The Role of Firm Characteristics in Pharmaceutical Product Launches

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Abstract

This paper examines the determinants of new pharmaceutical launches since 1980 in the G7 nations using discrete-time hazard models. Despite the obvious incentive to amortize the large sunk costs of drug development over many markets, entry occurs in only 4% of the opportunities. The results indicate that firm characteristics, such as domestic status and experience in the local market, are important in explaining product launches in addition to market characteristics. Also, the interaction between the innovating firm and target country is a critical component of profitability. New drugs are 1.5 times more likely to be launched in markets that share a border or a language of a drug company's country of headquarters, even for multinational firms. The effect of competition depends on the characteristics of both the potential entrant and the incumbents: domestic entrants prefer to compete with domestic incumbents. Although this is an industry with the potential for ubiquitous licensing and low transportation costs, the specific match quality between the innovating firm and market conditions remains an important determinant of entry.

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I. Introduction

This paper examines the influences of market structure, firm and product characteristics on the launch of new drugs in the largest pharmaceutical markets, the G7 nations. Despite the incentives to amortize large and sunk development costs over many markets, only one-third of the prescription pharmaceuticals sold in one of these countries (the US, Japan, Germany, France, Italy, the UK, and Canada) are also marketed in the other six. Economic theory suggests that entry is a function of market size, the level of competition, and the fixed costs associated with product launch. Research in strategic management suggests that firms are heterogeneous: some are better suited to a particular market than others. Joint testing of economic and strategic hypotheses is rare, largely because it requires a setting with a clear set of potential entrants and separate markets. Disentangling these various effects is an empirical challenge, but one for which this setting is ideal. An identical product is launched (or not launched) in different markets, yielding three sources of variance to exploit: variation across countries, variation across therapeutic classes, and changes over time.

Besides the obvious effects on available medical treatments in a country, there are a number of reasons why the entry patterns of new pharmaceuticals are important. Understanding them 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. Theories on entry suggest that some features of this industry will result in "too little" entry in equilibrium. In addition, identifying the sources of competitive advantage in this industry has implications for industry structure and, perhaps, the regulation of entry within a country, as well as managerial decisions such as the choice of a licensing partner.

My main finding is that firm-level characteristics and their interaction with other variables are at least as important in understanding competition as the "usual suspects" like market size and entry barriers. In particular, market characteristics alone correctly predict entry for only about 30% of the sample. Including firm characteristics improves this prediction substantially. These firm variables affect entry in several ways. First, there is a great deal of heterogeneity in firms' cost of entry, related to country-of-origin, size, and experience. Second, these costs vary within a firm across markets; i.e., the interaction of firm and market characteristics matters. Similarities between the country of headquarters and the target country, such as a shared border or language, greatly increase the likelihood of product launch. Finally, entry also depends on the interaction between a potential entrant's characteristics and those of the incumbent competitors. The effect

of competition on profitability also depends on the characteristics of both the potential entrant and the incumbents: domestic entrants prefer to compete with domestic incumbents, and are more sensitive to foreign competition than are foreign entrants.

The following section reviews the theoretical and empirical literature on entry. It also provides a brief description of the pharmaceutical industry and presents the rationale for examining market, firm, and product characteristics in this setting. I explain the empirical model in Section III and the data in Section IV. Section V presents the results, and Section VI concludes.

II. Background on entry and the pharmaceutical industry

A. The literature on entry

A wealth of theoretical work exists on the welfare consequences of free entry when firms must incur fixed costs. Many theories predict too little entry relative to the social optimum (Spence (1976), Dixit and Stiglitz (1977)): the marginal entrant is welfare enhancing. Others (von Weizäcker (1980), Perry (1984)) generate the opposite result, especially in homogenous product markets. Then, an additional entrant reduces welfare by merely "business stealing" while incurring fixed costs. Mankiw and Whinston (1986) demonstrate the conditions under which there is too much or too little entry. In general, with imperfect competition, a fixed cost of entry, and homogeneous products, the marginal entrant decreases welfare, although this effect decreases as the fixed entry cost approaches zero. But in settings where variety is important – so that the marginal entrant adds to product diversity – the welfare effects of entry are ambiguous. Accounting for the incentives to invest in innovation adds yet more complexity: it is necessary to compare the dynamic efficiency resulting from innovation with the static inefficiency of market power – and prices in excess of marginal cost – in the short run. While this paper does not speak directly to the effects of entry on social welfare in pharmaceutical markets, more entry is likely to be welfare enhancing in this setting.[1]

Several general findings emerge from the empirical literature on entry. Both market size and the degree of competition influence the entry decision. The number of firms in equilibrium increases at a decreasing rate with the size of the market, and profit margins fall as the number of competitors increases (Bresnahan and Reiss (1987, 1990, 1991), Berry (1992), Scott Morton

[1] This is because different chemicals are not perfect substitutes for each other, so the benefit of an increase in product diversity probably exceeds the business stealing effect. In addition, the costs of developing a drug for many markets are not much greater than the costs of developing a drug for a single market, so the fixed entry cost is relatively small for launch in any additional market. Finally, the dynamic efficiency of innovation incentives is generally considered important for pharmaceuticals.

(1999)). Second, firms tend to enter in markets that are similar to those they already compete in. Berry (1992) shows airlines that serve one or both of the cities in a city pair market are more likely to enter that market (though this may reflect network effects rather than similarity). Scott Morton (1999) demonstrates that generic drug firms in the US tend to enter product markets that match well to their existing products. Finally, the match between a product and a market is important. For example, Mazzeo (2002) finds that competing motels strategically differentiate themselves from each other in quality space to soften price competition. All these studies of entry have the advantage of requiring little or no data on price and quantity, which is often expensive and difficult to obtain. However, these authors relied on a single cross-section of markets, which precludes simultaneous consideration of market, firm, and product characteristics.[2]

B. Background and studies on the pharmaceutical industry

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.[3] 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. These markets also differ on a number of other dimensions, of which regulation is the most notable. The entry of pharmaceuticals is restricted by the Food and Drug Administration in the US or an equivalent agency in other countries. The price of drugs is also regulated in most countries, including four of the G7 markets. For a more detailed description of price controls, see Jacobzone (2000) or Kyle (2005).

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, and are responsible for half of all drugs available somewhere in the world. Table 1 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

[2] Toivanen and Waterson (2001) observe entry decisions over time into fast-food markets in the UK, but like Berry (1992), assume all heterogeneity is at the firm level.
[3] Figures are annual totals for 2000. Source: IMS Health.

markets. Drugs with small domestic markets like Denmark, Switzerland, and the Netherlands spread to more foreign markets than drugs with large home markets. Pharmaceutical firms tend to specialize in certain therapeutic categories,[4] 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.[5] 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. [6]

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 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.[7] 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. Lichtenberg and Philipson (2002) 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)) and entry costs (Djankov et al. (2002)). 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)). Parker (1984) shows regulation is related to large differences across countries in the number and mix of products introduced before 1978. More recently, Kyle (2005), Danzon, Wang and Wang (2005), and Lanjouw (2005) all find evidence that price controls have deterred entry in pharmaceutical markets since the early 1980s. Thus, there is much reason to expect regulation to influence entry.

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[4] For a breakdown of the top twenty firms' specializations, see DiMasi (2000).
[5] Paraxel's Pharmaceutical Statistical Sourcebook 1999, p. 49.
[6] IMS Health Inc.
[7] 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.

Regulation also affects drugs and firms differentially within a country, particularly in the costs of gaining regulatory approval (Dranove and Meltzer (1994), Carpenter (2003)). 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, there is substantial evidence of significant firm and product heterogeneity in research productivity (Henderson and Cockburn (1996) and Cockburn and Henderson (1994, 1998)), and 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.

III. Model

This paper assumes that potential entrants for a market take existing market structure as given and compete simultaneously in time t. 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. This set excludes drugs currently under development for that therapeutic class, for which outcomes are uncertain and regulatory approval may be years away.

A discrete-time hazard model corresponds to a static, reduced-form model of entry in which firms launch a new drug when they expect positive profits, and otherwise stay out of a market. Let i index drugs, j index firms, k index therapeutic classes, and l index countries. A market is thus a class-country-year triple. I estimate the following equation as a logit, where P(t) is the probability of a drug's launch:

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

This approach has the advantage of being flexible as well as accounting for right-censored observations, and its main purpose is descriptive. However, it also 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 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 by, for example, using entry in one country to deter a competitor's launch in another. While firms in an oligopolistic setting (such as most drug markets) are likely to react to the behavior of their competitors, most firms in this industry have few drugs on the market and are active in a small number of countries. For the large multinationals, with more multimarket contact, this assumption may be more problematic.

An alternative to the discrete-time logit is a continuous-time hazard model. Since drug launches are observed at annual intervals in this dataset, a discrete-time model is probably most appropriate. As the interval of observation becomes small, the results from a discrete-time logit converge to those from a proportional hazard model,[8] and the results from a continuous-time hazard model are similar to the discrete-time results presented here.

Despite the strong and sometimes uncomfortable assumptions necessary, estimating a static reduced-form model can provide insights into the sources of unobserved heterogeneity that may inform future research. In particular, these models are numerically stable and robust enough to estimate a large number of coefficients and fixed effects, which is a far greater challenge in a structural setting such as that of Berry (1992). The estimation here offers several advantages over previous work. The set of potential entrants is clear, so the dependent variable is reliably defined. Unlike most previous studies, which use a single cross-section, the panel structure of this dataset permits a richer set of controls. It is also one of few studies to focus on the entry patterns of highly R&D-intensive products, the management of which is likely to be quite different from single-outlet, local firms with relatively undifferentiated products.

IV. Data

I obtained information on all drugs developed between 1980 and 2000 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.

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

I examine entry into only the G7 markets, which account for about 70% of total pharmaceutical revenue. Entry incentives should be greatest for these large markets, and other important factors, such as patent law, are relatively uniform across this subset. This permits a closer examination of the role of *firm* characteristics in the entry decision, without worrying as much about differences across countries that are important, but often unobserved or difficult to quantify.

The OECD Health Data 2000 dataset provides population, GDP, data on access to health care, and other demographic information for the G7 markets considered here. 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." Canada, France, Italy, and Japan are price-controlled countries; the US, UK, and Germany do not use explicit price controls.

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. 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.[9]

Unfortunately, while I have information on when a drug is launched in a country and what therapeutic classes it is approved for somewhere in the world, I do not know which therapeutic classes a drug is approved for in each country. Therefore, I assume that when the drug is launched in a country, it is a competitor in all of its therapeutic classes, but entry into each therapeutic class is not a separate or independent decision. For this reason, for each drug-country pair, I use only one entry equation (for its primary therapeutic class), but treat the drug as a competitor in all its therapeutic areas once launched.[10] In general, exit is rare, since a drug may continue to be an important therapy even after its patent expires, especially in nations without a significant generic segment. While a firm may reduce its advertising efforts for a particular drug, it generally does not withdraw the product from a market. It is therefore assumed that there is no

[9] There is evidence that "gray market" trade in pharmaceuticals across borders has been increasing, however. See OECD Joint Group on Trade and Competition (2001).

[10] I experimented with (1) treating a drug as a competitor/potential entrant in only its primary therapeutic class and (2) using a non-primary therapeutic class for the entry decision (which changes the values only of the competition and class fixed effect variables). The results were almost identical.

exit for economic reasons.[11] Possible obsolescence is controlled for in the estimation by allowing older drugs to have a different impact on entry than newer therapies.

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. 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, I follow Dranove and Meltzer (1994) in using Medline citations; the construction of variables using citations is described in the Appendix. 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.[12]

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. 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 specifications, with the unfortunate implication that the estimated fixed effect for each country is the net impact of many variables.

Table 2 presents summary statistics for data used in estimation. The sample contains 1482 unique molecules produced by 286 firms in 134 therapeutic classifications, for a total of 13445 country-class-year markets. There were 86755 entry opportunities, only 3445 (4%) of which had a product launch. The mean number of drugs competing in markets with entry opportunities is 1.8. Figure 1 shows the distribution across therapeutic classes within several countries over

[11] However, Lichtenberg and Philipson present evidence that 18% of the drugs approved between 1970 and 1979 in the US are no longer marketed in 1999.

[12] Reported adverse interactions and contraindications can be obtained for drugs launched in the US. Results are largely unchanged by including these measures of quality in regressions using the subset of the data for which this information was collected.

1980-2000. Most markets are highly concentrated, and over one-fourth have no entry at all. Remarkably, 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. On average, it takes about 3.4 years after a new treatment is first launched elsewhere for an empty market to experience its first entrant (see Table 3), and another 4 years after that for a second drug to enter the market. This suggests rather large welfare consequences related to launch delays, but there is quite a bit of variance around these numbers, and systematic patterns are difficult to identify. Figure 2 shows the launch pattern for the average drug: it is clear that the probability of additional G7 launches after one year is rather low, and the average drug is only in 2 of the G7 markets.

Variables measured at the drug-year level include age, the number of countries in which the drug has been introduced, and its importance as measured by its share of total Medline citations within its therapeutic class. The probability of entry is expected to be concave in the number of launch countries if there are 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. A positive coefficient is expected on the importance measure, either because important drugs are more profitable or because regulators respond to political pressures and approve them more quickly.

Several firm-level variables are included. A firm with a presence in many markets may have more resources to draw on, which would make entry more likely. The dummy variable "multinational" (defined here as a firm active in at least 10 countries) captures this effect. A firm's experience in a country is defined as the count of drugs it markets in that country, and an alternative measure, "experience years" (equal to the number of years a firm has been active in the country), is also used. These capture economies of scope: experience with the regulator, firm reputation, and the presence of a detailing force and distribution channels may be spread across all a firm's products within a country. The number of drugs a firm has within a country-class market measures expertise in the local market.

All firm variables apply to the innovating firm, which may license a drug to another firm for marketing in particular countries. If licensing were efficient, then only the firm portfolio variables should matter, as an innovating firm might choose not to license out a drug that could cannibalize sales of its other products. The other characteristics of the innovating firm, in

particular the firm-country interactions, would be irrelevant. To the extent that licensing markets work well, this specification is biased against finding any significance on most firm-level variables.

Three additional dummy variables capture similarities between the country of headquarters of the originating firm and the target country; these indicate whether the headquarters country shares a border, language, or regulatory structure with the potential market. Firms may prefer to enter markets that share characteristics with their home market, with which they are likely to be most familiar. This could stem from a better understanding of neighboring culture, easier communication, or familiarity with regulations. (Sharing a border may also be related to lower transportation costs, though in the case of pharmaceuticals such costs are usually trivial.) If labor markets were completely efficient, a firm could hire managers with the necessary language skills or experience in the target country; in this case, the coefficients on these variables should be zero.

I believe that drugs are not homogeneous products, which would suggest that competition from drugs that are closer substitutes would have more of an effect on profits. The characteristics of competing firms may also affect profits if, for example, an incumbent has a particularly large sales force or is favored by physicians for some reason. Several (admittedly crude) measures of competition are used in the estimation to allow for the possibility that drugs or firms may have asymmetric effects on their competitors' profits. These include the number of "old" incumbent drugs (those launched more than 5 years ago), the number of "new" incumbents, the number of incumbent drugs made by domestic firms and the number made by foreign firms.

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. In general, additional country-level variables such as the number of doctors per capita, pharmaceutical spending, and life expectancy proved insignificant[13] and so only a parsimonious set of variables is presented here. Specifications that include country-therapeutic class fixed effects control for other unobserved market characteristics.

[13] 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)? In addition, once demeaned by country and year, these measures have little variation.

V. Results

Tables 4-6 present results of discrete-time logit duration models. All specifications include drug age, year, and therapeutic class fixed effects, the coefficients of which are not reported; Models 3-6 include country-therapeutic class interactions.

Table 4 displays the parameter estimates for market characteristics (note: Models 4 and 5 include alternative measures of competition, the coefficients for which are presented in Table 6). Models 1 and 2, which do not include country fixed effects, are most useful for examining the effect of country-level characteristics. All of the countries in the sample are large and relatively wealthy, so perhaps it is not surprising that population and per capita GDP are not especially important determinants of entry for this set.[14] In the specification that includes only country characteristics, the coefficients on population and its square have the expected signs, but the coefficient on GDP is not statistically different from zero. However, the use of price controls appears to discourage entry once firm characteristics are controlled for (Model 2). At the median of all continuous variables, price controls decrease the probability of entry by about 21%.

The parameter estimates for variables capturing the extent of competition in Models 1-3 demonstrate the consequences of mismeasuring market size. The probability of entry appears to be increasing in the number of current competitors in Model 1, which controls only for year and therapeutic class effects. Such an interpretation overlooks the fact that the number of drugs in a market reflects underlying *country-specific* demand for a therapy, which is inadequately captured by population and wealth. As an example, consider lafutidine, a new antiulcer medication developed by a Belgian company, which was launched in Japan but not in the US. While quite a large market in both countries, Japan already had 18 antiulcer treatments, compared to 9 in the US. However, the Japanese have a much higher rate of stomach cancers and other gastrointestinal disorders,[15] so demand for antiulcer drugs is especially large relative to other countries. Without accounting for the difference in demand for antiulcer treatments between these two countries, one would erroneously conclude that entry is more likely in markets with more competition.

If country-therapeutic class interactions are included, as in Model 3, the coefficients on the various measures of competition are negative and significant. Competition from older drugs appears to have a greater impact than that of more recently introduced products, perhaps because brand-name capital takes time to develop or because doctors have "sticky" prescribing habits.

[14] Market size and wealth have much greater effects when estimated on a sample of countries with more variance. See Kyle (2003).
[15] Source: Merck Manual.

The coefficients on the squared terms of the number of competitors are positive, indicating that the decline in expected profits is steeper when the number of competing drugs is low. This is to be expected: if each drug takes 1/N of the market, where N is the number of drugs, then moving from monopoly to duopoly typically entails a greater drop in per-firm profits than the difference between nine and ten competitors.

It should be noted that these results are also consistent with unobserved heterogeneity in the fixed costs of entry across firms where the order of entry into a market is determined by fixed costs. In other words, the 10^{th} entrant takes longer to get into the market not because profits are being competed away, but because the 10^{th} entrant has higher fixed costs than the 5^{th}, for example. Markets with many potential competitors experience more entry, which is consistent with the hypothesis that firms have heterogeneous costs. Such markets get more idiosyncratic draws from the distribution of firm fixed costs and therefore experience more actual entry in expectation.

Table 5 displays parameter estimates for firm and product characteristics included in Models 2-5. These coefficients are fairly robust across all specifications. Profits appear to be concave in the number of countries in which a drug has been launched. This result is consistent with firms introducing their products first in the most profitable countries, and with economies of scope from clinical trials or other data required for regulatory approval common to many countries. The probability of entry is increasing in its importance: the larger a drug's share of the citations in its therapeutic class, the more likely its launch.

More interestingly, the diffusion of a new drug depends largely on the characteristics of its originator. The percentage of correct predictions of entry increases from 31% to 58% when firm characteristics and interactions with market characteristics are included for models without country-class fixed effects, and from 51% to 64% for models with them. Experience in a country increases the likelihood of entry. On average, marketing three additional drugs in a country or an additional three years of marketing any drug in a country offsets the effect of competing with one additional drug. This suggests economies of scope in local distribution through familiarity with the regulator or the establishment of marketing and distribution forces, as well as firm reputation built up over many years of marketing in a country. However, it is impossible in this model to distinguish whether the firm has exogenously low fixed costs in a given country, and therefore introduces more products, or whether it achieves lower costs through economies of scope. Entry is less likely if the firm has a larger number of drugs in its portfolio or if it already markets a drug in the same country-therapeutic class market; these effects are of little economic significance.

Particularly striking is the importance of domestic status, even after measures of market experience are included. The probability of launch in the home country of the firm is 3.4 times greater than the average. A firm may have relatively low fixed costs in its domestic market for many reasons; perhaps it receives some favoritism by the local regulator, is allowed more generous pricing in the interest of keeping the domestic industry strong, or enjoys superior marketing ability in its native environment. Alternatively, domestic firms may be most familiar with the therapeutic needs of their home country, and therefore concentrate their drug development in those areas. Japanese firms have developed many of the antiulcer treatments available today in response to the local demand for such products, to continue with the example used earlier.

Similarities between a firm's home market and the target country seem to matter for the entry decision. Sharing a border and a language increases the probability of entry by 53% at the median of all continuous variables based on the estimates from Model 2, though the effect of a common regulatory structure is not estimated precisely.[16] In other words, these similarities provide almost half of the advantages associated with domestic status. These effects are present even for multinational firms. In specifications that include interactions of the multinational dummy with all other variables (not included to save space), the effect of a shared language or border for multinationals is one-third to one-half the size of the coefficient for small local firms, but still large and significant. The estimated home country advantage for multinationals is about 41% the size of that for local firms. Thus, even the largest pharmaceutical firms with a global presence prefer to stay as to close to home, in some sense, as possible. These effects are illustrated in Figure 3, which shows the predicted probability of entry for foreign firms with no shared language or border, multinational firms, "similar" firms, and domestic firms over the range of continuous firm-level variables and at the median of all market-level variables.

If firms have very different fixed costs of entry across markets, do they also have different impacts on the variable profits of their competitors? Some suggestive evidence of asymmetric competitive effects is provided in Table 8. Models 4 separates competition from domestic and foreign incumbents, and Model 5 includes interactions of these competition measures with the

[16] The importance of some variables differs from country to country. Results for specifications estimated by a drug's country of origin are available from the author, and are summarized as follows. The coefficients on domestic status in Italy and Japan are significantly larger than those for other countries. The effect of similarities in regulatory structure becomes clearer. Swiss, French, and Italian firms seek launch in free-pricing countries with a *different* regulatory structure than their home markets. US and UK firms, whose domestic markets lack price controls, seem to prefer similar free-pricing markets, and shared language or borders matter much less. However, examining this limited set of countries does mean that the coefficients on the "common" variables are driven by a small number of country-pairs and should be interpreted with some caution.

characteristics of the potential entrant. From Model 4, it appears that foreign incumbents have a more negative effect on variable profits than do domestic firms. This makes intuitive sense given the earlier results: if foreign firms face higher entry costs, then those that manage to enter probably do so with particularly high-quality drugs. However, not all potential entrants are affected the same way. The results from Model 5 indicate that domestic firms are far less affected by competition from other domestic firms than from foreign firms. There are a number of possible explanations for this pattern. If the set of drugs from foreign firms that are launched in a country is of higher quality than the set of drugs from domestic firms, then we might expect firms to differentiate strategically, as in Mazzeo (2002). This would imply that domestic firms would prefer to compete with foreign drugs and vice versa, to segment the market. However, especially in price-controlled countries, high quality drugs may not be permitted to charge higher prices, and such market segmentation may be impossible. Under those conditions, it is reasonable that the sales of lower quality drugs are more affected by the presence of many high quality competitors. The presence of many domestic incumbents may also be correlated with a regulator that favors domestic firms, so that many domestic incumbents signals especially low entry barriers to a domestic potential entrant. Alternatively, domestic firms may find it easier to collude with each other than with foreign firms. Addressing that possibility is beyond the scope of this paper, but may be interesting future research.

VI. Conclusion

This paper integrates predictions of economic theory with the views of strategic management in considering the relative impacts of firm and market characteristics on the entry patterns of pharmaceuticals. I find that expected profits decline in the number of competitors provided that market-specific demand is controlled for. Thus, results are consistent with predictions of industrial organization oligopoly models and the findings of previous studies of entry. Price controls are estimated to have a negative effect on entry, and drug characteristics are related to profits in expected ways. In addition, there is evidence of economies of scale in global production and economies of scope within a market. Firm characteristics, such as experience in a country and domestic status, are found to have an enormous bearing on the diffusion of a new drug.

While both market structure and firm/product characteristics have substantial effects on the entry pattern of a new drug, this research demonstrates that the interaction between them is crucial. Similarities between a firm's home market and a potential launch market greatly increase the probability of launch; a common border and language provides about half the advantage of

domestic status. In addition, the effect of incumbents on the launch decision of a potential entrant depends in part on whether both are domestic or have different origins. This is an important dimension of entry that most previous research has been unable to address.

There are several important implications for public policy from this research. The characteristics of most pharmaceutical markets point towards "too little" entry, so an understanding of the impediments to launch is important. For example, price controls appear to reduce the probability of a new drug's entry. The costs of deterring existing 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, these results demonstrate that domestic firms are able to access their local markets at a lower cost than are foreign firms. While it is possible that local firms develop treatments for local needs more efficiently than foreign firms, an industrial policy that favors the drugs of domestic firms may result in crowding out of superior foreign products. This research also demonstrates the importance of understanding local pharmaceutical markets. The match between an innovating firm and the local market appears to be a critical aspect of profitability. The findings suggest that there are gains from licensing to domestic firms or to firms with a large presence in a market.

These results indicate that there are important sources of competitive advantage that merit additional exploration. More information about pharmaceutical firms, such as their financial health, their patenting activities, and their licensing practices, would be very valuable. 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 examines the nature of competition in these markets may be appropriate.

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Table 1: 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 2: Summary Statistics

Number of drugs	1482
Number of firms	286
Number of therapeutic classes	134
Years covered	1980-1999
Number of markets (country-class-year observations)	13445
Number of entry opportunities (drug-country-class-year observations)	86755
Number of entry events	3445

Frequency	Variable	Definition	Obs	Mean	Std Dev	Min	Max
Drug-year	Drug importance	Drug's share of stock of Medline citations for class	18914	0.01	0.07	0	1
	Age	Number of years since drug's first launch anywhere	18914	8.26	5.17	0	15
	Number of countries launched in		18914	5.40	5.91	0	27
Firm	Multinational	Firm has launched drugs in 10+ countries	286	0.33	0.47	0	1
Firm-year	Portfolio	Total number of firm's drugs	4034	5.03	8.94	1	81
Firm-country	Domestic firm	All refer to the firm's country of headquarters and the target country	1982	0.11	0.31	0	1
	Common language		1982	0.12	0.33	0	1
	Common border		1982	0.11	0.31	0	1
	Common regulations		1982	0.36	0.48	0	1
Firm-country-year	Country experience	Count of firm's other drugs launched in country	23538	1.64	4.48	0	51
	Country-class experience	Count of firm's drugs in country-class market	23538	0.09	0.38	0	5
	Experience years	Number of years firm has marketed in country	23538	4.07	6.99	0	40
Country	Price controls	Country uses price controls	7	0.43	0.53	0	1
Country-year	Population	Population in 10s of millions	140	9.16	7.03	2.45	27.29
	GDP per capita	GDP per capita in US$1000s	140	17.09	5.20	7.84	31.94
Country-class-year	Number of new drugs in market	Count of drugs in market launched less than 5 years ago	13445	1.75	1.89	0	14
	Number of old drugs in market	Count of drugs in market launched more than 5 years ago	13445	2.88	3.84	0	34
	Number of potential competitors	Count of drugs launched in class elsewhere in the world	13445	9.49	8.37	1	66
	Number of domestic drugs in market	Count of drugs in market launched by firms headquartered in country	13445	1.15	1.86	0	18
	Number of foreign drugs in market	Count of drugs in market launched by firms headquartered in country	13445	3.63	3.97	0	30

Table 3: Years between launches in a country-therapeutic class market

	Years since last entry event	
Entry order	Mean	Std. Dev.
1	3.43	4.20
2	4.01	3.83
3	2.81	2.84
4	2.35	2.53
5	2.08	2.10
6	2.00	2.16
7	1.43	1.58
8	1.67	1.62
9	1.30	1.64
10	0.96	1.34

The first entry event in a market occurs an average of 3.43 years after the drug is first launched elsewhere, the second entry event occurs an average of 4.01 years after the first entry, etc.

Table 4: Parameter Estimates for Market Characteristics

	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
Included Fixed Effects	Year, Age, Class	Year, Age, Class	Year, Age, Class*Country	Year, Age, Class*Country	Year, Age, Class*Country
Explanatory variables	Country	Country, Firm, Country*Firm	Country, Firm, Country*Firm	Country, Firm, Country*Firm	Country, Firm, Country*Firm
Observations Used	80300	80300	80300	80300	80300
Log Likelihood	-11894.1431	-10328.8186	-9660.9739	-9674.7924	-9666.2711
Percent of correct no-entry outcomes	96.04	96.26	96.51	96.51	96.51
Percent of correct entry outcomes	30.56	57.07	64.18	63.94	65.73
Number of new drugs in market	0.066**	0.090**	-.155**		
	(0.023)	(0.024)	(0.029)		
N new drugs squared	0.000	0.000	0.008*		
	(0.002)	(0.003)	(0.003)		
Number of old drugs in market	0.034*	0.046**	-.224**		
	(0.015)	(0.016)	(0.022)		
N old drugs squared	-.001	-.001	0.004**		
	(0.001)	(0.001)	(0.001)		
Number of potential competitors	-.013**	-.016**	0.056**	0.051**	0.050**
	(0.005)	(0.005)	(0.006)	(0.006)	(0.006)
Population (10s of millions)	0.065**	0.041*	-.122	-.120	-.119
	(0.016)	(0.018)	(0.094)	(0.094)	(0.094)
Population squared	-.002*	-.001	0.010**	0.010**	0.010**
	(0.001)	(0.001)	(0.002)	(0.002)	(0.002)
GDP per capita ($1000s)	-.038	-.081**	-.041	-.063	-.061
	(0.020)	(0.021)	(0.040)	(0.041)	(0.042)
Price controls	-.046	-.214**	-.320*	-.219	-.229
	(0.042)	(0.045)	(0.163)	(0.161)	(0.161)

* = significant at the 5% level, ** = significant at the 1% level.

Table 5: Parameter Estimates for Firm Characteristics

	Model 2	Model 3	Model 4	Model 5
Included Fixed Effects	Year, Age, Class	Year, Age, Class	Year, Age, Class*Country	Year, Age, Class*Country
Explanatory variables	Country, Firm, Country*Firm	Country, Firm, Country*Firm	Country, Firm, Country*Firm	Country, Firm, Country*Firm
Observations Used	80300	80300	80300	80300
Log Likelihood	-10328.8186	-9660.9739	-9674.7924	-9666.2711
Percent of correct no-entry outcomes	96.26	96.51	96.51	96.51
Percent of correct entry outcomes	57.07	64.18	63.94	65.73
Country experience	0.020**	0.014*	0.013*	0.014*
	(0.006)	(0.006)	(0.006)	(0.006)
Experience years	0.020**	0.013**	0.013**	0.013**
	(0.004)	(0.005)	(0.005)	(0.005)
Country-class experience	-0.031	-0.052	-0.052	-0.073*
	(0.030)	(0.032)	(0.032)	(0.032)
Portfolio	-0.015**	-0.010**	-0.009**	-0.009**
	(0.003)	(0.003)	(0.003)	(0.003)
Drug importance	1.297**	1.232**	1.261**	1.253**
	(0.245)	(0.265)	(0.265)	(0.265)
Number of countries launched in	0.436**	0.468**	0.468**	0.468**
	(0.015)	(0.016)	(0.016)	(0.016)
Number of countries launched in squared	-0.012**	-0.012**	-0.012**	-0.012**
	(0.001)	(0.001)	(0.001)	(0.001)
Multinational firm	0.326**	0.398**	0.394**	0.398**
	(0.075)	(0.079)	(0.079)	(0.079)
Domestic firm	1.664**	1.981**	1.992**	2.053**
	(0.064)	(0.076)	(0.076)	(0.107)
Common language	0.347**	0.606**	0.608**	0.609**
	(0.066)	(0.079)	(0.079)	(0.079)
Common border	0.230**	0.072	0.070	0.056
	(0.064)	(0.075)	(0.074)	(0.075)
Common regulatory structure	0.010	-0.087	-0.084	-0.091
	(0.046)	(0.051)	(0.051)	(0.051)

* = significant at the 5% level, ** = significant at the 1% level.

Table 6: Parameter Estimates for Domestic vs. Foreign Competition

	Model 4	**Model 5**
Included Fixed Effects	Year, Age, Class*Country	Year, Age, Class*Country
Explanatory variables	Country, Firm, Country*Firm	Country, Firm, Country*Firm
Observations Used	80300	80300
Log Likelihood	-9674.7924	-9666.2711
Percent of correct no-entry outcomes	96.51	96.51
Percent of correct entry outcomes	63.94	65.73
Number of domestic incumbents	-0.098**	-0.110**
	(0.024)	(0.025)
Number of foreign incumbents	-0.138**	-0.131**
	(0.013)	(0.013)
Number of domestic incumbents *Domestic entrant		0.086**
		(0.027)
Number of foreign incumbents *Domestic entrant		-0.057**
		(0.016)

* = significant at the 5% level, ** = significant at the 1% level.

Figure 1: Distribution of the Number of Drugs in a Market, Selected Countries

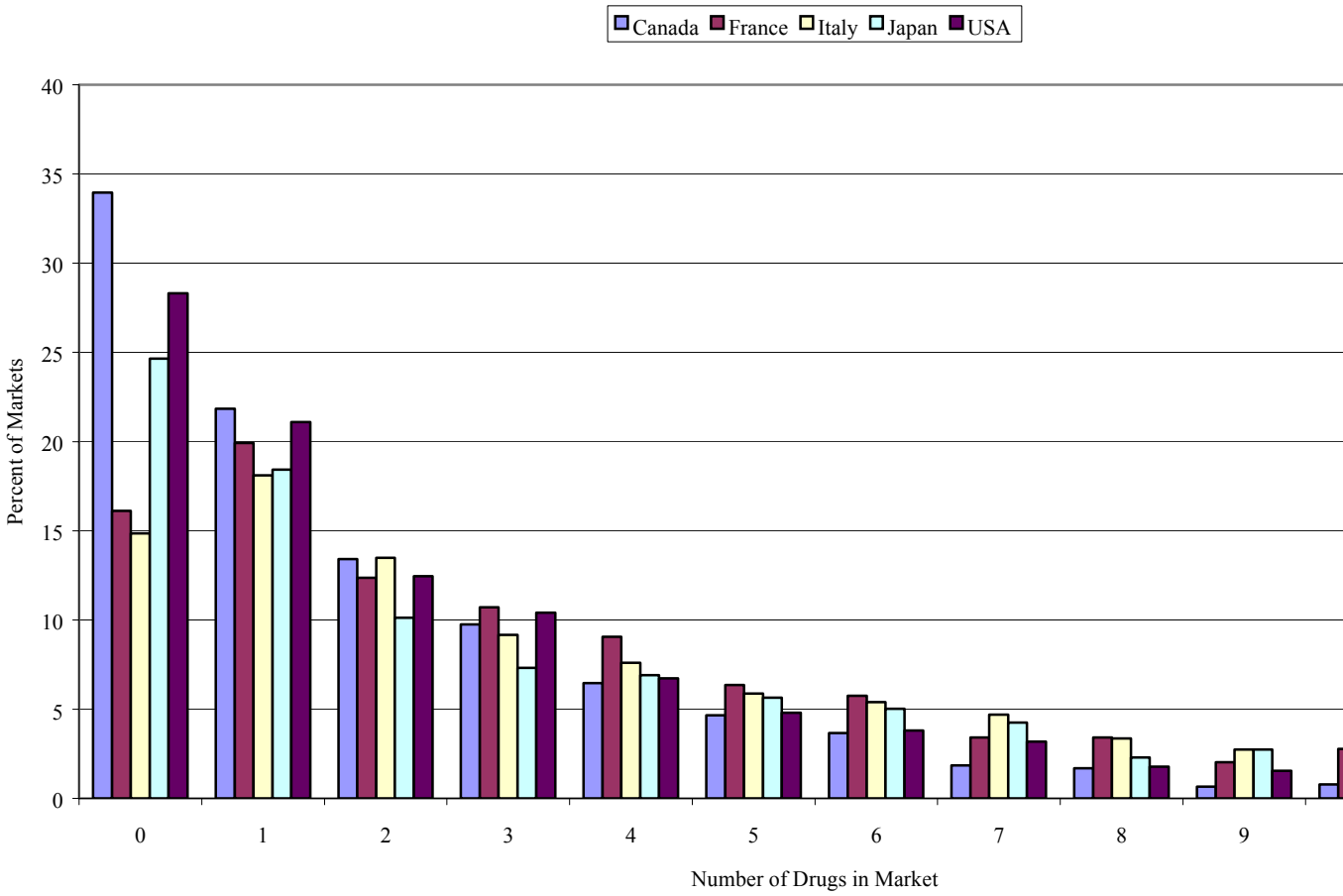


Figure 2: Launch patterns by age of drug

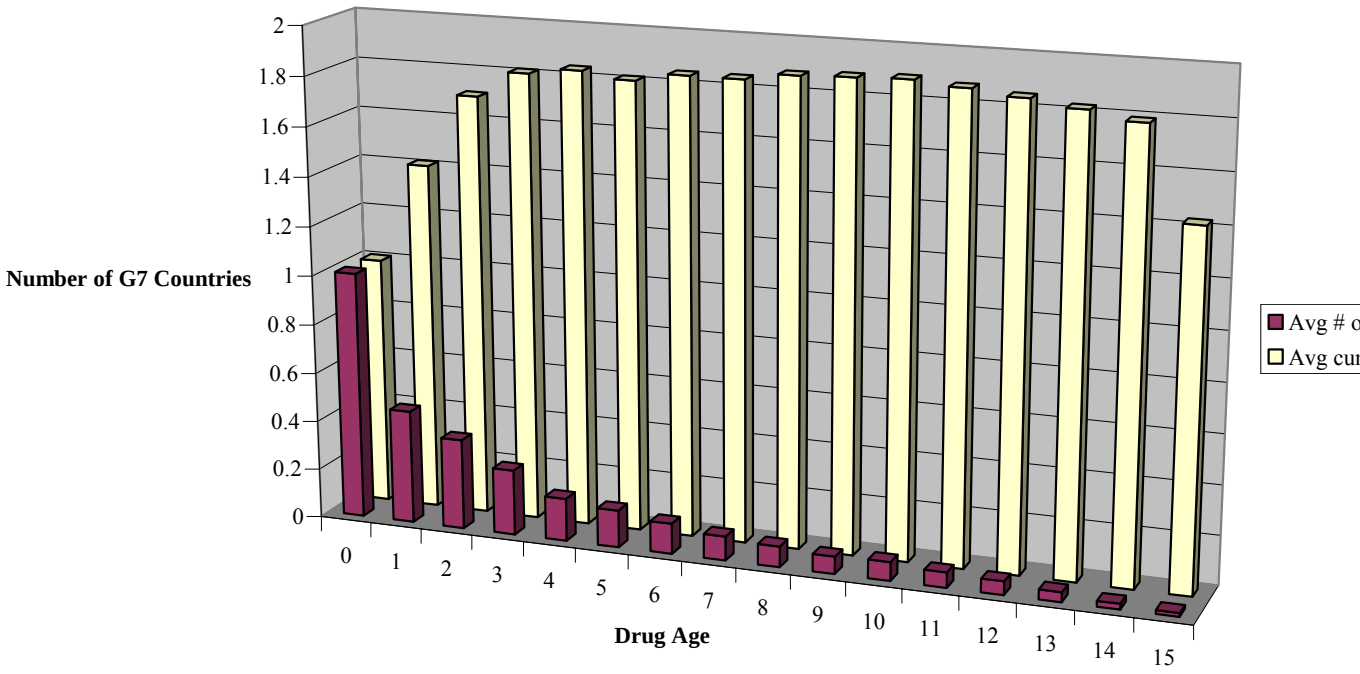
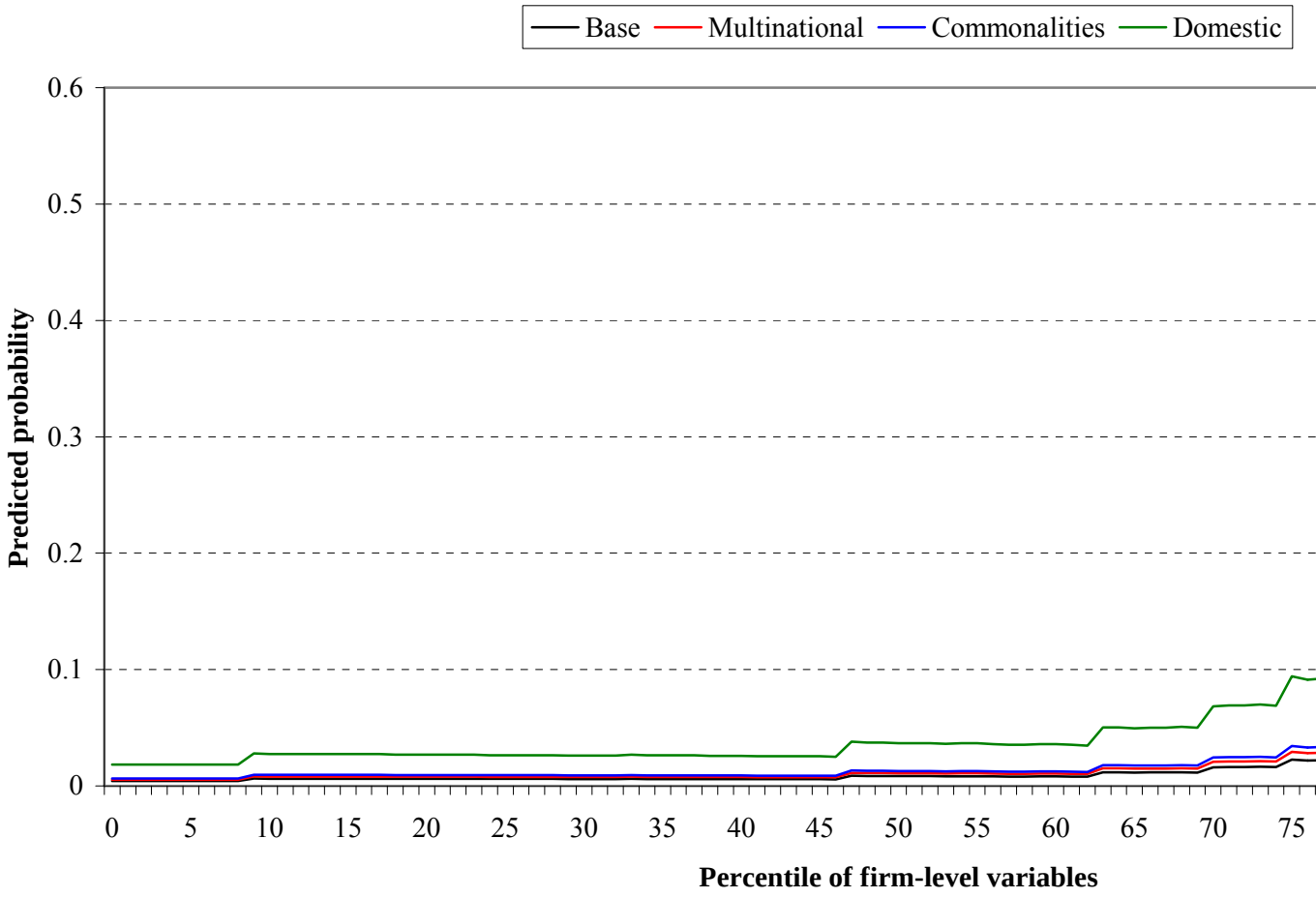


Figure 3: Predicted Probabilities of Entry Based on Firm Characteristics



Probabilities are calculated at the mean of all market-level variables.

Appendix: Construction of variables using MEDLINE citation data.

The description of MEDLINE from the National Library of Medicine website is as follows:

> MEDLINE is the NLM's premier bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the health care system, and the preclinical sciences. MEDLINE contains bibliographic citations and author abstracts from more than 4,000 biomedical journals published in the United States and 70 other countries. The file contains over 11 million citations dating back to the mid-1960s. Coverage is worldwide, but most records are from English-language sources or have English abstracts.

All MEDLINE citations that were classified as a clinical trial, meta-analysis, practice guideline, or randomized controlled trial, and pertained to humans, were downloaded from the National Library of Medicine website (http://www.ncbi.nlm.nih.gov/PubMed/) for 1965 through 2000, a total of 307,527 articles. To match the drugs in Pharmaprojects to the Medline data, the drug's generic name, chemical name, and its synonyms (such as brand names in different countries) were located in the title and abstract of citations, resulting in 764,384 drug mentions. For 81% of drug mentions, there is a field for the affiliation of the lead author; the geographic locations of the lead authors were identified from this field for all but ~1% of these mentions.

"Global drug importance" is defined as a drug's share of the stock of drug mentions for its therapeutic class from articles by foreign authors. The stock was computed using 5, 10, and 15% rates of depreciation; the results from the regression analysis are robust to the assumed rate (15% is the rate used for the reported results). The most class citations pertain to anticancers, anti-infectives, and antidiabetics. Not surprisingly, the anti-AIDS/anti-HIV therapeutic classes account for an increasing share of citations over time (about 10% in 2000).

In using this data, one must assume that a drug's importance is positively correlated with the number of studies and publications that refer to it, and that Medline's coverage is not biased towards a particular country. There are several unavoidable weaknesses. The measure of importance might reflect not therapeutic value but safety concerns, if a potentially dangerous drug is the subject of more studies. Large pharmaceutical firms may have more resources to devote to the funding of clinical trials that are published in Medline journals, thus biasing "importance" towards larger firms. Although the Medline database includes publications from more than 100 countries, its coverage is most complete for English-language journals, which could lead to an upward bias for the importance of drugs from English-speaking nations. Finally, it is possible that the search algorithm misses mentions of drugs in abstracts that are not in English or finds fewer matches if abstracts from non-English articles are often unavailable. These shortcomings are acknowledged, but alternative objective measures of drug importance are few.