulation (capsule, syrup, powder etc.) and amounts, strength or concentration of the active ingredient(s); (4) the date the product goes on sale; and (5) the therapeutic class of the product using the World Health Organization's 'ATC' Anatomical Therapeutical Chemical classification system at the third level. This database covers all therapeutic classes, but not all countries. Coverage of countries increased over time, with product launches observed in 45 countries in 1982, increasing to 66 in the early 1990s, and to 76 by the end of the sample. In two cases country was coded by IMS as a region: French West Africa, consisting of Benin, Cameroon, Congo, Cote d'Ivoire, Gabon, Guinea, and Senegal; and Central America consisting of Costa Rica, El Salvador, Guatemala, Honduras, and Panama. Notably, India was not included in this database during this period.

The drug launch data for India were obtained from a second source, the "FirstIndia" dataset of product sales compiled by ORG MARG, a market research company. This covers the period 1967 to 1997 but only for a partial set of therapeutic classes, namely antibiotics, cancer, and antiulcer. There were 498 observations on brand name, active ingredient(s), therapeutic class, and launch date.

Identifying drug launches in these data consistently across countries and over time was a serious challenge. In the data, 14 percent of records had no listing of active ingredients, only a brand name, for about one fifth of which the active ingredient could be 'recovered' through lookup of the brand name or through parsing of the composition field. Moreover, 24 percent of records were for multi-ingredient or combination products: in some cases more

than 20 ingredients were listed. About 20 percent of products fell into categories in which active ingredients were prohibitively difficult to identify consistently (vaccines, biologics, hormones, allergens, immune globulins etc.), appeared to be for non-prescription products such as nostrums, over-the-counter, or proprietary formulations, herbal and homeopathic medicines, or were for 'non-drug' medical products, such as blood-testing strips, imaging contrast agents, non-medicinal or inactive ingredients or excipients, diagnostics, and surgical solutions.

As a preliminary step, we therefore excluded 17,452 records for products whose ingredients could not be identified. After a very careful effort to identify brand names of known drugs, we believe that no instances of launches of new drugs were excluded for this reason. We further excluded 37,199 records in therapeutic classes largely populated with non-prescription or hard to identify products,[38] and 2,274 records for vaccines.

Remaining records were 'unpacked' to give one observation per ingredient per product, with the exception of 29 combination drugs given a distinct non-proprietary name in the British Pharmacopeia where ingredients were combined.[39] This created an additional 29,784 observations, and was done to be 'over-inclusive' in identifying drug launches: while many drug products combine active ingredients, treating all combinations of new and old chemical entities as distinct products would result in spuriously high counts of new products, and under-identification of launches of new entities.

In principle each active ingredient is unambiguously identified by the generic name, in practice these are not fully standardized, or may use spelling variations from different languages, or may not have been assigned. After excluding non-drug or hard-to-identify products and ingredients, we observe 9,065 distinct active ingredients in the remaining 115,123 observations on country and ingredient. Considerable effort was invested in coding these consistently, to avoid under-identification of drug launches. A variety of online and hardcopy reference sources were consulted, including: the *ChemIDplus* database main-

[38] Products in the following therapeutic classes: toothpaste and dentifrices, digestives, vitamins, mineral supplements, tonics, laxatives, anti-anemics, topical antihaemorrhoidals, certain dermatologicals (emollients and protectives, wound and ulcer preps, anti-pruritics, disinfectants, medicated dressings, acne, miscellaneous), parenteral nutrition, bacterial immunostimulants, smoking cessation, herbal cough and cold, ophthalmics, otologicals, allergens, herbal and homoeopathic medicines. These were identified through the ATC codes (A1A, A9, A11, A12, A13, A6, B3A, B3B, C5A, D2, D3, D4, D8, D9, D10, D11, K, L3X, N7B, R5F, S, T, V) or through manual examination. Vitamins and non-prescription or OTC drugs were identified from reference sources such as the Physicans's Desk Reference for Nonprescription Drugs and Dietary Supplements. Herbal and homeopathic products were identified by hand inspection, lookup in Physicians' Desk Reference for Herbal Medicine, or being manufactured by a company specializing in herbal products e.g. Arkopharma, Weleda.

[39] These are the drug combinations with demonstrated synergistic effects: co-amoxiclav, co-amilofruse, co-amilozide, co-amoxiclav, co-beneldopa, co-bucafapap, co-careldopa, co-climasone, co-codamol, co-codaprin, co-cyprindiol, co-drydamol, co-erynsulfisox, co-fluampicil, co-flumactone, co-hycodapap, co-methiamol, co-oxycodapap, co-phenotrope, co-proxamol, co-simalcite, co-spironozide, co-tenidone, co-tetroxazine, co-triamterzide, co-trifamole, co-trimazine, co-trimoxazole, and co-zidocapt.

tained by the US National Library of Medicine, the *WHO-MedNet* database, the University of Alberta *DrugBank* database, the *DrugBase* database published by Wissenschaftliche Verlagsgesellschaft Stuttgart, the *Health Canada Non-Medicinal Products Database*, the FDA's *Inactive Ingredients* Database, the Kyoto University and University of Tokyo *KEGG DRUG* database, and current and historical editions of the *Martindale Complete Drug Reference* published by The Pharmaceutical Press, the *Merck Index*, the *Index Nominum* published by the Swiss Pharmaceutical Society, and the *USP Dictionary of United States Adopted Names (USAN) and International Drug Names* published by the U.S. Pharmacopeial Convention. When possible, generic chemical names were matched to the WHO's listing of International Nonproprietary Names (INNs); when an INN was not available, the USP USAN, British Approved Name, or Japanese Approved Name was used.

As a further measure to avoid under-identification of country launches, the parts of active ingredient names corresponding to salts, esters or non-covalent derivatives were removed to arrive at the 'active moiety'. This corresponds roughly to the New Chemical Entity in U.S. usage. Treating different salts, esters and derivatives as distinct entities would result in a significantly larger number of new drugs. For each of the 2,265 such chemical entities in the source dataset we determine the first worldwide launch date, based on the earliest of (1) the first date it appears in the IMS or ORG MARG datasets, (2) the first date it appears in the FDA's drugs@fda approvals database, (3) the first date it was listed as approved for marketing in any country in the Pharmaprojects database. To avoid problems with left-censoring of launch dates in 1982 in the IMS data, we exclude any drugs for which the first worldwide launch date defined this way was before 1983. We also exclude drugs that were only launched in Japan and Taiwan and/or Korea, which appear to reflect medical practice idiosyncratic to this region. This leaves us with 642 drugs, for which we observe 17,189 drug-country observations on the timing of launches.

To prepare this dataset for survival analysis, we use the first worldwide launch date to determine t=0 for each molecule, and then for each drug-country combination create annual observations for the time-varying and non-time varying covariates described below for each year until either the drug is launched in that country or is censored. Care was taken to exclude country-years where a drug was not at risk of launching (as observed in these data), for example if data were not reported for that country until after the first worldwide launch date, or if the drug were in a therapeutic class not covered in these data for that country, for example antihypertensives in India. This gives a total of 298,605 observations on 38,180 drug-country combinations, with the launch date was censored for 20,991 drug-country combinations.

Explanatory variables

Patent Protection

We construct measures of the availability and duration of patent protection for (a) pharmaceutical products and (b) chemical processes is coded for each country-year, along with presence of enforcement mechanisms.

Two sources were used. Data compiled by Ginarte and Park (1997) and Park (2008) who give dummy variables coded every 5 years 1960-2000 for up to 120 countries on (1) 'Coverage'—i.e., availability of patent protection for different classes of subject matter, here the relevant category is chemicals and pharmaceuticals, process and product; (2) patent term, measured as years from filing or years from grant; (3) treaty membership in PCT, Paris Convention and UPOV; and (4) presence of various enforcement mechanisms and other factors impacting the scope of rights, such as preliminary injunctions, requirements to work, contributory infringement, compulsory licensing etc. This information was cross-referenced against the text of relevant statues and treaties, published in *World Patent Law and Practice: Patent Statutes, Regulations, and Treaties* by John P. Sinnott and William J. Cotreau (New York: M. Bender, 1974, seriatim), and *Patents Throughout the World*, an annually updated looseleaf publication (New York: West Group). The Statutes, Regulations, and Treaties information are taken as definitive regarding dating of changes in patent term, coverage of pharmaceuticals and chemical processes, patent term extensions, duration of term for foreign versus domestic applicants, and provide some ability to 'back fill' the Ginarte-Park data to identify more precisely changes in the patent regime. There are occasional inconsistencies and conflicts between national law and multinational treaties e.g. Andean Pact, Bangui Agreement. In these cases, the provisions of the national law are taken as definitive.

Using these data we define: Patent_Term = Max (Years from grant +2, Years from filing). The distribution of country/year observations by patent term is as follows:

Patent_Term	0	3	7	10	12	14	15	16	17	18	19	20	22
No. obs	9	17	21	77	59	15	83	35	175	39	38	694	12

Using the patent term, we define the following process and product patent regimes:
Short_Process=1 if chemical processes patentable and $0 <$*Patent_Term* ≤ 12
Short_Product=1 if pharmaceutical products patentable and $0 <$*Patent_Term* ≤ 12
Medium_Process=1 if chemical processes patentable and $13 \leq$*Patent_Term* ≤ 17
Medium_Product=1 if pharmaceutical products patentable and $13 \leq$*Patent_Term* ≤ 17
Long_Process=1 if chemical processes patentable and *Patent_Term* > 17
Long_Product=1 if pharmaceutical products patentable and *Patent_Term* > 17

Pro-patent Index = sum of dummies for whether:

a) patent term is the same for domestic and foreign applicants

b) preliminary injunctions are available

c) infringer can be liable for contributory infringement

d) burden of proof of infringement is reversed for process inventions

e) patents cannot be revoked for failure to work

f) there is no requirement to work the patent, or can be satisfied by importation

g) there is no compulsory licensing

h) term extensions are available for pharmaceuticals

Price Controls

Each country's price control regime was coded as None/Some/Extensive from the sources listed in Lanjouw (2005). The designation 'Some' means that the country has formal price control regulation but it covers only a subset of drugs. 'Extensive' means that the regulation covers most drugs and/or is viewed in the sources as particularly restrictive. In the regressions a dummy variable for price control regime = Extensive is used.

Demographic and Income Variables

Age distribution: For each country-year, the total population, and percentage of the population over 65 years old are taken from the World Bank, *World Development Indicators*. We also used the percentage of the population under 5 years old, but found no effect in the regressions.

Income per capita: For each country, annual values of real GDP per capita (RGDPCH) are taken from the Penn World Table version 6.2

Income inequality: We use the Gini coefficient as reported in the World Bank's World Development Indicators. Since there are rarely more than two observations per country 1975-2005, missing values are interpolated using first-observation-carried-back for years prior to the first observed value, and then last-observation-carried-forward subsequently.

Health care expenditures: For each country, total health care expenditure as percent of GDP is taken from the World Bank's World Development Indicators. This is only consistently available 1990 onwards, and missing data are interpolated using first-observation-carried-back for years prior to 1990.

Health Institutions

We use the following dummy variables:

EDL = 1 if the country has adopted an Essential Drug List

NDP =1 if the country has adopted a National Drug Policy

NF = 1 if the country has adopted a National Formulary

Each of these variables varies across countries and time. Taken from sources listed in Lanjouw (2005).

Local Technical Capacity

Chemicals Patents is a count of U.S. patents by application date in any of the IPC classes corresponding to chemical engineering and manufacturing, as indexed by the American Chemical Society (these include Pesticides, Medicial Preparations, Chemical Methods and Processes, Inorganic Chemistry, Fertilizers, Organic Chemistry, Macromolecules, Dyes and Paints, Petrochemicals, Soaps and Oils, Beverages and Vinegar, Microbiology and Fermentation, Sugar, and Analyzing Materials); plus Chemical or Physical Laboratory Apparatus, Biocides and Pest Repellants, and Apparatus for Enzymology or Microbiology. This count is constructed for each country/year, based on the country of the inventor(s) listed on the patent, and then converted to a stock using a 15 percent depreciation rate.

Governance

Rule of Law and Regulatory Quality index values and rank order (for 181 countries) published in World Bank, *Worldwide Governance Indicators* for 1996, 1998, 2000, 2002 (not available before 1996). We use first-observation-carried-back for years prior to 1996, then last-observation-carried-forward.

Instrumental Variables

Political_ Constraints: a measure of credible policy commitment (the degree of political constraints on policy change). It is derived from a spatial model of political interaction and is based on the number of independent veto points in the different branches of the political system and the distribution of political preferences both across and within these branches. Higher values represent greater political constraints (and thus greater policy commitment). For details see Henisz (2000).

Executive_ Orientation: a dummy variable that codes whether the executive comes from a right, left or center party with respect to its orientation on economic policy. Both of these variables vary both across countries and over time. Source: *World Bank Database of Political Institutions: Changes and Variable Definitions* (Philip Keefer, December 2009).

Ethnolinguistic_ diversity: a measure commonly used as an indicator of difficulty in reaching and committing to political decisions. This index varies across countries and over time. For details, La Porta et al. (1999).

Legal_ Origin: The historical origins of the legal system for each country is coded as either common law (U.K.), French law, German law, Socialist or Scandanavian (fixed for each country over time). For details, see La Porta et al. (1999).

Regional Trade Agreements (RTA): the cumulative number of regional trade agreements that the country has entered as of a given year. This varies across countries and over time. These data were compiled from Table 3 of Baier and Bergstrand (2007), supplemented with the WTO web site (http://www.wto.org/english/tratop_e/region_e/summary_e.xls). We thank Keith Head for providing a clean version of these data.

Table 1. Summary Statistics (country-year observations)

Variables	Mean	Std. Dev	Minimum	Maximum
Policy Regimes				
Short_Process	0.11	0.31	0.00	1.00
Medium_Process	0.22	0.42	0.00	1.00
Long_Process	0.60	0.49	0.00	1.00
Short_Product	0.07	0.25	0.00	1.00
Medium_Product	0.16	0.37	0.00	1.00
Long_Product	0.59	0.49	0.00	1.00
Pro-patent Index	0.42	0.23	0.00	1.00
Price Controls	0.40	0.49	0.00	1.00
Health Institutions				
National Drug Policy	0.82	0.39	0.00	1.00
Essential Drug List	0.74	0.44	0.00	1.00
National Formulary	0.83	0.38	0.00	1.00
Other Variables				
Population (millions)	49.44	119.05	0.41	1034.17
GDP/cap (thousands)	12.58	8.83	1.12	48.59
Health/GDP (percent)	4.48	8.83	0.20	15.78
Gini Coefficient	39.25	10.05	19.49	63.00
% Pop Age 65+	8.40	4.95	1.40	18.07
Bureaucratic Quality	67.96	24.71	16.67	100.00

Table 2. Global Diffusion of New Drug Launches

No. of countries	Sample			
	All drugs		FDA-approved drugs	FDA priority review drugs
	N	(%)	(%)	(%)
1-3	145	23	13	13
4-10	101	16	12	10
11-25	133	21	20	16
26+	263	41	55	62

Notes: Table shows the number of countries in which each drug is launched during the period 1983-2002, with no adjustment for censoring of launch lags or for changes in the number of countries present in the data.

Table 3. Diffusion Times for Drug Launches

	Time by which 25% launched (years)		
	All Drugs	FDA-approved drugs	FDA Priority Review drugs
Income Level			
Low Income	8.98	6.99	5.99
Middle Income	4.05	3.01	2.99
High Income	2.01	1.97	1.02
Patent Regime			
None	7.99	4.02	4.01
Short	6.00	4.42	3.99
Medium	5.43	3.99	3.98
Long	2.56	1.99	1.45
Price Regulation			
Weak/None	2.99	1.99	1.97
Strong	4.98	3.06	3.01
Overall	3.41	2.45	2.00

NOTES: Table entries are based on the estimated Kaplan-Meier survivor function, which adjusts for censoring of launch lags. Countries are categorized as Low, Middle, or High income based on the World Bank's categories and their GDP per capita at PPP in 2001. Based on 298,605 observations. FDA-approved sample has 163,853 observations, and the FDA-priority-reviewed sample 64,778.

Table 4. Weibull Model of Drug Launch: Proportional Hazard Coefficients

	(1)	(2)	(3)	(4)
Elapsed time	0.614**	0.618**	0.611**	0.611**
	(0.006)	(0.006)	(0.006)	(0.006)
Log(population)	0.074**	0.076**	0.077**	0.083**
	(0.007)	(0.007)	(0.007)	(0.007)
Log(GDP/cap)	0.247**	0.023	0.015	0.048*
	(0.015)	(0.018)	(0.020)	(0.023)
Log(Health/GDP)		0.313**	0.259**	0.275**
		(0.017)	(0.018)	(0.018)
Price Controls	-0.153**	-0.171**	-0.140**	-0.153**
	(0.018)	(0.018)	(0.019)	(0.019)
Pro-patent Index	0.372**	0.169**	0.154**	0.220**
	(0.051)	(0.052)	(0.054)	(0.056)
Short_Process	0.117	0.175**	0.180**	0.179**
	(0.065)	(0.066)	(0.067)	(0.067)
Medium_Process	0.199**	0.171**	0.159**	0.164**
	(0.053)	(0.053)	(0.055)	(0.055)
Long_Process	0.017	0.031	0.004	0.053
	(0.063)	(0.059)	(0.060)	(0.060)
Short_Product	0.130*	0.020	-0.064	-0.019
	(0.065)	(0.066)	(0.066)	(0.066)
Medium_Product	0.077	0.174**	0.142**	0.130**
	(0.042)	(0.041)	(0.042)	(0.042)
Long_Product	0.335**	0.303**	0.260**	0.229**
	(0.058)	(0.054)	(0.054)	(0.055)
FDA-approved drug	1.357**	1.375**	1.355**	0.540**
	(0.024)	(0.024)	(0.025)	(0.065)
Gini Coefficient			0.014**	0.012**
			(0.001)	(0.001)
% Pop Age 65+			0.026**	0.024**
			(0.003)	(0.003)
BQ* FDA drugs				-0.001
				(0.001)
BQ* non-FDA drugs				-0.012**
				(0.001)
Rule of Law index				0.001
				(0.011)
National Drug Policy			0.028	0.009
			(0.032)	(0.032)
Essential Drug List			0.189**	0.204**
			(0.032)	(0.033)
National Formulary			0.098**	0.093**
			(0.027)	(0.027)
ATC Dummies	YES	YES	YES	YES
No. Observations	298,605	298,605	298,605	298,605
log-likelihood	-45,413	-45,237	-45,122	-45,034

NOTES: * significant at 5 percent and ** significant at 1 percent. Standard errors clustered on country-drug in parentheses.

Table 5. Weibull Model of Drug Launch: Robustness Analysis

	(1) Drug Random Effects	(2) Level 2 Therapeutic Class Effects	(3) FDA-approved drugs	(4) Low/Middle Income	(5) Interactions of Patents with Price Controls	(6) Local innovation Capacity
Price Controls	-0.214**	-0.157**	-0.181**	-0.205**	-0.040	-0.147**
	(0.020)	(0.019)	(0.021)	(0.029)	(0.037)	(0.019)
Pro-patent Index	0.370**	0.229**	0.231**	-0.036	0.220**	0.187**
	(0.054)	(0.055)	(0.061)	(0.096)	(0.055)	(0.057)
Short_Process	0.185**	0.168*	0.134	0.172*	0.325**	0.171*
	(0.068)	(0.067)	(0.075)	(0.079)	(0.073)	(0.067)
Medium_Process	0.138*	0.163**	0.140*	0.188**	0.174**	0.156**
	(0.057)	(0.054)	(0.061)	(0.062)	(0.055)	(0.055)
Long_Process	0.019	0.049	0.037	0.034	0.025	0.046
	(0.062)	(0.060)	(0.066)	(0.068)	(0.061)	(0.061)
Short_Product	-0.023	-0.006	-0.048	-0.017	-0.015	-0.028
	(0.067)	(0.066)	(0.073)	(0.076)	(0.066)	(0.066)
Medium_Product	0.175**	0.144**	0.112*	0.064	0.144**	0.131**
	(0.044)	(0.041)	(0.046)	(0.047)	(0.042)	(0.042)
Long_Product	0.279**	0.239**	0.191**	0.241**	0.328**	0.232**
	(0.057)	(0.054)	(0.059)	(0.074)	(0.061)	(0.055)
Short_Process x Price_controls					-0.368**	
					(0.080)	
Long_Product x Price_controls					-0.124**	
					(0.043)	
Stock of Chemicals patents						0.001**
						(0.001)
log-likelihood	-38903	-43681	-35101	-20602	-45023	-45030

NOTES: * significant at 5 percent and ** significant at 1 percent. Standard errors clustered on country-drug in parentheses. 298,605 observations, except for columns (3) and (4) which have 163,853 and 168,684 respectively. All equations also include the other explanatory variables in column (4) of Table (4).

Table 6. Hazard Model of Drug Launch: Instrumental Variable (FIML) Estimates

	(1)	(2)	(3)	(4)	(5)	(6)
	Baseline	Country Random Effect	Political Constraints, Executive Orientation	+ Ethno-Linguistic Diversity	+ Legal Origins	+ Number RTA's
Price Controls	-0.155**	-0.189**	-0.491**	-0.497**	-0.596**	-0.566**
	(0.020)	(0.023)	(0.025)	(0.027)	(0.025)	(0.026)
Pro-patent Index	0.147**	0.164**	0.211**	0.221**	0.212**	0.170**
	(0.056)	(0.068)	(0.058)	(0.059)	(0.058)	(0.057)
Short_Process	0.143**	0.151**	0.211**	0.214**	-0.099	0.098
	(0.065)	(0.074)	(0.067)	(0.068)	(0.068)	(0.068)
Medium_Process	0.121**	0.105*	0.344**	0.352**	0.177**	0.269**
	(0.053)	(0.057)	(0.053)	(0.053)	(0.050)	(0.051)
Long_Process	0.026	-0.118	0.431**	0.446**	0.423**	0.313**
	(0.053)	(0.078)	(0.059)	(0.051)	(0.058)	(0.059)
Short_Product	-0.032	0.021	0.031	0.025	0.155**	0.009
	(0.065)	(0.075)	(0.068)	(0.068)	(0.069)	(0.068)
Medium_Product	0.156**	0.142**	0.425**	0.423**	0.440**	0.362**
	(0.041)	(0.044)	(0.041)	(0.042)	(0.039)	(0.040)
Long_Product	0.173**	0.311**	0.721**	0.719**	0.676**	0.639**
	(0.054)	(0.065)	(0.051)	(0.055)	(0.052)	(0.054)
log-likehood	-90666	-86631	-605230	-603247	-593124	-585949

NOTES: * significant at 5 percent and ** significant at 1 percent. 298,605 observations. All regressions include a piece-wise linear specification of the baseline duration dependency (dummies for years t=0,...,9 and t>9), the full set of controls for demographic variables, bureaucratic quality, and therapeutic category dummies (as in Table 4, column (4) and Table 5.) Columns (1) and (2) are single equation estimates. Columns (3)-(6) are estimates using the approach developed by Lillard (1993), i.e. FIML estimation of a four-equation system in which the process patent, product patent and price control regimes are all treated as endogenous and are estimated as ordered probit regressions for patent regimes and probit for price controls. The same set of instruments is used in each of the policy regime equations, but varies across specifications in the table (as indicated in the column headings). Heteroskedastic-robust standard errors in parentheses.

Table 7. Impact of Policy Regimes on Launch Lags

Panel A: Median lag to predicted 25% diffusion using baseline coefficients

	All drugs	**FDA-approved drugs**	**Low income**	**Middle income**	**High income**
Benchmark	4.63	3.01	8.85	4.91	2.60
Regime 1: Short_Process	3.45	2.25	6.61	3.67	1.94
Regime 2: Long_Product	3.18	2.07	6.09	3.38	1.79
Regime 3: Price controls	5.95	3.87	11.38	6.31	3.35
Panel B: Median lag to predicted 25% diffusion using FIML coefficients on policy variables					
Regime 1: Short_Process	3.28	2.13	6.27	3.48	1.84
Regime 2: Long_Product	1.42	0.93	2.72	1.51	0.80
Regime 3: Price controls	10.34	6.73	19.77	10.98	5.82
No. observations	38,180	26,319	3,350	17,976	16,854

NOTES: Table entries are median values of 38,180 observations on the 25th percentile of the estimated Weibull failure function. In Panel A parameters are from from the Weibull model in Table 4, column (4), and in Panel B the estimated coefficients on policy variables are from Table 6, column (3).

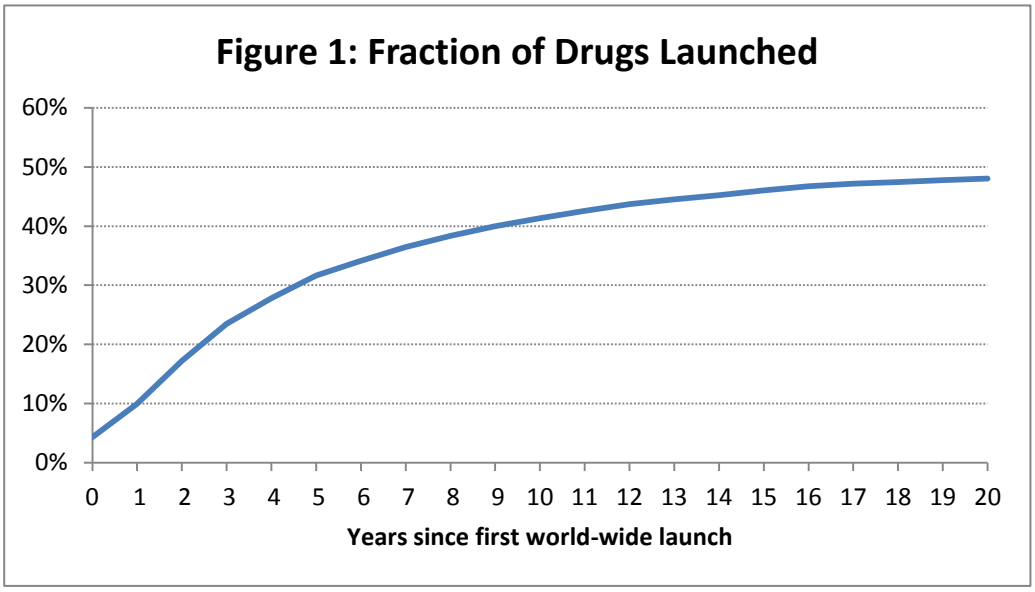
Figure 1: Fraction of Drugs Launched
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Years since first world-wide launch

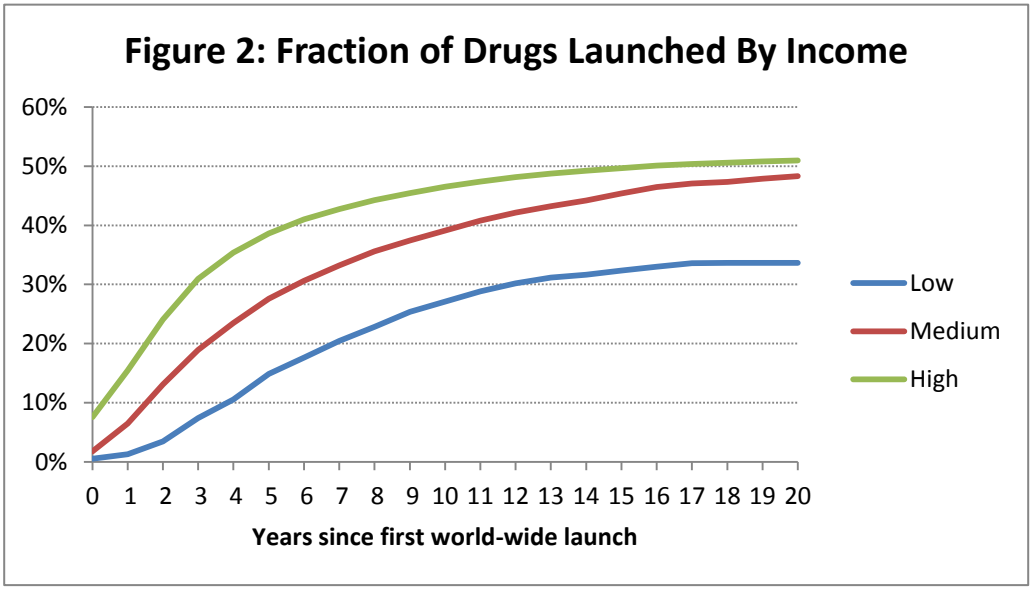
Figure 2: Fraction of Drugs Launched By Income
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Years since first world-wide launch
Low
Medium
High

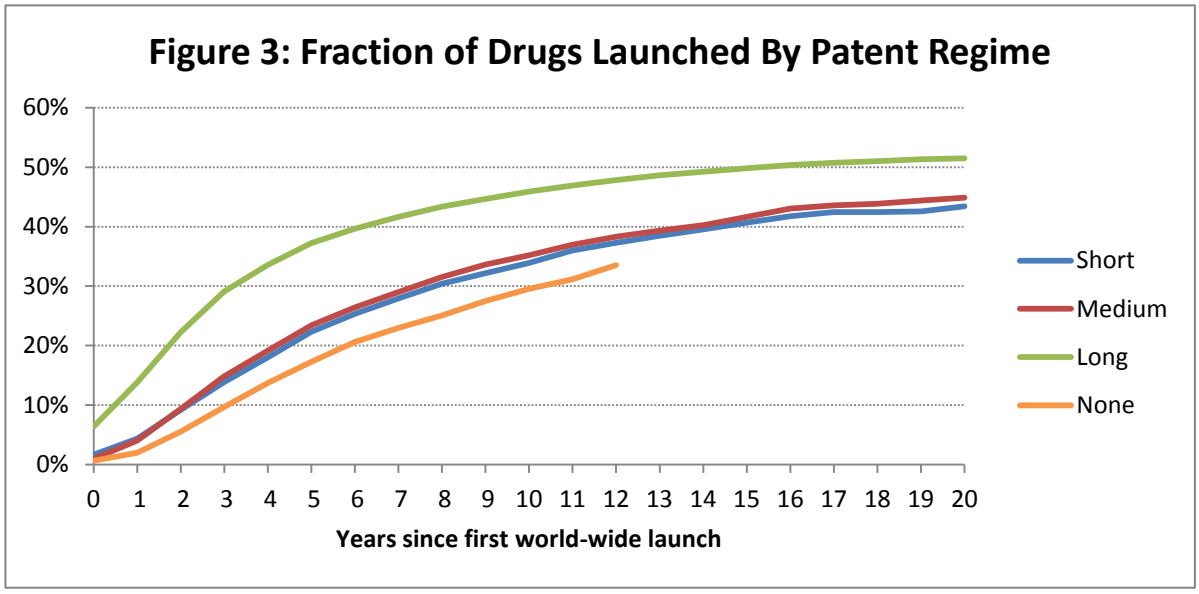
Figure 3: Fraction of Drugs Launched By Patent Regime
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Years since first world-wide launch
Short
Medium
Long
None

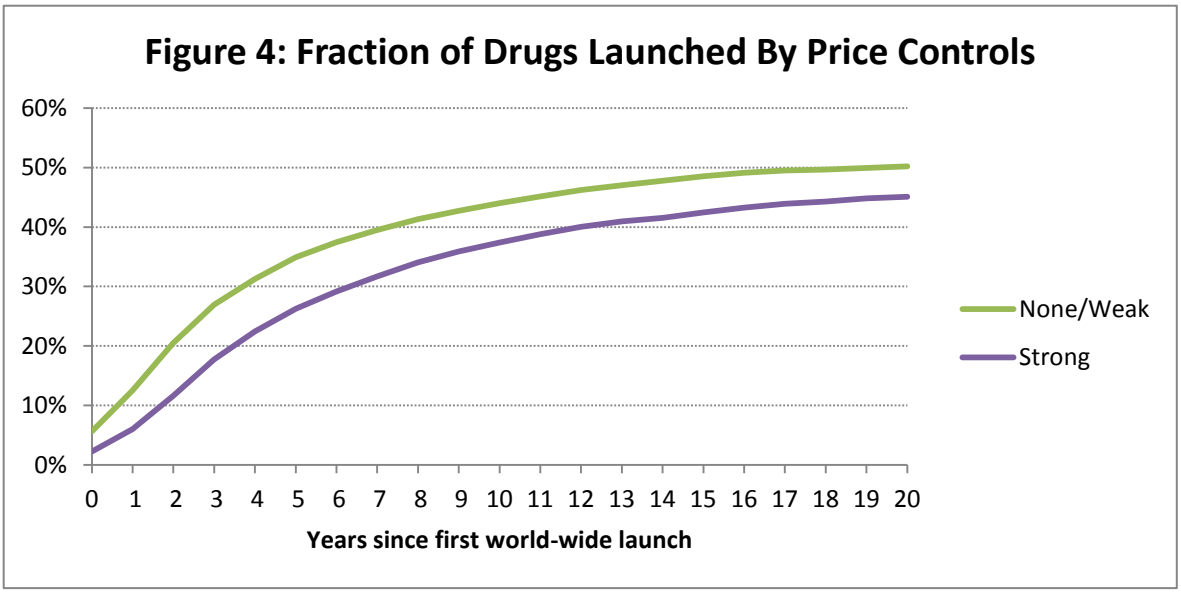
Figure 4: Fraction of Drugs Launched By Price Controls
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Years since first world-wide launch
None/Weak
Strong

Table A.1: Policy Regimes and Drug Launches by Country

Country	Product Patent Regime	Process Patent Regime	Price Control Regime	Percent of Drugs Launched Within 5 Yrs	Percent of Drugs Launched & FDA-approved
ARGENTINA	N,S,M,N	S,M,L	S,N	45.3	56.5
AUSTRALIA	M,L	M,L	N	27.3	38.2
AUSTRIA	N,L	L	S	44.4	58.0
BANGLADESH	M	M	N	9.7	11.0
BELGIUM	L	L	S	36.3	47.5
BENIN	S,L	S,L	S	12.2	14.0
BOLIVIA	L	L	N	8.6	10.1
BRAZIL	N,M,S	N,S	S,N	31.6	42.0
BULGARIA	L	L	N	18.3	21.1
CAMEROON	S,L	S,L	S	12.2	14.0
CANADA	L	L	N	37.5	54.6
CHILE	M	N,M	N	28.8	36.6
COLOMBIA	N,M,L	N,M,L	S,N	31.5	42.5
COSTA RICA	N,S,L	L,S,L	N	28.5	36.6
COTE D'IVOIRE	S,L	S,L	S	12.2	14.0
CZECH REPUBLIC	L	L	N	41.9	46.9
DENMARK	M,L	M,L	N	44.9	59.4
DOMINICAN REPUBLIC	M	M	N	21.3	26.8
ECUADOR	N,M,L	M,L	S	22.1	28.5
EGYPT	N	M	S	10.3	13.8
EL SALVADOR	M	M	N	28.5	36.6
FINLAND	L,N,L	L	S,N	43.5	59.1
FRANCE	L	L	S	37.5	44.2
GABON	S,L	S,L	S	12.2	14.0
GERMANY	L	L	N	55.0	67.9
GREECE	M,L	M,L	S	35.7	46.8
GUATEMALA	N	M,S	S,N	28.5	36.6
GUINEA	S,L	S,L	N	12.2	14.0
HONDURAS	L,M	L,M	N,S	28.5	36.6
HONG KONG	L	L	N	27.7	37.3
HUNGARY	N,L	L	N	36.6	41.2
INDIA	N	S	S,N	8.2	10.9
INDONESIA	N,M,L	N,M,L	N	19.5	25.9
IRELAND	L	L	N	38.5	50.8
ISRAEL	L	L	S	24.0	34.0
ITALY	L	L	S,N	52.3	60.3
JAPAN	L	L	N	31.9	34.4
JORDAN	L	L	S	12.9	15.8
KUWAIT	N,L	S,L	S	21.5	25.4
LATVIA	L	L	N	20.1	23.2
LEBANON	N,L	M,L	S	19.7	22.3
LUXEMBOURG	L	L	S	25.4	29.5
MALAYSIA	L,M	L,M	N	20.2	27.1
MEXICO	N,L	N,L	N,S,N	37.4	48.7
MOROCCO	L,N,L	N,L	S	13.7	16.1
NETHERLANDS	L	L	N	39.4	50.4
NEW ZEALAND	L	L	N	28.8	39.0
NORWAY	L	L	N	47.0	53.5
PAKISTAN	M,L	M,L	S	14.8	16.9
PANAMA	M	M	N,S	28.5	36.6
PARAGUAY	N	M	S	19.4	23.7
PERU	N,M,L	N,M,L,N	S,N	20.6	26.4
PHILIPPINES	L	L	N	31.8	40.4
POLAND	L	L	N	34.2	39.6
PORTUGAL	N,L	M,L	N	24.6	28.3
PUERTO RICO	L	L	N	48.7	59.6
RUSSIA	L	L	N	14.3	16.7
SAUDI ARABIA	L,M	L,M	S	13.7	19.5
SENEGAL	S,L	S,L	N	12.2	14.0
SINGAPORE	L	L	N	25.5	33.3
SLOVAK REPUBLIC	L	L	N	34.4	39.5
SLOVENIA	L	L	N,S	28.7	33.8
SOUTH AFRICA	L	L	N,S	28.8	39.0
SOUTH KOREA	M,L	M,L	S,N	42.6	46.9
SPAIN	N,L	L	S	39.1	47.5
SWEDEN	L	L	S,N	38.9	53.0
SWITZERLAND	L	L	N	44.4	58.4
TAIWAN	L	L	N	28.3	35.1
THAILAND	N,L	M,L	N	30.4	40.9
TUNISIA	N	L	S	8.2	9.2
TURKEY	M,L	M,L	S	25.1	33.5
UK	L	L	N	50.6	66.5
UAE	N	S	N	21.1	25.0
URUGUAY	N,M	M	N	37.6	43.9
USA	L	L	N	53.1	80.0
VENEZUELA	N,M,L	N,M,L	N	24.6	32.1

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