Pharmaceutical Price Controls and Entry Strategies

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June 30, 2003

Abstract

This paper examines the use of price controls on pharmaceuticals, while controlling for both market structure and of firm (and product) characteristics, in estimating the extent and timing of the launch of new drugs around the world. Price controls are found to have a statistically and quantitatively important effect on pharmaceutical launches. Drugs invented by firms headquartered in countries that use price controls reach fewer markets and take longer to diffuse than products that originate in countries without price controls. Price controls have a non-uniform impact on firms in different countries; in particular, Italian and Japanese firms tend to introduce their products in price controlled markets more quickly than American or British firms. Companies delay launch into price-controlled markets, and are less likely to introduce their products in additional markets after entering a country with price controls. Overall, the results suggest that a country's use of price controls not only has a substantial impact on entry into that market, but into other countries as well.

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I. Introduction

The diffusion rate for new, patented technologies depends on the strategies implemented by innovators for entry into market segments. The influence of regulation on launch decisions has been highlighted by many economists (most recently, Djankov, La Porta, Lopez-de-Silanes, and Schleifer (2002)). This paper examines the use of price controls on pharmaceuticals, while controlling for both market structure and of firm (and product) characteristics, in estimating the extent and timing of the launch of new drugs around the world.

Pharmaceutical markets provide an interesting empirical puzzle to explore. Developed nations differ from each other in the number of drugs that compete in a market as well as in the mix of available products. Over the past 20 years the US has had an average of three drugs (unique chemical entities) per therapeutic class, or medical condition for which a drug is prescribed. Italy, with a population of about 57 million, has an average of five drugs per therapeutic class. Switzerland has an average of four drugs per class for a population of just 7 million. Only one-third of the prescription pharmaceuticals marketed in one of the seven largest drug markets (the US, Japan, Germany, France, Italy, the UK, and Canada) are also marketed in the other six. This is a strikingly low figure given the size and wealth of these countries and the substantial trade between them, and since pharmaceutical firms should have incentive to spread the large sunk costs of drug development over as many markets as possible. In addition, some markets have no entrants at all, despite the availability of treatments in other countries.

The entry patterns of pharmaceuticals are important to understand for several reasons. The cost of untreated conditions in markets with no entry may be substantial. In addition, there are many monopoly and duopoly markets. Competition usually results in lower prices, and given the widespread concern about the cost of pharmaceuticals, it is valuable to know what impedes further entry into a market. This study also contributes to the debate on the effect of regulations, particularly price controls, by examining their impact on the market structure of pharmaceutical markets within a country. Finally, understanding entry in this setting may provide insights into the diffusion of other new technologies, particularly those characterized by large development costs, relatively low marginal or transportation costs, and that are susceptible to creative destruction by subsequent innovators.

Price controls are found to have a statistically and quantitatively important effect on pharmaceutical launches. Drugs invented by firms headquartered in countries that use price controls reach fewer markets and take longer to diffuse than products that originate in countries without price controls. Price controls have a non-uniform impact on firms in different countries;

in particular, Italian and Japanese firms tend to introduce their products in price controlled markets more quickly than American or British firms. Companies delay launch into price-controlled markets, and are less likely to introduce their products in additional markets after entering a country with price controls. Overall, the results suggest that a country's use of price controls not only has a substantial impact on entry into that market, but into other countries as well.

The following section gives a brief overview of the pharmaceutical industry and outlines regulatory regimes in the countries included in this study. Section III describes the expected impact of price regulation on product launch decisions. The empirical model is explained in Section IV, and Section V describes the data used in this research. Results are presented in Section VI, and Section VII concludes.

II. Description of Industry and Regulatory Regimes

Expenditures on health care range from 5% of GDP in South Korea to over 13% in the US, and the share of pharmaceutical sales in total health expenditures account for anywhere from 4% in the US to nearly 18% in France and Italy. The US is the largest single market at $97 billion of annual revenue; the five largest European markets amount to $51 billion, as does Japan.[1] Table 1 provides revenues from the major markets and the distribution of revenues across broad therapeutic classifications. This table illustrates that the importance of certain therapies can vary substantially across countries. For example, nearly 22% of revenues in the US derive from drugs for the central nervous system, while in Japan this figure is only about 6%. Italian expenditures on anti-infectives are over twice those of the UK.

The industry is highly fragmented: there are thousands of small firms around the world, only several hundred of which are research-based and have brought at least one drug to market. About forty multinational firms dominate the market. These firms, listed in Table 2, are responsible for half of all drugs available somewhere in the world and spent over $44 billion on research and development in 1999. Table 3 lists the number of firms in each major market, the number of drugs they have developed, and the average number of countries to which those drugs diffuse. The US is the origin of over a quarter of all drugs, and these products reach an average of about nine markets. Though many drugs are invented in Japan, they are launched in fewer foreign markets. Drugs with small domestic markets like Denmark, Switzerland, and the Netherlands spread to more foreign markets than drugs with large home markets. Pharmaceutical

[1] Figures are annual totals for 2000. Source: IMS Health.

firms tend to specialize in certain therapeutic categories,[2] and competition within therapies is relatively concentrated. A new drug is reported to require an average of 7.1 years to develop at a cost of $500-600 million.[3] In 2000, pharmaceutical companies spent approximately $8 billion on sales and marketing and distributed samples worth an additional $7.95 billion in the US alone.[4]

These markets differ on a number of dimensions, of which regulation is perhaps the most notable. The entry of pharmaceuticals is restricted and in many countries, so is the price. Each nation has an agency or ministry devoted to pharmaceutical evaluation, which have heterogeneous standards for establishing safety and efficacy and which vary in how quickly they evaluate new drug applications. Some require that some clinical trials be performed on domestic patients and are less accepting of foreign data. Some European countries require proof of cost-effectiveness. During the 1990s, mean approval times ranged from 1.3 years in France for 1990, to 4.8 years in Spain for 1991.[5] In addition to differences in agency funding and bureaucratic efficiency, the number of drugs under review varies considerably across years and countries. There has been a gradual move towards harmonization of regulatory standards for all major markets, particularly within the European Union. Under the EU's Mutual Recognition Procedure, enacted in 1995, a drug approved in one member state (the Reference Member State) must be granted marketing authorization in other member states (the Concerned Member States) within two months unless a Concerned Member State objects through a formal process. Another option is the Centralized Procedure, in which a drug is submitted to the European Medicines Evaluation Agency for marketing approval in all EU nations. However, the drug's manufacturer must still negotiate with individual countries over price under either the Mutual Recognition Procedure or the Centralized Procedure.

Price regulation has many variants. Most countries have adopted some form over the last thirty years or so. A few countries do not officially regulate prices, but may have considerable power in determining prices if the government, as the largest provider of health care, has monopsony power. For example, firms must negotiate price with the National Health Service in the UK. In countries with more explicit price controls, the government fixes the price for a drug based on some determination of therapeutic value, the cost of comparable treatments, the contribution of the drug's manufacturer to the domestic economy, the prevailing price in other countries, and manufacturing cost; the weight given to each factor differs by country. In some cases, price controls apply only to "listed" drugs, those the government will reimburse through its

[2] For a breakdown of the top twenty firms' specializations, see DiMasi (2000).
[3] Paraxel's Pharmaceutical Statistical Sourcebook 1999, p. 49.
[4] IMS Health Inc.
[5] Thomas et al. (1998), p. 790.

public health insurance. Negotiations between pharmaceutical firms and national governments may be lengthy and tense, and drug companies often blame this process for delays in product launch. In a recent article in the *Financial Times*, Pfizer chairman Hank McKinnell stated "[w]e introduce our new products later and later on the French market, and if the government continues to put pressure on prices, there will be no more [new products]."[6] Broadly speaking, northern European countries and the US have fewer or less intrusive price controls, while southern Europe has more extensive government intervention.[7]

Several countries (South Korea, Mexico, Spain, and the UK) regulate the profits of pharmaceutical firms. The government negotiates with manufacturers and sets a rate of return according to complicated formulas accounting for operating costs, promotion expenditures, and R&D spending. During the 1990s, many countries also enacted price freezes or mandatory price cuts in response to the increasing cost of pharmaceuticals. Most Canadian provinces do not permit prices to increase by more than the rate of inflation, and the US Congress has threatened similar laws – and extracted non-binding commitments from major pharmaceutical firms to hold the rate of price increases.[8] Three other sorts of regulation or government intervention are worthy of remark: policies on generic drugs, the use of demand-side controls, and restrictions on advertising. These are not explicitly considered here, but are described in Appendix A.

Countries also differ in subtle non-regulatory aspects. The number and size of pharmacies are highly varied across countries, as are distribution and dispensing margins (see Figure 1). Physicians have diverse prescribing habits; in Japan, physicians both prescribe and dispense drugs, and they tend to prescribe lower doses than elsewhere in the world and combinations of drug therapies. Consumer compliance and trust of doctors is multifarious. Herbal and "alternative" therapies are more widely used in Europe than in the US, though their popularity in the US is increasing. Finally, the practice of licensing products to one or more firms for launch is far more prevalent in some countries than others. It is particularly common in Italy, Spain, Japan, and South Korea.

III. Launch decisions and pharmaceutical regulation

Many prior studies on the pharmaceutical industry identify factors that should be important in the decision to launch a new drug. Competition in pharmaceuticals exists both within a chemical (branded versus generic, prescription versus over-the-counter) and between

[6] "Drug companies hit out at French price controls," *Financial Times*, June 10, 2001.
[7] See Jacobzone (2000) for a detailed summary of regulations in each country.
[8] Ellison and Wolfram (2000).

different chemicals that treat the same condition. The generic segment garners significant market share within a few years of patent expiration when entry occurs, but not all therapeutic classes (and very few countries) attract such entry.[9] While many have shown that generic competition has indisputable significance (at least in the US), there is substantial justification for focusing on competition *between* drugs. In a recent paper, Lichtenberg and Philipson (2000) estimate the loss in sales from entry by new drugs for the same therapeutic classification and find that entry by such drugs reduces the PDV of a drug by considerably more than generics. These results are broadly consistent with other studies that emphasize the importance of intermolecular competition, such as Stern (1996) and Berndt et al. (1997). In the context of a study on the diffusion of innovation, the creative destruction of intermolecular competition is more interesting than generic competition, which exists only for older drugs.

In addition to competition, the regulatory environment has a significant bearing on prevailing prices (Danzon and Chao (2000a, 2000b)). Countries with stringent regulation of entry combined with relatively little price regulation, such as the US and the UK, have highly concentrated domestic industries whose products diffuse more extensively into foreign markets (Thomas (1994)). The one study that explicitly addresses international entry (Parker (1984)) shows regulation is related to large differences across countries in the number and mix of products introduced before 1978. Thus, there is much reason to expect regulation to influence entry.

Regulation also affects drugs and firms differentially within a country, particularly in the costs of gaining regulatory approval (Dranove and Meltzer (1994), Carpenter (2002)). Product characteristics, like therapeutic novelty or indication, and firm characteristics, such as experience with the FDA and domestic status, are related to the speed at which a new drug receives regulatory approval in the US. Data from three other large pharmaceutical markets (the UK, France, and Germany) displays a similar pattern in time-to-market of important drugs, and reveals a strong home country advantage: the drugs of domestic firms are approved earlier than those of foreign firms. Beyond the non-uniform effects of regulation, Scott Morton (1999) finds evidence of important firm-specific differences in the entry decisions of generic drug firms. Firm-specific costs are therefore likely to be important in drug launches. For a more thorough review of the economics literature on entry, see Kyle (2003).

[9] Generic competition in the US is the focus of Caves et al. (1991) and Grabowski and Vernon (1992), among others. Hudson (2000) looks at the determinants of generic entry in the US, the UK, Germany, and Japan. Ellison et al. (1997), who estimate demand for a class of antibiotics, and Berndt et al. (1997), who examine the antiulcer market, consider competition both within and between drugs.

An important consequence of price controls that relate the domestic price to the prices in foreign markets is that pharmaceutical firms now have incentive to launch their products first in countries where they have the freedom to set a higher price, since this will influence the price in markets with price controls. Price controls may have an additional effect in Europe through parallel imports, permitted between the 15 EU member states, which enable wholesalers to arbitrage price differences between EU countries. Launching a drug in a country with stringent price controls may depress global revenues if wholesalers in countries with higher prices purchase drugs in price-controlled markets for domestic resale.

IV. Model

The approach taken in this paper assumes that potential entrants for a market take existing market structure as given and compete simultaneously in time t. Let i index drugs, j index firms, k index therapeutic classes, and l index countries. A market is thus a class-country-year triple. Define the reduced-form profit function as

$$\Pi_{ijklt} = N_{klt}\delta + M_{klt}\theta + X_{klt}\beta + Z_{jklt}\gamma + W_{ikt}\alpha + \varepsilon_{ijklt}$$

where N is the number of competing drugs in the market, M is the number of potential entrants, X is a vector of market characteristics, Z is a vector of firm characteristics, and W is a vector of drug characteristics.[10] Firms enter if their expected profits are at least zero, and any firm that elects not to enter must expect negative profits from entry. Included in W are the characteristics of markets the drug has already been launched in, since entry into a price-controlled market may affect subsequent launch strategies.

This paper takes two estimation approaches to examine the effect of price regulation on the launch decision. One is to estimate whether the number of countries a drug is launched in depends on whether it originates in a price-controlled country. A second approach is to estimate whether price controls delay a drug's launch in a country using a hazard model. These are described in greater detail below.

A. Negative binomial model

The number of countries in which a drug is launched may be estimated as a Poisson or negative binomial process such that

[10] Product quality is considered exogenous. Once a drug has been developed and tested, its efficacy is fixed: a firm cannot re-position a low-quality drug as a high-quality product. In reality, some "tweaking" is possible, such as once-a-day dosing formulations, but such changes are second order.

$$\text{Prob}(C_i = c_i) = \frac{e^{-\mu_i}\mu_i^{c_i}}{c_i!}$$

where c is the count of markets launched in drawn from a negative binomial distribution with parameter μ, and

$$\log\mu_i = N_{klt}\delta + M_{klt}\theta + Z_{jklt}\gamma + W_{ikt}\alpha + \varepsilon_i$$

with ε reflecting cross-sectional heterogeneity or specification error. This estimation approach is useful for examining the extent of diffusion over a drug's lifetime as a function of its characteristics and its origins (for example, whether its inventor is located in a market with price controls).

By simply estimating the count of countries entered, each country is essentially assigned equal weight. Since countries vary considerably in size, treating each country equally implies a greater weight per capita given to residents of small countries. The US market is approximately twice the size of the largest five European markets combined, but with the negative binomial estimation approach, a drug launched in those five countries is measured as having diffused further. An alternative measure of diffusion is the total population with access to a new drug. Therefore, the following equation is estimated using ordinary least squares:

$$\log(\text{total population}) = N_{klt}\delta + M_{klt}\theta + Z_{jklt}\gamma + W_{ikt}\alpha + \varepsilon_i$$

B. Discrete-time hazard

The probability that a drug is launched during a time interval t can be written as

$$P(t) = a(t) + N_{klt}\delta + M_{klt}\theta + X_{klt}\beta + Z_{jklt}\gamma + W_{ikt}\alpha$$

where a(t) is a series of intercepts for each year of a drug's age (or time at risk). A convenient transformation for estimation is the logit, i.e.

$$\log\left(\frac{P(t)}{1 - P(t)}\right) = a(t) + N_{klt}\delta + M_{klt}\theta + X_{klt}\beta + Z_{jklt}\gamma + W_{ikt}\alpha$$

This method has the advantage of being quite flexible as well as accounting for right-censored observations. While the negative binomial estimation described above speaks to the extent of a drug's diffusion, the discrete time hazard captures both the speed of diffusion and the effect of the characteristics of potential markets on the launch decision.

Use of the discrete-time logit requires several strong assumptions. To include N as an explanatory variable, we must assume that one drug's entry does not induce another's exit. The justification for such an assumption is provided in Section V. If M, the number of potential entrants, is included and treated as an exogenous variable, then the threat of future competition is

allowed to affect current entry decisions, but one must believe that firms do not behave strategically. This assumption is highly suspect. The number of drugs developed to treat a condition is almost certainly a function of the global profits associated with that disease. Firms in an oligopolistic setting (which most drug markets are) are very likely to react to the behavior of their competitors.

Since drug launches are observed at annual intervals in this dataset, a discrete-time model is probably more appropriate than a continuous time model such as the Cox Partial Maximum Likelihood Estimator, or proportional hazards model. As the interval of observation becomes small, the results from a discrete-time logit converge to those from a proportional hazard model. [11] While only the estimates from the discrete time model are reported in this paper, results from continuous time models are quite similar.

V. Data

Information on all drugs developed between 1980 and 2000 is obtained from the Pharmaprojects database, which is maintained by the UK consulting firm PJB Publications. This dataset includes the drug's chemical and brand names, the name and nationality of the firm that developed it, the identity of licensees, the country and year in which it was patented, its status (in clinical trials, registered, or launched) in the 28 largest pharmaceutical markets, and the year of launch where applicable. Each drug is assigned to up to six therapeutic classes. The system of classification used by Pharmaprojects is adapted from the European Pharmaceutical Market Research Association; there are 17 broad disease areas (for example, dermatological conditions) and 199 more specific classes (such as antipsoriasis treatments). The sample of drugs used in this research is restricted to those that are new chemical or molecular entities by dropping new formulations of existing products, OTC licensing opportunities, antidotes, and diagnostic agents.

The OECD Health Data 2000 dataset provides population, GDP, data on access to health care, and other demographic information for OECD countries. Of the 28 countries in Pharmaprojects, 21 are also OECD members. The regulatory structure of each country is classified as "price control regime" using the summary tables from Jacobzone's "Pharmaceutical Policies in OECD Countries: Reconciling Social and Industrial Goals." Table 4 lists the countries included in this study, whether they have price controls, and the year such controls were enacted. While this is a crude indicator of policy, the variety of regulations in these nations is difficult to categorize neatly.

[11] See Amemiya (1985), pp. 433-455, or Allison (1984) for a more complete discussion of duration models.

A market is defined as a country-therapeutic class-year triple. This definition assumes that drugs with the same therapeutic classification are substitutes, and that there is no substitution between therapeutic classes. Of course, the latter assumption is a strong one. Different classes of products may be appropriate for the same condition. A patient with migraine headaches might be prescribed a treatment specifically for migraines, an NSAID, or a narcotic; these represent three distinct classes. Other therapeutic classes may be complements – drugs that have nausea as a side effect are often prescribed in conjunction with an anti-nausea treatment, for instance. In addition, this market definition requires that there be no trade in unapproved products across international borders: launching a drug in the US must not enable access to the Canadian market. While the move to a common market in Europe weakens the assumption of separate markets, negotiation with health ministries is still necessary for the drug to be reimbursed. Competition from drugs approved in nearby countries but without local insurance coverage is probably weak. A drug is "at risk" for entry into all markets beginning in the year of its first launch into any country. After launch in a market, it drops out of the risk set for that country. Any drug that has been approved somewhere in the world for a particular therapeutic class is a potential entrant into that therapeutic class in all other countries.

Drug quality, or the therapeutic advance a treatment represents, is likely an important factor in both the fixed costs of entry (if regulators accelerate approval of breakthrough therapies, or if regulatory approval is more difficult to obtain for a novel type of therapy with which regulators are unfamiliar) and in variable profits. Unfortunately, objective measures of quality are difficult to obtain. Previous studies have used the ratings of therapeutic novelty assigned by the FDA upon application for approval, but these are unavailable for drugs that did not seek entry into the US. Pharmaprojects also ranks drugs according to their novelty, but this ranking is retrospective, so a drug that represented a therapeutic advance at its initial launch ten years ago may be rated an established therapy in the current database. The "Essential Drug List" of the World Health Organization is another possibility, but it is updated infrequently and most of the drugs on the list are more than twenty years old. Therefore, this research follows Dranove and Meltzer (1994) in using Medline citations; the construction of variables using citations is described in Appendix B. Other aspects of drug quality are the number and severity of adverse interactions and side effects, dosage form, and dosage frequency. Systematic data on these characteristics is unavailable, particularly for drugs not marketed in the US. The inclusion of a drug fixed effect should mitigate the bias from omitting better measures of quality, and the results presented later are unaffected by adding such fixed effects.

Quantifying the regulatory barrier to entry, as well as the severity of price regulation, is nearly impossible. One indication is the time between application and approval of a drug. However, not only is this unavailable in all markets, but is also likely to be a function of drug quality, firm characteristics, the number of other drugs under review, and perhaps the decisions of regulators in other countries, and is therefore an imperfect measure. The existence of price regulation in a country is captured by a dummy variable, which obscures differences in the implementation of such policies, as described in Section II. All regulatory variables are vulnerable to endogeneity problems, as such policies may be reactions to (the perception of) high profits earned by pharmaceutical companies. Only four countries (Canada, Mexico, the Netherlands, and Sweden) enacted price controls during the sample period. Other omitted variables include the importance of generic competition within a country (or therapeutic class), the degree to which marketing of pharmaceuticals is regulated, the cost of marketing in each country, heterogeneity in prescribing behavior, and other subtle but important distinctions between countries. These effects are subsumed in the country fixed effects included in some regression models, with the unfortunate implication that the estimated fixed effect for each country is the net impact of many variables.

Table 5 presents summary statistics for data used in estimation. The sample contains 1604 unique molecules produced by 310 firms in 147 therapeutic classifications, for a total of 58,624 country-class-year markets. There were 298,960 entry opportunities, only 7,385 (2.5%) of which had a product launch. The mean number of drugs competing in markets with entry opportunities is 2.8. The distribution of the number of competitors over all markets is shown in Figure 2, both for the entire time period and as of 2000; Figure 3 shows the distribution across therapeutic classes within several countries over 1980-2000. Most markets are highly concentrated, and over one-fourth have no entry at all. Over 28% of all potential markets are empty in the US, even though it accounts for twice the revenues of Japan and Europe. The large fraction of "0" markets reflects both that some drugs are never launched in a country and that some drugs are only introduced years after they first become available elsewhere. However, even as of 2000, 15% of markets are empty.

Variables measured at the drug-year level include age, the number of therapeutic classes in which it competes, the number of countries in which the drug has been introduced, and its share of the stock of domestic and foreign Medline citations for its therapeutic class. Figure 4 shows the distribution of the number of countries in which a drug has been launched as of 2000. Most drugs enter only one country, usually the domestic market. There may be economies of scale in global production, as clinical trial data is accumulated and used in subsequent

applications, or if regulators are exposed to less political risk in approving a drug that has already been accepted by their counterparts in other countries. The probability of entry is thus expected to be concave in the number of launch countries. A drug's value should decline with age, due to the limited period of patent protection and competition from newer therapies, so entry is predicted to be convex in age. Drugs that compete in multiple therapies and important drugs that are the subject of many scientific studies should be more profitable; positive coefficients on these variables are expected.

Several firm-level variables are included. International experience is the count of the number of countries in which the firm markets any drug. A firm with a presence in many markets may have more resources to draw on, which would make entry more likely. However, such firms may also be less dependent on any single market and therefore be more selective in the timing of their launches. Thus there is no clear prediction for the effect of international experience. A firm's experience in a country is defined as the count of drugs it markets in that country, and its experience in a therapeutic class is the count of other drugs it produces for that class. These capture economies of scope: experience with the regulator and the presence of a detailing force and distribution channels may be spread across all a firm's products within a country, and there may be benefits to specialization within a therapeutic class. The number of drugs a firm has within a country-class market measures expertise in the local market.

Finally, country-level demographics provide rough measures of market size and demand. Ideally, incidence rates at the level of country-class would be included, but these are difficult to obtain and may also be endogenous if pharmaceuticals reduce the occurrence of disease. Instead the stock of Medline citations is computed for each therapeutic class authored by foreigners (as a measure of the global importance of the therapeutic class) and authored by domestic scientists (as a measure of the local importance). In general, additional country-level variables such as the number of doctors per capita, pharmaceutical spending, and life expectancy proved insignificant[12] and so only a parsimonious set of variables is presented here.

VI. Results

A. Extent of diffusion

Table 6 provides estimation results from the negative binomial models and OLS models of the number of countries launched in and the log of total population reached, respectively. Each

[12] This is likely because what these variables measure is unclear. A long life expectancy may indicate good health, but does this reflect low demand (healthy people don't need drugs, so little entry) or is it the result of available treatments (lots of entry)?

is estimated allowing for a 4, 8 and 12 year lag since a drug's initial launch. All specifications include year and therapeutic class fixed effects.

In general, the coefficients are consistent with expectations. Important drugs diffuse more widely, and pharmaceuticals invented by firms that are active in many countries are likely to reach more markets. However, firms with many drugs in their portfolios and those with competing drugs in the same therapeutic class tend to launch their drugs in fewer countries. This suggests some effort on the part of multiproduct firms to match a market to the most appropriate treatments.

The most striking result from these estimations is the effect of a drug's origins on its diffusion. Pharmaceuticals invented by French, Italian, and Japanese firms are launched in fewer countries and reach fewer people than drugs originated by American, British, and Swiss/other firms (the omitted category). While the differences narrow somewhat 12 years after a drug's first introduction, the results suggest that drugs invented by firms in countries with price controls tend to be less successful on the global market.

One interpretation of this pattern is that the incentives created by price control regimes spur firms in these countries to introduce new products that are slightly different from, but not a huge advance over, their existing products, because the prices of their existing products are ratcheted down by regulators over time. Thomas (2001) believes this is particularly true for Japanese firms. However, all pharmaceutical firms should face these incentives. That is, a British firm should be able to reap the same rewards from introducing a "me-too" product on the Italian market as an Italian firm, unless the British firm faces higher entry costs or expects a lower price (and lower profits) than the Italian firm in Italy. This suggests that price controls or other entry regulations may be used by governments as a tool of industrial policy to favor domestic firms.

An alternative interpretation is that countries with price controls happen to have populations with idiosyncratic needs, and domestic firms are better suited to developing drugs for those needs. Returning to the example of antiulcer treatments in Japan, one could argue that the populations of other countries have less demand for ulcer drugs, so ulcer drugs invented in Japan are less likely to be launched in those markets. Absent a reason why only countries with price controls would have such idiosyncratic needs, however, this interpretation seems incomplete.

B. Time to launch and entry strategies

Results from the discrete time hazard models are presented in Tables 7a-7d. All models include year and therapeutic class fixed effects, though the individual coefficients are not

reported. Country fixed effects are not included since the variable of greatest interest, the use of price controls, has little intracountry variation. Model 1 is the most parsimonious specification; Model 2 includes dummy variables for the country of headquarters of a drug's inventor; and Model 3 adds interactions of the headquarters dummies with price controls. Finally, Models 4 and 5 include dummy variables indicating prior launch in other countries and interactions with price controls.

Results for the non-regulatory variables are robust across all specifications, as is evident from Table 7a. As would be expected, relatively rich countries and those with large populations are likely to be launched in quickly. The existence of competing drugs in a market is associated with increased rates of entry as well, although this is most likely due to the correlation of previous entry with unobserved demand in that country.[13] Domestic firms tend to enter the market with short delays, as do firms with extensive international experience or that have launched many other products in the market. The speed of diffusion increases with a drug's importance and the number of other markets it has entered, but falls with age, as the patent nears expiration and more innovative products may have been developed (see coefficients reported in Table 7b).

Table 7c provides results for regulatory variables and country-of-origin dummy variables. Consistent with the results discussed above, the coefficients on the dummy variables indicating the country of a drug's origin show that Italian and Japanese firms are particularly slow in introducing their products into other markets. The effect of price controls is quite substantial. The coefficient on the main effect of the price control dummy ranges from -.183 to -.329, depending on the specification, and these estimates are all statistically significant at the 1% level. Using results from Model 1, this implies slope coefficients from -.0005 to -.006 with all other variables at the 25th percentile and 75th percentiles, respectively. The coefficient on the use of price freezes is also negative, though not statistically significant. Interestingly, price controls do not affect all firms in the same way. In particular, Italian and Japanese firms appear to prefer markets with price controls relative to most other firms. Whether this is the result of geographic proximity (of Italian firms to other southern European countries with price controls, or Japanese firms to Australia and South Korea) or skill in competing in price-controlled markets is unclear.

Models 4 and 5 estimate the hazard of entry conditional on markets that a drug has already entered. That is, conditional on being in country i, what is the probability of launch in country j? If, as outlined in the discussion of price regulation in Section III, entry in a price-controlled markets affects profits in other countries, then pharmaceutical companies should

[13] If these models are estimated using country-therapeutic class interaction fixed effects, the effect of competition on additional entry is negative. However, this specification does not permit consideration of regulatory effects.

choose to enter price-controlled markets last, if at all. Entry in Italy, for example, should be associated with fewer launches in the future, and especially into other countries with price controls that reference the Italian price. The estimates from these variables are in Table 7d, and the results indicate that these effects are indeed present. Prior launch in the price-controlled markets of Australia, Belgium, France, Greece, Italy, Japan, or Spain reduces the likelihood of entry into one of the remaining markets. If one of the remaining markets also uses price controls, prior entry into Australia, France, Italy, and Japan further reduces the probability of launch 15-25%.

This pattern is consistent with firms' preference for entry into markets with free pricing first, reaping profits from high prices for as long as possible, and launching their products in price-controlled markets as late as possible given the constraints of a limited period of patent protection and the threat of entry by competitors in these markets. It suggests that the effect of price controls is not isolated to an individual market, but rather affects the diffusion of a drug into other markets as well.

VII. Conclusion

While firm and product characteristics have substantial effects on the entry pattern of a new drug, this research demonstrates that the impact of price regulations used in many developed countries also has a large bearing on diffusion. Price controls delay or reduce the probability of launch in countries that impose them, and these effects carry over into other markets as well. Price controls have differential impacts on firms headquartered in different countries, influencing both the number and types of markets entered.

There are two implications for public policy from this research. Price controls appear to reduce the probability of a new drug's entry, and disproportionately affect Swiss, British, and American firms. These companies are responsible for over 40% of all drugs developed between 1980 and 2000, and are generally considered the most innovative. The costs of deterring their products, over and above the possible long-run effects on incentives to invest in costly R&D and the development of future products, should be balanced against any short-run savings from lower prices. Second, the effect of price controls is not isolated to a single market, but influences the global launch decisions of pharmaceutical firms and thus impacts the extent and timing of a new drug's diffusion. These results have particular salience as individual states in the US adopt price control measures to control Medicaid costs, and as the federal government considers similar legislation.

However, some important caveats warrant mention. Price controls may be an endogenous response to some other factor not captured in the regressions presented here. They may also be correlated with an omitted variable, such as other industrial policies or drug safety regulation, that is in fact responsible for the patterns observed, rather than price regulation. In addition, this research makes no statements about the effect of price controls on total social welfare. It may well be that the increased use of pharmaceuticals that results from lower drug prices more than outweighs the costs associated with delays to market or reduction in incentives for R&D. Estimation of welfare would require considerably more detailed information on prices and consumption. Future work should also incorporate better measures of country-specific demand and costs associated with product launch, such as indicators of regulatory stringency and advertising. Lastly, a structural approach that addresses the problem of endogenous entry by competitors and responses by governments and that examines the nature of competition in these markets may be appropriate.

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Summary stats
Relative effects

Table 1: Revenues from major pharmaceutical markets and distribution across broad therapeutic classes, 2000

Millions of $US	US	Japan	Germany	France	Italy	UK	Canada	Spain	Brazil	Mexico	Argentina	Aust/NZ
	97385	51434	14424	13283	9035	8888	5524	5290	5153	4905	3422	2849
Pct of revenues by class												
Cardiovascular	17.51%	19.19%	23.45%	24.95%	24.26%	22.94%	23.77%	22.74%	14.63%	8.03%	16.42%	23.73%
CNS	21.76%	6.05%	12.94%	15.23%	11.67%	18.13%	19.01%	17.56%	13.82%	11.76%	15.28%	16.74%
Alimentary	14.71%	15.69%	16.13%	14.96%	14.45%	16.09%	14.54%	15.05%	16.55%	18.94%	17.59%	16.04%
Anti-infective	9.62%	11.50%	8.58%	10.25%	11.70%	4.71%	6.28%	7.88%	8.62%	17.49%	9.94%	6.18%
Respiratory	10.13%	6.93%	8.81%	9.15%	8.48%	13.09%	8.20%	10.74%	10.13%	11.17%	7.63%	11.65%
Musculo-skeletal	5.50%	6.72%	4.62%	4.73%	5.80%	5.23%	6.12%	5.29%	8.34%	7.54%	7.83%	5.05%
Genito-urinary	7.02%	2.06%	6.06%	6.05%	6.00%	5.99%	5.70%	4.99%	10.75%	6.97%	7.54%	4.49%
Cytostatics	2.68%	6.53%	5.12%	2.65%	4.53%	3.05%	3.51%	4.18%	0.45%	0.53%	1.49%	3.16%
Dermatologicals	3.60%	2.73%	3.72%	3.42%	3.27%	4.04%	4.54%	3.67%	7.63%	5.97%	6.28%	5.41%
Blood agents	1.61%	7.13%	2.93%	2.63%	4.06%	1.35%	1.88%	2.93%	1.36%	1.47%	1.69%	1.37%
Sensory organs	1.83%	3.17%	1.52%	1.89%	2.17%	1.79%	2.23%	2.06%	2.81%	2.14%	3.16%	2.42%
Diagnostic agents	1.30%	3.59%	2.24%	1.48%	1.26%	1.34%	1.81%	0.04%	0.12%	0.14%	0.64%	0.81%
Hormones	1.18%	2.26%	2.14%	1.72%	1.79%	1.34%	0.76%	2.74%	2.25%	1.75%	2.51%	0.49%
Miscellaneous	1.39%	2.54%	1.27%	0.58%	0.33%	0.42%	1.45%	0.06%	1.09%	4.87%	1.46%	1.97%
Hospital solutions	0.00%	3.91%	0.33%	0.09%	0.17%	0.11%	0.02%	0.04%	0.12%	0.29%	0.06%	0.00%
Parisitology	0.15%	0.01%	0.15%	0.22%	0.07%	0.39%	0.18%	0.04%	1.34%	0.92%	0.47%	0.49%

Source: IMS Health, "World-wide Pharmaceutical Market" Feb. 2001. Figures are revenues from retail pharmacies, in millions of $US at current exchange rates. Figures for Japan include both pharmacy and hospital sales.

Table 2: Top 40 (by R&D spending) pharmaceutical firms

Firm	Nationality	R&D Spending	Number of Drugs
Pfizer	USA	$4,035.0	43
Glaxo SmithKline	UK	$3,704.9	78
Johnson & Johnson	USA	$2,600.0	43
Aventis	France/Germany	$2,592.9	79
Roche Holding	Switzerland	$2,462.7	46
AstraZeneca	UK	$2,454.0	28
Novartis	Switzerland	$2,233.3	40
Pharmacia Corporation	USA	$2,123.6	54
Merck & Company	USA	$2,068.3	33
Bristol-Myers Squibb Company	USA	$1,802.9	27
Eli Lilly & Company	USA	$1,783.6	17
American Home Products Corporation	USA	$1,513.8	30
Bayer Group	Germany	$1,270.9	25
Abbott Laboratories	USA	$1,194.0	8
Schering-Plough Corporation	USA	$1,191.0	9
Sanofi-Synthelabo	France	$970.5	54
Boehringer Ingelheim	Germany	$880.4	27
Amgen	USA	$822.8	4
Takeda Chemical Industries	Japan	$728.9	27
Schering AG	Germany	$728.7	16
BASF Group (Knoll)	Germany	$707.4	23
Sankyo Company	Japan	$607.5	16
Yamanouchi Pharmaceutical Company	Japan	$517.2	15
Merck KGaA	Germany	$477.0	11
E.I. du Pont de Nemours & Company	USA	$442.0	6
Eisai Company	Japan	$440.6	12
Fujisawa Pharmaceutical Company	Japan	$429.9	11
Akzo Nobel	Netherlands	$426.1	22
Novo Nordisk	Denmark	$393.1	6
Chugai Pharmaceutical Company	Japan	$377.3	6
Genentech	USA	$367.3	10
Baxter International	USA	$332.0	8
Daiichi Pharmaceutical Company	Japan	$322.2	9
Shionogi & Company	Japan	$255.0	11
Solvay	Belgium	$244.0	6
Taisho Pharmaceutical Company	Japan	$219.2	3
Nycomed Amersham	UK	$203.8	8
Kyowa Hakko Kogyo Company	Japan	$199.9	5
Ono Pharmaceutical Company	Japan	$189.6	8

Source: PharmaBusiness: 24, Nov. 2000. Figures are millions of 1999 dollars spent on healthcare research and development.

Table 3: Origin and diffusion of pharmaceuticals

Country	Number of firms	Number of drugs	Avg countries in which launched
USA	83	420	8.9
Japan	71	301	4.4
France	14	195	7.3
Germany	21	147	6.9
UK	17	128	9.2
Switzerland	11	110	9.5
Italy	33	100	4.5
Spain	13	37	2.7
Netherlands	5	36	8.1
South Korea	5	18	1.2
Denmark	3	17	13.3
Canada	6	8	6.0
Norway	1	8	9.0
Belgium	2	7	8.3
Hungary	2	7	5.7
Finland	1	6	6.0
Sweden	6	6	6.3
Argentina	3	5	2.2
Australia	2	5	3.0
Czech Republic	2	3	9.0
Austria	2	2	1.0
Israel	1	2	5.5
Brazil	1	1	1.0
Croatia	1	1	15.0
Cuba	1	1	2.0
Ireland	1	1	1.0
New Zealand	1	1	1.0

Table 4: Countries in sample

Country	Price Controls	Year
Australia	Y	1951
Austria	Y	1976
Belgium	Y	1963
Canada	Y	1987
Denmark	N	
France	Y	1945
Germany	N	
Greece	Y	1978
Ireland	N	
Italy	Y	1978
Japan	Y	1950

Country	Price Controls	Year
Mexico	Y	1993
Netherlands	Y	1996
Portugal	N	
South Korea	Y	1977
Spain	Y	unknown
Sweden	Y	1993
Switzerland	Y	1962
Turkey	Y	1928
UK	N	
USA	N	

Table 5: Summary Statistics

Number of drugs	1604
Number of firms	310
Number of therapeutic classes	147
Years covered	1980-1999
Number of markets (country-class-year observations)	58,624
Number of entry opportunities (drug-country-class-year observations)	298,960
Number of entry events	7,385

Frequency	Variable	Definition	Obs	Mean	Std Dev	Min	Max
Firm-country-year	Country experience	Count of firm's other drugs launched in country	85824	1.140	3.291	0	51
	Own in market	Count of firm's drugs in country-class market	85824	0.055	0.302	0	10
Country-class-year	Number of new drugs in market	Count of drugs in market launched less than 5 years ago	58777	1.042	1.503	0	15
	Number of old drugs in market	Count of drugs in market launched more than 5 years ago	58777	1.828	2.981	0	35
	Number of potential competitors	Count of drugs launched in class elsewhere in the world	58777	8.841	8.740	1	82
Drug-year	Drug age	Number of years since drug's first launch anywhere	21161	9.284	6.874	0	40
	Number of countries launched in		21161	6.040	6.6358	0	27
	Drug importance	Drug's share of stock of Medline citations for therapeutic class	21161	0.011	0.071	0	1
Firm-country	Home country	Dummy = 1 if firm is headquartered in country	6494	0.044	0.205	0	1
Firm-year	International experience	Count of countries in which firm has launched any drugs	4437	9.158	9.239	0	28
	Class experience	Count of firm's drugs in therapeutic class	4437	1.204	0.797	1	17
	Portfolio	Total number of firm's drugs	4437	0.037	0.230	0	3
Country-year	Population	Population in 10s of millions	420	4.538	5.527	0.34	27.29
	GDP per capita	GDP per capita in US$1000s, PPP	420	14.265	6.279	2.25	31.94
	Price controls	Dummy = 1 if country uses price controls	420	0.508	0.501	0	1
	Price freeze	Dummy = 1 if country has a price freeze in effect	420	0.147	0.355	0	1

Table 6: Extent of diffusion

Variable	Negative binomial models Y = number of countries entered			Linear models Y = Log(total population reached)		
	4 year lag	8 year lag	12 year lag	4 year lag	8 year lag	12 year lag
	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)
Number of potential entrants	0.0124*	0.0251**	0.0208**	0.012*	0.026**	0.021**
	(0.0055)	(0.0057)	(0.0065)	(0.006)	(0.007)	(0.008)
International experience	0.0412**	0.0488**	0.047**	0.030**	0.039**	0.037**
	(0.004)	(0.0043)	(0.005)	(0.004)	(0.005)	(0.006)
Own in class	-0.0227	-0.0202	-0.007	-0.017	-0.023	-0.010
	(0.0193)	(0.0188)	(0.021)	(0.020)	(0.022)	(0.025)
Portfolio	-0.006**	-0.0085**	-0.0082**	-0.004	-0.007**	-0.007**
	(0.0021)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Drug importance	0.7011	1.551**	1.5242**	0.092	1.811**	1.309*
	(0.413)	(0.545)	(0.483)	(0.470)	(0.620)	(0.596)
US firm	0.1066	-0.0042	0.0392	0.114	0.013	0.106
	(0.0826)	(0.087)	(0.0957)	(0.090)	(0.106)	(0.120)
UK firm	0.2763*	0.0382	-0.1072	0.315*	0.022	-0.128
	(0.111)	(0.12)	(0.1357)	(0.126)	(0.146)	(0.170)
French firm	-0.3212*	-0.2359	-0.174	-0.332*	-0.214	-0.156
	(0.1293)	(0.1211)	(0.1272)	(0.134)	(0.143)	(0.155)
German firm	-0.16	-0.1987*	-0.1917	-0.177	-0.237*	-0.246
	(0.0949)	(0.0965)	(0.1061)	(0.101)	(0.114)	(0.129)
Italian firm	-0.3651**	-0.4435**	-0.3201*	-0.381**	-0.489**	-0.412**
	(0.1416)	(0.1309)	(0.1356)	(0.133)	(0.141)	(0.155)
Japanese firm	-0.5754**	-0.627**	-0.5827**	-0.570**	-0.655**	-0.650**
	(0.0949)	(0.0983)	(0.1093)	(0.095)	(0.109)	(0.127)
Observations	1144	1033	867	1144	1033	867
Log Likelihood	4328.7397	7977.3365	8423.0633	0.3669	0.3828	0.3931

*= 5% significance, ** = 1 %. All specifications include year and therapeutic class fixed effects.

Table 7a: Timing of diffusion, non-regulatory variables

Variable	Discrete time hazard models				
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)
Number of new drugs in market	0.107**	0.108**	0.108**	0.105**	0.104**
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
Number of old drugs in market	0.029**	0.029**	0.029**	0.030**	0.028**
	(0.005)	(0.005)	(0.005)	(0.005)	(0.005)
Number of potential entrants	-0.007*	-0.006	-0.006	-0.007*	-0.007*
	(0.003)	(0.003)	(0.003)	(0.003)	(0.003)
Population	0.075**	0.073**	0.073**	0.067**	0.066**
	(0.007)	(0.007)	(0.007)	(0.007)	(0.007)
Population squared	-0.004**	-0.004**	-0.004**	-0.003**	-0.003**
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
GDP per capita	0.057**	0.057**	0.057**	0.057**	0.057**
	(0.004)	(0.004)	(0.004)	(0.004)	(0.004)
Experience in country	0.043**	0.044**	0.045**	0.042**	0.041**
	(0.004)	(0.004)	(0.004)	(0.004)	(0.004)
Domestic firm	1.621**	1.609**	1.589**	1.628**	1.629**
	(0.050)	(0.050)	(0.051)	(0.050)	(0.051)
International experience	0.015**	0.014**	0.014**	0.012**	0.012**
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Own in class	-0.065**	-0.066**	-0.065**	-0.071**	-0.071**
	(0.016)	(0.016)	(0.016)	(0.016)	(0.016)
Own in market	0.054	0.054	0.053	0.066*	0.067*
	(0.030)	(0.030)	(0.030)	(0.030)	(0.030)
Portfolio	-0.016**	-0.019**	-0.019**	-0.016**	-0.016**
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Drug importance	0.969**	0.962**	0.959**	1.220**	1.246**
	(0.177)	(0.177)	(0.177)	(0.178)	(0.178)
Number of countries launched in	0.420**	0.417**	0.417**	0.414**	0.415**
	(0.009)	(0.009)	(0.009)	(0.012)	(0.012)
Number of countries launched in squared	-0.012**	-0.012**	-0.012**	-0.011**	-0.011**
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Observations	298960	298960	298960	298960	298960
Log likelihood	-27160	-27133	-27124	-26880	-26848

*= 5% significance, ** = 1 %. All specifications include year and therapeutic class fixed effects.

Table 7b: Timing of diffusion, age effects

Variable	Discrete time hazard models				
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)
Age = 0	-4.823**	-4.703**	-4.661**	-4.558**	-4.592**
	(0.222)	(0.225)	(0.227)	(0.228)	(0.229)
Age = 1	-5.667**	-5.542**	-5.498**	-5.322**	-5.363**
	(0.223)	(0.226)	(0.228)	(0.229)	(0.230)
Age = 2	-6.131**	-6.004**	-5.960**	-5.773**	-5.814**
	(0.223)	(0.227)	(0.229)	(0.230)	(0.231)
Age = 3	-6.591**	-6.464**	-6.420**	-6.174**	-6.212**
	(0.224)	(0.228)	(0.230)	(0.231)	(0.232)
Age = 4	-7.126**	-6.998**	-6.955**	-6.670**	-6.709**
	(0.226)	(0.230)	(0.232)	(0.233)	(0.234)
Age = 5	-7.497**	-7.367**	-7.325**	-7.033**	-7.073**
	(0.228)	(0.232)	(0.233)	(0.234)	(0.235)
Age = 6	-7.752**	-7.621**	-7.578**	-7.281**	-7.321**
	(0.230)	(0.233)	(0.235)	(0.236)	(0.237)
Age = 7	-8.019**	-7.887**	-7.845**	-7.537**	-7.576**
	(0.232)	(0.236)	(0.237)	(0.238)	(0.239)
Age = 8	-8.296**	-8.163**	-8.120**	-7.799**	-7.838**
	(0.234)	(0.238)	(0.240)	(0.240)	(0.241)
Age = 9	-8.607**	-8.470**	-8.428**	-8.113**	-8.152**
	(0.238)	(0.242)	(0.243)	(0.244)	(0.245)
Age = 10	-8.679**	-8.539**	-8.497**	-8.178**	-8.219**
	(0.240)	(0.244)	(0.245)	(0.246)	(0.247)
Age = 11	-8.798**	-8.658**	-8.616**	-8.289**	-8.328**
	(0.242)	(0.246)	(0.247)	(0.248)	(0.249)
Age = 12	-9.116**	-8.974**	-8.932**	-8.631**	-8.670**
	(0.249)	(0.253)	(0.255)	(0.255)	(0.256)
Age = 13	-9.013**	-8.872**	-8.829**	-8.532**	-8.572**
	(0.250)	(0.253)	(0.255)	(0.256)	(0.256)
Age = 14	-9.258**	-9.117**	-9.074**	-8.798**	-8.838**
	(0.258)	(0.262)	(0.263)	(0.264)	(0.265)
Age = 15	-10.156**	-10.013**	-9.971**	-9.788**	-9.836**
	(0.236)	(0.240)	(0.241)	(0.242)	(0.243)
Observations	298960	298960	298960	298960	298960
Log likelihood	-27160	-27133	-27124	-26880	-26848

*= 5% significance, ** = 1 %. All specifications include year and therapeutic class fixed effects.

Table 7c: Timing of diffusion, regulatory and country-of-origin effects

Variable	Discrete time hazard models				
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)
Price controls	-0.228**	-0.224**	-0.329**	-0.243**	-0.183**
	(0.027)	(0.027)	(0.058)	(0.028)	(0.036)
Price freeze	-0.066	-0.068	-0.069	-0.068	-0.057
	(0.047)	(0.047)	(0.047)	(0.047)	(0.047)
US firm		-0.047	-0.113*	-0.032	-0.034
		(0.041)	(0.054)	(0.042)	(0.042)
UK firm		0.203**	0.214**	0.188**	0.183**
		(0.054)	(0.071)	(0.056)	(0.056)
French firm		0.141*	0.070	0.166*	0.161*
		(0.063)	(0.085)	(0.065)	(0.065)
German firm		0.050	0.023	0.066	0.066
		(0.048)	(0.062)	(0.049)	(0.049)
Italian firm		-0.234**	-0.395**	-0.190*	-0.195*
		(0.075)	(0.103)	(0.077)	(0.077)
Japanese firm		-0.155**	-0.290**	0.032	0.032
		(0.050)	(0.067)	(0.054)	(0.054)
Price controls*US firm			0.135		
			(0.074)		
Price controls*UK firm			-0.030		
			(0.095)		
Price controls*French firm			0.143		
			(0.113)		
Price controls*German firm			0.052		
			(0.085)		
Price controls*Italian firm			0.326*		
			(0.137)		
Price controls*Japanese firm			0.272**		
			(0.088)		
Observations	298960	298960	298960	298960	298960
Log likelihood	-27160	-27133	-27124	-26880	-26848

*= 5% significance, ** = 1 %. All specifications include year and therapeutic class fixed effects.

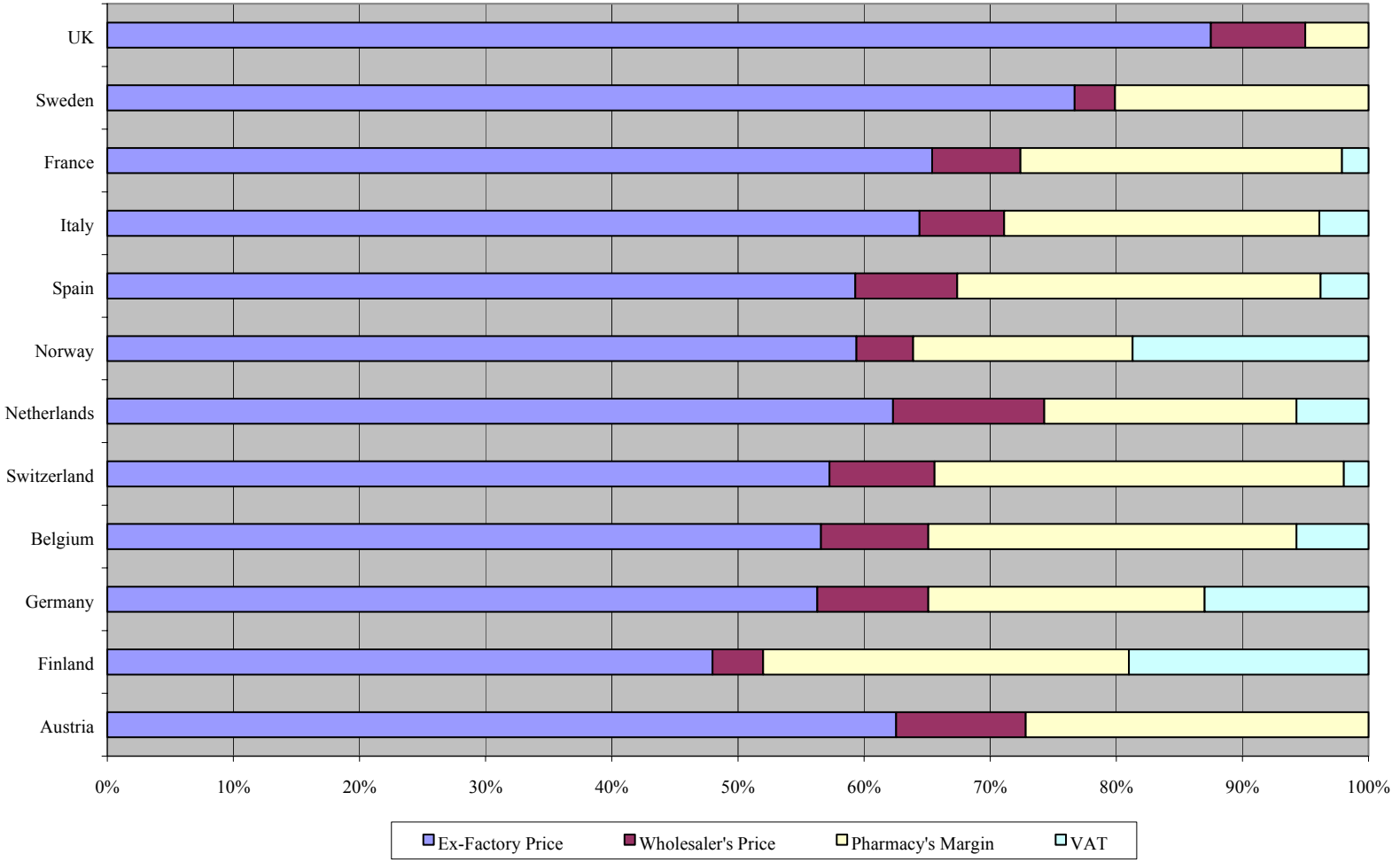
Table 7d: Timing of diffusion, regulatory and prior launch effects

Variable	Discrete time hazard models		
	Model 4	**Model 5**	**Model 5**
	Main effect		Price control interaction
	Coef. (Std Err)	Coef. (Std Err)	Coef. (Std Err)
Australia	-0.427**	-0.304**	-0.240*
	(0.053)	(0.074)	(0.100)
Austria	0.025	-0.030	0.103
	(0.046)	(0.063)	(0.086)
Belgium	-0.357**	-0.350**	-0.022
	(0.045)	(0.061)	(0.084)
Canada	0.031	0.091	-0.119
	(0.047)	(0.066)	(0.089)
Denmark	0.075	0.097	-0.042
	(0.045)	(0.062)	(0.084)
France	-0.073	0.007	-0.164*
	(0.040)	(0.053)	(0.072)
Germany	-0.048	-0.059	0.024
	(0.037)	(0.051)	(0.069)
Greece	-0.153**	-0.187**	0.054
	(0.050)	(0.068)	(0.092)
Ireland	0.016	0.013	0.009
	(0.046)	(0.066)	(0.088)
Italy	-0.221**	-0.120*	-0.201**
	(0.039)	(0.052)	(0.073)
Japan	-0.487**	-0.372**	-0.249**
	(0.044)	(0.054)	(0.074)
Mexico	-0.039	-0.083	0.082
	(0.050)	(0.071)	(0.094)
Netherlands	0.123**	0.087	0.058
	(0.044)	(0.061)	(0.083)
Portugal	0.040	-0.059	0.190*
	(0.046)	(0.064)	(0.086)
South Korea	0.153**	0.031	0.231**
	(0.048)	(0.068)	(0.090)
Spain	-0.377**	-0.461**	0.174*
	(0.043)	(0.062)	(0.082)
Sweden	0.103*	0.091	0.021
	(0.045)	(0.063)	(0.086)

Switzerland	0.197**	0.173**	0.049
	(0.039)	(0.053)	(0.071)
Turkey	0.004	-0.035	0.068
	(0.083)	(0.118)	(0.156)
UK	0.214**	0.268**	-0.108
	(0.043)	(0.058)	(0.079)
USA	-0.053	-0.038	-0.012
	(0.040)	(0.056)	(0.073)

*= 5% significance, ** = 1 %. All specifications include year and therapeutic class fixed effects.

Figure 1: European price structure of pharmaceuticals



Source: European Federation of Pharmaceutical Industry Associations (EFPIA), 1998 in: Pharmaceutical Pricing and Reimbursement in Europe, 1999.

Figure 2: Distribution of the Number of Drugs in a Market

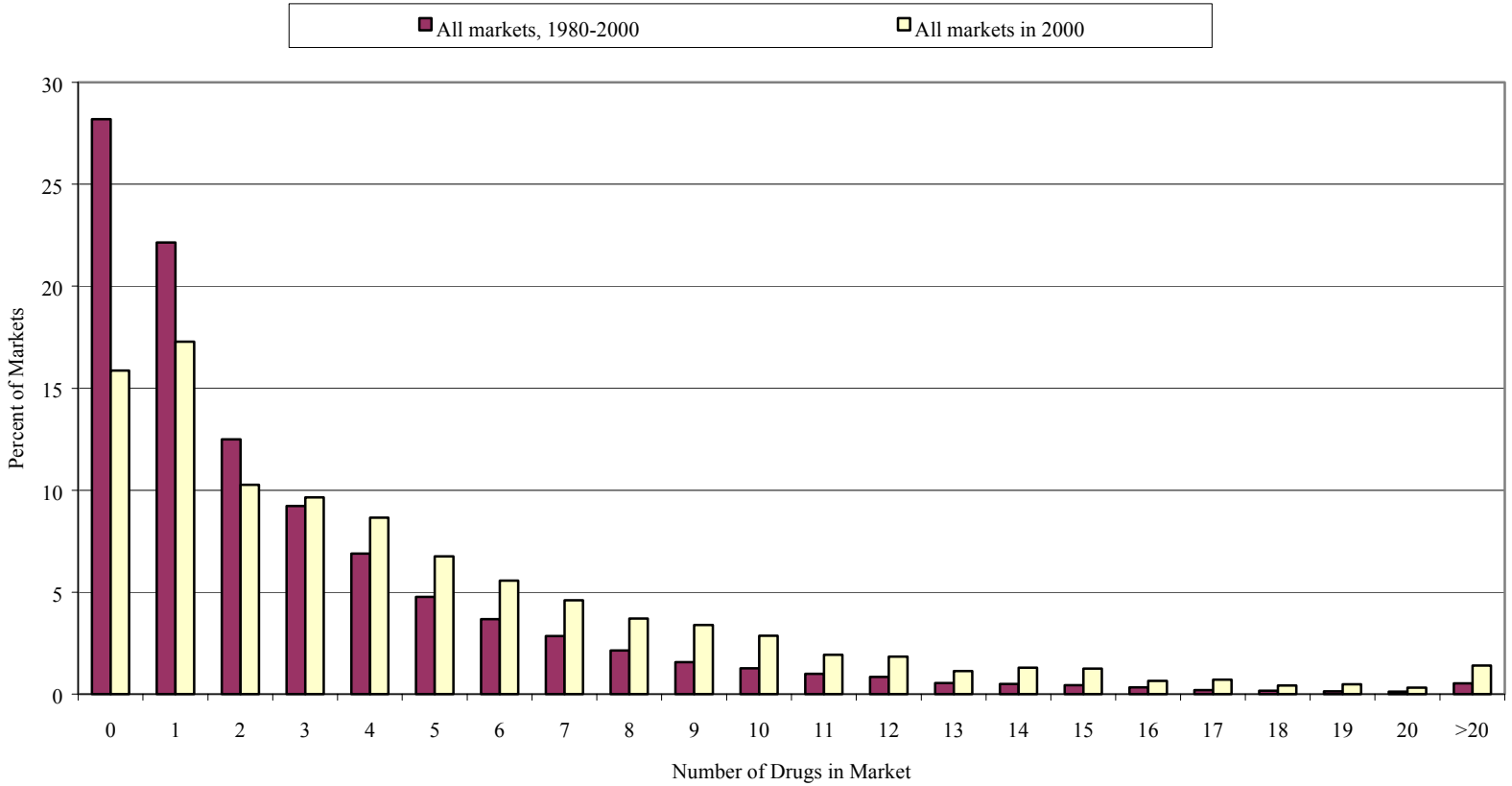


Figure 3: Distribution of the Number of Drugs in a Market, Selected Countries

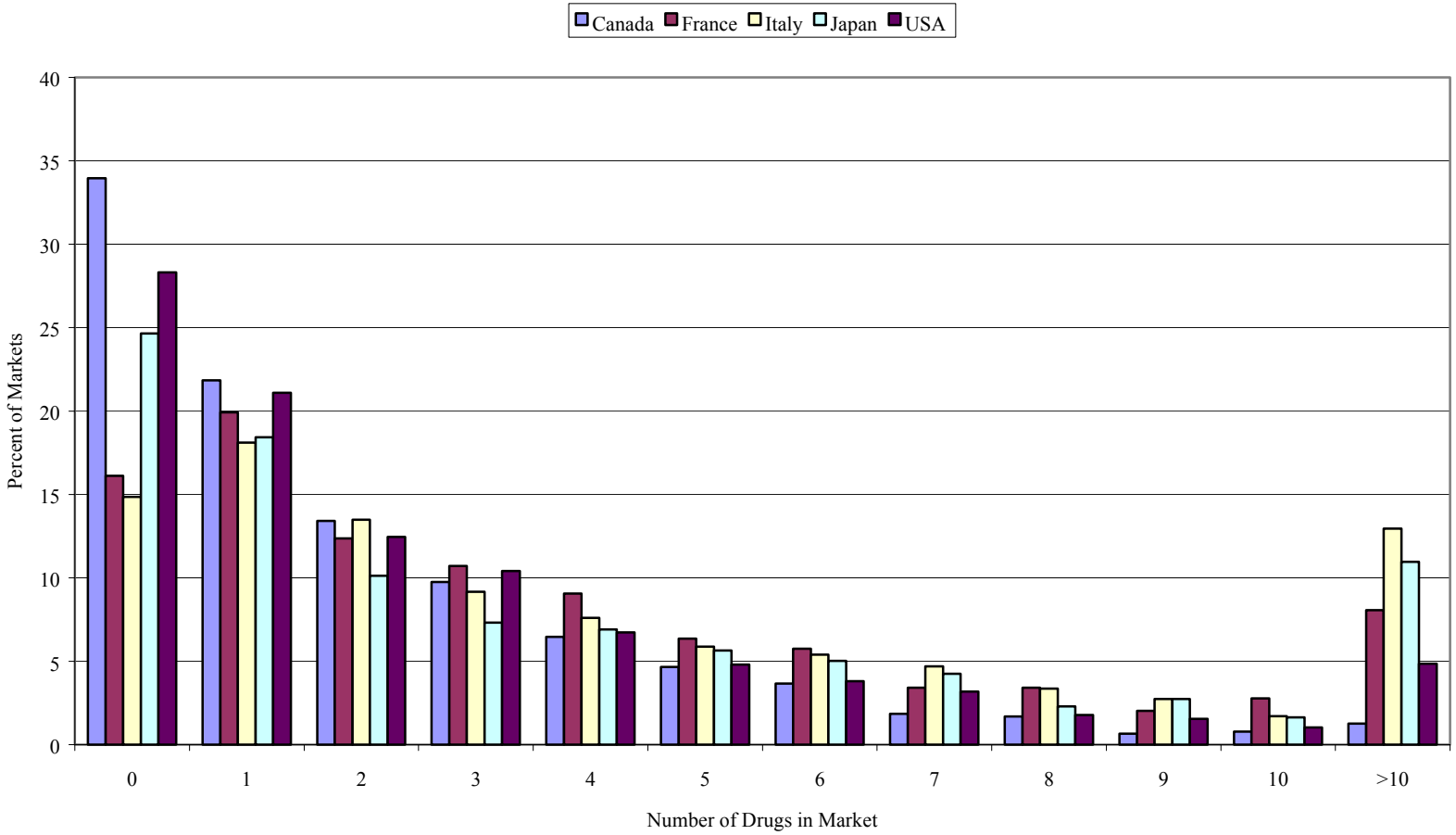
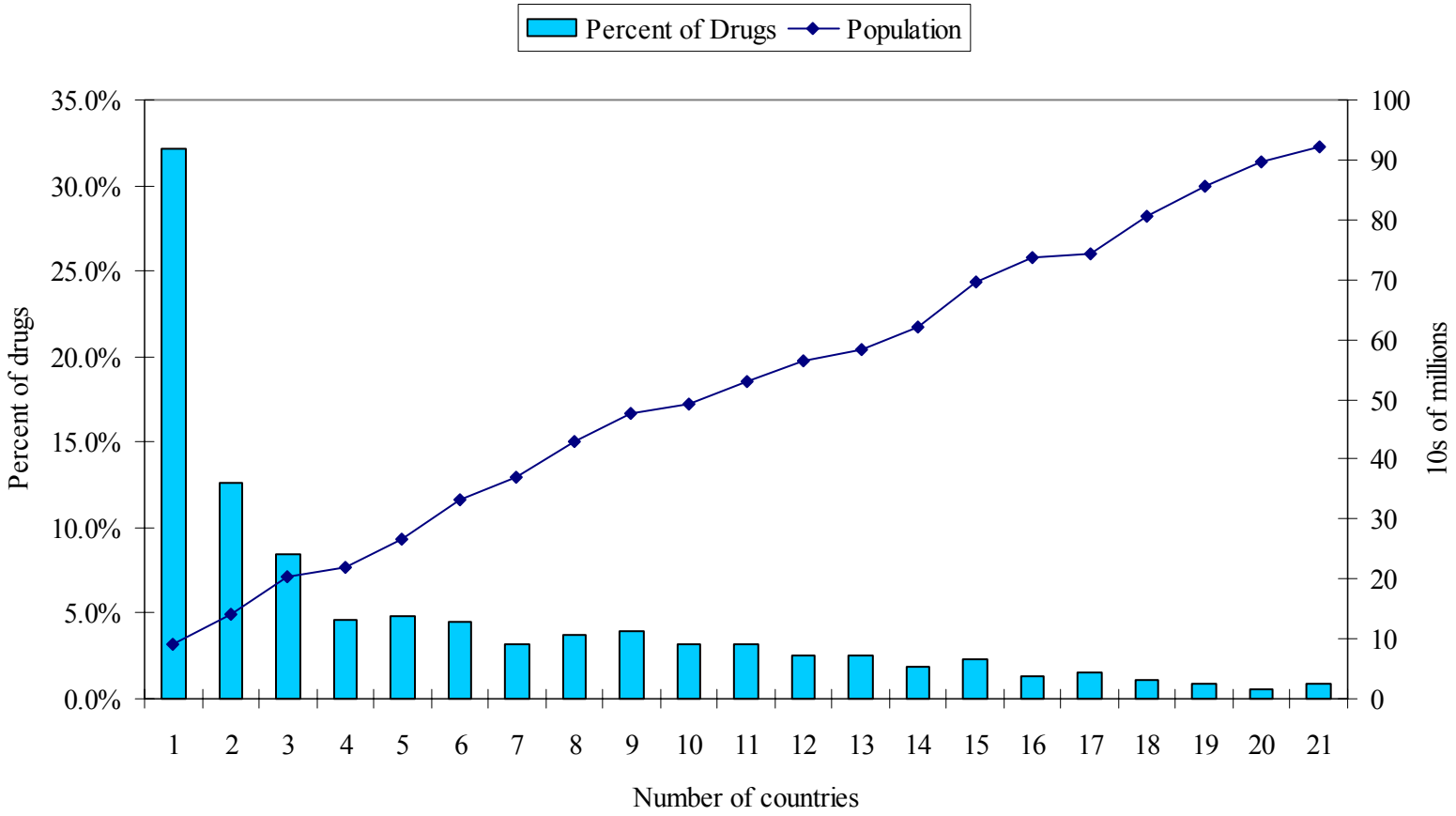


Figure 4: Distribution of the number of OECD countries entered and population reached



Appendix A: Additional regulatory information

Generic Drugs

Countries differ in the amount of testing required for approval of generic products, and many have made policy changes over the past several decades. Even the generic drug industry in the US, where generic penetration is highest, achieved significance only after the Waxman-Hatch Act of 1984. European countries have only recently adapted their policies to encourage generic entry, such as providing incentives for pharmacists to fill prescriptions with generics, encouraging doctors to prescribe generics, or requiring patients covered by the government health plan to accept generics. In most countries, though, generics garner only a small market share.

Demand-side Controls

Reference pricing is a regime in which the government sets a price at which it will reimburse a treatment for a condition. The patient must then pay the difference between that reference price and the price of the treatment he elects to take. The reference price is usually determined by a formula that accounts for the average cost of alternative therapies, the cheapest available treatment, etc. Reference pricing is relatively new, beginning first in Germany in 1989, and is in limited use in about six major markets. Most countries require a patient co-payment for a prescription covered under the government insurance plan, which varies across patients (by income or age), therapeutic class, type of drug, etc. and may be fixed or a percentage of total cost. Some governments, notably Britain and Germany, monitor or limit the prescribing behavior of physicians. Many countries provide guidelines for prescribing and some impose financial sanctions on doctors who deviate. Others also limit the volume a physician may prescribe of a particular drug or restrict him to a fixed budget. In the US, health maintenance organizations attempt similar controls on cost. For a detailed treatment of the many varieties of regulation, see Jacobzone (2000). These distinctions amount to variations in the price sensitivity of patients and doctors in different countries.

Advertising

Prescription drug advertising is highly regulated in all countries, in its content and in some cases its quantity as well. Only three countries (the US, China, and New Zealand) permit direct-to-consumer advertising, and the US only recently relaxed its position on this. Italy restricts the number of minutes a firm may detail a drug. One consequence of this policy is extensive licensing of the same drug to several firms, so that the total number of detailing minutes

is increased. France and Spain set targets for limiting promotional expenditures to a percentage of revenues or selling price.