Strategic R&D Investment Decisions in the Pharmaceutical Industry

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October 22 2015

Abstract

Do pharmaceutical firms respond to the actions of their competitors in R&D, and how much? Answering this has implications on the impact of a faster FDA approval process - something pharmaceutical companies are pushing for. While a faster approval process leads to quicker realization of profits and more remaining time on the firm's patent, it also intensifies competition reducing per-firm profits. Which effect dominates depends on the degree of competition. To this end, I estimate a dynamic investment model using Phase-3 data. Solving the new equilibrium, I find an expedited process is beneficial only when competitors are far from launching.

1 Introduction

Pharmaceutical firms spend a significant portion of their time and investment in the research phase testing and proving the safety and efficacy of their drugs. The profits are realized only upon launch of the product, so drugs which fail part way through the process generate no revenues to offset the substantial costs accumulated over the development process. Finally, unlike most industries, even after significant investment and results the launch of a firm's product in a market is not certain. This is because the Food and Drug Administration (FDA), the regulatory authority that oversees the entire R&D testing, can approve or reject a firm's petition to launch in the market. The outcome of this regulatory process is fairly uncertain with unpredictable review times.[1] Pharmaceutical firms view this process as delaying marketing of their new drugs and deterring innovation.[2] This effect is further exacerbated by the short remaining patent life of most drugs.[3]

Many firms, investors and industry lobbyists have repeatedly called for a faster FDA approval process. However, it is unclear if this is necessarily beneficial for firms. From the perspective of a focal firm, an early launch is beneficial because 1) the firm gets more years on its patent to market the drug and 2) profits are realized sooner. However, the possibility of an early launch makes the market lucrative to other firms as well, potentially leading to a more crowded market reducing the focal firm's profits.[4] Thus, while a faster approval process can increase the NPV of profits, it can also intensify competition among firms leading to lower per-firm profits. Which effect dominates depends on the extent to which firms are impacted by competition. The theoretical literature does not provide a clear direction of this impact: on one hand competition can encourage innovation if the potential innovator is able to usurp market share from the incumbent with its new product but on the other hand the presence of competition can deter the incentive to innovate if the potential innovator is able to take only a share of the total industry profits.[5]

Using observed data to empirically measure this impact is hard because observed market structure and innovation rates are equilibrium responses and hence co-determined. The ideal way to measure the impact of competition on innovation is by observing market structure change due to exogenous reasons. Empirical work that uses this strategy include Aghion

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[1]Firms quote this uncertainty as a disclaimer in their forward-looking press release statements.

[2]For example "In recent years, Mr Pharma will complain, the FDA's approval process has become slower", Big Pharma's gripes about the FDA, Economist, July 2011 and "FDA approval of new products is deterring new investment in innovation," Medtronic chief rues US approval process, Oct 2011, Financial Times

[3]Grabowski and Kyle (2007) estimate that market exclusivity periods range from 10-15 years, compared to the 20-year patent term awarded

[4]This is similar to a lowering of the entry threshold described in Bresnahan and Reiss (1991)

[5]See Gilbert (2006) for a review of the theoretical and empirical literature on competition and innovation.

et al. (2004) who use changes in market structure caused by government policy changes and MacDonald (1994) who uses changes in import policies. However, exogenous variation of market structure in most industries is scant. For example, Cockburn and Henderson (1995) using detailed investment data at the drug discovery level find that investment is weakly correlated across firms after controlling for technological opportunity. However, as they point out, this could be the case simply because observed investments are equilibrium responses. This calls for a structural model that endogenizes market structure and innovation taking into account industry-specific features (e.g., Goettler and Gordon 2011). I use both approaches to measure this impact, relying on the structural parameters to evaluate the counterfactual of a faster FDA approval process.

First, I exploit the unique feature of the pharmaceutical industry - the uncertainty of the FDA approval process – to measure if firms respond to competitors' states. While firms might know the average approval probabilities in expectation, the exact outcome of the FDA review process is uncertain, i.e. FDA approvals and rejections conditional on filing are fairly exogenous. Using this in a reduced form regression, I find evidence that firms respond to competitors' states and competition has a negative impact on investment: specifically, a firm's probability to continue investment decreases if the firm's competitor received an FDA approval and increases if the competitor received an FDA rejection.

Second, I build a structural model that accounts for the endogeneity of market structure and innovation. Using a dataset on firm entry, continuation and exit decisions in Phase 3 clinical trials across different markets in the pharmaceutical industry, I estimate a structural model to measure the impact of competition on firms' continuation decisions. The structural model takes four main aspects of the pharmaceutical industry into account: the forward-looking behavior of firms, their strategic decision making, market heterogeneity and the uncertainty of the FDA approval process. As firms incur huge costs in the research phase which can take up to 10-12 years and as profits are realized only upon successful launch of the product, it is the forward-looking nature of firms that justifies investing large amounts in the research phase. Thus it is important to account for dynamics to model this industry. Second, the model should be able to account for equilibrium responses of firms. For example, a firm may exit a market while in the research phase if it observes that one of its competitors has launched. This is because if the share of profit of the focal firm decreases with the number of launched firms it no longer justifies continued investments in the research phase. Third, one needs to account for the fact that some markets can be more lucrative than others by accommodating the presence of unobserved heterogeneity in markets. Lastly, the launch outcome is not determined by the firm but by the FDA review process. I thus estimate a dynamic oligopoly model allowing for unobserved heterogeneity.

I estimate the model using the underlying approach outlined in Arcidiacono and Miller (2011). The estimation recovers two types of markets and the estimates indicate a significant and negative impact of competition on firms' investment decisions. Using these estimates, I then solve for the dynamic equilibrium under a faster approval process. I simulate the effect of a faster FDA approval process by reducing the probability that a drug remains in-review but keeping overall approval and rejection rates the same.

The results indicate an expedited approval process is beneficial only when competitors are far from launching. Compared to the current regime, a faster approval process can be disadvantageous (in terms of firm profits) if competitors are close to launching. The intuition behind these findings is that under an expedited approval process, a competitor that has filed launches sooner, reducing the focal firm's access to monopoly profits.

I also find that ignoring these strategic considerations in R&D leads one to misleadingly conclude an expedited approval process is always beneficial: the expected value of filing after R&D investment is overestimated by as much as 120%-443%.

1.1   Contribution

Empirical work studying competition in the pharmaceutical industry has focused largely on the impact of competition from generic entry on branded drugs' pricing and advertising levels (e.g., Caves et al. 1991, Ching 2010, Ellison and Ellison 2011). However, little research exists on firm strategic behavior *prior* to the launch stage when firms' products are not yet in the market. This paper finds evidence suggesting strategic behavior in the pre-launch stage and investigates the implications of such strategic effects on the implementation of an expedited approval policy.

This paper is also closely related to the literature studying innovation and investment levels in a competitive environment using the Ericson and Pakes (1995) framework. While investment decisions from the perspective of post-launch activities such as advertising, learning about demand uncertainty and brand building have received empirical attention (e.g., Borkovsky et al. 2014, Dubé et al. 2005, Ellickson et al. 2012, Hitsch 2006, Vitorino 2014), R&D investments that influence new product launches[6] have received relatively little empirical attention primarily due to lack of data that allows one to observe R&D efforts pre-launch. Perhaps closest in this regard is Goettler and Gordon (2011) who estimate a structural model that endogenizes innovation to evaluate the counterfactual if Intel would innovate more in the absence of AMD. Unlike their setting where the market structure is

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[6]R&D investments that influence existing product quality or existing capacity have been the focus of empirical works such as Gowrisankaran and Town (1997), Ryan (2012). See Doraszelski and Pakes (2007) for a review of other empirical applications.

fixed at two firms, I observe varying market structures both within and across markets. This allows me to infer the degree of competition from firms' exit decisions rather than relying on product substitution in the post-launch market. This feature is especially important in the pharmaceutical industry where a large number of molecules (nearly 95% in the data) do not reach the launch stage.

The paper is organized as follows. Section 2 gives an overview of the pharmaceutical industry, describes the data and highlights a few empirical regularities in a reduced-form setting, Section 3 builds the structural model, Section 4 discusses the estimation strategy and Section 5 presents the results. Section 6 evaluates the counterfactual of a faster approval process and Section 7 concludes.

2   Industry Background and Data

Drug development is a time-intensive and expensive process. Firms vying to enter a market after discovery of a chemical compound have to perform pre-clinical, Phase I, Phase II and Phase III trials before they can launch their product. Getting to the final launch phase is a low probability event - for every 250 compounds that enter pre-clinical testing only 1 wins FDA approval.[7]

Pre-clinical trials for the drug involve testing the compound on animals. Based on the findings firms may decide to file an Investigational New Drug filing with the FDA which can either approve or reject the filing. If approved, the drug has to pass successfully through three more phases – Phase I which involves testing on a small group of healthy individuals, Phase II which involves testing on a small group of patients with the disease to prove that the drug has the intended effects on the patients and Phase III which involves testing on a large-scale to establish safety and efficacy of the drug. Figure 1 illustrates the various phases a pharmaceutical firm needs to go through before final launch and the approximate time it takes to complete each phase.

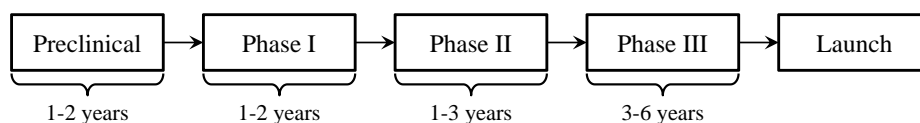| Preclinical	Phase I	Phase II	Phase III	Launch
1-2 years	1-2 years	1-3 years	3-6 years	

Figure 1: Pharmaceutical research and development process

To answer the questions posed in this paper we need firm actions in the R&D stages prior to a New Drug Application (NDA) as well as FDA-determined launch outcomes at

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[7]Source: Pharmaceutical Research and Manufacturers of America citing data from the Tufts University Center for the Study of Drug Development

the market-firm-year level. I focus on drug development efforts post-Phase 2 clinical trials.[8] This is because Phase 3 is by far the most expensive of all four research phases (DiMasi et al. 2003) and because these data are largely publicly available as the FDA requires that all drugs in controlled clinical investigation other than Phase 1 trials be registered on a publicly-available database. The dataset used in the paper comes from Adis R&D Insight - an aggregator that collects this information across all firms and markets over time.

Specifically, an observation in the data consists of the date a firm entered Phase 3 clinical trials in a particular disease indication and the date if it exited, filed or launched. The data consists of a total of 294 disease indications[9] in the period 1995-2008. Markets were classified by how firms defined their research. In most cases this procedure led to a one-to-one mapping between disease indication classifications and markets. In a few instances, manual coding was required to classify similar disease indications into a single market. For example, the coded market for Type-1 diabetes is sometimes referred to as Type-1 diabetes and other times as Type-1 diabetes mellitus in the raw data.

The pharmaceutical industry is characterized by four main features: forward-looking firms, heterogeneous markets, uncertainty in FDA outcomes and strategic firms. I now provide evidence of each of these characteristics from the data:

Forward-looking firms

Firms spend an average of 4.6 years in Phase 3 clinical trials. Figure 2 shows the number of years spent in research by various firms across different markets. During this period the firm does not earn any profits. Investments are made in expectation of profits if and when a firm's drug launches in the market. This is clear evidence of firms' forward-looking behavior and warrants a model that takes these dynamics into account.

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[8]I refer to time spent in research as investment. R&D investments in dollar amounts by disease-indication are rarely disclosed by firms.

[9]To ease the computational burden I restrict the considered drugs to those affiliated with the top 15 firms by sales. I further consider only the first drug that a firm entered a market with (thus potentially ignoring complementarities within a market). This brings down the number of markets from 513 to 294.
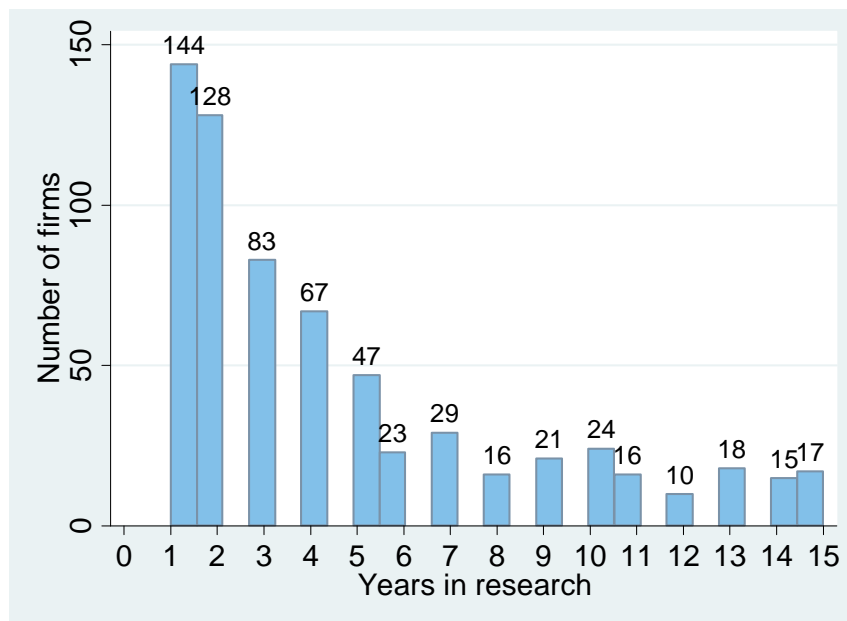
Figure 2: Distribution of years spent in research across all firms and markets

Heterogeneous markets

The number of drugs in Phase 3 trials per market ranges from 1 to 10: Table 1 shows the distribution of number of drugs per market. 52% of markets have just 1 drug that has entered Phase 3 in that indication while few markets have more than 4 drugs that entered the market. This is an indication of substantial market-specific heterogeneity: some markets see more firms investing in them while others see relatively fewer firms.

This market-specific heterogeneity is also evidenced in the number of launched firms per market shown in Figure 3. The average number of launched firms in a market is 0.57 with 176 markets having no launched product during the time-span in the data, 88 markets having 1 firm that has launched successfully, 20 markets with 2 launched firms and 10 markets with greater than 3 launched firms.

The R&D investment data is further supplemented, where available, with market-specific descriptives such as prevalence and whether the indication disproportionately affects people of a specific age, race or gender. These data come from epidemiology reports from MedTrack, publicly available government data sources such as NIH and SEER as well as medical journal articles. Lastly, data from MedTrack which tracks realized sales of launched products, provides a crude measure of the indication-specific market-size in dollar amounts. These figures are observed only conditional on launch - however, averaging across all drugs and years of realized sales within a disease-indication gives an approximate measure of the market potential specific to a given indication. Table 2 provides the summary statistics of these market

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descriptives.

Table 1: Number of drugs in research per market

Number of drugs per market	Number of markets	% of markets
1	152	52%
2	56	19%
3	35	12%
4	21	7%
5	8	3%
6	7	2%
7	4	1%
8	6	2%
9	2	1%
10	3	1%
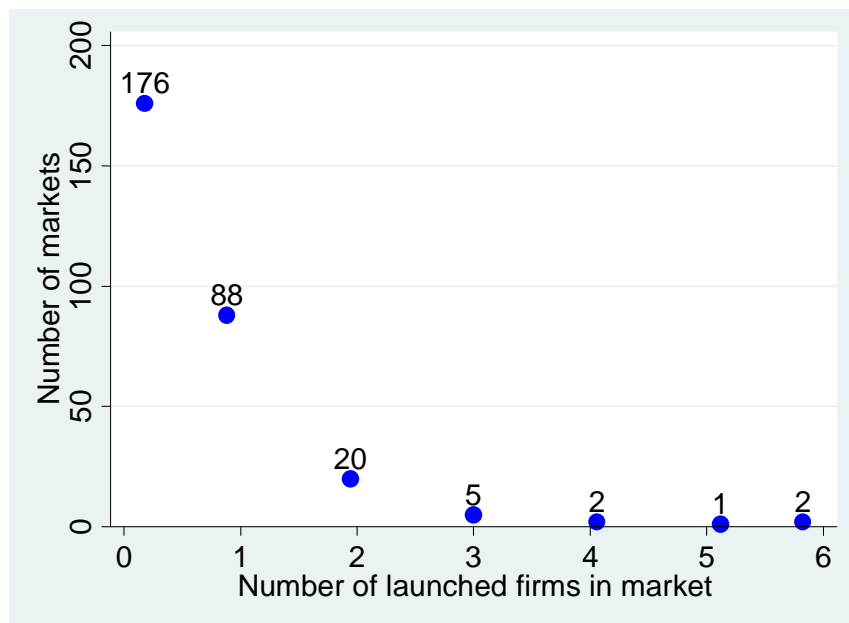
Figure 3: Number of launched firms per market

Table 2: Market Characterisitcs

| | Mean | Std. Dev | Percentiles | | | N Obs |
			10th	50th	90th	
Prevalence (per 10,000)	628	1,056	0.74	130	2,000	158
Varies with						
Age	0.25	0.43	0	0	1	215
Race	0.41	0.49	0	0	1	215
Gender	0.53	0.50	0	0	1	215
Market size ($ millions)	$ 468	$ 438	$ 41	$ 349	$ 1,054	213

Uncertain FDA Approval process

After entering Phase 3 clinical trials, a firm in a market can take one of three actions - continue investment (i.e. remain in Phase 3), exit the market or file for an NDA. After a firm files with the FDA, whether the firm's petition is approved, rejected or remains in further review is entirely determined by the FDA. The table below summarizes the transitions between phases across all drugs, markets and time. The second row of the table is indicative of firms' endogenous actions: 86.9% of the time an incumbent continues on in its R&D efforts, 7.6% of the time it files for an NDA and 5% of the time it decides to exit the market. The third row is indicative of the FDA determined exogenous outcomes: of those that are filed, 26.2% are approved, 2.3% are rejected by the FDA and 71.6% continue to remain in review. Both this and Figure 4 which shows the distribution of years spent in review across all firms in the data, indicate that 1) approval on filing is not guaranteed and 2) realization of the outcome is not always quick. Conditional on an outcome (approval/rejection) the average time spent in review is 1.49 years.

Table 3: Phase Transitions across all drugs, firms, market and years

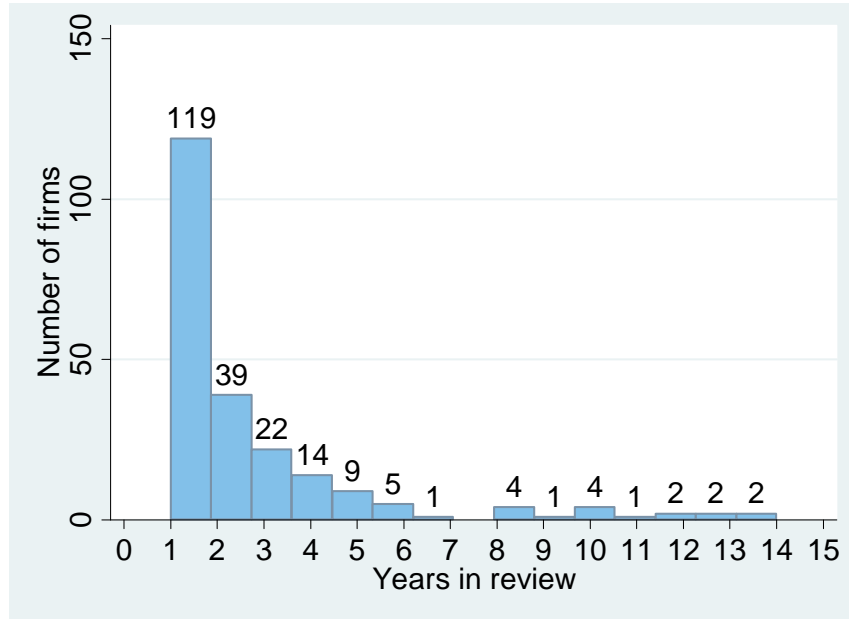|	Not entered	Entered P3	Filed NDA	Launched	Exited	N Obs
Not entered	84.7%	15.3%	0%	0%	0%	3,912
Entered P3	0%	86.9%	7.6%	0.6%	5.0%	3,045
Filed NDA	0%	0%	71.6%	26.2%	2.3%	573
Launched	0%	0%	0%	100%	0%	1,213
Exited	0%	0%	0%	0%	100%	1,188

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Figure 4: Distribution of Years in FDA review across all firms and markets

Strategic interactions between firms - Reduced form evidence

I now provide reduced-form evidence showing the impact of competitor's states on a firm's investment decisions. Table 4 regresses the decision to continue or exit on the firm's own state as well as the competitor's state controlling for market-, firm- and time- fixed effects. The first set of results under the column Endogenous actions shows that a firm is more likely to continue investment if a competitor has exited the market, and this probability increases as the number of competitors that have exited the market increases. The second column includes the FDA determined outcomes of approvals and rejections. The results indicate that a firm is less likely to continue investment in R&D when a competitor has launched successfully in the market, with more competitors having an increasingly negative effect. The results also indicate that endogenous as well as FDA-determined exits have a similar effect on a firm's decision to continue investment.

Endogeneity concerns stem from two sources 1) firm-determined outcomes are equilibrium responses and 2) an omitted variable, such as a scientific discovery specific to a disease-market, can lead to biased estimates. Concerns related to (1) are mitigated by the regression on FDA-determined outcomes. To the extent that the firm files only if it expects a positive outcome, this can still be at best interpreted as a correlational regression. To overcome this concern, I turn to a structural model in Section 3 that explicitly endogenizes firm actions. Concerns related to (2) should lead us to underestimate the effect of competition leading to an upward bias of the estimate. To see this, a market-time specific event, such as a scientific

discovery that makes Phase 3 clinical trials easier for all firms, will likely cause us to see more launched firms in the market and more firms investing in R&D efforts. This will lead to a positive coefficient on the Number of competitors launched coefficient, while the estimated coefficient reported in Table 4 is significantly negative.

Table 5 shows a similar regression but on the decision to enter Phase 3 clinical trials or not. Here we see a negative impact of the number of firms in research on the focal firm's decision to enter Phase 3 with the probability further declining as the number of competitors in research increases. Surprisingly, we also that as the number of exits increase, firms are less likely to enter the market. This could be driven by market-time specific trends or by a learning phenomena where firms learn, from the actions of their competitors, that certain markets are hard to do research in. Including the FDA-determined outcomes, we see that launched competitors have an increasingly negative effect on a firm's decision to enter.

Tables 11 and 12 in Appendix A show that these patterns hold even when all firms (and not just the top 15) are included.

Market-specific variables (market potential, prevalence, age, race and gender) were found to be poor indicators of firms' entry and investment decisions in Phase 3. Appendix B shows regressions of firms' endogenous decisions on market characteristics. The coefficients on the market characteristics are insignificant. This is possible because these variables likely affect firms' decision early-on in the drug discovery phase, rather than in late-stage clinical trials. Market fixed-effects, on the other hand, have a much higher explanatory power highlighting the importance of unobserved heterogeneity. Moreover, not including market fixed-effects leads to insignificant estimates on competitors' states. This finding informs the structural model, where I recover the estimates by (unobserved) market-type, instead of relying on market-specific observables in the state-space.

Table 4: Decision to continue or exit as a function of competitor's states

Continue/Exit	Endogenous actions		FDA outcomes	
	Coefficient	t-stat	Coefficient	t-stat
Number of competitors exited				
1	3.00	6.6	3.12	6.54
2	4.66	6.41	4.74	6.48
3	4.96	4.83	5.63	4.93
4	4.67	2.78	4.30	2.6
5	6.37	4.75	5.13	3.39
6	7.63	4.62	4.83	2.63
7	20.23	0.02	18.05	0.01
Number of competitors in research				
1	0.10	0.27	0.02	0.04
2	0.48	0.9	0.23	0.41
3	0.36	0.53	-0.28	-0.38
4	0.98	1.09	0.76	0.74
5	-0.64	-0.5	-1.62	-1.19
6	-1.58	-1.11	-3.04	-1.87
7	0.00		0.00	
Number of competitors in filed status				
1	-0.48	-1.12	-0.52	-1.03
2	-1.33	-1.29	-0.54	-0.49
3	12.33	0	12.99	0.01
Number of competitors exited due to FDA				
1			3.73	2.87
Number of competitors launched				
1			-0.29	-0.49
2			-1.41	-1.59
3			-2.15	-1.99
4			-4.80	-2.73
5			9.33	0
6			-7.89	-3.36
Own state (Reference: Research Year >4)				
Research year 1	1.41	3.16	1.33	2.9
Research year 2	0.81	1.98	0.71	1.69
Research year 3	0.64	1.57	0.45	1.07
Research year 4	0.78	1.74	0.71	1.56
Fixed-effects	Market, Firm, Time			
Log likelihood	-218.46		-205.73	
N obs	1159		1159	
N markets	294		294	

Note: The first column Endogenous actions reports estimates that include only firm-driven outcomes. The second column under FDA outcomes includes FDA-determined approvals and rejections, i.e., Number of competitors exited due to FDA and Number of competitors launched.

Table 5: Decision to enter Phase 3 or not as a function of competitor's states

Enter/Not enter	Endogenous actions		FDA outcomes	
	Coefficient	t-stat	Coefficient	t-stat
Number of competitors exited				
1	-1.33	-4.65	-1.35	-4.59
2	-1.64	-3.68	-1.84	-4.00
3	-2.75	-2.95	-2.96	-3.48
4	0.00	0.00	0.00	0.00
5	-3.14	-2.23	-3.32	-2.25
6	-4.14	-2.40	-3.88	-2.11
7	0.00	0.00	0.00	0.00
Number of competitors in research				
1	-0.61	-3.21	-1.18	-5.86
2	-1.51	-5.62	-2.30	-8.05
3	-1.75	-4.69	-2.52	-6.45
4	-1.60	-3.31	-2.73	-5.60
5	-2.64	-3.17	-3.32	-4.33
6	-2.12	-0.47	-2.75	-1.05
7	-1.21	-1.06	-2.76	-2.38
Number of competitors in filed status				
1	-0.45	-1.97	-1.03	-4.22
2	0.23	0.45	-0.42	-0.88
3	-13.17	-0.02	-12.24	-0.04
Number of competitors exited due to FDA				
1			-3.31	-5.72
Number of competitors launched				
1			-2.27	-7.48
2			-2.97	-6.64
3			-2.57	-3.88
4			-4.06	-3.96
5			-4.53	-3.23
6			0.00	0.00
Fixed-effects	Market, Firm, Time			
Log likelihood	-896.38		-839.32	
N obs	3874		3874	
N markets	294		294	

Strategic interactions between firms - Anecdotal evidence

Figure 5 taken from Recap, a company that provides insights for the biopharmaceutical industry, sheds some light into the causal reasons why firms abandon their compounds in late-stage clinical trials. The figure shows that of the 66 compounds (out of 559 compounds in Recap's Bioportfolio Index which contains only biotech companies) that abandoned clinical

trials in Phase 3, 12% state "Pipeline prioritization" as their reason for leaving Phase 3. This includes market and competitive dynamics like market size and level of market saturation.
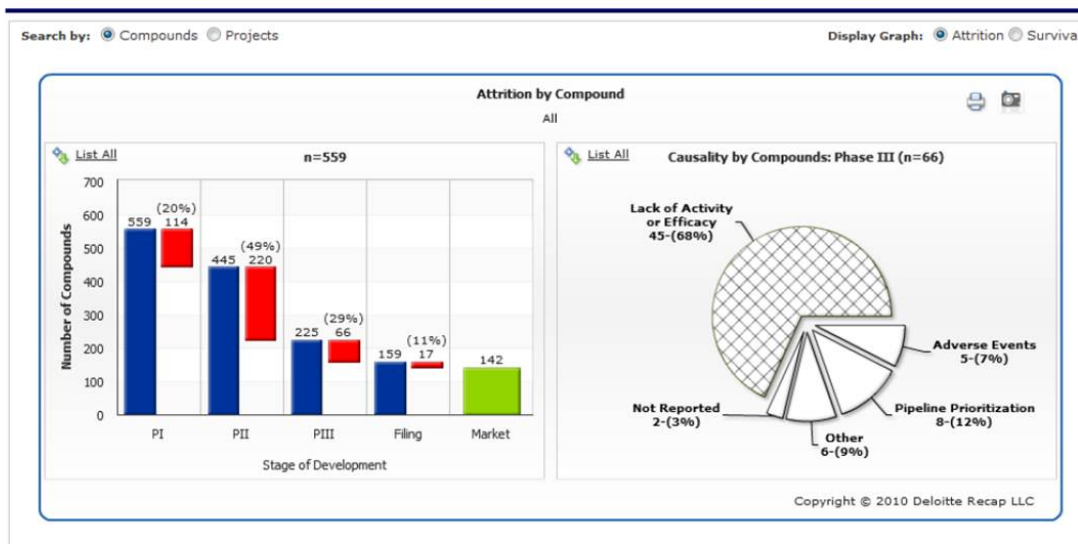
Figure 5: Evidence suggesting competitive considerations account for 12% of Phase 3 clinical trials abandonment

While this provides preliminary evidence of the impact of competition on firm's decisions, I next develop a model that explicitly endogenizes innovation and market structure taking into account the specifics of the industry as described above.

3   Model

I now describe the model that governs a firm's decision to enter Phase 3 clinical trials or not; and conditional on entry to continue investment in these clinical trials, file for a NDA or exit the market. These decisions are influenced by 1) the structural parameters which include the cost to enter Phase 3 clinical trials, continuation costs of research and profitability by market type, 2) the firm's own state 3) the competitors' states and 4) privately observed shocks (e.g., adverse side-effects in clinical trials can cause the firm to exit). The payoff is positive only if a firm launches its product in the market. Payoffs in the investment stages reflect the cost of continuing research.

Outcomes which are not in the firm's control include Approval and Rejection by the FDA, i.e. once a firm has chosen to file for an NDA the outcome after this step is determined by the FDA.

I now briefly go over the reasons a firm can exit the market and explain how these are captured in the model. A firm can exit the market due to one of three reasons 1) adverse effects of the drug on the patient population that are discovered during research 2) pipeline prioritization arising from competitive considerations or 3) FDA rejection after the firm has filed for an NDA.

Adverse effects

If a firm's drug has adverse effects on its desired patient population, the firm will have to withdraw testing and exit the market. This effect is captured through the error term ε_{ex} present in the utility from exiting the market. A large positive shock captures the effect of an adverse event while a negative shock captures the effect of a windfall. Competitors are assumed to know these error shocks only in expectation.

Pipeline prioritization

This captures a firm's decision to endogenously exit or continue investment in the clinical trials as influenced by its competitors states and actions. This influence is captured through the state space in the firm's consideration - the extent of this influence is empirically estimated.

FDA rejection

A firm, when it is reasonably confident that it has all the data to justify a launch, submits the relevant documents to the FDA who then reviews them. Based on its review the FDA may reject the petition of the firm to launch in the market. I capture this as a probability pr_e associated with exit conditional on filing. These probabilities are directly inferred from the data, and conditional on filing are assumed to be exogenous.

3.1 States and State Transitions

The state space consists of those variables that are observed to the researcher - x_t, and those that are unobserved to the researcher - s. Both variables are known to the firm $i, i \in \{1 \dots I\}$. The unobserved state allows for market-specific heterogeneity. A market's type is assumed to be fixed over time, i.e. it cannot transition from one state to another. Markets are assumed to be independent. Firm i's observed state in period t is denoted by x_{it} where

$x \in \{0, 1, 2, 3, 4, 5, \text{Exit}, \text{File}, \text{ExitFDA}, \text{Launch}\}$. 0 indicates the firm has not yet entered the market, 1...5 denote the research year[10] the firm is in, Exit indicates the firm has exited the market, File indicates the firm has filed for an NDA and is waiting to hear of an outcome from the FDA, ExitFDA indicates the FDA rejected the firm's NDA while Launch indicates the firm won FDA approval. Note that Exit, ExitFDA and Launch are all absorbing states, i.e. once a firm has reached this state it continues to remain in this state. Next I describe the state transitions that determines a firm's next period state given its current state and action.

If a firm has not yet entered Phase 3 in year t it can choose action d_{it} where $d \in \{\text{ne},\text{e}\} \equiv$ {Not Enter, Enter}. Its next period state is then given by:

$$x_{it+1} = (x_{it} + 1).1 \, (d_{it} = \text{e}) + 0.1 \, (d_{it} = \text{ne}) \tag{1}$$

where $1\,(.)$ is the indicator function.

If a firm is an incumbent it can choose action d_{it} where $d \in \{\text{c},\text{f},\text{ex}\} \equiv$ {Continue,File,Exit}. Its next period state is given by:

$$x_{it+1} = \begin{array}{l} x_{it} + 1 \text{ if } d_{it} = \text{c} \\ \text{File if } d_{it} = \text{f} \\ \text{Exit if } d_{it} = \text{ex} \end{array} \tag{2}$$

Once a firm's state changes to File, its next period state is determined exogenously by the FDA, i.e.,

$$x_{it+1} = \begin{array}{l} \text{Launch with probability } pr_l \\ \text{ExitFDA with probability } pr_e \\ \text{File with probability } pr_f = 1 - pr_l - pr_e \end{array} \tag{3}$$

where pr_l and pr_e are exogenous launch and exit probabilities directly informed by the data.[11]

A firm's transition conditional on entry into Phase 3 is captured in the schematic shown in Figure 6.

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[10]to limit the state space, I assume that once a firm has reached state 5 it continues to remain in state 5 until it exits or files.

[11]These probabilities can be allowed to be a function of the years spent in research prior to filing. This will allow for knowledge accumulation as captured by Doraszelski (2003) and can accommodate, for example, higher approval probabilities if the firm spent more years in research. However, in the data, I do not find evidence supporting this: FDA approval probabilities are almost equal across all levels of investment.
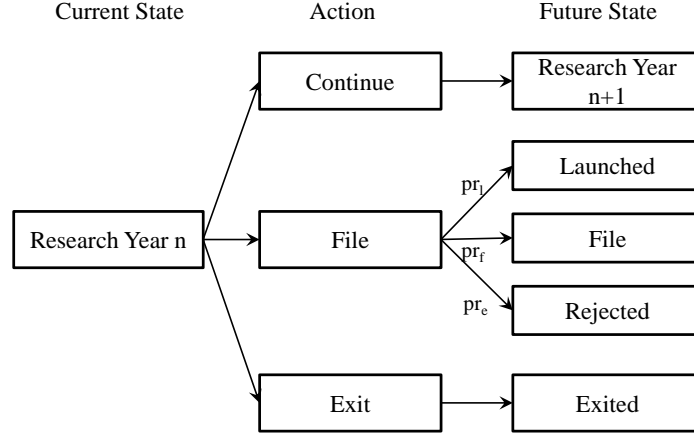
Figure 6: Schematic of a firm's transition from a research year to the next state

3.2 Per-period utility

I now specify the current-period payoffs associated with each possible action a firm can take. For an entrant with two possible choices, the per-period utility of staying out of the market and entering the market are given by Equations 4 and 5 respectively:

$$u_{ne} = 0 + \varepsilon_{ne} \tag{4}$$

$$u_e = -c_{enter} + \varepsilon_e \tag{5}$$

where c_{enter} is the cost associated with entering Phase 3.

For an incumbent with three possible choices, the utility from continuing research, filing for an NDA and exiting the market are given by Equations 6-8:

$$u_c(x_t) = -c_r(x_{it}) + \varepsilon_c \tag{6}$$

$$u_f(x_t) = -c_f(x_{it}) + \varepsilon_f \tag{7}$$

$$u_{ex} = 0 + \varepsilon_{ex} \tag{8}$$

where $c_r(x_{it})$ is the cost of continuing research and is allowed to depend on firm i's own state. This allows the cost of research to be a flexible function of the firm's investment. $c_f(x_{it})$ reflects the likelihood that a firm is more or less likely to file with the FDA when its level of investment is x_{it}. For example, if $c_f(x_{it})$ is decreasing in x_{it}, then the more years a

firm spends in research the more likely it is to file with the FDA. On the other hand, if this function is increasing in x_{it}, then the firm is less likely to file with the FDA reflecting the fact that the firm was not able to garner positive results over the years of research.

If the firm has reached the launch phase, it earns profits which are allowed to depend on the number of competitors who are also in the launch stage. I assume the following form of the payoff function:

$$u_l(x_t) = \pi + \delta \sum_{-i} 1(x_{it} = \text{Launch}) \tag{9}$$

where $\sum_{-i} 1(x_{it} = \text{Launch})$ is the total number of competing firms in the launched state. π is the profit potential of the market when there are no competitors and δ is the impact of additional competitors on profits.

This payoff function deviates from the typical payoff used in the literature which uses product substitutability as revealed by consumer purchase decisions in the marketplace to infer the degree of competition. This is because unlike most industries, the pharmaceutical industry has a very high failure rate - in the data only 5.71% of all drugs reach a launch stage. Inferring competition from marketplace substitution is nearly impossible because one does not observe such substitution for most of the drugs in the data. As a result, I focus on recovering δ which reveals competitive behavior as inferred from firms' exit decisions in R&D.

The structural parameters are represented by the vector $\theta = \{c_{enter}, c_r, c_f, \pi, \delta\}$.

3.3   Value functions

The choice-specific value functions if a firm is a potential entrant can be given by the following equations:

$$V_{ne}(x_t, s) = u_{ne} + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}(V_{ne}(x_{t+1}, s), V_e(x_{t+1}, s)) \cdot f_{ne}(x_{t+1}|x_t) \tag{10}$$

$$V_e(x_t, s) = u_e + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}(V_c(x_{t+1}, s), V_f(x_{t+1}, s), V_{ex}(x_{t+1}, s)) \cdot f_e(x_{t+1}|x_t) \tag{11}$$

The summation is over all the possible states $\left(\dim \prod_{-i} |x_{-i,t+1}|\right)$ that all of firm i's competitors can be in, in the next time-period.[12] The probability of each of these states

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[12] Although each firm can be in 10 possible states, implying a summation over 10^{I-1} possible future states just one-period ahead, a simplification occurs because each firm can be in a maximum of 3 future states. To

occurring is given by $f_j(x_{t+1}|x_t)$ if j was the action chosen by i in period t. i's own state in the next period can be determined from the state transition equations described in Equations 1-3.

The choice-specific value functions for an incumbent firm is given by the following equations:

$$V_c(x_t, s) = u_c(x_t) + \beta \sum_{x_{t+1}} \text{Emax}_{\varepsilon'}(V_c(x_{t+1}, s), V_f(x_{t+1}, s), V_{ex}(x_{t+1}, s)) . f_c(x_{t+1}|x_t) \quad (12)$$

$$V_f(x_t, s) = u_f(x_t) + \beta \sum_{x_{t+1}} (pr_l . V_l(x_{t+1}, s) + pr_e . V_{exFDA}(x_{t+1}, s) + pr_f . V_{fFDA}(x_{t+1}, s)) . f_f(x_{t+1}|x_t)$$
$$(13)$$

$$V_{ex}(x_t, s) = 0 \quad (14)$$

Once a firm has filed with the FDA the corresponding value functions are:

$$V_l(x_t, s) = u_l(x_t, s) + \beta \sum_{x_{t+1}} V_l(x_{t+1}, s) f_l(x_{t+1}|x_t) \quad (15)$$

$$V_{fFDA}(x_t, s) = 0 + \beta \sum_{x_{t+1}} (pr_l . V_l(x_{t+1}, s) + pr_e . V_{exFDA}(x_{t+1}, s) + pr_f . V_{fFDA}(x_{t+1}, s)) . f_{fFDA}(x_{t+1}|x_t)$$
$$(16)$$

$$V_{exFDA}(x_t, s) = 0 \quad (17)$$

Note: although these are subscripted for launch, file and rejection these are not choice-specific as these outcomes are not determined by the firm.

3.4   Equilibrium

Firms are assumed to be symmetric in their actions and their strategies are assumed to be Markov Perfect. A firm chooses that action that maximizes its value function conditional on the current state space and its expectation of other firms strategies:

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see this, if a firm is an entrant it can be in only 2 possible states next period; if it is an incumbent it can be in only 3 possible states next period; and if it has filed it can be in only 3 possible future states next period. This results in a smaller state space of maximum dimension 3^{I-1} one-period ahead.

$$V\left(x_t, s|d_{it}^*, d_{-i}\right) \geq V\left(x_t, s|d_{it}', d_{-i}\right) \tag{18}$$

4 Estimation

The parameters are recovered using the EM Algorithm described in Arcidiacono and Miller (2011). The estimation recovers 1) the probability q_{ms} that market m belongs to type s, 2) the overall population probability of the unobserved states π_s, 3) the type-specific CCPs as a function of observed states and 4) the type-specific structural parameters θ.

I first specify the likelihood of the data and how to obtain the conditional choice probabilities (CCPs) from the data and then list the steps used in estimation. To ease the computational burden, if a market contains more than four incumbents, I use only the first four firms that entered the market.

4.1 Likelihood

Assuming the ε's follow a Type-1 i.i.d extreme-value distribution the choice-specific value functions for an incumbent can be written as:

$$v_c\left(x_t, s; \theta\right) = -c_r\left(x_{it}\right) + \beta \sum_{x_{t+1}} \left(\Gamma + ln\left[e^{v_c(x_t,s;\theta)} + e^{v_f(x_t,s;\theta)} + e^{v_{ex}(x_t,s;\theta)}\right]\right).f_c\left(x_{t+1}|x_t\right) \tag{19}$$

$$v_f\left(x_t, s; \theta\right) = -c_f\left(x_{it}\right) + \beta \sum_{x_{t+1}} \left(pr_l.V_l\left(x_{t+1}, s; \theta\right) + pr_e.V_{exFDA}\left(x_{t+1}, s; \theta\right) + pr_f.V_{fFDA}\left(x_{t+1}, s; \theta\right)\right).f_f\left(x_{t+1}|x_t\right) \tag{20}$$

$$v_{ex}\left(x_t, s; \theta\right) = 0 \tag{21}$$

where $v\left(.\right) = V\left(.\right) - \varepsilon$, and Γ is the Euler function.

Equation 19 can be further simplified by using the fact exiting the market is a terminal action:

$$v_c\left(x_t, s; \theta\right) = -c_r\left(x_{it}\right) + \beta \sum_{x_{t+1}} \left(\Gamma + ln\frac{\left[e^{v_{ex}(x_t,s;\theta)}\right]}{p_{ex}\left(x_{t+1}, s; \theta\right)}\right).f_c\left(x_{t+1}|x_t\right) \tag{22}$$

where

$$p_{ex}\left(x_t, s; \theta\right) = \frac{e^{v_{ex}(x_t,s;\theta)}}{e^{v_c(x_t,s;\theta)} + e^{v_f(x_t,s;\theta)} + e^{v_{ex}(x_t,s;\theta)}} \tag{23}$$

But $p_{ex}(x_t, s; \theta)$ is the conditional choice probability of exiting the market and can be estimated directly from the data. Replacing $p_{ex}(x_t, s; \theta)$ with $\hat{p}_{ex}(x_t, s)$, equation 22 simplifies to

$$v_c(x_t, s; \hat{p}, \theta) = -c_r(x_{it}) + \beta \sum_{x_{t+1}} (\Gamma - ln(\hat{p}_{ex}(x_{t+1}, s))) . f_c(x_{t+1}|x_t) \tag{24}$$

which requires computation of only one-period ahead conditional choice probabilities. This idea has been illustrated in Hotz and Miller (1993). Arcidiacono and Ellickson (2011) provide a review of empirical applications that use this simplification along with detailed derivations.

Note that the same simplification cannot be applied to $v_f(x_t, s; \theta)$ because once the firm has filed with the FDA it no longer has a choice to make - all further decisions are made by the FDA. Thus to compute $v_f(x_t, s; \hat{p}, \theta)$, I simulate out V_l and V_{fFDA} using $\hat{p}$ for T time periods. Note that a further simplification can be made when the value function is linear in θ (Bajari, Benkard and Levin (2007)). For a given state vector and CCPs, firm actions can be forward simulated. Once any given firm has filed, whether it receives an approval or rejection by the FDA is simulated by drawing probabilities from a uniform distribution NS times. In Equations 25 and 26, terms $1(\text{Launch}_i)$ and $\sum_{-i} 1(\text{Launch}_i)$ are pre-computed prior to the maximization step, resulting in value functions linear in π and δ:

$$V_l(x_{t+1}, s; \theta) = \sum_{t=0}^{T} \beta^t \left(\pi + \delta \sum_{-i} 1(\text{Launch}_i) \right) \tag{25}$$

$$V_{fFDA}(x_{t+1}, s; \theta) = \sum_{t=0}^{T} \beta^t \left(\pi.1(\text{Launch}_i) + \delta \sum_{-i} 1(\text{Launch}_i) \right) \tag{26}$$

The choice-specific value functions for an entrant can be written as:

$$v_e(x_t, s; \hat{p}, \theta) = -c_{enter} + \beta \sum_{x_{t+1}} (\Gamma - ln(\hat{p}_{ex}(x_{t+1}, s))) . f_e(x_{t+1}|x_t) \tag{27}$$

$$v_{ne}(x_t, s; \hat{p}, \theta) = 0 + \beta \sum_{x_{t+1}} (\Gamma + ln [exp(v_e(x_{t+1}, s; \theta)) + exp(v_{ne}(x_{t+1}, s; \theta))]) . f_{ne}(x_{t+1}|x_t)$$

$$\tag{28}$$

$$= \beta \sum_{x_{t+1}} \left(\Gamma + ln \frac{[exp(v_e(x_{t+1}, s; \theta))]}{p_e(x_{t+1}, s; \theta)} \right) . f_{ne}(x_{t+1}|x_t)$$

$$= \beta \sum_{x_{t+1}} (\Gamma + v_e(x_{t+1}, s; \theta) - ln(p_e(x_{t+1}, s; \theta))) . f_{ne}(x_{t+1}|x_t)$$

$$= \beta \sum_{x_{t+1}} \left(\Gamma - c_{enter} + \beta \sum_{x_{t+2}} \left(\Gamma - ln\left(\hat{p}_{ex}\left(x_{t+2}, s\right)\right)\right) . f_e\left(x_{t+2}|x_{t+1}\right) - ln\left(p_e\left(x_{t+1}, s; \theta\right)\right)\right) . f_{ne}\left(x_{t+1}|x_t\right)$$

which requires evaluation of two-period ahead CCPs.

The likelihood of the data for an incumbent and an entrant are given by equations 29 and 30 respectively:

$$l_{imts}\left(y_{imt}|x_t, s; \hat{p}, \theta\right) = \frac{exp\left(v_c\left(x_t, s; \theta\right)\right).1\left(y_{imt} = \text{c}\right) + exp\left(v_f\left(x_t, s; \theta\right)\right).1\left(y_{imt} = \text{f}\right) + 1.1\left(y_{imt} = \text{ex}\right)}{exp\left(v_c\left(x_t, s; \theta\right)\right) + exp\left(v_f\left(x_t, s; \theta\right)\right) + 1} \tag{29}$$

$$l_{imts}\left(y_{imt}|x_t, s; \hat{p}, \theta\right) = \frac{exp\left(v_e\left(x_t, s; \theta\right)\right).1\left(y_{imt} = \text{e}\right) + exp\left(v_{ne}\left(x_t, s; \theta\right)\right).1\left(y_{imt} = \text{ne}\right)}{exp\left(v_e\left(x_t, s; \theta\right)\right) + exp\left(v_{ne}\left(x_t, s; \theta\right)\right)} \tag{30}$$

where y_{imt} is the action taken by firm i in market m in time t.

Aggregating across all firms and years, the likelihood of market m of unobserved-type s is given by:

$$l_{ms}\left(y_m|x, s; \hat{p}, \theta\right) = \prod_{i=1}^{I}\prod_{t=1}^{T} l_{imts}\left(y_{imt}|x_t, s; \hat{p}, \theta\right)$$

Aggregating across all types and markets, the log-likelihood of the data is:

$$l\left(y|x; \hat{p}, \theta\right) = \sum_{m=1}^{M}\sum_{s=1}^{S} q_{ms}ln\left(l_{ms}\left(y_m|x, s; \hat{p}, \theta\right)\right) \tag{31}$$

where q_{ms} is the probability that market m is of type s.

4.2   CCP estimation

To get the conditional choice probabilities, $\hat{p}$, I use a parametric approximation. θ_{CCP} denotes the parameter vector describing the CCPs. For incumbents, I estimate a logit on the probabilities of continuing, filing and exiting the market and for entrants, I estimate a logit on the probabilities of entering and not entering. q_{ms} are used as weights in the logit likelihood.

The continuation function is specified as a linear combination of

$$\left(1, \sum_{-i}\left(x_{-it} = \text{Exit}\right), \sum_{-i}\left(x_{-it} \in \{1, ..., 5\}\right), \sum_{-i}\left(x_{-it} = \text{File}\right), \sum_{-i}\left(x_{-it} = \text{ExitFDA}\right), \sum_{-i}\left(x_{-it} = \text{Launch}\right), x_{it}\right).$$

The function for the entry choice probabilities is specified as a linear combination of $\left(1, \sum_{-i} (x_{-it} = \text{Exit}), \sum_{-i} (x_{-it} = \text{Launch})\right)$.

4.3 EM Algorithm

I operationalize the EM algorithm with starting values $\pi_s^1, \theta_{CCP}^1, \theta^1$ where the superscript denotes the lth iteration of the EM algorithm. Following Arcidiacono and Miller (2011), I update $q_{ms}, \pi_s, \theta_{CCP}, \theta$ as follows

1. $q_{ms}^{l+1} = \frac{\pi_s^l l_{ms}\left(y_m|x,s;\theta_{CCP}^l,\theta^l\right)}{\sum_{s=1}^S \pi_s^l l_{ms}}$

2. $\pi_s^{l+1} = \frac{\sum_{m=1}^M q_{ms}^{l+1}}{M}$

3. Obtain θ_{CCP}^{l+1} using the specification in Section 4.2 and q_{ms}^{l+1} as weights.

4. $\theta^{l+1} = \underset{\theta}{\text{argmax}} \sum_{m=1}^M \sum_{s=1}^S q_{ms}^{l+1} ln\left(l_{ms}\left(y_m|x,s;\theta_{CCP}^{l+1},\theta\right)\right)$

These steps are repeated till $|\pi^{l+1} - \pi^l| < tol$.

4.4 Identification

Here I briefly go over the identification of the second stage parameters $\theta = [c_{enter}, c_r, c_f, \pi, \delta]$. Firms' decisions to continue investment can either be due to high expected revenues or low research costs. Because I do not observe expected revenues or costs of research, only the relative valuations can be identified. I normalize the revenue parameter π to 1 unit for estimation. All other parameters are interpreted relative to this normalization.

The observed rate of entry identifies the entry cost c_{enter}. If in two markets with identical revenues, we observe fewer entries in one of the markets, it must be that the entry cost in that market is higher. The continuation rate identifies the cost of research c_r relative to the cost of exiting. If firms exit sooner after entry into a market it implies high continuation costs. Similarly, the observed filing rate identifies the cost of filing c_f. The competitive impact parameter δ is identified based on firm's responses to launched competitors. If we observe more exits when there are more launched competitors it implies a negative effect of competition on revenues.

5 Results

I recover 2- (unobserved) types of markets using the EM algorithm. The number of unobserved types was chosen by performing a latent-class CCP estimation using 1-, 2- and 3-

types without imposing any structure from the model. The model fits were then compared using the Bayesian Information Criterion (BIC):

$$BIC = -2.ln\left(l\left(y|x_{CCP}, \theta_{CCP}\right)\right) + k.ln\left(n\right)$$

where x_{CCP} is the vector of states used in the CCP estimation, k is the number of parameters in the model, n is the sample size and $l\left(y|x_{CCP}, \theta_{CCP}\right)$ is the likelihood of the data. The BIC across all models are listed in Table 6. The BIC is lowest for the model with 2-types, providing support for a model with 2 unobserved market types.

Table 6: Latent class CCP estimation using the Data provides evidence for 2- unobserved types

Number of unobserved market types	1	2	3
BIC	5150.53	5081.73	5215.40

The CCP estimates, θ_{CCP}, for continuation and filing for incumbents, and entering for entrants are shown by type of market in Table 7. Table 8 presents the structural parameter estimates θ.[13] The main parameter of interest, δ, is significantly negative for both types of markets. Entry costs are fairly high, indicating that firms have to get a large positive draw of the random shock, ε_e, to enter Phase-3. Type-1[14] markets include indications like cerebral ischaemia, cystic fibrosis and myeloid leukaemia. These markets experience a higher negative impact of an additional competitor, as reflected in the higher values of δ for Type-1 markets.

The FDA approval probabilities (Table 9) are recovered directly from the data. Conditional on being in-review, a firm has a 26.2% chance of receiving approval, 71.6% chance of remaining in review and 2.3% chance of receiving rejection. This translates to an ex-ante in-review probability curve shown in Figure 8.

To highlight the impact of competition, I simulate out the equilibrium value functions for the Type-2 market.

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[13]Estimates allowing for filing costs are not reported here. The filing costs were insignificant for Type-1 markets which form a majority of the markets. For Type-2 markets, the filing costs were found to be an increasing function of years spent in research. Along with the empirical fact that FDA-approvals are equal across all levels of investment, this provides suggestive evidence that firms cannot get better outcomes by investing more years in R&D and that the random shocks that reflect adverse effects/positive outcomes are more likely to drive firms decisions.

[14]I define a market as Type-1 if $q_{ms=1} > 0.5$

Table 7: CCP Estimates: θ_{CCP}

	Type - 1		Type - 2	
	Coefficient	t-stat	Coefficient	t-stat
Incumbent (base outcome: exit)				
Continue				
Constant	4.090	16.59	4.350	11.11
Number of competitors launched	-0.199	-0.71	-0.303	-1.92
Number of competitors exited	0.120	0.55	0.110	0.53
Number of competitors in research	-0.318	-2.87	-0.093	-0.90
Number of competitors in filed status	-0.121	-0.30	0.397	1.63
Number of competitors exited due to FDA	1.788	0.55	0.785	3.51
Own state: Research Year 1	-1.546	-6.47	-2.057	-5.63
Own state: Research Year 2	-1.698	-6.57	-1.980	-5.64
Own state: Research Year 3	-1.153	-3.59	-1.659	-4.55
Own state: Research Year 4	-0.652	-1.75	-1.464	-4.18
File				
Constant	0.362	2.24	0.480	1.81
Entrant (base outcome: not enter)				
Enter				
Constant	-1.753	-26.72	-1.809	-31.29
Number of competitors launched	1.282	0.68	0.577	3.03
Number of competitors exited	0.252	0.13	0.972	3.98
% Type-m	74.64%		25.36%	
Number of markets	294			

Table 8: Structural Parameter Estimates: θ

		Market Type-1		Market Type-2	
		Coefficient	t-stat	Coefficient	t-stat
Entry cost	c_{enter}	39.43	16.75	21.42	21.70
Research cost (Year 1)	c_{r1}	7.90	7.24	5.94	5.31
Research cost (Year 2)	c_{r2}	10.39	5.31	6.19	3.91
Research cost (Year 3)	c_{r3}	9.89	4.66	5.20	3.36
Research cost (Year 4)	c_{r4}	11.09	6.16	8.80	3.49
Research cost (Year 5)	c_{r5}	11.81	13.68	4.61	3.47
Competitive impact	δ	-1.26	-5.29	-0.80	-2.47
% Type-m		74.64%	16.04	25.36%	5.45

The revenue parameter π is normalized to 1. Standard errors are computed using bootstrap with replacement over 40 draws.

Table 9: FDA Approval Probabilities conditional on Firm's filing for an NDA

Probability of	Remaining in-review pr_f	Approval pr_l	Rejection pr_e
Current FDA	71.60%	26.20%	2.30%

Impact of competition on expected profits

Using the estimates for the Type-2 market and the model in Section 3, I simulate out the equilibrium responses of firms for T=20 periods to evaluate the impact of competitors on a firm's payoff conditional on launching. The equilibrium I consider is Markov perfect, where firms' strategies depend only on the current state variables. In equilibrium, each firm behaves optimally and has rational expectations about competitors' actions. To solve for the equilibrium, I backward simulate the dynamic game starting at T=20. Each period, I solve for the equilibrium at each possible state.

In Figure 7, I plot the value function conditional on launching as a function of competitors' states. Each line represents the value function evaluated at four different states; the base line is the value when no other firm has entered R&D. The dotted line plots the value when 0, 1, 2 or 3 of the firms' competitors have entered Phase-3. This line shows that as the number of competitors that have entered Phase 3 increases, the NPV of profits decreases, but not by much - this is because firms know that after entry the competitor still has many years remaining before it might launch in the market. However, if the competitor has filed, there is a 26.2% probability that it will get approved and this causes the NPV to decline further. Lastly, as the number of competitors that have launched increases, profits decline the most.
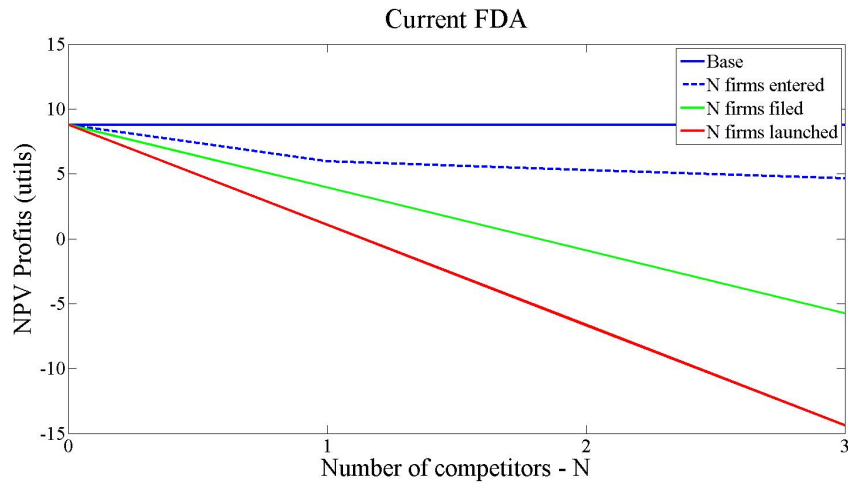

Figure 7: Impact of competition on profits conditional on launching

6 Counterfactual

Effect of a Faster FDA Approval Process

To measure the impact of a faster FDA approval process, I modify the FDA's probability of approval so that the time in-review is effectively reduced. Table 10 presents the current FDA probabilities as well as the probabilities used in this counterfactual evaluation and Figure 8 plots these probabilities over time. In the data, the probability of a firm staying in-review is 71.6% while in the counterfactual I reduce this to 31.6%. I adjust the per-period approval probability to 62.9% to ensure that overall approval and rejection probabilities are the same over a span of 20 years, i.e. $\sum_{t=1}^{T} pr_f^{t-1} \cdot pr_l = \sum_{t=1}^{T} pr_{f,faster}^{t-1} \cdot pr_{l,faster}$ where $pr_{f,faster}$ is the in-review probability in the counterfactual of a faster FDA approval.

Table 10: FDA Approval Probabilities conditional on Firm's filing for an NDA

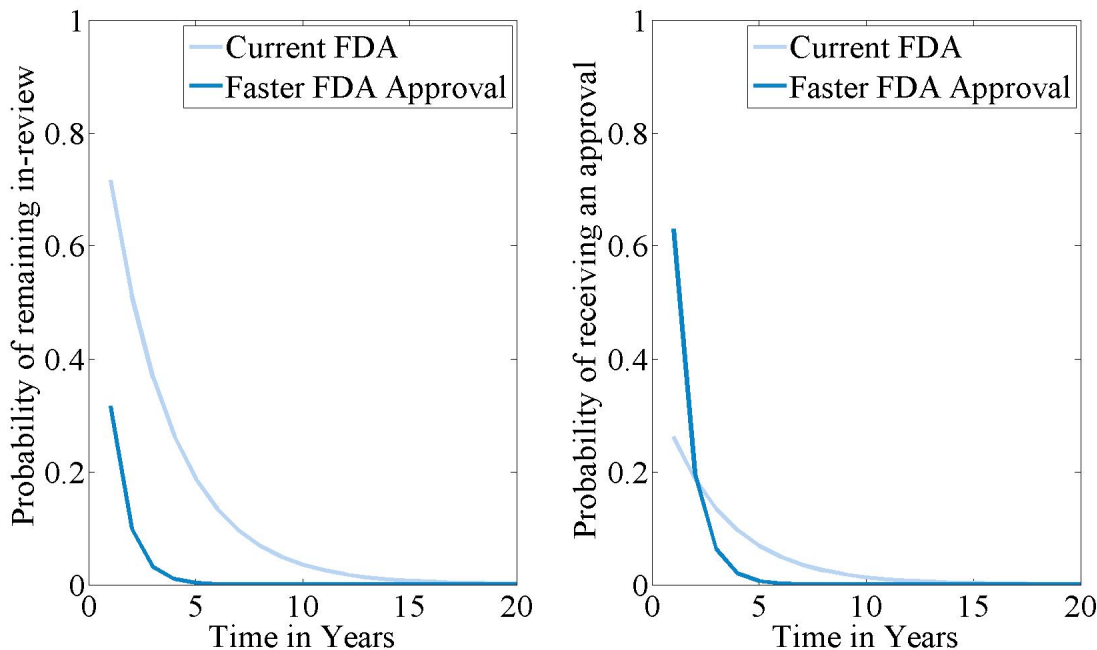| Probability of	Remaining in-review	Approval	Rejection
Current FDA	71.60%	26.20%	2.30%
Faster FDA Approval	31.60%	62.99%	5.41%

Figure 8: Ex-ante probabilities of remaining in-review and approval

I then recompute the new equilibrium under the counterfactual of a faster approval process. I first compare the impact of competition on profits across the two scenarios: current

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FDA approval rates and a faster FDA approval. I then highlight the implications of ignoring strategic effects. The left panel in Figure 9 reproduces Figure 7 for comparison. The right panel shows that the NPV declines much more rapidly, in the counterfactual of a faster FDA process, when competitors are closer to launching. The line depicting NPV as a function of the number of firms filed is much steeper in this counterfactual: this is because unlike in the current FDA, competitors remain in-review for shorter periods of time which in turn reduces the launched firm's term as a monopolist.
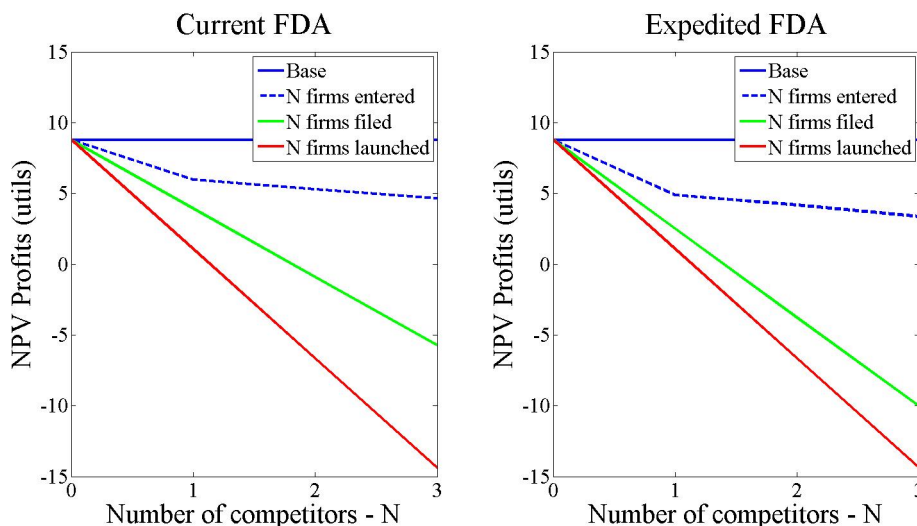

Figure 9: Impact of competition on profits - faster FDA approval reduces NPV of profits when competitors have filed

Quantifying the effects: Competitive intensity vs. reduced time to market

To quantify the extent to which each effect dominates, I compare the value functions solved by computing the dynamic equilibrium under a faster FDA approval process to the value functions if firms acted without any strategic behavior, i.e., ignored the states of their competitors.[15] Figure 10 plots the File value functions, v_f, under the 2 scenarios along with the base case scenario of the current approval process. The state space chosen is such that the firm's competitors are far from launching (one competitor has just entered R&D and the other two have not entered). As can be seen, the focal firm benefits from an expedited approval process: the File value function is 19% higher compared to the current FDA approval process. In other words, the benefit from the reduced time to market and the longer time remaining on a firm's patent[16] outweighs the competitive effects. The bias, if firms did not

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[15]there is no equilibrium computation in the non-strategic case.

[16]since I evaluate value functions for 20 periods, all remaining periods after a firm launches is considered as time remaining on the firm's patent.

consider their competitor's strategic responses is in the order of 120%.

Next, I repeat the same exercise but when the firm's competitors are close to Launch (one competitor has filed and the other two have not entered). Figure 11 shows that the focal firm is worse-off under an expedited approval process because competitive effects outweigh any potential gain from a faster approval process. Compared to the current regime, the focal firm's access to monopoly profits is lower when competitors are likely to get an approval soon. Moreover, when competitors' states are not accounted for, one can misleadingly conclude a large positive impact of an expedited FDA process.
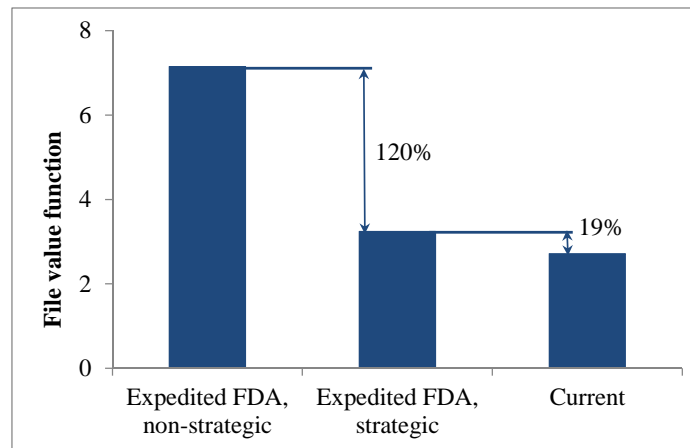

Figure 10: Reduced time to market and longer remaining patent life dominates when competitors are far from Launch.
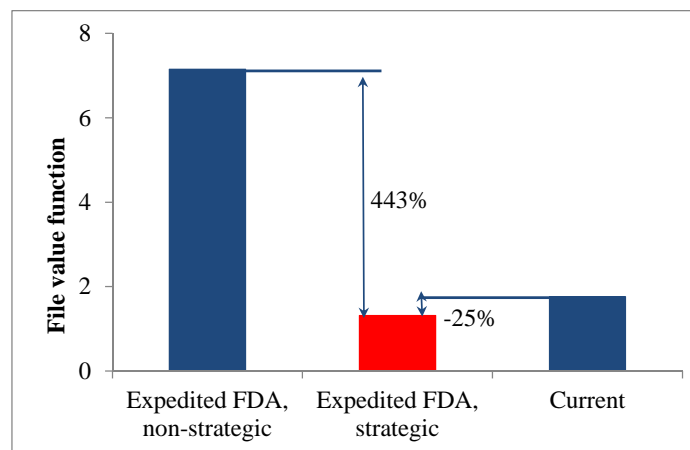

Figure 11: Competitive effects dominate when competitors are close to Launch.

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7   Conclusion

This paper finds that a faster FDA process, something pharmaceutical firms are pushing for, is not always beneficial from a profit-maximizing firm's viewpoint. While the reduced time to market and the longer time remaining on a firm's patent can increase the NPV of the flow of profits, this makes the market more attractive thus intensifying competition which can exert a downward pressure on firm profits. Using a dataset on Phase 3 clinical trial entry, continuation and filing decisions and FDA outcomes at the firm-market-year level a dynamic model of oligopoly was estimated accounting for unobserved heterogeneity in markets. This paper finds evidence - both model-free as well as from the structural parameters - that competition has a negative impact on firms' continuation decisions in R&D.

This paper focused only on the Phase 3 stage of R&D. Acquiring data on the earlier Phases of research can shed further light on the dynamics that occur in this industry. Because firms manage a portfolio of products, it is possible that firm decisions across markets are not independent. Exploring complementarities across markets is a direction for future work, where one might find that a launched competitor not only effects the market the focal firm is in, but spurs investment in another market belonging to the firm's portfolio. It was also assumed that conditional on being in a research state, all firms are equal. While this assumption seems reasonable given that these firms constitute the top 15 firms in the US pharmaceutical industry, relaxing this assumption and accounting for firm heterogeneity is a direction for future work.

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A Strategic Interactions - Reduced Form Evidence (All Firms)

Table 11: Decision to continue or exit as a function of competitor's states (All Firms)

Continue/Exit	Endogenous actions		FDA outcomes	
	Coefficient	t-stat	Coefficient	t-stat
Number of competitors exited				
1	2.86	8.53	3.00	8.79
2	3.06	6.62	3.15	6.69
3	4.28	5.32	4.22	5.56
4	3.51	4.02	3.93	4.39
5	2.97	1.77	3.48	1.99
6	5.04	3.7	3.94	2.82
7	5.32	3.73	3.74	2.52
Number of competitors in research				
1	-0.47	-1.4	-0.45	-1.32
2	-0.57	-1.48	-0.45	-1.13
3	-1.47	-3.07	-1.55	-3.16
4	-0.79	-1.29	-1.05	-1.59
5	-0.52	-0.5	-0.59	-0.49
6	-2.31	-2.03	-2.64	-2.19
7	-3.64	-2.49	-3.58	-2.42
Number of competitors in filed status				
1	0.14	0.42	0.18	0.51
2	0.65	0.85	0.77	0.93
3	-1.64	-1.27	-1.47	-1
Number of competitors exited due to FDA				
1			1.85	2.79
Number of competitors launched				
1			0.15	0.33
2			-0.51	-0.79
3			-0.69	-0.84
4			-1.75	-1.57
5			-3.48	-1.8
6			-4.77	-2.47
Own state (Reference: Research Year >4)				
1	1.47	4.62	1.47	4.54
2	0.87	3.03	0.84	2.9
3	0.60	2.16	0.56	2
4	0.90	2.95	0.86	2.79
Fixed-effects	Market, Firm, Time			
Log likelihood	-434.47		-426.39	
N obs	2374		2374	
N markets	513		513	

Table 12: Decision to enter Phase 3 or not as a function of competitor's states (All Firms)

Enter/Not enter	Endogenous actions		FDA outcomes	
	Coefficient	t-stat	Coefficient	t-stat
Number of competitors exited				
1	-1.81	-7.85	-1.93	-8.08
2	-2.13	-4.76	-2.31	-5.01
3	-3.31	-5.01	-3.19	-5.39
4	-3.25	-2.87	-3.95	-3.71
5	0.00		0.00	
6	-5.19	-3.67	-4.81	-3.39
7	-6.57	-3.86	-5.97	-3.37
Number of competitors in research				
1	-1.07	-6.77	-1.49	-9.05
2	-1.64	-7.17	-2.15	-9.08
3	-2.10	-7.43	-2.94	-9.94
4	-2.72	-6.62	-3.25	-7.74
5	-3.23	-6.03	-4.20	-8.16
6	-1.89	-1.63	-2.96	-2.62
7	-11.25	-0.03	-14.17	-0.02
Number of competitors in filed status				
1	-0.20	-1.01	-0.62	-3.10
2	0.45	1.06	0.36	0.89
3	-0.46	-0.62	-1.06	-1.49
Number of competitors exited due to FDA				
1			-3.18	-6.41
Number of competitors launched				
1			-1.90	-7.75
2			-2.39	-6.35
3			-2.91	-5.67
4			-4.39	-4.53
5			-2.94	-2.20
6			0.00	0.00
Fixed-effects	Market, Firm, Time			
Log likelihood	-1323.4		-1249.99	
N obs	5911		5911	
N markets	513		513	

B Market Characteristics

Table 13: Market Characteristics Poor Predictors of Firm Decisions in Phase-3

	Continue/Exit		Enter/Not Enter	
	Coefficient	t-stat	Coefficient	t-stat
Market Characteristics				
Market size ($ millions)	0.00015	0.61	-0.00014	-1.01
Prevalence (per 10,000)	-0.00020	-1.80	0.00012	1.83
Age	-0.39	-1.63	0.11	0.80
Race	0.25	0.91	-0.09	-0.57
Gender	-0.08	-0.34	0.01	0.04
Number of competitors exited				
1	-0.55	-1.98	-0.03	-0.14
2	-0.68	-1.76	-0.20	-0.55
3	-0.18	-0.27	0.44	0.85
4	-0.31	-0.35	0.78	0.68
5	-0.04	-0.03	0.00	
6	-1.23	-1.00	1.16	0.93
7	-1.92	-1.41	2.00	1.24
Number of competitors in research				
1	-0.05	-0.17	0.39	2.50
2	-0.07	-0.20	0.59	3.07
3	-0.94	-2.46	0.56	2.31
4	-0.87	-1.67	1.05	3.10
5	-0.41	-0.32	-0.03	-0.06
6	-0.04	-0.03	-0.14	-0.06
7	-0.93	-1.26	0.00	
Number of competitors in filed status				
1	-0.15	-0.52	-0.28	-1.46
2	0.93	1.30	0.33	0.79
3	0.70	0.52	0.95	1.41
Number of competitors exited due to FDA				
1	0.12	0.22	-1.43	-2.54
Number of competitors launched				
1	-0.15	-0.53	0.51	2.49
2	0.49	0.99	0.52	1.47
3	-0.40	-0.55	1.02	2.59
4	-1.28	-2.06	-0.91	-1.03
5	-0.71	-0.80	0.71	0.53
Own state (Reference: Research Year >4)				
1	0.22	0.65		
2	-0.03	-0.10		
3	-0.05	-0.14		
4	0.52	1.21		
Fixed-effects	Firm, Time			
Log likelihood	-381.48		-970.76	
N obs	1704		2356	
N markets	125		125	