Innovation and consumer welfare: Impacts of price regulation in the pharmaceutical industry

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Abstract

Patent protection involves a well-known welfare tradeoff between *ex-ante* innovation incentives and *ex-post* market distortions. The recently enacted price regulation on patented drugs in the United States signifies a shift to mitigate the latter damage at the expense of potential losses in research and development. I estimate static demand and dynamic model of pharmaceutical firms' continuation decisions in clinical trial. I use the estimates to evaluate the welfare effects of the price regulation, accounting for both consumers' welfare gain from decreasing drug prices and potential welfare loss from missing future development of better drugs. Counterfactual simulations demonstrate that the implementation of price regulation, imposing a price cap 10% lower than the oligopoly price on the highest revenue-generating drug, result in up to a 7% increase in consumer welfare.

1 Introduction

Patent protection serves as an incentive for innovation, yet it allows patent holders to set prices above marginal costs once they invent products. The effectiveness of patent protection, including factors such as patent duration and price regulation on patented goods, entails a welfare tradeoff between fostering *ex-ante* innovation and potentially causing *ex-post* market distortions. Striking the right balance is critical for the well-designed patent system.

While this tradeoff has been acknowledged for a long time (Clark, 1915; Nordhaus, 1969; Scherer, 1972), our understanding of the quantitative impacts of different patent systems on R&D incentives and consumer/social welfare remains surprisingly limited. The empirical literature on innovation has predominantly focused on R&D investments as an outcome variable. Evaluating innovation and its policy implications, however, should be grounded in welfare considerations, for the value of innovation diminishes significantly if the resulting goods are not affordable. This issue is particularly pertinent in the ongoing policy debate in the United States concerning the price regulation of patented drugs. The Inflation Reduction Act (hereafter IRA), enacted in 2022, provides Medicare the authority to negotiate drug prices for medications in the late stages of patent life, in response to substantial increase in drug prices over the past few decades. In contrast, controversy surrounds this action, particularly fueled by research-based global pharmaceutical companies. These companies, potentially facing losses of billions of dollars due to this legislation, argue against it, expressing concerns about discouraging R&D investment. It

is crucial to recognize that an ill-designed policy lacking a robust evaluation may impose significant welfare costs in the future.

Addressing the question naturally aligns with structural models, as welfare evaluation and various policy counterfactuals are essential. To this end, this paper develops and estimates a structural model of pharmaceutical firms' R&D decisions in clinical trials. Notably, the model explicitly integrates demand estimation, allowing for the evaluation of consumer welfare and profit estimates without relying on a reduced-form profit function. The estimated model enables me to assess anticipated policy impacts through counterfactual simulation.

The empirical analysis relies on two distinct datasets, each utilized for the demand estimation and the dynamic estimation. The first dataset, used for demand estimation, comes from a publicly available, nationally representative survey of the United States. This survey captures individual expenditures on each prescribed drug. For dynamic estimation, I leverage a database that compiles comprehensive development information for drug projects from their initiation. The focus of this analysis is on the diabetes drug market due to its substantial market size and the intensive nature of R&D within this therapeutic area.

In my model, firms make R&D choices to pursue future FDA approvals for introducing new drugs to the market, and subsequently, firms sell their approved drugs in static markets. The incorporation of vertical differentiation of products is crucial to address questions related to innovation. However, accurately measuring drug quality, which includes factors such as efficacy, side effects, drug interactions, and ease of use, poses a challenge. Since drug quality is arguably a stable, drug-specific property, I opt to estimate drug quality as unobserved characteristics in demand estimation, as in Berry et al. (2016), Hashmi and Van Biesebroeck (2016) and Khandelwal (2010). Non-parametric estimates of the drug quality reveal a steady escalation, closely mirroring the observed pattern of market turnover. Newer therapeutic-class drugs have gained significant market shares, despite charging much higher prices.

In the clinical trial stage, firms decide whether to continue or discontinue their drug development projects. The profits derived from demand estimation are incorporated into a dynamic clinical trial stage, serving as payoffs from continuation. One challenge in linking the demand model with the dynamic clinical trial model arises from the fact that approximately 90% of drugs in development fail during clinical trials, making it impossible to directly recover the drug qualities of these unsuccessful drugs. To address this, I assume that firms draw drug quality from a quality distribution. The mean of quality distribution is allowed to exogenously change over time based on estimates of marketed drug quality. Employing the forward-simulation technique developed by Bajari et al. (2007), I estimate dynamic parameters to fit both estimated quality distribution of marketed drugs and clinical trial decisions. A pivotal parameter for counterfactual results is one governing how firms' R&D respond to expected profits. The identification of R&D responsiveness to expected profits hinges on variations of expected profits due to factors such as scientific failure risk, market competition, and market size.

Computing the equilibrium of the model poses a challenging task. Although the two-step estimation method circumvents the need to solve for equilibrium during estimation, it becomes necessary for conducting counterfactual simulations. The value functions and policy functions are time-dependent, influenced by changing exogenous market and clinical trial characteristics. Furthermore, expected values from entry depend on distributions of products characteristics in the market such as quality levels of marketed drugs, whether

they are generic or branded, and the remaining years of patent protection. These factors significantly expand the state space and makes the model non-recursive, rendering standard value or policy function iteration approaches impractical. To tackle this challenge, I employ an algorithm that significantly reduces computation time by combining a Pakes and McGuire (2001)-type algorithm with functional approximation.

Using the estimated model, I analyze the effects of price regulation on patented drugs on pharmaceutical firms' R&D response and resulting consumer welfare. Specifically, I examine a counterfactual scenario that mirrors the anticipated U.S. price regulation, wherein only a branded drug with top sales is subject to a price cap, representing a 10% decrease from the unregulated oligopoly price. My counterfactual simulations suggest that the price regulation can lead to an increase in consumer surplus ranging from 0.5% to 7%, despite a predicted decrease in the continuation probability of clinical trials ranging from 0.2% to 4%.

This paper proceeds as follows. The following paragraphs discuss how this paper relates to the existing literature. In Section 2, I discuss industry background. Section 3 describes the data and descriptive statistics. In Section 4, I present a model. I describe estimation in Section 5 and results in Section 6. Finally, in Section 7, I discuss computation method of counterfactual simulation and a theoretical consideration about a policy design problem. Section 8 concludes.

Related literature

This paper is related to the literature studying the role of patent on R&D and its welfare consequence (Nordhaus, 1969; Moser, 2005; Budish et al., 2015; Moscona, 2020). Theoretically, an unambiguous prediction is that stronger patent protection induces more R&D investment. In contrast to the theoretical clarity, previous empirical work to study the impact of patent protection on technological progress are limited (Bryan and Williams, 2021). Sakakibara and Branstetter (2001), Lerner (2009) and Qian (2007) find little evidence that stronger patent protection encourages innovation, while Moser (2005), Budish et al. (2015) and Moscona (2020) find patent protection affects the direction and the level of innovation.

Since direct measures of R&D investment are easy to access such as clinical trial starts and new drug approvals, pharmaceutical industries have attracted many empirical studies of innovation. A number of papers assess impacts of market profitability on R&D incentive in different settings and they broadly reach consensus of its positive effect (Acemoglu and Linn, 2004; Blume-Kohout and Sood, 2013; Finkelstein, 2004; Duggan and Scott Morton, 2006; Dranove et al., 2020). Cunningham et al. (2021) build a model about and empirically confirm the presence of "killer acquisitions", where incumbent firms acquire inventors of competing products and then discontinue their projects in order to preempt competition. However, research that directly connects to welfare-relevant outcomes are limited.

Demand estimation is of vital importance to discuss consumer welfare. There are many papers that implement IO type demand estimation in the pharmaceutical context (Dunn, 2012; Chaudhuri et al., 2006; Dubois and Lasio, 2018; Maini and Pammolli, 2023; Björnerstedt and Verboven, 2016; Crawford and Shum, 2005a). Among them, Dunn (2012) estimates BLP-type of demand model of anti-cholesterol drugs and finds quality-adjusted price decreases over time. Although the motivation to estimate demand model is the same (*i.e.*, to evaluate welfare gain of production introduction), he does not consider pharmaceutical companies' R&D investment and thus cannot investigate the key tradeoff

of patent protection and price regulation that this paper studies. Another related paper in this literature is Chaudhuri et al. (2006) who investigate price change and the associated welfare loss from patent protection. Again, firms R&D is not modeled and they only estimate downside of patent protection. Rao (2020) and Khmelnitskaya (2023) are the only studies I am aware of that model and estimate dynamic game of pharmaceutical firms' clinical trials. My model of clinical trial stage builds on them. The contribution of this paper is to develop a framework to connect the clinical trial model to demand estimation, and to provide an estimation and computation strategy. This enables me to investigate welfare implications of R&D as well as a variety of market-related counterfactuals.

My model is estimated using a conditional choice probability (CCP)-based method (Hotz and Miller, 1993) with forward simulation (Bajari et al., 2007). My method builds on the literature using dynamic games to study innovation (Goettler and Gordon, 2011; Hashmi and Van Biesebroeck, 2016; Igami, 2017; Igami and Uetake, 2019; Yang, 2020). These papers primarily concentrate on exploring the relationship between competition and innovation, examining products that some firms have produced rather than newly invented products protected by patents. Consequently, their frameworks cannot be readily applied to address the specific questions posed in this paper. One technical contribution of this paper is to develop a framework to incorporate innovative goods, where most of goods fail during R&D phase and do not reach to marketing. The difficulty is that we cannot observe demand data of these un-commercialized goods. I boil down a variety of differentiation of developed drugs into a single dimension of quality index, which makes a difference of demand.

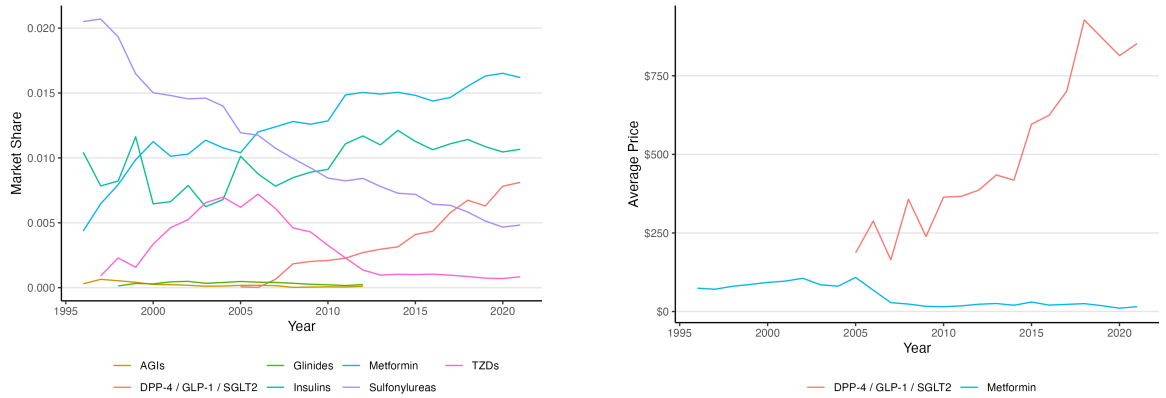
Several papers study the effects of regulations on innovation. Most of the papers are reduced-form empirical studies looking at the effects of labor laws regulations on innovation (Acharya et al., 2013; Griffith and Macartney, 2014). An exception is Aghion et al. (2023) who build endogenous growth model to assess the equilibrium impact of labor regulatory burden on innovation and calibrate the model by using French firm-level panel data. As far as I know, no paper has studied the welfare effect of patent-relevant price regulation.

Computing equilibrium of my model is a nontrivial task because all the information of market goods becomes state variable. To address this challenge, I employ several techniques. First, I use an alternative equilibrium concept, Ifrach and Weintraub's (2017) moment-based Markov equilibrium (MME), rather than Markov perfect equilibrium. Applications of the MME include Corbae and D'Erasmo (2021); Caoui (2022); Jeon (2022). Second, I approximate the value function (Kalouptsidi, 2017). Finally, I combine these techniques with simulation-based value function iteration similar to methods considered by Collard-Wexler (2013).

2 Industrial background

Drug Development

Drug development is a resource-intensive and time-consuming process, with a relatively low likelihood of final FDA approval. The entire process is carefully structured, regulated, and incurs significant costs. The process of developing pharmaceutical products involves multiple stages, each with specific milestones and regulatory requirements. Following the identification of potential drug compounds through routine discovery processes, they undergo preclinical evaluations to assess efficacy and toxicity. If successful, it can begin



(a) Share dynamics

(b) Average price dynamics

Figure 1: US diabetes drug markets. Average price dynamics of first-line medicine, metformin, and new class drugs.

clinical research with human subjects. The clinical testing period involves three phases. In Phase I, the drug is tested on 20 to 100 healthy subjects to test the safety of the drug. In Phase II, the drug is tested on a small group of patients with the disease to prove the drug has the intended effects on the patients. Phase III is conducted to assess the drug's effectiveness on a large sample of patients. Notably, successful completion of each phase is necessary before progressing to the next. The FDA plays a crucial role in approving investigational new drug applications and new drug applications, with close communication between pharmaceutical firms and the FDA throughout the process.

Diabetes Drug Market

I particularly focus on diabetes drugs for the estimation of the model with two following reasons. First, diabetes is one of the most research-intensive diseases in the last two decades. In my data, diabetes amounts to the highest number of drugs which have conducted preclinical development. Second, the number of diabetic patients is relatively high compared to other research-intensive diseases such as cancer. This is necessary to obtain sufficient samples of data the demand estimation uses, detailed more later.

The U.S. diabetes drug market has experienced a notable development with the introduction of new-generation drugs since the late 2000s. Therapeutic classes known as DPP-4 and GLP-1 were initially approved around 2005, and a more recent class, SGLT-2, entered the U.S. market in 2013. Currently, the FDA has granted approval to a dozen drugs within these novel classes, with no generic counterparts available yet. While these drugs have demonstrated efficacy in treating type 2 diabetes mellitus and have captured a portion of the market share (Figure 1 (a)), they have not exhibited a distinct superiority over metformin. Metformin, widely used as a first-line medication and available in generic form, presents a more cost-effective alternative. The high cost associated with the new-generation drugs poses a significant barrier, with these medications being more than ten times expensive than generic metformin and experiencing escalating prices in the last decade (Figure 1 (b)).

Medicare Drug Price Negotiation Program

IRA, enacted into law in 2022, provides the Centers for Medicare & Medicaid Services (CMS) the authority to directly negotiate the prices of certain high expenditure, single source drugs without generic or biosimilar competition.[1] The substantial increase in drug prices over the past few decades has become a cause for concern, leading to widespread demands for government intervention. In response to public pressure, the government enacted drug price regulations. The White House documents that "Millions of Part D enrollees depend on these vital treatments to treat life-threatening conditions including diabetes, heart failure, and cancer, but many struggle to access their medications because of prohibitive costs" regarding drugs selected in a first negotiation cycle. Countering this claim, global pharmaceutical firms have employed lobbying efforts and legal challenges to impede the enactment and implementation of laws related to drug price regulations.

Annually, CMS will select drugs for negotiation, and the resulting negotiated prices from the first cycle will be effective in 2026. In the initial cycle, CMS selected ten drugs for negotiation, with four of them being diabetes drugs.

In order to be eligible for negotiation, drugs must be at least seven years (for small-molecule drugs) or eleven years (for biologics) past its FDA approval or licensure date. In addition, medicines qualify for price negotiation if they are covered under Medicare Part D, Medicare's outpatient prescription drug benefit program, and are single source brand-name drugs without generic or biosimilar competition. CMS selected ten from 50 medications with the highest Medicare Part D covered prescription drug costs.

A type of the price regulation will be price ceiling. CMS propose maximum fair price to the firms of the ten drugs. In developing an initial offer, CMS will start with evidence related to therapeutic alternatives and then consider other factors, such as costs of R&D and production and distribution of the selected drug. By September 1, 2024, CMS will publish any maximum fair prices agreed upon between CMS and participating drug companies.

3 Data and Descriptive statistics

Demand Data

I use data from Medical Expenditure Panel Survey (MEPS) to obtain market shares and prices of diabetes drugs. The survey is publicly available and nationally representative in the US, and recodes details on the individual's medical expenditure on each prescribed drug, insurance, demographic characteristics (age, sex, income, education, medical history) and health conditions. The yearly dataset covers from 1996 to 2021.

Each drug in MEPS is linked to FDA's National Drug Code (NDC). I identify a corresponding drug name and a dosage form (e.g., 50 mg or 100mg) for each NDC by using publicly available database, Find-A-Code. I supplement information on manufacturers, Anatomical Therapeutic Chemical (ATC), brand and generic names, whether drug is generic or branded and FDA's approval data from several sources including FDA's Orange Book and public databases called DrugBank and KEGG.

[1] `https://www.cms.gov/files/document/fact-sheet-negotiation-process-flow.pdf` and `https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf`

For the analysis that follows, I aggregate across all dosages of the same drug because they are the same invented product from the development perspective. I use drugs of ATC code A10 as diabetes drugs. Regarding mixture drugs, which contain two molecules in a single medicine, I treat them as single-molecule drugs with more novel molecules (the other of Metformin or Glimepiride), whose producers are left unchanged. I define potential consumers by using ICD code, a medical classification list, and disease history variables of each individual in MEPS. I limit the sample to those with disease history of either diabetes, hypertension, cholesterol metabolism or some other minor disease. The restricted samples cover more than 99% consumptions and individuals who buy diabetes drug. percentage of no drug consumers.

MEPS records *Quantity* and *Expenditure* variables for each prescription. Individuals prescribe multiple drugs including the same drug many times with possibly different quantities during one year. I assume each observation is independent and an individual with N observation at a year does makes N choices among alternatives including outside option. I assume consumers buy q_j quantity as a single good j at each choice, and I calculate it as an average of *Quantity*. The quantity of product j in the usual economic meaning thus corresponds to just the number of observations buying drug j, and the market share is defined as:

$$ms_{jt} = \frac{\#\text{obs. buying } j}{\#\text{individuals buy no drug} + \sum_{k \in J_t} \#\text{obs. buying } k},$$

where J_t is a set of drugs sold in year t. To construct the price variable, I use total expenditures including both the amount paid by the insurer and the amount paid out-of-pocket by the individual, and call this *Expenditure*. *Expenditure* of the same drug and year substantially differ across individuals, reflecting complex U.S. medical and insurance systems. However, it is necessary for demand estimation to specify prices that individuals in sample do not actually consume. Although one can possibly estimate a demand model with price dispersion, I decide to construct single price variable with a consideration of the scope of the paper. I define price of drug j at period t, denoted by P_{jt} as follows; First, I regress *Expenditure* on *Quantity* without constant for each year, call the coefficient p_{jt}, which is intended to measure price for one unit of *Quantity*. Price P_{jt} is then calculated as $P_{jt} = p_{jt}q_j$. Pirce is adjusted in 2021 U.S. dollars.

Summary statistics is provided by Table 1 and 2 for every two years. The market size of potential consumers grows substantially during 2000s, while the share of outside option is fairly stable. The highest share except for the outside option is increasing. The number of branded drugs increases during 2000s and hits the peak around 2010. Most notably, the average price of branded drugs drastically increases in 2010s, while the generic price is also increasing.

year	market size	outside share	max inside share
1998	1.26e+8	0.32	0.14
2001	1.75e+8	0.35	0.18
2004	2.27e+8	0.31	0.14
2007	3.03e+8	0.32	0.20
2010	3.57e+8	0.36	0.22
2013	3.47e+8	0.33	0.26
2016	3.54e+8	0.35	0.25
2019	3.12e+8	0.30	0.29

Table 1: Summary Statistics

year	# brand	# generic	mean price brand	mean price generic	s.d. price
1998	12	6	136.27	74.13	73.67
2001	16	7	197.86	129.43	98.80
2004	20	5	209.45	122.72	88.42
2007	24	4	398.40	55.64	508.14
2010	23	6	605.36	126.81	313.76
2013	18	5	957.82	164.93	770.68
2016	16	6	2561.23	310.93	3034.84
2019	20	7	2086.69	288.59	1040.11

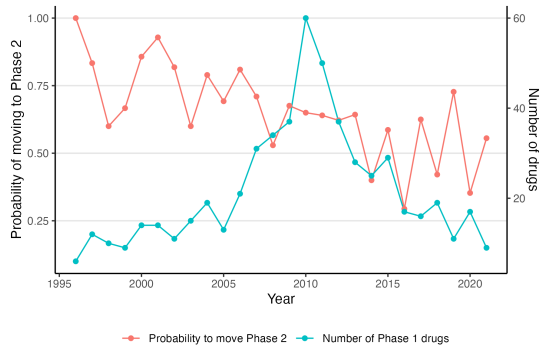
Table 2: Summary Statistics

Clinical Trial Data

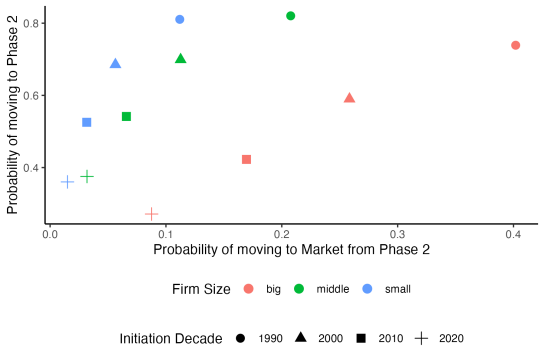
The data source used for the dynamic estimation is Pharmaprojects database, which has been used in earlier research studying drug development (e.g., Blume-Kohout and Sood (2013); Cunningham et al. (2021)). Pharmaprojects contains comprehensive information starting from 1989 until now, tracking drug projects from early-stage development through to launch or discontinuation. Using Pharmaprojects, I identify dates of phase transition for all drug-disease-company-country pairs, and restrict the samples to those in U.S. and with type-1 and type-2 diabetes. I exclude reformulation of existing drugs, which include mixture drugs, to focus on novel drug development.

An outcome variable used in the analysis is whether to continue development from Phase I to Phase II. Pharmaprojects makes a determination about project discontinuation (including *"No Development Reported"*, *"Discontinued"*, and *"Suspended"*) very carefully and conservatively. Therefore, dates recorded in Pharmaprojects as discontinuation are not the dates companies make discontinuation decisions. Probably, the more appropriate modeling to match the reality and the data would be firms making decisions whether to progress projects to the next phase or to wait without any progress, in which firms will face the same choice if choosing the latter. However, this makes it significantly complicated to solve and identify the model without much benefit, and thus I decided to choose a much simpler model. Since phase transition dates are reliable information as firms decision timing, I calculate average duration from the entry into Phase I and the entry into Phase II and assume that all firms have to make decisions after the time passed. Figure 2 panel (a) presents the probability of choosing continuation of development and the number of projects in each year. The continuation probability decreases in 2000s and

stays around 50% in 2010s. The number of projects, which is treat as exogenously given, sharply increases around 2010.



(a) Phase transition probability from Phase I to II, and Number of Phase I projects



(b) Phase transition correlation

Figure 2

A key parameter in counterfactual simulation is the responsiveness of continuation decision to expected profits. The identification of it depends on the degree of positive correlation between expected profits and continuation decisions. Table 3 shows results of logistic regressions predicting continuation of Phase II by the number of opponent projects in each phase and market. Even though coefficients are statistically insignificant due to small sample size, mostly firms negatively respond to the competitiveness. Figure 2 panel (b) plots correlation between continuation probability from Phase I to II (y axis) and success probability to reaching FDA approval (x axis) for different decades and different firm sizes. The firm size is defined using the number of projects in the data. Strong positive correlation within a firm size will be an important variation to estimate the responsiveness parameter, and the second column of Table 3 also captures the correlation. Interestingly, Figure 2 panel (b) shows negative correlation conditional on age. This might also suggest the selection during clinical trials, since bigger firms conduct more projects and they can selectively pick some projects showing promising results. Since one firm's products steal shares their own shares each other, big firms having many projects under development would adopt a more stricter criterion of development continuation decisions. The interesting factors, the selection and multi-product firms, are not taken into consideration in this version of the paper.

4 Model

In this section, I present a dynamic differentiated-good oligopoly model. Time is discrete with infinite horizon, $t = 0, 1, \cdots$. The model consists of two parts: static demand and Bertrand competition, and dynamic clinical trial stage. In the clinical trial stage, a firm makes a decision of trial continuation only once, for simplicity. Khmelnitskaya (2023) decomposes the reason of development discontinuation into strategic and scientific components, and finds that the strategic factor plays little role in exit of late phases. Also, it is straightforward to incorporate multiple decisions of one project. Building and estimating Ericson and Pakes (1995)-type models, where incumbent firms have scope of future R&D investment of new products, is left for further research.

	Model 1	Model 2
Intercept	2.16 (0.68)	
# Phase1	−0.04 (0.03)	−0.04 (0.03)
# Phase2	0.05 (0.07)	0.05 (0.07)
# Phase3 + Registered	−0.03 (0.06)	−0.03 (0.06)
# Market	−0.07 (0.05)	−0.06 (0.05)
Company size big		1.66 (1.54)
Company size middle		2.23 (1.15)
Company size small		2.33 (1.00)
Probability of approval		0.76 (3.35)
AIC	738.41	866.84
BIC	760.20	903.16
Log Likelihood	−364.20	−425.42
Deviance	728.41	850.84
Num. obs.	577	692

Table 3: Development Continuation Decision

Clinical trial stage

There are four phases in the clinical trial stage: Phase I, II, III and FDA filing, denoted by $k = 1, \cdots, 4$, respectively. I focus on firms' decisions whether to continue development from Phase I to II and treat everything else exogenous. At every period t, new firms enter Phase I. Each firm draws its drug quality q_i from quality distribution $F_t(\cdot)$. I allow $F_t(\cdot)$ evolves deterministically. I assume firms do not observe not only others' draws but also their own draw of quality of the clinical trial stage and only knows its distribution and how it evolves. Once drug j is launched, q_j becomes public information. The number of firms to enter Phase I follows Poisson distribution with rate λ_{0t}. After the entry, firms have to wait certain time to complete Phase I. The time to required for Phase I is assume to follow an exponential distribution with rate λ_1 and thus the process that a firm's completion is Poisson. An implication of the Poisson process is memoryless property, *i.e.* remaining expected duration for the completion does not depend on how much time has elapsed already. This assumption, though unrealistic, greatly reduces required state space, since firms do not have to track how many periods other firms have waited and only have to track the number of the firms conducting Phase I. When the Poisson clock ticks, firm i draws private shocks $(\varepsilon_{it}^{out}, \varepsilon_{it}^{in})$ and decides whether to continue $(a_{it} = 1)$ or discontinue $(a_{it} = 0)$ its project in the next period. This decision is done at the end of each period after state is realized. If $a_{it} = 0$, firms terminates the development and gets ε^{out}. I assume ε_{it}^{out} and ε_{it}^{in} are independently and identically distributed (i.i.d.) Type-1 extreme value with cumulative distribution function $\exp(-\exp(-\varepsilon/\sigma_\varepsilon))$, where σ_ε is the scale parameter. If $a_{it} = 1$, firm incurs cost c_{lt} at the period and moves to Phase II at the beginning of the next period, where subscript l denotes one of three firm sizes $FS = \{small, middle, big\}$.

From Phase II, everything is exogenous. The time required for each $k \neq 1$ follows an exponential distribution with rate λ_k. At the end of each stage $k = 2, 3, 4$, firm drops out from the clinical trial with probability $1 - \rho_{klt}$ due to a scientific reason. I allow ρ_{klt} for each k to vary across three firm sizes and decades to match the data better. Let y_i denote a binary variable indicating firm i succeeds its clinical trial or not. I allow any correlation between q_i and y_i. Since no firm observes quality of drugs under development,

the conditional distribution $F_t(\cdot|y=0)$ is irrelevant for the entire game (as explained soon, the profit only depends on marketed drug competitors). So, I am agnostic about $F_t(\cdot|y=0)$, and with an abuse of notation, let $F_t(\cdot)$ denote $F_t(\cdot|y=1)$. If firm passes all the phases, it moves to market stage launches the drug and its quality becomes public.

Market stage

Utility for a consumer i from drug j is given by

$$u_{ijt} = \alpha \ln p_{jt} + X_{jt}\beta + q_{m(j)} + \xi_{jt} + \epsilon_{ijt},$$

where $m(j)$ is j's molecule. After patent of brand drug j expires, generic firms enter the market and sell the same molecule drug $m(j)$. Characteristics X_{jt} include (1) a brand indicator, (2) dummy variables indicating first four years after the entry, which is meant to capture gradual share taking. Drug quality $q_{m(j)}$ is estimated as a molecule fixed effect, since the quality considered here is time-invariant drug-specific characteristics which is constant whoever sells it. ξ_{jt} is a market shock and an idiosyncratic shock ϵ_{ijt} follows type-I Gumbel distribution.[2] Utility from outside option is normalized as $u_{i0t} = \epsilon_{i0t}$. Consumer i choose option $j \in \{0, 1, \cdots, J_t\}$ in period t if $u_{ijt} > u_{ij't}$ for all $j' \neq j$.

On the supply side, I assume a Nash equilibrium in strategic price setting for differentiated goods. Let me denote by π_{ft} the variable profit of multi-product firm f in market t. In the clinical trial stage, I have not addressed firm heterogeneity of incumbency yet and treat all firms as identical new entrants. Still, I allow for multi-product ownership in the market observed in data and these firms maximize total profits. Firm f selling products $j \in F_{jt}$ maximizes its profit:

$$\pi_{ft} = \max_{\boldsymbol{p}_{jt}} \sum_{j \in F_{jt}} (p_{jt} - mc_{jt}) ms_{jt} M_t, \tag{1}$$

Following Dubois et al. (2022), I assume generic firms set competitive prices. Marginal costs mc_{jt} and market level shock ξ_{jt} are i.i.d random variables following probability distribution F_{jt}^{mc} and F_t^{ξ}, and realized before price setting each period. Let $\pi_{jt}(q_t, X_t)$ denote j's equilibrium profit given quality vector $q_t \equiv \{q_{it}\}_{i=1}^{n_t}$ and characteristics vector $X_t \equiv \{X_{it}\}_{i=1}^{n_t}$ where n_t is the number of drugs at period t.

Continuation value, State and Equilibrium

Since period payoff π_{jt} and many factors in the clinical trial stage are time-variant, the strategy and the equilibrium are also non-stationary. Since a firm's action is a simple binary discrete choice, a strategy is characterized by a cutoff strategy $\mu_{lt} : S_t \to \{0, 1\}$ such that $a_{it} = 1$ if and only if $\mu_{lt}(s_t) \geq \varepsilon_{it}^{out} - \varepsilon_{it}^{in}$. Using the logit formula, firm's conditional choice probability (henceforth, CCP) to take $a_{it} = 1$ under strategy μ, denoted by $\Psi(\cdot)$, which is the probability that a firm will play action a_{it} at state s_{it} before observing

[2] In order to capture flexible substitution pattern, I am considering nested logit error and random coefficient specification. Especially, in this specification, the model does not predict that generic entry of molecule m takes share of the brand-name drug of the same molecule. Therefore, when calculating expected profits used in the clinical trial stage, I assume that after patent expiration the drug exits from market, earns zero profits and generic drug immediately enters the market.

realization of $(\varepsilon_{it}^{in}, \varepsilon_{it}^{out})$, is given by

$$\Psi(\mu_{lt}(s_t)) = \frac{\exp\left(\frac{\mu_{lt}(s_t)}{\sigma_\varepsilon}\right)}{1+\exp\left(\frac{\mu_{lt}(s_t)}{\sigma_\varepsilon}\right)}. \tag{2}$$

Given the opponents' (symmetric) strategy $\mu(s) = \{\mu_{lt}(s)\}_{t=0,l\in FS}^{\infty}$, continuation value of firm j completes Phase I at t is given by:

$$\int_{-\infty}^{\infty} V_{lt}^{\Psi(\mu)}(s_t, q) dF_t^q(q) - c_{lt} + \varepsilon_{it}^{in},$$

$$\text{where} \qquad V_{lt}^{\Psi(\mu)}(s_t, q) = \left(\prod_{k=2,3,4} \rho_{klt}\right) \mathbb{E}_{\Psi(\mu)}\left[\sum_{m=t+\tau}^{t+\tau+T_i} \beta^m \pi_m(\boldsymbol{q}_m, \boldsymbol{X}_m) \,\middle|\, s_t\right],$$

where s is a state detailed below and T_i is remaining duration of patent protection after market launch, which is stochastic and assumed to be i.i.d..[3] The expectation in the second line is taken over (1) time required for clinical trial τ (2) iid static variable (mc, ξ) (3) T which itself is iid but affects other future market state variables (4) market state variables (q, X) whose evolution is determined in equilibrium. In the clinical trial stage, I assume firms only track (or observe) the number of firms in each phase $(n_{kt})_{k=1}^4$ but not year other firms enter in Phase I and their firm sizes, which actually affect their own profitability in market. Other firms' strategy μ affects state evolution, and thus, the expectation uses CCP $\Psi(\mu)$. In this sense, the environment is dynamic game even though firm's choice is only once, since past and future strategy other firms take is payoff-relevant. If other firms use strategy μ', firm i's optimality implies

$$\mu_{lt}(s; \mu') = \int_{-\infty}^{\infty} V_{lt}^{\Psi(\mu')}(s_t, q) dF_t^q(q) - c_{lt}. \tag{3}$$

Since market states (q, X) are vectors of continuous variables and thus very high-dimensional, it is almost computationally infeasible to solve the model if I keep the distribution as it is. Therefore, I assume firms only keep track of the following moments of the state: (1) the highest effective quality which equals $\max_j\{q_{m(j)} + X_j\beta\}$ for each brand and generic drugs (2) the number of brand and generic drugs (3) the sum of effective quality of all drugs for each brand and generic drugs (4) quantile statistics of drug age, which is not directly relevant with static profits but needed to calculate evolution of the other moments. To distinguish from the genuine state variables, I call the moments plus $(n_{kt})_{k=1}^4$ moment-based state, denoted by $\theta_t = \theta(s_t)$.

The equilibrium concept I consider is a non-stationary version of MME proposed by Ifrach and Weintraub (2017).

Definition 1. Non-stationary MME comprises a continuation strategy $\mu_t(\theta)$ that satisfies the following conditions:

(1) Firm strategy μ satisfies the equilibrium condition:

$$\mu_{lt}(\theta) = \int_{-\infty}^{\infty} V_{lt}^{\Psi(\mu)}(\theta_t, q) dF_t^q(q) - c_{lt} \quad (\forall t, l, \theta)$$

[3]Usually, companies register their developing drugs to patent before FDA approval, and thus they have much shorter years of market exclusivity than 20 years after FDA approval. Yet, some drugs are approved to extend its patent protection, so the duration is highly random.

(2) The perceived transition kernel is given by:

$$\hat{P}_\mu = \Phi P_\mu$$

where $\hat{P}_\mu$ is the transition kernel of the moment-based state when firms use strategy μ, P_μ is that of the underlying state, and Φ is an operator such that $\hat{P}_\mu$ approximates the process of the moment-based state, P_μ.

The non-stationarity complicates the computation of the equilibrium. I describe the algorithm in the counterfactual section. Let me denote $EV_{lt} = \int_{-\infty}^{\infty} V_{lt}^{\Psi(\mu)}(\theta_t, q) dF_t(q)$, which is equilibrium expected profit, for the notational simplicity.

Discussion

Interpretation of c_{lt}— An interpretation of c_{lt} needs caveats. First, the cost term captures the expectation of all possible expenses that will be paid until the end of the production, except for the marginal costs. This will include not only clinical trial costs of Phase II and III but also costs associated with application to FDA approval, market entry costs and fixed costs of production.

Second, I do not explicitly incorporate the disqualification of drug safety which should have determined $1 - \rho_1$, and instead allow all firms to make continuation decisions about the development. This point is also related to the selection issue I argue next. If firm have some knowledge about their own drug quality, these firms are no longer identical and optimal continuation probability should be increasing in their posterior. Therefore, in the current model, an estimate of c_{lt} also reflects overall disqualification rate of Phase I. However, this assumption may not be that harmful for counterfactual results unlike it may sound, if I properly estimate σ_ε. This is because σ_ε determines how much firms response to the continuation value and the continuation cost, and thus, even if some firms face prohibitively expensive costs due to the safety issue and does not response to the change of the continuation value at all, my estimate takes these firms into account overall. Third, I allow the continuation cost to vary over time. The cost shift may reflect costs associated with quality update of developed drugs and/or other factors such as labor costs and legal burdens.

Firm information about its own quality— In the model, firms are assumed to have no additional information about their own drugs under development except for the prior distribution. This assumption is unrealistic and abstracts away the important selection issue discussed in the conclusion. To incorporate the selection of high quality drugs, it will be natural to assume a firm to observe noisy signal of its quality. Variance of the noise term will be identified from the failure rate in the late phases.

5 Estimation

In this section, I present estimation strategy. The estimation takes two steps. In the first step, I estimate demand parameters and back out marginal cots. In the second step, profits calculated from the demand estimation are plugged into the clinical trial stage and using forward simulation technique I estimate dynamic parameters c_t and $f_t(q)$.

Demand and Period competition

I estimate demand parameters using aggregate market share and Berry's (1994) inversion provides the linear relationship

$$\ln(ms_{jt}) - \ln(ms_{0t}) = \alpha \ln p_{jt} + X_{jt}\beta + q_{m(j)} + \xi_{jt},$$

where ms_{jt} is j's market share at period t.[4]

Following Dubois et al. (2022), I construct instruments in a sprit of BLP-type IV. In particular, in the IV estimation, I use the following variables as instruments for p_{jt}: for each drug j in each year t, the number of products in j's ATC-4 class and the number of drugs in novel ATC-4 classes including DDP-4, GLP-1 and SGLT2, as these classes were getting more and more popular after the introduction around 2010. Since these variables indicate the competitiveness of markets, price will correlate with them, while the independence from ξ_{jt} is valid if the serial correlation of ξ_{jt} disappears between sufficiently large year gap as entry might correlate with ξ_{jt}.

Marginal costs is estimated from the first-order condition of equation (1) for every market t:

$$mc_t = p_t + (\Omega_t \odot S^t(p_t))^{-1} ms_t(p_t), \tag{4}$$

where Ω_t is ownership matrix at period t and $S^t i, j(p_t) = -\partial ms_{jt}/\partial p_{it}$. Since each mc_{jt} and ξ_{jt} are non-parametrically identified and estimated, estimated empirical distributions of $\hat{mc}_{jt}$ and $\hat{\xi}_{jt}$ are consistent estimators of F^{mc}_{jt} and F^{ξ}_{t}. I allow F^{mc}_{jt} to differ across brand and generic drugs.

Once demand parameters and marginal costs are estimated, I can compute profits π for hypothetical market structure. The algorithm to compute Bertrand NE follows Morrow and Skerlos (2011), in which prices are going to be iteratively updated by using the first order condition with an initial guess and it usually takes a few seconds.

In the dynamic estimation, I forward simulate the life-time expected profits of entering market, EV_{lt} for all t and l. This needs to repeatedly compute Bertrand NE under a huge number of hypothetical market structures (with different drugs, qualities, mc, xi, and year.) It is almost infeasible to run Morrow and Skerlos's (2011) for every time. Instead, using a polynomial function, I approximate Bertrand NE profit of firm i by i's information (q_i, X_i, mc_i, ξ_i) and several statistics of market level distribution of these variables. I carefully distinguish between state variables (q, X) and iid static variables (mc, ξ) and use the latter information as much as possible to make the state space compact. To this end, I simulate more than 200 thousand of firms' profits under different market structures with sufficient variation of these variables, and the approximation achieves $R^2 \approx .97$.

Dynamic model: Quality update and Cost of innovation

A set of parameters to be estimated in the dynamic game part is $c_{lt}, F_t(q)$ and σ_ε. I parameterize $F_t(q)$ as follows:

$$F_t(q) = \Phi\left(\frac{q - (\gamma_0 + \gamma_1 t_{96})}{\sigma_q^2}\right),$$

[4]As MEPS dataset contains individual prescriptions, expenditures, and detailed individual characteristics, it would be better, in terms of efficiency gain and strong IV, to use individual data directly following Berry et al.'s (2004) approach.

where $t_{96} = t - 1996$ and $\Phi(\cdot)$ is the cumulative distribution function of the standard normal. Flexibility to allow for c_{lt} needs a careful examination. The parameter σ_ε is estimated as a correlation between outcome a_{it} and expected profit EV_{lt} conditional on cost. This means that EV_{lt} needs to be more flexible than c_{lt} and the variation of EV_{lt} within the same cost must be sufficient. Through examining several specifications, I decide to use c_l. I estimate the set of parameters, $\Theta = \{\Theta_c, \Theta_q, \sigma_\varepsilon\} = \{\{c_l\}_{l \in FS}, \{\gamma_0, \gamma_1, \sigma_q\}, \sigma_\varepsilon\}$, by maximum likelihood. I set a reference year 1996 because it is the earliest sample in my dataset. Note that since I do not consider he selection issue of quality, a quality distribution of observed market drugs estimated demand estimation is unbiased. So, I first estimate Θ_q directly from the estimated $\hat{q}$, denoted by $\hat{\Theta}_q^{mrk}$. However, to make the clinical trial data fit better, I allow these parameters to change in the final estimation. This is particularly important for recent clinical trial observations in which no drug has ever approved and thus no quality estimate is obtainable.

To estimate these dynamic parameters, I use a two-step estimation method which is de facto standard in the dynamic game estimation literature (Bajari et al., 2007; Aguirregabiria and Mira, 2007; Pakes et al., 2007; Pesendorfer and Schmidt-Dengler, 2008). In the first step, I estimate CCP Ψ_t directly from the data. I use a logistic regression with flexible regressors. To accommodate the non-stationarity of the value and policy function, I allow the CCP to vary across years in the estimation. I also estimate parameters governing state transitions, which contain duration rates $(\lambda_k)_{k=1}^4$, the probabilities passing each phase $(\rho_k)_{k=2}^4$ and an empirical distribution of the duration between market entry and patent expiration. In the second step, I compute $V_{lt}^{\Psi}(s_t, q)$ using forward simulation, in which I simulate the evolution of the state s_t (actual state not moment-based state) and action a_{it} by drawing from the choice probabilities $\hat{\Psi}_t$ and the state transition process. Each simulation sequence starts from the actual state s_t in the data and fix entry quality q. During simulation, some other firms enter the market with some qualities. I draw them from $F_t(q; \hat{\Theta}_q^{mrk}.)$. In addition, to simulate years after the last sample period, I use the value of the last year. For every simulated path, I can compute all the period payoff and thus discounted profits of the path. Then, $V_{lt}^{\Psi}(s_t, q)$ is computed simply by summing them for all the paths

$$\hat{V}_{lt}^{\hat{\Psi}}(s_t, q) = \frac{1}{R} \sum_{r=1}^{R} \sum_{k=t}^{T^r} \beta^{k-t} \pi(s_k^r).$$

Substituting the simulated expected value into the optimality condition (3) and CCP (2) yields the probability of action:

$$\Pr(a_{it} = 1 | s_t) = \frac{\exp\left(\frac{\widehat{EV}_{lt}(s_t) - c_l}{\sigma_\varepsilon}\right)}{1 + \exp\left(\frac{\widehat{EV}_{lt}(s_t) - c_l}{\sigma_\varepsilon}\right)},$$

$$\text{where} \quad \widehat{EV}_{lt}(s_t) = \int_{-\infty}^{\infty} \hat{V}_{lt}^{\hat{\Psi}}(s_t, q) d\Phi\left(\frac{q - (\gamma_0 + \gamma_1 t_{96})}{\sigma_q^2}\right)$$

The integration part is computed following Tauchen's (1986) method, and grid points of q_t are taken according to the Gauss-Hermite quadrature. Since the weights on each grid changes as Θ_q change, I cannot use the Gauss-Hermite quadrature directly here. The continuation actions and estimated quality distribution of marketed drugs constitute the

likelihood function. Thus, the log-likelihood function can be written as

$$l(\Theta) = \underbrace{\sum_t \sum_{i \in I_t} [a_{it} \ln \Pr(a_{it} = 1|s_t) + (1 - a_{it})(1 - \Pr(a_{it} = 1|s_t))]}_{\text{clinical trial continuation decisions}} + \underbrace{\sum_t \sum_{j \in J_t} \phi \left(\frac{\hat{q}_j - (\gamma_0 + \gamma_1 t_{96})}{\sigma_q^2} \right)}_{\text{marketed drug quality}},$$

where I_t is a set of firms that face continuation choice at year t and J_t is a set of marketed drugs that entered Phase I at year t.

Identification

The distribution of quality $F_t^q(\cdot)$ is identified from the data of marketed drugs. Since the selection issue is abstracted away so far, observed quality is consistent with the underlying distribution. Given the identification of $F_t^q(\cdot)$, expected profits $\int_{-\infty}^{\infty} V_t^{\Psi(\mu')}(s_t, q) dF_t^q(q)$ is also identified from demand parameters. Once the expected profits from continuation are identified, the problem is boiled down the usual logit estimation, in which cost parameters and the scale of the error term $(\varepsilon^{in}, \varepsilon^{out})$ are identified since the coefficient on the expected profits is fixed as 1. The cost parameters are pinned down average continuation probabilities, while the scale parameter is identified from the positive correlation between outcome probability and the expected profits conditional on costs. The latter is numerically equivalent to the inverse of a coefficient attached to the expected profits under which the scale parameter is normalized as 1. In the estimation, however, there is efficiency gain from estimating $F_t^q(\cdot)$ using not only estimated marketed drug quality but also clinical trial decisions.

Discussion

The model is nonstationary by nature, since the market size and the exogenous entry rate are time-dependent. This means year itself is a state variable. Basically, each year, one has an only single observation, the data are very sparse compared to the huge state space. This implies the difficulty to estimate the CCP precisely, and it is Igami's (2017) and Igami and Uetake's (2019) motivation to avoid using the standard two-step estimation method. They instead use finite-period models and the full-solution method, which fill in the gap of the sparsity by solving policy function directly. However, in my environment, their full-solution approach is inappropriate and infeasible. It is inappropriate, because there is no natural terminal period. It is infeasible, because the number of possible states is too many to solve backward. Thus, I follow the two-step estimation approach and fill states of no observation by estimating CCP using polynomial structure, which is a standard approach many application studies take.

One possible remedy for the finite sample bias of CCP estimation is proposed by Aguirregabiria and Mira (2007). They recommend to replace imprecisely estimated CCP by policy function after estimating parameters using the CCP. The policy function can be obtained by solving the model with parameters estimated using CCP. Furthermore, there are benefits to repeat this iteration until convergence.

6 Results

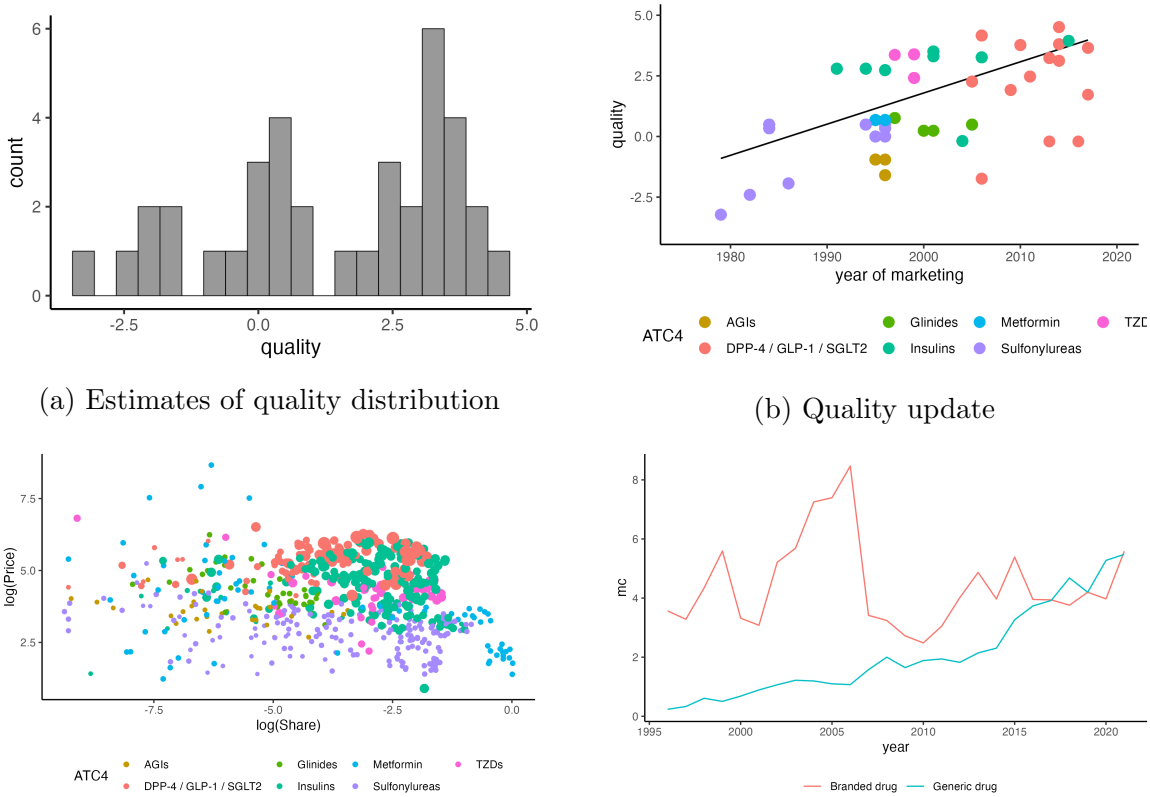
Demand parameters

Table 4 presents estimates of the demand estimation. The IV estimate in the second column shows more elastic price sensitivity than the OLS estimates in the first column. Corresponding own- and cross-price elasticity are -1.103 and 0.031, respectively. Compared to the literature, these values are smaller in absolute levels (for example, -1.430 and 0.142 in Dubois et al. (2022)). Also, a coefficient on the brand dummy is estimated as negative, but the literature robustly shows it is positive. A likely reason is that instrumental variables do not work well. Even though the F-statistics shows sufficient relevance of IVs (Stock and Yogo, 2002), the estimated coefficients on the IVs in the first stage regression are mostly positive, which is an opposite sign because these IVs are supposed to proxy degree of market competition. I scrutinize the data and find that counter-intuitively firms did not decrease, or even increased, prices after the patent expires, even controlling year and firm fixed effects. This might be the case in the reality interestingly but potentially indicates a problem in constructing price variable.

Model:	OLS	IV
log(Price)	-0.4204 (0.1042)	-1.013 (0.2190)
Brand Dummy	-1.512 (0.2587)	-0.9574 (0.2978)
Fixed-effects		
First 5 Years After Entry	Yes	Yes
Molecule	Yes	Yes
Fit statistics		
R^2	0.44289	0.39529
Observations	649	649
F-test (1st stage), log(Price)		32.326

Heteroskedasticity-robust standard-errors in parentheses

Table 4: Demand parameter estimates



(a) Estimates of quality distribution

(b) Quality update

(c) Market share, price and quality

(d) Estimates of marginal costs

Figure 3: Estimates of unobserved quality and maginal costs

Drug quality for each molecule is non-parametrically estimated as fixed effects. The result is presented in Figure 3. Panel (a) shows its histogram, and Panel (b) presents estimates along the year of market entry, colored by ATC4 classes. The estimates of quality distribution reveals a strong increasing pattern, mostly coinciding with different therapeutic classes. The OLS estimates regressing quality on Phase I entry year[5] are used in forward simulation as quality distributions of competitors. The estimates of quality successfully capture an intuitive sense of what quality is intended to measure. That is high-quality products are well sold even if prices are high. Panel (c) of Figure 3 depicts the situation, where larger dots are higher quality.

Average of estimated marginal costs for both branded and generic drugs is displayed in Panel (d) of Figure 3.

Period profits are derived from Bertrand NE. Polynomial approximation of log of the profit is very successful using not only ones own information such as quality, marginal cost and market shock ξ_{jt} but also information regarding market distributions of these variables such as maximum and mean for each brand and generic drugs.

Dynamic parameters

The estimate of conditional choice probabilities is presented in Table 5. Similar to Table 3 in section 3, the estimates of coefficients on the number of competitors in each phase

[5]Due to the omission of data on when marketed drugs entered Phase I in Pharmaprojects, I utilize a time frame of seven years prior to FDA approval. This duration represents the sample average years taken from Phase I to approval for drugs with recorded entry dates.

and market are overall negative without statistical significance. I also include maximum quality value for both branded and generic drugs in market. These variables have also negative impacts.

	Model 1
# Phase1	−0.04 (0.06)
# Phase2	0.05 (0.12)
# Phase3 + Registered	−0.03 (0.11)
# Market	−0.15 (0.17)
max quality brand	−0.34 (0.96)
max quality generic	−0.00 (0.30)
Fixed-effects	
Every three year	Yes
Firm size	Yes
Fit statistics	
Log Likelihood	−422.34
Num. obs.	692

Table 5: CCP: logit on the continuation choice

Figure 4 compares actual and fitted values of continuation probability for each year. The estimated CCP captures the same trend of the actual data. For the policy function after the last year of the sample, I use the one of the last year.

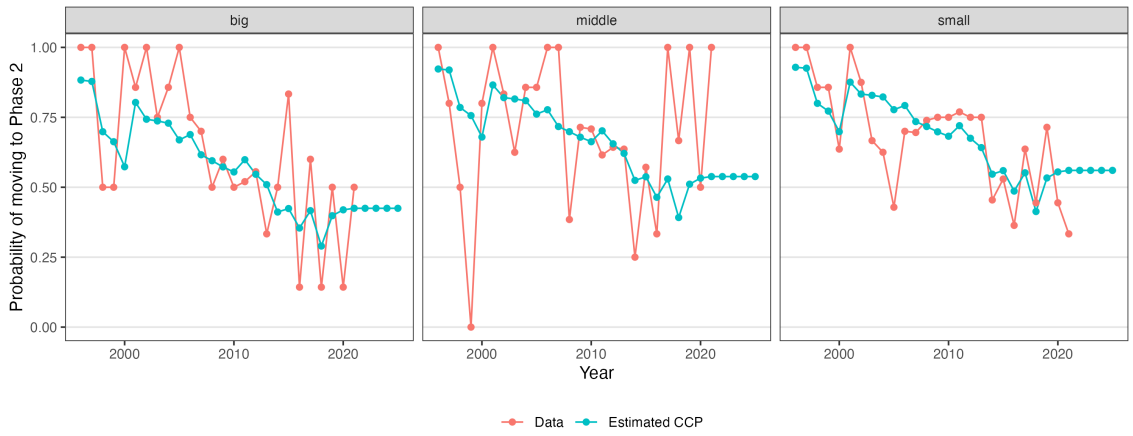
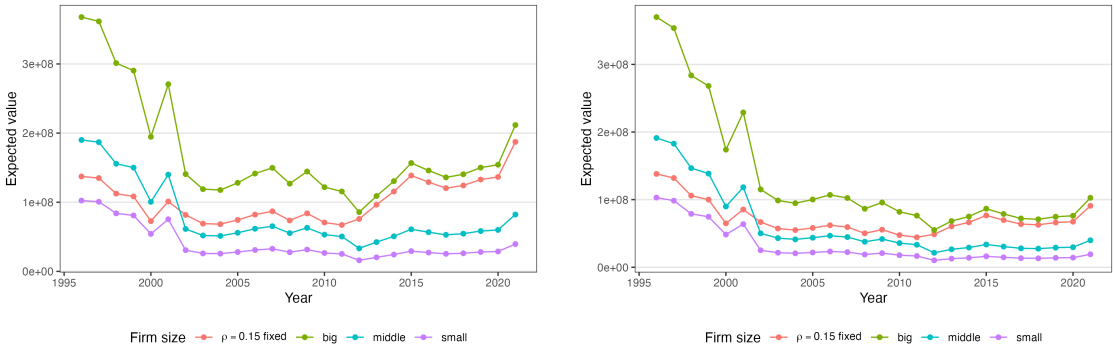


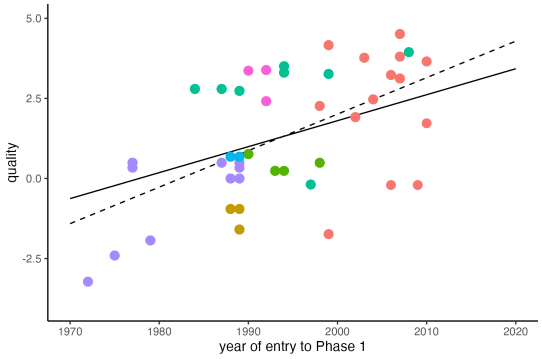
Figure 4: CCP fitting

I fix discount factor $\beta = 0.9$. Expected value EV_{lt} calculated by the simulation is presented in Figure 5 panel (a), where the quality distribution used in the figure is estimated only from marketed drugs. The red line fixes the success rate $\rho_2 * \rho_3 * \rho_4 = 0.15$ to see roles of other factors more clearly. Note that the only difference between firms with different sizes is this rate in my model. Expected discounted profits decrease in the first decade and increase in the last decade. Two factors are likely to govern this trend. On the one hand, as the years go on, more and more high-quality drugs enter the market and the profitability of newer drug decreases fixing quality. On the other hand, quality distribution improves over time, expanding market size of inside share. Even though mean

of quality distribution increases linearly, expected profits can increase in a convex form, due to the logit demand. Therefore, the latter force exceeds the former in late years. By adjusting success rates for each firm size, I obtain EV_{lt} for each firm size.



(a) $\hat{\Theta}_q = \hat{\Theta}_q^{mrk}$ (b) $\hat{\Theta}_q = \hat{\Theta}_q^{Full}$



(c) Quality update: solid $\hat{\Theta}_q = \hat{\Theta}_q^{Full}$
dashed $\hat{\Theta}_q = \hat{\Theta}_q^{mrk}$

Figure 5: Simulated expected life-time profits

Table 6 provides estimates of the dynamic parameters. The first column presents the full estimation of Θ, while the second column's estimates are the result fixing $\Theta_q = \hat{\Theta}_q^{mrk}$. The likelihood ratio test rejects the null that $\Theta_q = \hat{\Theta}_q^{mrk}$ with a significance level of 0.05. Figure 5 panel (b) shows corresponding expected profits under the estimates of full model $\hat{\Theta}^{Full}$, and panel (c) compares between means of quality distribution under $\Theta_q = \hat{\Theta}_q^{mrk}$ and $\Theta_q = \hat{\Theta}_q^{Full}$. MLE adjusts mean quality of late years downward to match clinical trial data better. This adjustment is critical for welfare evaluation in counterfactual experiments. Estimates of continuation costs for small and middle firms are negative. Since costs should be positive, the underestimation suggest that σ_ε is too large. The last column of Table 6, the result when fixing σ_ε to be 1, shows much higher and positive cost estimates. As σ_ε captures the degree of positive correlation between EV_{lt} and the outcome a_{it}, this implies either that the variation of EV_{lt} is too small or that the model is too much misspecified and some specification adjustments will be necessary. In order to obtain valid results of welfare analysis in counterfactual simulation, reliable estimates of σ_ε is crucially important, since it governs how much firms reduce R&D investments under price regulation. A more trustworthy identification strategy about σ_ε must be required, which is left for future work.

	Full	Fix Θ_q	Fix $\sigma_\varepsilon, \Theta_q$
γ_0	1.48 (0.247)	1.554	1.554
γ_1	0.081 (0.015)	0.114	0.114
σ_q	1.655 (0.161)	1.633	1.633
c_small	-4.483 (2.882)	-5.814 (3.221)	1.869 (0.131)
c_middle	-2.649 (2.649)	-3.317 (3.462)	4.186 (0.173)
c_big	6.173 (2.787)	9.74 (1.852)	11.423 (0.182)
σ_ε	8.635 (4.326)	11.496 (3.787)	1
Fit statistics			
log-likelihood	-519.225	-606.413	-684.409

Table 6: Dynamic parameter estimates. Figures are in .1 billions of dollars. Standard errors presented in parentheses do not account for static estimation in the first stage and simulation errors of forward simulation. These values represent the lower bounds of correct standard errors.

7 Counterfactual simulation and Discussion

In this section, I discuss welfare implications of IRA's price negotiation. To mimic anticipated regulation form, I consider a counterfactual scenario where a branded drug which achieves the biggest revenues in the market is imposed a price cap. I set the price cap as 10% decrease of unregulated oligopoly price. First, I present results ignoring strategic interaction in the clinical trial stage. More specifically, instead of computing equilibrium of the entire dynamic model under counterfactuals, I recompute static equilibrium under the regulation with and without new product entry. Then, I calculate the continuation probability in the clinical trial using modified expected value computed by multiplying average static profit change rate with the original EV. Table 7 presents the result of change rates of total consumer surplus, firms' R&D continuation probability and consumer surplus leaving R&D decision unchanged.

year	Consumer Surplus	Cont. Prob.	CS w/o R&D response
2000	0.059	-0.028	0.071
2005	0.038	-0.028	0.043
2010	0.016	-0.030	0.019
2015	0.015	-0.035	0.018
2020	0.008	-0.026	0.010

Table 7: Counterfactual simulation

In the following, I first present the computation algorithm to solve the model, second explain measure of consumer surplus and offer some theoretical considerations.

Solving the model is not a simple task. Since the model does not have a recursive structure due to non-stationarity and multiple stages, simple iteration algorithms such as value or policy function iteration approach do not work here. As such, I use the following algorithm. The algorithm solve value functions backward and thus avoids to conduct forward simulation from each state in Phase I to the end of patent life.
Algorithm:

1. Randomly pick up M state points (not moment-based state) to roughly cover a reasonably wide range of state space. Keep M states in memory until the end.

2. Randomly draw mc's and ξ's for every firms and every year and calculate firms' static profits under states picked in step 1. Repeat this sufficiently many times enough to integrate out non-state random variables, mc and ξ. Take the average of simulated profits for each branded drug in each state. Note that the expectation has to be taken before taking log. Then, approximate log of the expected profits of branded drugs by a flexible polynomial function of both moment-based states and a year variable. This serves as the value function of the last year of the support of patent protection, denoted by $W_{\bar{T}}(\theta, t)$. Note $W_{\bar{T}}(\theta, t)$ does not depend on policy function.

3. Guess an initial guess of equilibrium CCP function $\Psi^0(\theta, t)$.

4. Given guessed CCP $\Psi^R(\theta, t)$ in the previous iteration R, simulate one-period state transitions k times from K states picked in step 1. Keep $M \times m$ state realizations in memory until the update of $\Psi^R(s)$. Let s_{ji} denote ith simulated state among m rooted from s_j with $j = 1, \cdots M$.

5. Update value functions backward using simulated state transitions as follows.

   a. In the market stage, an expected flow profit $E\pi(s)$ is given $W_{\bar{T}}(\theta, t)$. The probability to remain in the market in next year from τ is given by $p^\tau = \frac{F^T(\tau+1)-F^T(\tau)}{1-F^T(\tau)}$. Calculate the average of the continuation value of τ-th year in market: $\tilde{W}_\tau(s_j) = E\pi(s_j)+\beta\left[p^\tau \frac{1}{m}\sum_{i=1}^m W^R_{\tau+1}(s_{ji}) + (1-p^\tau)\frac{1}{m}\sum_{i=1}^m W^{R,r}_\tau(s_{ji})\right]$, where $W^{R,0}_\tau(\cdot)$ is an initial guess. Estimate polynomial approximation $W^{R,r+1}_\tau(s_j)$ using M data points of $\tilde{W}_\tau(s_j)$. Repeat the iteration until convergence. Convergence is evaluated using coefficients of polynomial functions.

   b. In the clinical trial stage, an expected flow profit is 0. The probability to remain in the same phase in next year from phase k, denoted by p^k is given by Poisson distribution, which is invariant how many years has passed in each phase. Calculate the average of the continuation value of Phase k: $\tilde{V}_k(s_j) = 0+ \beta\left[p^k \frac{1}{m}\sum_{i=1}^m V^R_{k+1}(s_{ji}) + (1-p^k)\frac{1}{m}\sum_{i=1}^m V^{R,r}_k(s_{ji})\right]$, where $V^{R,0}_k(\cdot)$ is an initial guess (if $k = 4$, $V^R_{k+1} = W^R_1$). For Phase 1, p^k is fixed to be 1, so that no iteration is necessary. Estimate polynomial approximation $V^{R,r+1}_k(s_j)$ using M data points of $\tilde{V}_k(s_j)$. Repeat the iteration until convergence. Convergence is evaluated using coefficients of polynomial functions.

6. Using Phase 1 value $V^R_1(s_j)$, calculate CCP $\Psi^{R+1}(\cdot)$. If coefficients of $V^R_1(\cdot)$ converges, then the iteration stops. If not, go back to step 4.

What level and what form of price regulation is optimal? Suppose that policymakers are primarily concerned with discounted value of consumer surplus and are able to commit future policy sequence. Then, a planner's problem is given by:

$$\max_{\{p_t(h_t)\}_{t=0,h\in\mathcal{H}}^\infty} \mathbb{E}\sum_{t=0}^\infty \beta^t \ln\left(\sum_{j\in J_t}\exp\{W^t_j(p_{jt}, q_j)\}\right),$$

subject to

(IC static) p_t satisfies Bertrand NE for non-patented drugs

(IC dynamic) Probability distribution of new entry of q_j must be supported by dynamic equilibrium,

where W_j^t is mean utility from good j at time t, h_t is a history of a state realization until time t and $\mathcal{H}$ is a set of all possible state realizations.

More generally, policymakers do not have to confine their attention to price regulation about innovation policies. Among countless alternatives of forms and magnitude of policy design, what is optimal? This question is unquestionably difficult to answer. However, some remarks are worth making. First, it would be a better approach to use some revelation-principle type argument to transform the extremely challenging question into well-defined optimization problem with more restricted domain of policy choices. As multiple policies will achieve the same outcome, it is redundant to search from unboundedly huge set of policies. Second, firms R&D decision depends only on expected values EV as long as firms are risk neutral. This observation should play a crucial role to find what kind of revelation-principle type argument is applicable to this particular environment, since (IC dynamic) condition in the planner's problem can be converted to planner's direct choice of EV and CCP. Third, appropriately employing duality will be a key. Consumer welfare faces inter-temporal tradeoff in terms of current price and future quality, and it might be able to consider some kind of indifference curve to compensate each other independently from firms' decision. It would be easier to choose expected values for firms given the indifference curve. Lastly, in terms of the implementation of solution to the planner's problem boiled down by revelation principle, price regulation would be more flexible than other innovation policy such as change of patent duration but hard to commit entire future contingent levels. The lack of commitment will be detrimental for firms' R&D incentive. Fining a way that is practically implementable and able to commit will be also a challenging task.

8 Concluding remark

In this paper, I develop a simple model of R&D investment in the pharmaceutical industry. The model is estimated using the standard two-step estimation method in the dynamic game estimation literature with forward simulation. The estimated model is leveraged for counterfactual experiments, examining the potential impacts of anticipated price regulation in the U.S. on both R&D and consumer welfares. Additionally, I propose a computation algorithm to facilitate solving the dynamic model in counterfactual simulation. I also provide a quick argument to approach an optimal policy design problem of innovation.

My analysis has some limitations. First, my dynamic model does not account for the selection of high-quality drugs during clinical trials. Throughout development processes firms must observe signals of drug quality, and approved drugs are likely to have relatively higher quality than a prior distribution. Neglecting the selection aspect leads to an overestimation of the underlying quality distribution, consequently inflating the downside of price regulations. Moreover, the analysis overlooks a crucial advantage of a patent system as an innovation policy over direct subsidies, namely its ability to screen out higher-quality inventions. Given that the quality or societal benefits of an invented good are often private information ex-ante and challenging for governments to evaluate, a patent

system provides an effective mechanism. To address this limitation, I plan to develop and estimate a model to address this selection issue in the next version. For example, selection issue under a dynamic game setting is considered in Crawford and Shum (2005b).

Another limitation in this version of the paper is that firms in the clinical trial stage are treated as entrants without any drugs in the market. However, it is crucial to note that the pharmaceutical industry is highly concentrated, and global research-based pharma giants own multiple drugs in the market while concurrently engaging in the development of new ones. Consequently, this version of the paper does not delve into the relationship between competition and innovation, which is one of the most important questions in Industrial Organization. An extension to incorporate competition might provide additional insights to the effects of price regulation and change of patent duration. Incumbent firms, concerned with potential cannibalization among their own products, may exhibit greater R&D incentives under conditions of earlier patent expiration or stronger price regulation. Furthermore, the pharmaceutical industry is characterized by frequent mergers and acquisitions and collaborative development of new drugs, presenting another crucial avenue for exploration in future research.

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