New Drug Development:
Estimating entry from human clinical trials

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Abstract

This paper analyses a detailed data set on drugs in human clinical trials around the world between 1989 and 2002. The data provides information on the probabilities with which drugs successfully complete the different phases of the trials and the durations of successful completions. The paper shows that success rates and durations can vary substantially across observable characteristics of the drugs, including primary indication, originating company, route of administration and chemistry. It suggests that analysis of this type of data can help us to answer questions such as: Do AIDS drugs get to market faster? Do Biotech drugs have higher probabilities of getting to market? This paper provides some general statistics for analyzing these questions.

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I. Introduction

The dynamics of drug development is one of the defining characteristics of the pharmaceutical industry. Despite its importance to the industry, there is little information on how long it takes for particular drugs to go through human clinical trials and the probabilities of successful completion. Recently, a number of authors have started making use of historical data on the development of drugs through human clinical trials in the US and elsewhere in the world (for example, Abrantes-Metz, 2003, Kyle, 2002, Danzon et al, 2003). These authors are using this data examine determine the relationship between drug characteristics and successful durations, market entry, and the use of licensing arrangements, respectively. This type of historical data has the potential to provide industry analysts with a much clearer picture of late stage pharmaceutical development and new drug entry. The current paper presents some summary statistics on duration and frequencies of successful completion of the human clinical trials. While this analysis is not sophisticated or detailed enough to provide answers to many of the questions researchers and practitioners are interested in, it does provided readers with some stylized facts to guide future work.

The paper analyzes a sample of drugs that have entered human clinical trials somewhere in the world between 1989 and 2002. The data provides information on entry and exit dates from the three different stages of the human clinical trials for the first indication that the drug was being developed (post-1989). The data also provides information on drug characteristics such as primary indication, chemical composition, route of administration and originating company. The analysis provides frequencies with which drugs with different characteristics successfully complete the different stages of the human clinical trials. For example, drugs that have been originally developed by one of the 10 largest drug companies have a higher than average probability of getting to market. The analysis also provides mean durations for drugs that successfully complete the different stages of the human clinical trials. For example, AIDS drugs are in human clinical trials for an average of 5 years, which is 3 years shorter than the average drug in the sample. In general, the results presented should not be interpreted as causal effects of drug characteristics on success rates or successful durations. Rather these results should be interpreted as central tendencies or simply as statistical observations of the drug development process.

Analysis of drug development and new drug entry must address four major questions. First, do "important" new drugs get through the regulatory process quicker than other drugs? In the US, the FDA offers a number of programs aimed to encourage development of important life-saving drugs, including prioritizing drugs at registration and offering fast tracks through human clinical trials and registration for specified drugs (particularly AIDS drugs). According to the FDA, priority drugs that successfully complete the review process have significantly shorter durations than standard drugs (FDA, 2003). Dranove and Metzler (1994) analyze the FDA's role in drug development durations by analyzing successful duration from discovery to market for US drugs. The authors find that economic indicators seem to be more important in determining durations than "scientific" indicators. This paper and Abrantes-Metz (2003) use more detailed data on the durations and failure rates for drugs in human clinical trials. This paper analyses successful durations through human clinical trials and the governmental review process by primary indication and finds significant differences across different indications. In particular, AIDS drugs and cancer drugs tend to have shorter successful durations. Note that these results should be interpreted with care, as the drugs analyzed are going through different regulatory environments throughout the world.[1] Note also that we have not controlled for the actions of the drug companies and their ability to determine success rates and durations.

Second, are there economies of scale or scope in drug development? Graves and Langowitz (1993) find a positive relationship between R&D expenditures and the number of new chemical entities produced. In their analysis of ten large pharmaceutical firms, Henderson and Cockburn (1996) find a similar relationship between the number of new drug patents and development output. Danzon et al. (2003) find that success rates are increasing with the overall number of drugs the firm has in development and the number of drugs in the relevant therapeutic area.[2] As stated above, the results presented below suggest that drugs discovered by larger companies have a higher probability of getting to market. However, the results also show substantial heterogeneity in the success rates for some of the largest firms. This heterogeneity suggests that firms may have different strategies for investing in drug development.[3] While there may be

[1] See Kyle (2002) for a discussion of the differences across countries.

[2] Danzon et al (2003) discuss the influence that alliances and licenses have on drug development success rates.

[3] It is interesting to consider the similarities between expenditure on new drugs and the expenditure on motion

advantages for larger firms in bringing drugs from discovery to market, it is not obvious that such advantages would be observable. For example, a larger firm may choose a strategy of investing in high risk "blockbuster" drugs. Such a firm may be observed to have a low probability of getting drugs to market, yet may be a very successful company.

Third, what effect does the drug's expected market return have on the probability of success and the time to market? Dranove and Metzler (1994) find that drugs with higher US and World sales have shorter durations to market. Kyle (2003) compares drug entry across countries and indications and finds that the probability of market entry is positively related to market size. DiMasi (2001) reports the results of a survey of drug companies that sponsored drugs through human clinical trials. The survey found that for over 30% of the drugs, whose development was discontinued between 1981 and 1992, the sponsors cited "economic reasons" as the explanation for why development was discontinued. These results suggest that expected market return is an important determinant of success probabilities and durations. The results presented below show that the probability of entry tends to increase with market size, except for drugs destined for very large markets. It is not clear how to interpret such results. One issue is that companies do not randomly choose which drugs to develop, and simple risk/return analysis suggests that companies may try to develop drug with lower probability of getting to market if those drugs are expected to have a higher return. In fact, Danzon et al (2003) find that drugs with a higher expected return have a lower probability of getting to market and argue that this result is consistent with equilibrium behavior. The analysis presented in this paper is not detailed enough to account for such endogeniety issues. The results also show that drugs destined for larger markets tend to spend longer in development. This result seems as odds with our expectation; however it is again not obvious how such results should be interpreted given that durations are heavily influenced by the drug companies.

Fourth, how do the drug's characteristics affect success frequencies and durations? Dranove and Metzler (1994) have some information on how some characteristics affect durations. However, the data is not detailed enough to determine how characteristics affect particular phases of the human clinical trials. The analysis presented in DiMasi (2001) is similar to this paper, however it is done on drugs in

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pictures (Goettler, 2002).

development prior to 1995. A recent change in the industry has been the introduction of biotechnology drugs into human clinical trials. The results show that biotech drugs tend to have higher probabilities of getting to market although their average durations are similar to the average durations over all drugs. The results also suggest significant differences between drugs with different routes of administration (ROA). Oral drugs seem to be quicker to market but with a lower probability of successful completion of human clinical trials. This result is consistent with an equilibrium story that oral drugs have higher expected returns, however these results are not based on a structural estimation so should be interpreted with care. For example, it may simply be the case that it is easier to conduct trials on oral drugs.

The paper proceeds as follows. Section II presents a brief description of the drug development process. Section III describes the data used in the analysis, and provides definitions of the variables used. Section IV presents and discusses the results. Section V concludes.

II. Human Clinical Trials

The process of drug discovery to market can be decomposed into six distinct periods. The first period is commonly known as Preclinical. In general, after preclinical analysis, a company wishing to launch a drug on the US market, for example, files an Investigatory New Drug (IND) application with the FDA. If accepted, the drug goes into human clinical trials, which has three basic phases, called Phase 1, Phase 2 and Phase 3 (the second, third and fourth periods, respectively). An IND may be filled for one or more phases. Generally, the phases are completed sequentially and after the Phase 3 trials have been completed, a company wishing to launch a drug on the US market will file a New Drug Application (NDA) with FDA and move into the fifth period. A drug that passes FDA review successfully is registered in the "Orange Book". Once registered, the drug moves into the sixth period and the company can launch the drug on to the US market. A similar process occurs in other countries.[4]

In preclinical trials, the pharmaceutical company uses genetic analysis, pharmacological tools and "animal models" to test for the safety and the effectiveness of the drug for particular disease indications. Unfortunately, because the data set analyzed below is based on information that is voluntarily given to the

public by the drug's sponsor, the information on preclinical trials is not very accurate. Note that according to the FDA, only 1 in 1,000 drugs pass the preclinical stage and are proposed for testing in humans (FDA, 2002). However, almost half the R&D expenditures occur in the preclinical stage of development (Levy, 1999)

The first phase of the human trials is called Phase 1. Phase 1 trials are generally carried out on a healthy volunteer population of between 20 and 80. According to the FDA, "These studies are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness" (FDA, 2003). Phase 2 trials involve several hundred patients with the disease condition, and are designed to give an early indication of the drugs effectiveness. Phase 3 trials are larger with patient numbers between several hundred and a few thousand, and are designed to give information on the balance between safety and effectiveness (Levy, 1999).

III. Data

Pharmaprojects contains information on 27,987 new branded drug entities that have reached the late stage development from 1980 to 2002. For the purposes of this study, we limited the sample size to the 3,328 drugs that have entered either Phase I, or Phase II, or Phase III of the human clinical trials somewhere in the world for the first time since 1989.[5] Note that information on every stage of development is available for only a limited number of drugs. The data is based on information that is voluntarily provided by the pharmaceutical companies in the form of press releases and academic conferences. Table (1) in the appendix presents information on the number of drugs for which we have information on the different phases of development. Note that of the drugs for which the data

provides information on Phase 3, just less than half have no information on the previous phases. It is thus necessary to be careful about interpreting results for drugs in Phase 1 and Phase 2 as there may be

[4] See Kyle (2003) for discussion of the differences between the drug development process in different countries.
[5] Note that these trials may or may not be taken place in the U.S. under direct FDA supervision.

substantial self-selection bias in the sample.[6] Although not reported, the good news is that most of the censoring of earlier phases occurs in the earlier years of the study (prior to 1994) suggesting that the censoring is not necessarily related to the expected success of the drug, but related to the standard left censoring problem in duration data.[7]

The length of time in each phase is determined by the time between the entry date of the particular phase and the entry date of the next phase. However, for Phase 3, the entry date of the next phase is the date on which the drug was launched somewhere in the world (for the first time). It should be noted that this phase explicitly includes time spent in government review after the Phase 3 clinical trials have ended. The measure of "success" is the probability of completing each phase of development, where successful completion of Phase 1 is defined as entry into Phase 2, similarly for Phase 2. For successful completion of Phase 3, we assume entry on to the US market.[8]

A number of measures are used to provide some information related to the topics discussed in the introduction. In relation to the drug's importance, the major measure is the drugs indication. The indication of the drug is generally its "primary indication", which is defined as the indication for which the drug is further along in its development. Most drugs are taken through human clinical trials for one indication prior to being tested for other indications. However, it should be noted that in the U.S., for example, doctors are free to prescribe approved drugs for any indication. Given this, it may not always be the case that the drug is intended for its "primary indication".

The measure of company size is "Big Pharma". A drug is categorized as either being originally developed by a big pharma firm or a non-big pharma firm. The drug's firm is a big pharma firm if the

[6] We may therefore expect to see that the drugs in the sample have a higher probability of getting to market than the average drug which enters the particular phase.

[7] In general data from any particular time interval is going to have a "left" censoring and "right" censoring problem. Left censoring refers to the fact that some durations began prior to the beginning of the sample period. Similarly, right censoring refers to durations that end after the end of the sample period. In this case the interval is a lot larger than the average duration for each phase, meaning that the censoring shouldn't be too large of a concern for the phase duration statistics.

[8] We are assuming that the objective of every drug is to be launched on the US market, which may be overstating things and thus we are including drugs that have no intention of going to the US market thus biasing the probabilities downwards.

company's world revenue for 2001 was one of the top ten in the pharmaceutical industry. One concern with using a measure of revenue is that it is endogenously determined, with successful drugs getting to market and creating revenue for the firm.[9] In the results we also report success probabilities and successful durations by individual company for the 8 companies with the largest number of drugs in the data base. In the life of a drug from discovery to market, there are many companies that are involved in its development, human clinical trials and marketing. In the results presented below the only company discussed is the drug's "originator". This is the company, according to Pharmaprojects, that discovered the drug. However, it may not be the company that sponsors the drug through the human clinical trials or takes the drug on to the market.[10] One advantage of using the drug's originator is that to some extent it is exogenous to the likely success of the drug in human clinical trials, particularly as only 1 in 1000 drugs ever makes it from discovery to human clinical trials. A disadvantage is that the originator, particularly a small company, is likely to license the drug to a large company in order for the larger company to take the drug through the trials and on to the market. We therefore may be underestimating the advantage to a drug of being sponsored by a large firm.

The measure of market size is the current world revenue for the drug's therapeutic class and pharmacological description. For example, the market size for the arthritis drug, Celebrex, is equal to the world revenue for arthritis drugs based on the Cox-2 inhibitor. The market size is then categorized into five discrete groups. This is a very crude measure of expected return, particularly as it does not account for the number of drugs in the market.[11] Unfortunately, we don't have more direct measures of market size, such as the actual revenue earned by the drug. We also don't have any information on the cost of drug development.[12] However, one advantage of this measure is that it provides some indication of the market size for drugs that have not yet reached the market.

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[9] Thanks to an anonymous reviewer for pointing this out.

[10] See Danzon et. al (2003) for a discussion of how licensing arrangements are related to success rates.

[11] Kyle (2002) finds that it is important to account for the number of drugs in the market when looking at market entry probabilities. [11] For discussion of drug development costs please see DiMasi et. al. (2003).

[12] For discussion of drug development costs see DiMasi et. al. (2003).

Finally, the data provides a number of other measures of drug characteristics including the drug's route of administration and the drug's original material. The drug's route of administration is categorized by a number of degrees of specificity. For example, a pill is categorized as "alimentary", and then "oral". We report results as specifically as possible while having enough drugs in the category for sensible statistics. The drug's original material is similarly categorized, so a particular biotech drug may be categorized as "biological", and then "recombinant protein". We report the statistics at the highest category level.

Table (2) represents the number of drugs in each phase of development according to their company size, material, route of administration and market size. Since 1989, first time entry drugs number 1,796 for Phase I, 1,879 for Phase II, and 1,025 for Phase III. Of the 398 drugs that have been launched worldwide, only 217 of them have been launched into the US market. 1,465 of the 3,328 drugs in the sample have been withdrawn or discontinued from development.

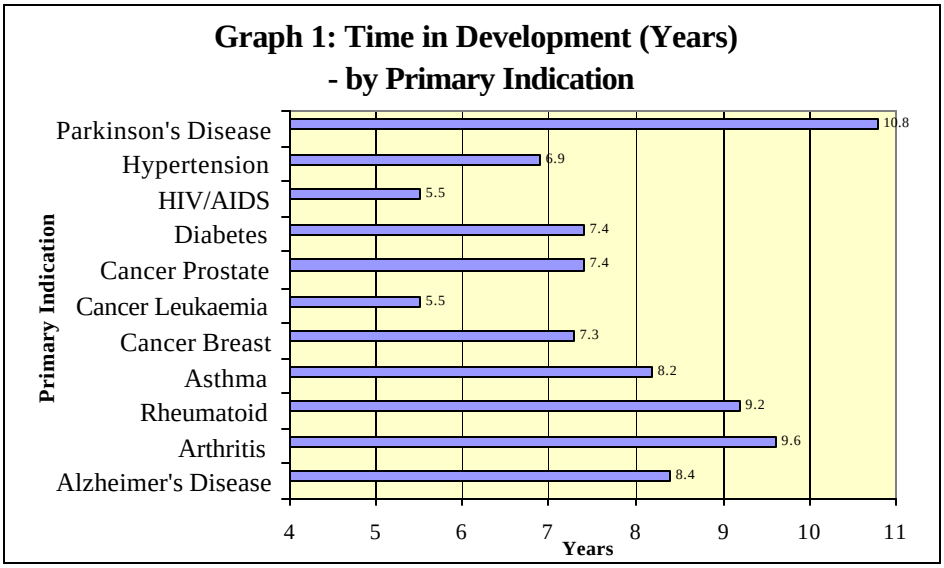
IV. Results

i) Do important drugs get to market faster?

In the US, the FDA has instituted policies that give pharmaceutical companies the opportunity to get "important" drugs to market. These policies include faster review of "priority" drugs and fast-tracking of human clinical trials for certain drugs. Priority drugs are defined by the FDA at the time of registration (generally after the completion of the Phase 3 clinical trials). The FDA also offers the opportunity for some drugs to shorten their time in human clinical trials and in this way, "fast-tracking" drugs to market. Time in development is calculated by adding together the average duration that drugs in the sample spend in each stage of development. On average, it takes just under 8 years for a drug to go from Phase I of human clinical trials to market launch in the US. The same figures for Phase II and Phase III drugs are 6.1 and 3.7 years respectively. More specifically, an average drug spends 1.7 years in Phase I, 2.4 years in Phase II, and 3.7 years in Phase III before launch.

Graph 1 presents a graph showing the estimated duration for the drugs in the data set by their primary indication. While it takes just 5.5 years on average for HIV/AIDS drugs to get from Phase I to the market, it takes drugs for Parkinson's disease almost twice that long to go through the same process. Drugs

for arthritis also spend more than 9 years, and asthma drugs spend more than 8 years in clinical trials on average. HIV/AIDS, anti-hypertension, and leukemia cancer drugs are some drugs that spend less than 7 years in clinical development. Again, this result is suggestive, but more sophisticated analysis is necessary to determine whether more important drugs get to market faster, and why.



ii) Are there economies of scale or scope in drug development?

While the data and the analysis is not nearly detailed enough to get at this question, we can present some summary statistics on the relationship between firm size (as measured by revenue) and success probabilities and successful durations. The probabilities are calculated by multiplying together the estimated probabilities of a drug moving from one particular stage in development to the next stage. The method of calculation can be expressed by the following equation:

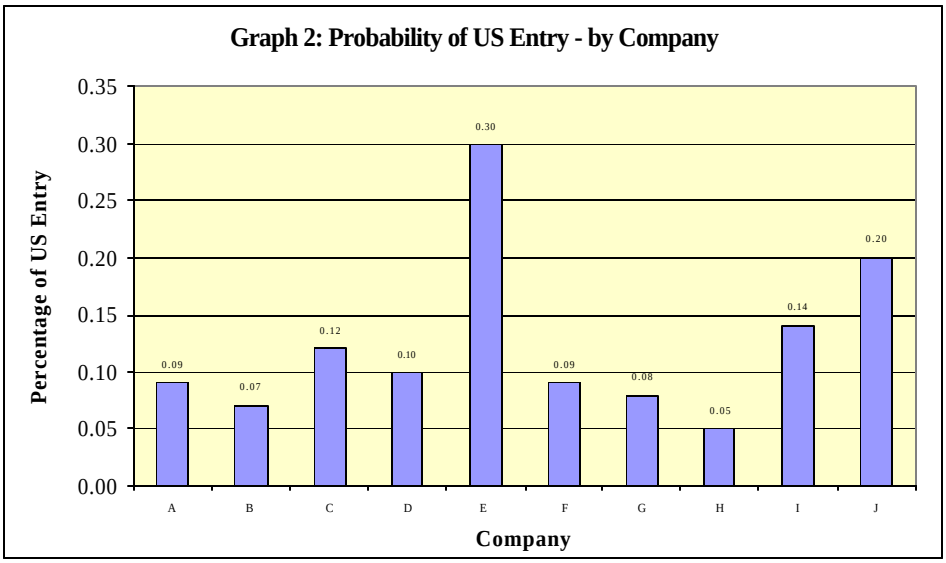
Pr (Launch=1|Phase I=1) = Pr (Launch=1|Phase III =1) x Pr (Phase III=1|Phase II=1) x Pr (Phase II=1|Phase I=1)

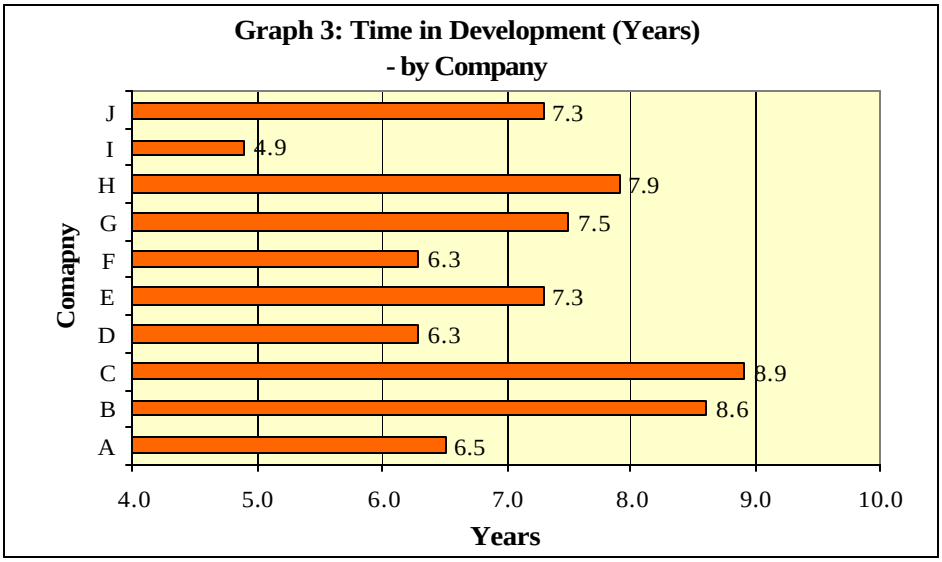
In words: probability of drugs being launched onto the market when they enter Phase I equals the product of the probability of drugs getting from Phase I to Phase II multiplied by the probability of the drugs in Phase II advancing to Phase III, multiplied by the probability of drugs in Phase III being launched onto the US market.

The reason behind this method is that information on all stages of clinical development is available for only a limited number of drugs. By studying this group of drugs exclusively, we would significantly reduce the sample size, and thereby, potentially exclude important information. Instead, we calculate the probabilities of the drugs in each phase of development getting to the next phase from the time they entered Phase I clinical trial until their launch to the market, and then multiplying the results together. The probabilities of drugs moving from a particular stage to the next are calculated using the number of drugs that have advanced to the next stage as numerator, and the sum of drugs that have been suspended, withdrawn or discontinued from that particular stage, or moved on to the next stage as the denominator. Drugs that are still active in that particular stage of development are not used in this calculation.

The results presented in Tables (4) through (9), show that drugs originally developed by Big Pharma firms are more likely to get to market, especially from Phase 3, where Big Pharma drugs have a 47% probability of getting to market, compared to 36% for non-Big Pharma drugs. Tables (5) and (6) show that this pattern holds for particular types of drugs such as drugs indicated for arthritis and drugs indicated for hypertension. In regards to successful durations, overall Big Pharma drugs are slightly quicker to market, but this pattern does not hold for the two subsets of drugs presented in Tables (8) and (9). We should be very careful interpreting such results as suggesting that that there are economies of scale or scope in pharmaceutical development, given both the discussion above on endogeniety and the heterogeneity in both success rates and successful durations for some of the larger companies.

Graphs (2) and (3) suggest that different companies may have different strategies in relation to drug development. It is particularly noteworthy that drugs from Company H have the lowest probability of getting to market, just 5% from Phase 1, and one of the longest successful durations at almost 8 years. On the other hand drugs invented by Company E have very high probabilities of entering the US market at 30% from Phase 1. Again these types of statistics are simply suggestive. We cannot conclude that the heterogeneity is due to such development strategies. We can however conclude that it will be difficult to empirically estimate economies of scale or scope given that company specific development strategies may influence observed probabilities of success.

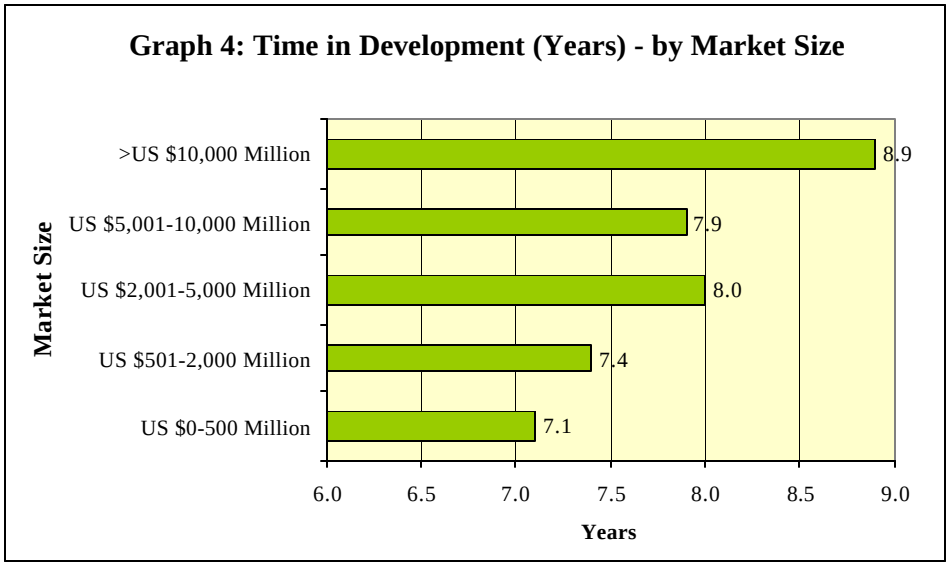




iii) What effect does the drug's expected market return have on success probabilities and durations?

The results presented in Table (4) show that as market size increases from less than $500 million to less than $10 billion, the probability of successfully completing each phase is generally increasing. Drugs with a market size of less than $500 million have just over a 1 in 4 chance of getting to market from Phase 3, while

drugs with markets between $500 million and $2 billion have a almost 1 in 2 probability of getting to market. However, the overall picture is far from clear. There are 100 drugs in Phase 1 that have a market size as being over $10 billion, of these drugs only 4 have reached the market in the US. Tables (5) and (6) present the success rates on two subsets of drugs, those indicated for arthritis and those indicated for hypertension. Arthritis drugs associated with a market size over $5 billion have a less than average probability of getting to market, while similar hypertension drugs have a greater than average probability of getting to market. Finally, it is not clear how to interpret such success rates as in equilibrium we would expect a negative relationship between expected return and successful probabilities (Danzon et. al., 2003).



In regards to successful durations, Graph (4) shows that time in development is generally increasing in market size, with large market drugs taking almost 2 years longer to get to market than small market drugs. The results presented in Tables (8) and (9) shows that this pattern also seems to hold for the two subsets of drugs (arthritis and hypertension). It is again not clear how to interpret such statistics given that companies decide whether or not to end development and how much to spend on continued development, based on their expectation of market return.

iv) What effect do drug characteristics have on success rates and successful durations?

Table (4) presents the success rates in regards to US entry from different phases of development for different categories of route of administration and different original materials. In regards to route of administration, oral drugs seem to have a relatively high probability of getting to market, but drugs delivered by subcutaneous injection have an even higher probability of getting to market. At more general category levels there is not much different between success rates for alimentary drugs and parenteral drugs (injections). In regards to original materials, biologicals seem to have higher success rates than other types of drugs. The most interesting result from Tables (5) and (6) is that almost all intravenous drugs get to market for arthritis, while no intravenous drugs get to market for hypertension. Similarly, a high percentage of biological drugs get to market for arthritis, while there is only one biological in the sample that has been developed for hypertension and that drug did not get passed Phase 1.

Table (7) presents the time in development for drugs with different characteristics. The table shows that drugs that would be relatively easy to administer, including orals, respiratory and transdermal (for example patches), are quicker to market than drugs delivered by injection. In particular, drugs delivered by intramuscular injection take over 9 years to get from Phase 1 to market, while transdermal drugs take less than 7 years to get from Phase 1 to market. It is not clear whether these results indicate that drugs with higher returns will get to market quicker or whether it is simply easier to conduct human clinical trials when drugs have particular routes of administration.

V. Conclusion

Drug development is one of the salient characteristics of the pharmaceutical industry. However, it is not an area of the industry for which we have a lot of information. Recently, a number of authors have started to make use of data on success rates and durations for human clinical trials (Abrantes-Metz et. al., 2003, Danzon et. al., 2003, and Kyle, 2002). This study analyzes the probability of success and the length of successful durations for 3,328 branded drugs that had entered either Phase I, Phase II or Phase III of the human clinical trials somewhere in the world between 1989 and 2002. Our basic summary is that approximately 1 in 8 drugs that entered Phase I are launched on the US market.[13] On average, this part of

[13] Our probability estimate is much lower than the FDA's. This is probably because the sample includes drugs that

the development process takes just under 8 years. This number is close to the FDA's own figure of 8.5 years in their tracking U.S. human clinical trials (FDA, 2002). The complete process of getting a drug to the market can be substantially longer. Bosch and Lee (1994) report that it takes a total of 12 years to get a new drug approval from the FDA. We excluded the preclinical period from our analysis since the Pharmaprojects data set is based on public information, and so focuses on drugs that have already made it to the late stage development.

There four major questions, that studies like this one, may be able to answer. Do more important drugs get to market quicker? Are there economies of scale or scope in drug development? What effect does the expected return have on the drug's development? What effect do characteristics of the drug have on the drug's development? We do find that HIV/AIDS drugs get to market quicker than the average drug. We find that drugs originally developed by the 10 largest pharmaceutical companies have slightly lower probabilities of US entry from Phase I, but spend substantially less time in all clinical development phases than the average drug. Drugs with the potential for extremely lucrative markets of US $10 billion or more tend to spend more time in development, and have a lower probability of actually reaching the market. Biological drugs have some what higher probabilities of making it to the US market, but this may vary across indications.

The results give, at best, partial answers to these questions. In some cases the results seem unintuitive, but as discussed above, answering these questions is quite complicated and requires careful analysis of these newly available data sets. It is hoped that the results discussed above increase our knowledge of the industry and create interest in more sophisticated econometric analysis such as that presented in Abrantes-Metz et al. (2003).

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were never intended for the U.S. market.

REFERENCES

Abrantes-Metz R.; Adams C. & Metz A. (2003). Pharmaceutical Development Phases: a Duration Analysis. The Federal Trade Commission.

Bosch, J. & Lee, I. (1994). Wealth Effects of Food and Drug Administration (FDA) Decisions. *Managerial and Decision Economics*, vol.15, 589-599.

Danson, P.; Nicholson, S. & Pereira, N. (2003). Productivity in Pharmaceutical-Biotechnology R&D: The role of experience and alliances. *National Bureau of Economic Research (NEBR) Working Papers*, no. W9615, April 2003.

DiMasi J.; Hansen, R. & Grabowski, H. (2003) The Price of Innovation: New estimates of drug development costs. *Journal of Health Economics*, forthcoming.

DiMasi J. (2001) Risks in New Drug Development: Approval success Rates for Investigational Drugs. *Clinical Pharmacology & Therapeutics*, May 2001, 297-307.

Dranove, D. & Meltzer, D. (1994). Do Important Drugs Reach the Market Sooner? *The RAND Journal of Economics*, vol.25, issue 3, 402-423.

FDA (2003). New Drug Approval Reports. http://www.fda.gov/cder/rdmt/default.htm.

FDA (2002), The FDA and the Drug Development Process: How the FDA insures that drugs are safe and effective, FDA Fact sheet.

Goettler, R. and Leslie, P. (2002). Movie Co-Financing. Stanford Business School.

Graves, S. & Langowitz, N. (1993). Innovative Productivity and Return to Scale in the Pharmaceutical Industry. *Strategic management Journal*, Vol. 14, Issue 8, 593-605.

Henderson, R. and Cockburn, I. (1996). Scale, Scope, and Spillovers: the determinants of research productivity in drug discovery. *RAND Journal of Economics*, Vol. 27, Issue 1, 32-59.

Kyle, M. (2002). Entry in Pharmaceutical Markets. Carnegie Mellon University, Dec. 2002.

Levy, R. (1999). The Pharmaceutical Industry. A Discussion of competitive and antitrust issues in an environment of change. *Bureau of Economics Staff Report*, Federal Trade Commission. March.

APPENDIX

Table 1: Drugs That Appear in Each Phase of Development

	Number	**Percent**
Phase 1 only	931	28%
Phase 2 only	786	24%
Phase 3 only	466	14%
Phase 1 and Phase 2 only	586	18%
Phase 1 and Phase 3 only	52	2%
Phase 2 and Phase 3 only	280	8%
Phase 1, Phase 2 and Phase 3	227	7%
Total	3328	100%

Table 2: Number of Drugs by Category

	Phase 1	Phase 2	Phase 3	US Launch	World Launch	Ceased
Big Pharma	268	304	176	60	80	339
Non Big Pharma	1528	1575	849	157	318	1126
Material						
Biologicals	450	387	187	43	81	165
Chemicals	932	1046	664	159	279	612
Natural Products	66	80	60	13	21	44
ROA						
Alimentary	403	487	372	103	161	222
Parenteral	492	539	323	76	141	219
Respiratory	48	56	21	5	9	29
Topical	64	68	71	22	38	37
Transdermal	28	28	26	5	9	22
Novelty						
Not Available	931	944	353	21	31	1465
All Preclinical	4	2	2	0	0	0
Established Strategy	178	210	212	74	153	0
New Formulation	84	104	115	29	57	0
Low Novelty	56	22	5	0	0	0
2nd, 3rd or 4th Compound	156	139	59	0	0	0
Leading Compound	387	459	279	93	157	0
Market Size						
US $0-500 Million	169	206	121	20	41	157
US $501-2,000 Million	521	581	330	94	144	436
US $2,001-5,000 Million	694	647	339	64	123	487
US $5,001-10,000 Million	230	259	123	28	58	222
> US $10,000 Million	138	154	91	7	22	141
Drug Age (Years)	**12.8**	**13.9**	**15.4**	**15.9**	**16.2**	**15.9**
(Standard Deviation)	(5.0)	(5.0)	(5.4)	(5.7)	(5.1)	(4.4)
N	**1796**	**1879**	**1025**	**217**	**398**	**1465**

Table 3: Primary Indication - Number of Drugs by Category

		Phase 1	Phase 2	Phase 3	US Launch	World Launch	Ceased
Alzheimer's Disease		22	31	13	2	2	26
Arthritis Rheumatoid		29	34	11	5	6	15
Asthma		42	49	18	4	8	29
Cancer							
	Breast	34	34	17	3	9	17
	Leukemia	15	22	9	5	6	12
	Lung	34	34	10	0	1	9
	Prostate	16	19	12	3	3	2
Diabetes		39	39	21	6	7	14
Hepatitis		26	21	11	3	7	6
HIV/AIDS		46	58	29	14	15	36
Hypertension		29	41	41	10	23	26
Parkinson's Disease		19	20	12	4	5	8
Thrombosis		28	31	17	4	8	23
N		**1796**	**1879**	**1025**	**217**	**398**	**1465**

Table 4: Probability of US Entry of Clinically Developed Drugs from Phase of Development (Number of Drugs in the Sample)

		Phase 1	Phase 2	Phase 3
All Drugs		**0.12**	**0.17**	**0.38**
		(1366)	(1218)	(542)
Big Pharma		**0.10**	**0.17**	**0.47**
		(217)	(219)	(127)
Non Big Pharma		**0.12**	**0.17**	**0.36**
		(1149)	(999)	(415)
Biologicals		**0.25**	**0.31**	**0.53**
		(309)	(218)	(75)
Chemicals		**0.19**	**0.25**	**0.45**
		(725)	(664)	(343)
Natural Products		**0.18**	**0.23**	**0.37**
		(50)	(45)	(30)
Alimentary		**0.28**	**0.34**	**0.51**
		(301)	(308)	(200)
	Oral	**0.29**	**0.35**	**0.51**
		(290)	(296)	(197)
Parenteral		**0.28**	**0.32**	**0.49**
		(405)	(343)	(147)
	Intravenous	**0.30**	**0.34**	**0.48**
		(209)	(195)	(86)
	Subcutaneous	**0.43**	**0.45**	**0.61**
		(43)	(39)	(18)
	Intramuscular	**0.39**	**0.45**	**0.69**
		(36)	(23)	(13)
Respiratory		**0.17**	**0.25**	**0.67**
		(36)	(27)	(6)
Topical		**0.27**	**0.37**	**0.50**
		(49)	(38)	(42)
Transdermal		**0.13**	**0.21**	**0.44**
		(23)	(17)	(9)
US $0-500 Million		**0.09**	**0.13**	**0.26**
		(133)	(128)	(69)
US $501-2,000 Million		**0.16**	**0.23**	**0.47**
		(418)	(391)	(186)
US $2,001-5,000 Million		**0.13**	**0.19**	**0.40**
		(506)	(400)	(159)
US $5,001-10,000 Million		**0.09**	**0.14**	**0.44**
		(178)	(172)	(64)
> US $10,000 Million		**0.04**	**0.06**	**0.13**

	(100)	(110)	(55)

Table 5: Probability of US Entry from Phase of Development (Number of Drugs in the Sample) - Arthritis*

	Phase 1	Phase 2	Phase 3
All Drugs	**0.30**	**0.36**	**0.61**
	(42)	(34)	(18)
Big Pharma	**0.43**	**0.57**	**1.00**
	(4)	(7)	(4)
Biologicals	**0.60**	**0.67**	**1.00**
	(20)	(12)	(3)
Chemicals	**0.24**	**0.32**	**0.62**
	(21)	(21)	(13)
Orals	**0.32**	**0.35**	**0.56**
	(11)	(16)	(9)
Intravenous**	**0.83**	**0.83**	**0.83**
	(9)	(4)	(6)
Large Market	**0.19**	**0.29**	**0.50**
	(12)	(12)	(10)

*By any Indication

** All Drugs Went Through Clinical Phases of Development

Table 6: Probability of US Entry from Phase of Development (Number of Drugs in the Sample) - Hypertension*

	Phase 1	Phase 2	Phase 3
All Drugs	**0.22**	**0.28**	**0.46**
	(34)	(41)	(28)
Big Pharma	**0.27**	**0.38**	**0.57**
	(7)	(6)	(7)
Biologicals**	**0.00**	**0.00**	**0.00**
	(1)	(0)	(0)
Chemicals	**0.25**	**0.32**	**0.46**
	(28)	(34)	(14)
Orals	**0.29**	**0.35**	**0.52**
	(17)	(27)	(16)

Intravenous**	**0.00**	**0.00**	**0.00**
	(5)	(6)	(2)
Large Market	**0.30**	**0.37**	**0.58**
	(25)	(31)	(19)

*By any Indication

**No Drugs Have Made to the Market

Table 7: Time in Development (Years)

		Phase 1	Phase 2	Phase 3
All Drugs		7.8	6.1	3.7
Big Pharma		7.1	5.5	3.4
Non Big Pharma		8.0	6.4	3.9
Biologicals		8.0	6.4	3.7
Chemicals		7.7	6.1	3.7
Natural Products		7.3	5.5	3.9
Alimentary		7.5	5.8	3.5
	Oral	7.5	5.8	3.5
Parenteral		8.2	6.6	4.0
	Intravenous	7.9	6.3	3.7
	Subcutaneous	8.7	7.1	4.2
	Intramuscular	9.2	7.4	4.6
Respiratory		6.7	5.1	3.3
Topical		7.7	6.4	4.5
Transdermal		6.8	4.9	2.9
N		**1796**	**1879**	**1025**

Table 8: Time in Development (Years) - Arthritis**

	Phase 1	Phase 2	Phase 3
All Drugs	7.9	6.4	3.7
Big Pharma	8.3	6.9	3.8
Biologicals	5.8	4.5	2.1
Chemicals	9.2	7.1	4.4
Orals	8.4	6.5	3.5
Intravenous	NA*	NA*	4.3
Large Market	9.5	8.0	4.8
N	**55**	**63**	**31**

**By any Indication

* Number of observations is insufficient for calculation

Table 9: Time in Development (Years) - Hypertension**

	Phase 1	Phase 2	Phase 3
All Drugs	7.3	6.4	3.2
Big Pharma	7.5	6.4	3.2
Biologicals	NA*	NA*	NA*
Chemicals	7.3	6.5	3.2
Orals	6.4	5.6	3.2
Intravenous	NA*	NA*	NA*
Large Market	7.1	6.4	3.4

N	**35**	**50**	**47**

**By any Indication

* Number of observations is insufficient for calculation