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IMPROVING REGULATION FOR INNOVATION: EVIDENCE FROM CHINA'S PHARMACEUTICAL INDUSTRY

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ABSTRACT

This study investigates how enhanced regulation can promote innovation, focusing on the impacts of a significant regulatory reform in China's pharmaceutical sector implemented in 2015. Inspired by regulatory practices in the U.S., the reform aimed to address application backlogs and reduce administrative waiting time for new drug development. Using data at the drug and firm levels during 2012--2021, we make three main findings: (1) drug categories experiencing improved approval times witnessed a surge in investigational new drug applications and related clinical trials; (2) despite little improvement in innovativeness (measured by novel targets unexplored by U.S. counterparts) within drug categories, the reform led to changes in firm composition, attracting innovative new firms and boosting overall drug innovativeness; and (3) the market recognized the improvement in drug innovation, as reflected in stock price adjustments post new drug registrations after the reform. Our findings demonstrate that regulatory barriers can hinder the entry of innovative firms and suggest that latecomers could boost their innovation potential by adopting specific, effective regulatory practices from frontier countries.

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1 Introduction

Medical innovation is crucial for improving health outcomes and extending life expectancy. Yet, the majority of scholarly work on this subject predominantly focuses on developed economies, the pioneers in medical innovation.[1] Developing and emerging economies, on the other hand, often lag in this area, with challenges arising from both governmental and market failures (Kremer, 2002). How can latecomers improve their potential in medical innovation? It appears that strategies that have shown some success in other sectors, such as fostering innovation through foreign direct investment (FDI) or government-led industrial policy, have not yet yielded significant results in the realm of medical innovation.[2] In this paper, we emphasize the potential effectiveness of overhauling regulatory practices that have fallen behind as a viable pathway to improve medical innovation in emerging markets.

A critical aspect of medical regulation is the time taken to approve various stages of new drug development, which varies significantly worldwide. As depicted in Figure 1, developed regions like Australia, Canada, Europe, Japan, and the U.S. typically have swifter approval processes. However, there is a marked variation in approval time among developing nations. For instance, emerging markets such as China and South Africa might experience approval processes that are up to four times lengthier than those in developed nations. Conversely, regulatory enhancements in the early 2010s in countries like Malaysia and Brazil resulted in notably reduced approval duration by 2016 (Patel, McAuslane and Liberti, 2019; Sani et al., 2020).

[1] Influential research has investigated the role of market size (Acemoglu and Linn, 2004; Finkelstein, 2004; Blume-Kohout and Sood, 2013; Dubois et al., 2015; Clemens and Rogers, 2020; Agha, Kim and Li, 2022), patent terms (Budish, Roin and Williams, 2015; Sampat and Williams, 2019), and regulatory practices (Stern, 2017; Chandra et al., 2022; Rogers, 2022). See Lakdawalla (2018) for an overview and more of our discussion later.

[2] The roles of FDI and state-led industrial policy in medical innovation remain to be systematically studied. Scholars have argued that because the pharmaceutical market is often controlled by nation-states or supernational organizations, making global market integration challenging (Zhou and Coplin, 2022). Furthermore, traditional state-led industrial policies, which have achieved some success in East Asia, have repeatedly fallen short when applied to the pharmaceutical and biotechnological sectors (Taylor, 2013).

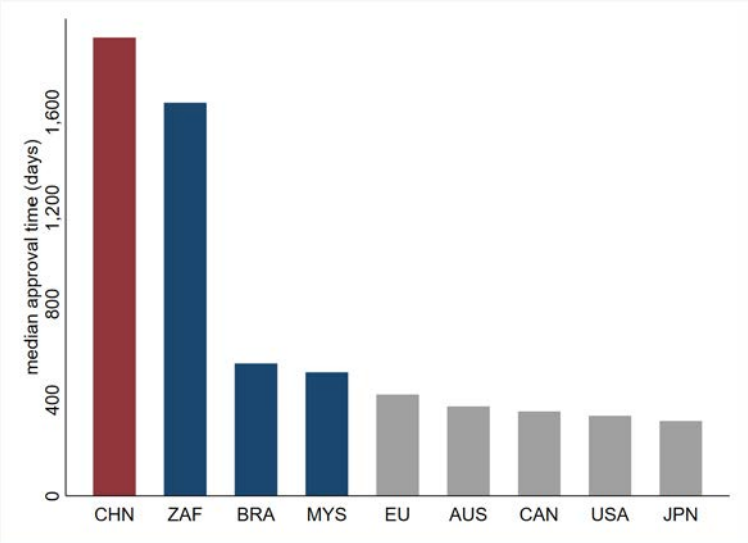


Figure 1: Median Approval Time for New Drugs Approved in 2016

Notes: The data (except for China) is drawn from reports by the Centre for Innovation in Regulatory Science (CIRS), based on the official statistics. The data for China is computed by the authors using China's drug application data. Blue bars refer to developing countries, whereas grey bars refer to developed countries.

To what extent can enhanced regulation foster medical innovation in emerging markets? This policy-relevant inquiry holds significant importance for many developing economies, yet it has received relatively limited attention from the medical innovation literature. We address this question by studying a pivotal case within these endeavors: a substantial regulatory reform introduced in China in 2015. Similar to various other emerging markets, the China Food and Drug Administration (CFDA) confronted a critical shortage of proficient personnel and limited regulatory expertise, which subsequently caused delays and backlogs in the processing of drug approval applications. In response, in 2015, CFDA adopted a strategy reminiscent of the Prescription Drug User Fee Act (PDUFA) enacted in the U.S.. This strategy involved the collection of user fees from applicants to facilitate the recruitment of personnel and the enhancement of systems, resulting in a significant reduction in the approval time for investigational new drugs (INDs), which serves as the critical first stage in the new drug development process. This reform presents an apt context to illuminate the impact on innovation when an emerging market adopts regulatory approaches employed by frontier countries such as the U.S.

Our study investigates the impact of regulatory reform on the quantity and novelty of drug innovation, utilizing the variation in reduction time at the drug level, measured across the three years before and after the regulatory reform (i.e., 2015–2017 vs. 2012–2014).[3] To guide our empirical analysis, we propose a straightforward framework. The essence of the reform—reducing waiting times—likely enhanced the expected returns from innovation. This change is expected to stimulate innovation efforts and attract new firms to the market. Consequently, we anticipate an increase in the quantity of innovation, driven by both existing and newly entering firms. However, the effect on the overall innovativeness of the pharmaceutical industry is more ambiguous. It hinges on whether the reform stimulates incumbent firms to be more innovative and induces the entry of more or less innovative firms, a question we address through empirical investigation. This investigation will also shed light on the cost of ineffective regulatory practices.

Our first set of analysis concentrates on the quantitative aspect, specifically the count of IND approvals and their related clinical trials. We examine the number of INDs across 109 drug categories during 2011–2021. Through a standard difference-in-difference approach, we find that a one-standard-deviation reduction (227 days) in approval time corresponds to a 68% increase in INDs during the period of 2018–2021. However, no such correlation existed prior to the regulatory reform. This finding is robust to considering a variety of drug characteristics. A closer examination of the firms reveals that incumbent companies are accountable for half of this upswing in INDs, with the remaining half attributed to new firms. This rise in INDs is also reflected in an increase in clinical trials across Phase I, II, and III. Additionally, our analysis at the firm level provides further support to the observations made at the drug level, reinforcing our findings.

In our subsequent analysis, we turn to understanding the implications of the reform on innovativeness of the drug industry. Motivated by the long-standing discussion on imitation and innovation in our context, we introduce a novel metric for innovativeness,

[3]Upon examining the relationships between reduction time and diverse drug characteristics, we unveil limited correlations. Notably, an exception is the connection between pre-reform approval time (or backlogs) and reduction time. These findings align with insights gleaned from our interviews, which attribute delays primarily to a shortage of evaluation personnel. Further elaboration can be found in Section 2.

focusing on whether drug applications adopt targets already established in the U.S. (or Europe). It is noteworthy that innovativeness can be influenced through two avenues: within-drug innovation and firm composition. We discover no substantiating evidence for a change in novelty within drug categories following the reform. Nevertheless, there is a sizable enhancement in drug novelty resulting from shifts in firm composition. The regulatory reform contributes to 38% of the increase in new targets observed in the post-reform period, with new firms playing a significant role in elevating aggregate innovativeness. Specifically, new firms account for 74% of the contribution to aggregate innovativeness, given their inclination for innovation and propensity to explore novel targets.

Our main analysis centers around INDs, a critical initial stage in new drug approvals. Notably, only a few INDs post-reform have progressed to the final approval stage of new drug applications (NDAs). To assess market reactions as an indicator of the reform's impact, we further explore stock market responses to NDAs before and after the reform. It's important to note that some INDs for post-reform NDAs may have been filed before the reform. Therefore, this analysis aims not to evaluate the market value of post-reform INDs directly, but rather to assess market reactions to the regulatory reform. By comparing the stock market reactions to the approval of new drugs with those of generic drugs, both before and after the regulatory reform, we find a notably positive stock market response to the final approvals of NDAs following the reform, a contrast to the limited response observed prior to the reform. This shift suggests that the market recognizes and values the improvements brought about by the regulatory changes. It supports our interpretation that the reform has led to increased expected returns, reflecting a positive market perception of the reform's impact on drug innovation.

Our primary contribution is to enhance our understanding of the relationship between regulation and innovation, especially medical innovation in emerging economies. Unlike developed nations such as the U.S., emerging countries like China grapple with application backlogs due to limited resources and human capital. These prolonged review processes amplify innovation costs, subsequently dampening the incentives to innovate.[4] This

[4]See, for example, DiMasi, Grabowski and Hansen (2016) and Martin et al. (2017).

presents significant opportunities for enhancement and introduces wide variations across drug categories, ripe for analysis. Most of the existing work on regulation in medical innovation focuses on evaluating the speed and safety trade-off of FDA review times, including the studies on the Prescription Drug User Fee Acts (PDUFA) in the U.S.—a precursor to the 2015 regulatory reform in China (Berndt et al., 2005; Philipson et al., 2008; Grabowski and Wang, 2008) and studies on more recent changes (Chandra et al., 2022; Rogers, 2022).[5] In developed economies, the central dilemma in medical regulation is balancing quantity and safety. Though this is crucial in emerging nations like China, there's an added dimension: the authenticity of the innovation's novelty. This raises inquiries such as, are these firms truly innovating or merely imitating their U.S. counterparts? Our study sheds light on this vital, relatively untapped domain of medical innovation in emerging markets.

Our study reveals an important link between quantity and novelty in innovation, due to firm entry. In our setting, quantity improvement leads to composition change, which implies novelty improvement at the aggregate level. To the best of our knowledge, this link has not been well studied in the literature on innovation, which commonly tends to analyze quantity and novelty separately (Romer, 1990; Grossman and Helpman, 1991). Our findings document that new firms play a considerable role in medical innovation. This pattern relates to a recent literature highlighting the substantial impact of firm entry in explaining China's economic growth (Khandelwal, Schott and Wei, 2013; Brandt and Lim, 2019). Our study adds new insights into the importance of understanding firm composition in the context of innovation. It also highlights the costs associated with ineffective regulation, specifically how it can deter more innovative firms from entering the market.

[5] Berndt et al. (2005) use a linear model to adjust for the preexisting downward trend and determine that PDUFA was responsible for approximately two-thirds of the reduction in review time from 1991 to 2002. Grabowski and Wang (2008) use a negative binomial regression model and, after accounting for various observable factors, find no correlation between the FDA's review time and the occurrence of adverse drug events. Philipson et al. (2008) utilize data on the distribution of approval and withdrawal times of drugs as well as the distribution of sales of the approved drugs to estimate producer and consumer surplus. The findings indicate that PDUFA remains highly cost-effective, even in the most conservative estimates. Chandra et al. (2022) study FDA's Breakthrough Therapy Designation (BTD) for drugs and find that a 23 percent reduction in development times did not have adverse effects on safety. Rogers (2022) examines FDA's deregulation for medical devices and documents improvement in both the quantity and quality of innovation.

Broadly speaking, our study adds to a growing literature on medical innovation mentioned above by emphasizing that regulatory practices can hinder or foster innovation. Additionally, our study joins an extensive literature on regulation and innovation across diverse domains (e.g., Van Reenen, Aghion and Bergeaud, 2023; Akcigit et al., 2023). Importantly, our study does not center around the impact of more or fewer regulations or wholesale adoption of regulatory approaches; rather, it reveals the value of pinpointing *specific* regulatory practices that have demonstrated efficacy in frontier countries.

2 Context

2.1 Drug Innovation in China

The Chinese pharmaceutical market is the world's second largest pharmaceutical market, with sales reaching $115 billion in 2015, trailing only behind the U.S.. However, the industry's challenges in innovating new drugs have been well-documented (Friedman, 2010; Ni et al., 2017), historically focusing mainly on the development and production of generics. As China accelerates its shift from being primarily a pharmaceutical manufacturing hub to a significant player in the global pharmaceutical R&D sector, its industry finds itself in the initial phases of this transformative journey. A comparison between the R&D pipelines of the top 20 Chinese pharmaceutical companies and their international counterparts over a decade (2012–2021) shows a considerable innovation gap: while multinational firms collectively introduced 313 new drugs, Chinese companies introduced around 31, highlighting a substantial disparity. This disparity extends to the novelty of new drugs in development, where most leading multinational companies have pipelines boasting over 50% of drugs with novel targets, whereas the majority of Chinese companies have less than 30% of products with innovative mechanisms of action (Kong et al., 2023). Overall, China's pharmaceutical innovation landscape is evidently in its early stages.

Since 2010, Chinese pharmaceutical companies have started building capabilities and investing in innovative drugs, with the number of IND applications growing by more than

30% annually in 2010–2020 (Su et al., 2022). However, it was widely recognized that the regulatory system did not keep up with the development of the pharmaceutical industry as of 2015. The China Food and Drug Administration (CFDA), the regulatory agency responsible for overseeing drug development and approval, faced intense criticism for its slow approval of clinical trials and new drugs. For example, in the year 2014, the CFDA received a total of 8,868 new applications. However, they managed to complete only 5,261 applications, leading to an accumulated backlog of 18,597 applications, which included unresolved cases from previous years.[6] As a contrast, in the U.S., starting from 2004, an IND application is deemed approved if the FDA does not reach a decision within 30 days of receiving the application. This streamlined process ensures that all submitted applications are cleared within a month, eliminating the possibility of a backlog.[7]

2.2 Regulatory Reform in 2015

As part of the government's efforts to promote innovation, the CFDA initiated a large-scale regulatory reform to promote drug innovation in 2015. The primary goal of the CFDA's regulatory reform is to tackle the backlog of drug approval applications and reduce processing times.

Figure 2 illustrates the process of new drug development and application. Initially, potential drug candidates undergo preclinical research in laboratory settings to establish their potential efficacy. Prior to clinical trials, a submission of an IND application to the regulatory authority, in this case the CFDA, is required. Clinical trials can commence only after receiving regulatory approval. A primary objective of the recent reform is to shorten the IND application process, highlighted by the red arrow in Figure 2. Following the completion of three stages of clinical trials, if the new drug demonstrates sufficient efficacy and safety, the drug developer will proceed with an NDA to the CFDA, the final regulatory approval needed before market release.

[6]National Medical Products Administration: "2014 Annual Drug Evaluation Report" http://www.cjpi.org.cn/zryyxxw/spypnb/webinfo/2017/01/1485614814619329.htm

[7]Title 21 of the Code of Federal Regulations (CFR) https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-C/section-312.40

In analysis, we focus on IND approvals as the main outcome. Additionally, we examine clinical trials and NDAs to help interpret our findings.

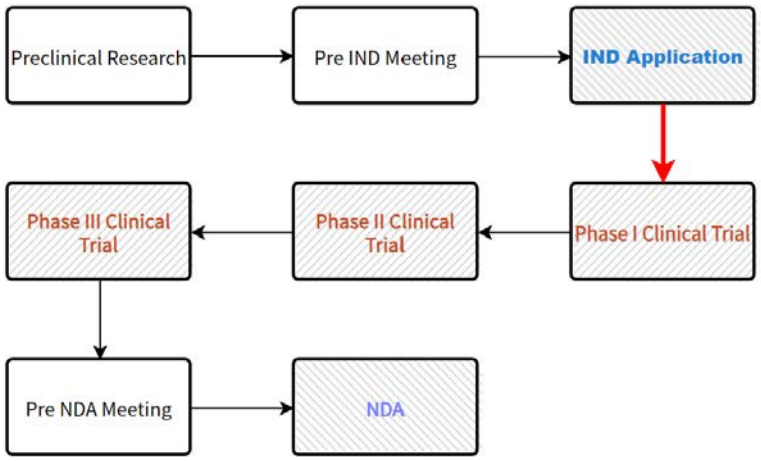


Figure 2: New Drug Development and Application Procedures in China

The CFDA was targeting a processing time of 60 or fewer working days for clinical trial applications. To achieve this, the CFDA has implemented a strategy similar to the Prescription Drug User Fee Act (PDUFA) in the U.S., collecting user fees from applicants to fund staff recruitment and system upgrades. The application fee was made transparent and publicly available, with a fee of 192,000 RMB for clinical trial applications of new drugs (the U.S. required a fee of $550,300 in 2015). Funding support from user fees has led to significant improvements of the evaluation personnel, with the number of evaluation staff increasing from around 70 at the start of the reform to approximately 800 by 2018 (Han et al., 2021).

To expedite the evaluation process, the CFDA has implemented several additional changes. First, the agency provides priority review tracks for drugs with significant clinical value at various stages of development, allowing them to skip the generic drug application queue. Second, fees for submitting applications and penalties for detected data falsification have been raised, as low fees and little punishment were previously blamed for con-

tributing to a high number of substandard applications. Third, the criteria for evaluating applications have been made clear and publicly accessible, ensuring that applicants have a clear understanding of what the regulator is looking for. This change helped China join The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) in 2017, further integrating China's pharmaceutical industry into the global market by complying with international standards.[8] In our analyses, we consider these changes as channels to achieve the targeted policy and do not attempt to separate each of these changes.

We provide a summary of the main policy documents regarding the approval time in Appendix A. Achieving the reduction in processing time was a gradual process, and in the following sections, we will gather data and analyze the implications of this development.

3 Conceptual Framework

To guide our empirical analysis, we introduce a straightforward conceptual framework, the specifics of which are detailed in Appendix B. This model illustrates our interpretation of the regulatory reform, showing its likely beneficial effects on the volume of innovation and its ambiguity impact on the overall novelty of innovation.

We consider a drug market featured by many different varieties and monopolistic competition. The quantity demanded for each variety ω is given by $x(\omega) = u(\omega)p(\omega)^{-\sigma}P^{\sigma}X$, where $u(\omega)$ and $p(\omega)$ are the novelty and the price of variety ω, respectively, and σ is the elasticity of substitution between varieties. P and X denote the aggregate price index and demand, respectively.

We assume consumption occurs at time $t = 0$. Drug varieties result from producers' innovation efforts. Nonetheless, to effectively serve the market at $t = 0$, a prospective drug producer must also await approval from the government regulatory bureau for drug innovation procedures, such as clinical trials. We presume the waiting time to be g. Thus,

[8] Source: Press release ICH Assembly meeting in Montreal, Canada, May/June 2017 https://www.ich.org/news/press-release-ich-assembly-meeting-montreal-canada-mayjune-2017

the expected return from application approval is:

$$\pi = (1+t)^{-g}(\tilde{\sigma}c)^{1-\sigma}P^{\sigma}X/\sigma \tag{1}$$

where $\tilde{\sigma} = \sigma/(\sigma-1)$ is the markup, and c is the production cost per unit of drug variety.

Firms are heterogeneous in their innovation capabilities, denoted by $\theta_i > 0$. They decide on their innovation intensity, k_i, where higher intensities correspond to a greater number of drug applications. The innovation costs are represented by $\psi_k(k_i)^{\gamma}$, with $\gamma > 1$ signifying a convex function. We assume that the expected number of new applications approved is given by $\theta_i k_i$. By multiplying θ_i, we posit that more innovative firms are likely to successfully generate more innovation outcomes given the same innovation intensity. In addition to selecting innovation quantities, firms can also choose the novelty of their drug applications. A higher novelty u will proportionally increase drug profits; however, enhancing novelty would necessitate costs $\psi_u u^{\phi}$ per unit of drug application, where $\phi > 1$ indicates that the costs are convex in novelty u.

There exist two separate categories of producers: incumbents and potential entrants (new firms). The measure of incumbents and potential entrants is denoted by M and M_e, respectively, both with innovation capacity distributions represented by $F(\theta)$. In order to initiate innovation and apply for drug approvals, potential entrants must bear an extra fixed entry cost, labeled as f. The fixed cost might include expenditures such as registration fees, which are not applicable to incumbents since they are already registered and may produce some established drugs concurrently. We assume that the fixed cost f for each firm is a random variable drawn from the distribution $G(f|\theta)$,[9] which allows for the possibility of more innovative firms having distinct fixed cost distributions, as they may have incentives to recruit highly educated individuals for better innovation. Finally, the production cost per unit of drug variety is identical (denoted by $c > 0$) for all firms.

[9] $G(\cdot|\theta)$ is a distribution function with $G(0|\theta) = 0$ and $\lim_{f\to\infty} G(f|\theta) = 1$.

Positive Impact on Innovation Quantity Using this simple framework, we can analytically explore the impact of a regulatory policy change. In our model, the regulatory policy change that reduces the waiting, $g' < g$, is reflected by an increase in the expected profits of drug applications. The rise in expected profits stimulates innovation for both incumbents and new firms. Additionally, when comparing these two outcomes, our model forecasts a more substantial proportional increase in innovation from new firms relative to incumbents. The discrepancy in responses between new firms and incumbents is due to the extensive margin of new firms (weighted by their innovation capacities), as higher innovation profits also drive increased entry by these firms.

Ambiguous Implication on Innovation Novelty Equally important, the overall change in novelty is ambiguous, which reflects the interplay of two forces. First, for incumbents, the rise in profits motivates them to enhance the novelty of their drugs. The extent of this enhancement varies and requires empirical investigation to determine its magnitude. Second, the average change in new firms' novelty is ambiguous, as the reform has an ambiguous impact on the composition of new firms' innovation capacities. On one hand, lowering entry barriers might lead to the entrance of less innovative firms. On the other hand, higher expected returns could encourage more innovative firms to make the necessary investments and enter the market. The interaction of these two forces creates an ambiguous outcome for the aggregate innovativeness of the industry. This nuanced effect is something we aim to unravel through our empirical examination,

4 Data and Measurement

Drug-level Approval Time Change Prior to the regulatory reform, the backlog problem affected drugs to different extents. The aim of the reform was to streamline and standardize the application process for all drugs, resulting in a more consistent approval time. This change in approval time allows us to examine the impact of regulatory reform on innovation outcomes at the drug level.

Figure 3 plots the average approval time and the number of IND applications by year. Consistent with the policy reform, the approval time for IND applications has experienced declines starting from 2015. Between 2011 and 2014, the approval time was around 500 days, and it declined to fewer than 100 days in 2021, representing a more than 80% decline in approval time.

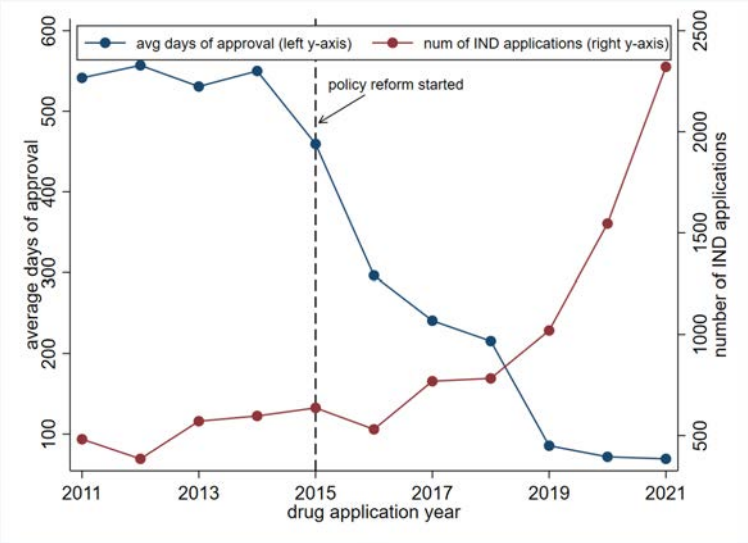


Figure 3: Average IND Approval Time across Years

Notes: The implementation of the reform commenced in August 2015.

To measure the drug-level change in approval time, we use China's medical registration data between 2011 to 2021. The data includes information such as applicant names, application dates, approval dates (if any), and targets. The drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification system, which divides them into different groups based on their anatomical, therapeutic, pharmacological, and chemical properties.[10] Our analysis uses 4-digit level ATC categories due to data availability. There are 287 ATC categories in our data, such as "anti-infectives and antiseptics for local oral

[10]The ATC classification system categorizes drugs into five levels. The first level is represented by a single letter and indicates the anatomical main group. The second level, consisting of two digits, indicates the therapeutic subgroup. The third level, represented by a single letter, indicates the therapeutic/pharmacological subgroup. The fourth level, also represented by a single letter, indicates the chemical/therapeutic/pharmacological subgroup. Finally, the fifth level, consisting of two digits, indicates the chemical substance.

treatment" (A01AB), which corresponds to anti-infective drugs used for oral diseases.

We focus on applications for INDs and also examine whether these INDs have translated into clinical trials. Since the full registration process for drug applications takes several years, very few drugs that began registration after the reform completed the entire process in our sample. Our data set includes 9,642 IND applications and 2,222 different applicants during the 2011–2021 period. Appendix Figure C.1 shows a strong correlation between the days spent on approval of first trials and the days spent from approval of the first trial to final registration for drugs that completed the entire registration process in our data set.

As the major reform occurred between 2015 and 2017, we measure the decline in approval time within three years (2015–2017) in the post-reform period relative to that within three years (2012–2014) in the pre-reform period to measure the magnitude of the reform. Some (relatively small) ATC categories do not have applications in either 2012–2014 or 2015–2017. We compute the decline in approval time for 109 ATC categories, covering 93% of drug applications during the 2011–2021 period. In addition, we employ pre-reform backlogs as an alternative measure.

We analyze the correlations between the decrease in approval time and various pre-reform characteristics across ATC categories. Existing literature suggests market size and market structure as crucial factors shaping innovation levels (Acemoglu and Linn, 2004; Aghion et al., 2005). To capture these two factors, we compute the number of applications and the Herfindahl-Hirschman index of INDs at the ATC level for the pre-reform period.[11] Furthermore, as we focus on post-reform innovation, we control for pre-reform innovation patterns at the ATC level. Specifically, we calculate the share of IND applications in all ATC-level applications as a proxy for ATC-level innovation capacity, as all applications encompass other types (e.g., applications for generic drugs) with lower innovation levels than IND. Additionally, we evaluate the level of innovativeness of IND applications at the ATC level by assessing the proportion of targets that have already been demonstrated in

[11]We calculate the Herfindahl-Hirschman index of IND applications by summing the squared shares of each firm's IND applications in relation to the total IND applications. This index serves as a measure of the concentration of innovation within the market.

the U.S.. Finally, recognizing that reductions in approval time in China may reflect global trends, we utilize U.S. drug application data to gauge the U.S.'s levels and declines of ATC-level approval time around the time of China's reform.

As reported in Appendix Table C.2, we do not find strong correlations between reduction time and these characteristics. In contrast, pre-reform approval time is highly correlated with reduction time (with a correlation of 0.60, see Appendix Figure C.3). It is also strongly correlated with the share of backlogs in 2012–2014 (with a correlation of 0.28, see Appendix Figure C.4).[12] These patterns align with our interview: the most significant regulatory challenge before the reform is the scarcity of evaluation personnel. The drug-level backlogs do not appear to be driven by drug characteristics but are more plausibly attributable to the availability of personnel resources.

Quantity and Novelty of Drug Innovation At the drug level, we use the number of IND applications to measure the quantity of innovation. As shown in Figure 3, the average yearly number of IND applications was 509 during 2011–2014 but rose to 1,087 during 2015–2021. We further collect data on clinical trials from the Chinese Clinical Trial Database. Among the post-2015 INDs, the shares that have progressed to Phase I, II, III clinical trials are 79%, 55%, and 34%. The rate from INDs to Phase III is akin to that of the U.S., as reported by Takebe, Imai and Ono (2018). Additionally, only 15% of the post-reform approved INDs have reached the NDA stage by the end of our study period, limiting our capability to examine the final drugs.

To complement this quantity-based approach, we propose a new measure to capture the novelty of drug innovation. Specifically, we examine whether the targets of each drug have been previously registered in the U.S. drug registration system (the data dates back to 1982) before the drug's application date. Our rationale for this measure is that innovative drugs often explore new targets that could treat previously incurable diseases or existing diseases more efficiently. Targets refer to biomacromolecules or biomolecular structures

[12]We compute the pre-reform share of backlogs as: among all the IND applications that were submitted in 2012–2014, the share of applications that had not been approved by the end of 2014.

that bind to specific drugs and produce therapeutic effects. Our conversations with industry experts suggest that drugs with targets that have already been developed in the U.S. are less likely to be truly innovative. For robustness, we also consider a similar measure using targets that have been explored by European firms.

Firm-level Data To study how firms respond to the regulatory change, we use applicant names in the medical registration data to identify firms involved in the applications. Thus, for each firm involved, we can obtain its number of IND applications and the characteristics of its IND applications in each year between 2011–2021. Our data involves 2,222 firms that had ever done IND applications during our sample period, and the average number of IND applications per firm was 4.88 in the 2011–2021 period, with great variation between firms: 40% of firms only made one application in the 2011–2021 period, whereas 10% of firms made more than 10 applications in the same period.

To identify both incumbent firms and new entrants following the regulatory reform, we utilized firm names to match our data with China's Business Registration Data for 2021.[13] China's Business Registration Data contains information on the year of establishment for all firms established before 2021. To evaluate the market responses after the medical regulatory reform, we also use firm names to match our data with the firm data from the CSMAR Database for firms that are listed in the stock market.

5 Regulatory Reform and Innovation Quantity

In this section, we study how the regulatory reform impacted the quantity of drug innovation. In Section 5.1, we provide suggestive evidence using the raw data. We then perform formal estimations regarding how the regulatory reform impacted the innovation quantities across different drug categories in Section 5.2 and across different firms in Section 5.3.

[13]Before matching datasets using firm names, we followed a similar procedure for cleaning and consolidating firm names as described in He et al. (2018).

5.1 Descriptive Evidence

In Figure 4, we plot the relationship between the reduction in approval time and the logged change in the number of IND applications at the drug level. We construct post-reform change in the number of IND applications by computing the log change in the average yearly number of IND applications in the post-reform period (2015–2021) relative to the pre-reform period (2011–2014). As shown, there is a positive correlation, indicating that the decrease in approval time may result in increased pharmaceutical innovation. We find that drug categories related to anticancer drugs, systematic hormonal preparations, cardiovascular system, and musculoskeletal system experienced larger reductions in approval time. These categories also experienced a larger increase in IND applications after the reform.

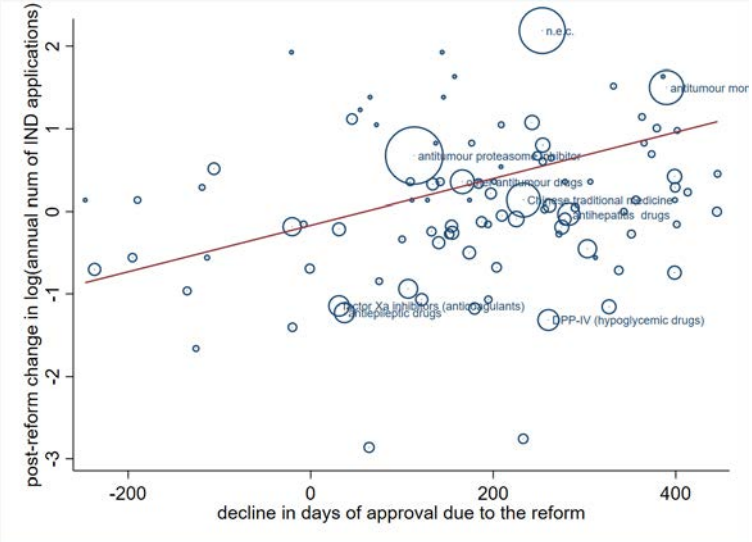


Figure 4: Relationship between Decline in Approval Time and Post-reform Growth in Number of IND Applications

Notes: This graph shows the post-reform change in the number of IND applications (y-axis) on the decline in approval time between 2015–2017 and 2012–2014 (x-axis), across 4-digit ATC categories. We truncate 5% of the decline in approval time to avoid extreme values on the two tails in the graph. The circle size reflects the amount of IND applications in the pre-reform period for each ATC category.

5.2 Drug-level Analyses

Research Design We now examine whether drugs that experienced a decline in approval time changed their innovative activities more systematically. Given that IND applications are count data and have many zeros, we use Poisson regressions for the formal empirical analysis. This approach has been recommended in recent literature (e.g., Tenreyro and Silva, 2006; Cohn, Liu and Wardlaw, 2022) to address issues related to zero values. Therefore, we will adopt the following regression equation:

$$y_{jt} = \exp(\beta_t decline_j + \alpha_t + \gamma_j + \mathbf{X}_j \times \alpha_t) + \epsilon_{jt} \tag{2}$$

where y_{jt} is the number of IND applications for ATC category j in year t. $decline_j$ is the decline in approval time within three years (2015–2017) in the post-reform period relative to that within three years (2012–2014) in the pre-reform period, which measures the impact of the policy reform on approval time for category j. We consider parameters β_t to capture the time-varying impact of the policy reform. For ease of interpretation, we standardize $decline_j$ with the standard deviation of $decline_j$ across different categories, and thus β_t represents the proportional change in the number of applications due to one standard-deviation decline in approval time (227 days). γ_j is ATC-level fixed effects, capturing time-invariant heterogeneity in the patterns of drug applications across different ATC categories. We set $\beta_{2014} = 0$ for the period immediately before the policy reform, and therefore β_t in other years corresponds to changes in β_t relative to year 2014.

$\mathbf{X}_j$ indicates a set of pre-reform characteristics at the drug level, including the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications (which also include other types of applications such as applications for generic drugs) in the 2012–2014 period. Specifically, considering that China introduced bioequivalence evaluation for generic drugs simultaneously with the reform for new drugs, the share of IND applications during the pre-reform period can

serve as a control for the potential substitution between generic and new drugs.[14] Appendix Table D.1 presents the summary statistics of the variables used in our empirical analysis.

Drug-level Results: INDs and Associated Clinical Trials Figure 5 presents the estimated values of β_t and their corresponding 90% confidence intervals for different years. The plot illustrates the relationship between the approval time and the number of IND applications after the regulatory reform. The results suggest a positive association between the decline in approval time and the number of IND applications, which has become significant since 2017. Specifically, after 2017, a one-standard-deviation decrease in approval time led to a more than 50% increase in the number of IND applications, indicating a substantial impact of the regulatory reform on medical innovations. Importantly, the analysis shows no systematic correlation between the decline in approval time and the number of IND applications before the regulatory reform in 2015. These findings provide reassurance that the observed association is not driven by pre-existing trends in the data. Appendix Table D.2 provides the estimates of β_t for regression (2), and we find that the coefficients are robust to incorporating controls.[15] Finally, in Columns (1)–(2) of Table 1, we provide the standard difference-in-difference estimates by exploiting the interactions between the decline in approval time and time dummies indicating the post-reform periods, which show that the impact becomes significant and round 51% during 2018–2021.

One particular concern is that firms may submit INDs solely for the purpose of signaling their efforts or to secure a position, without actually making any significant contributions. To investigate this, we link IND data with China's clinical trial data using the applicant name and drug name. The analysis reveals that, prior to the reform, only 61% of INDs were

[14] We also experimented with keeping only IND and generic drugs' applications and then computing the share of IND applications in ATC-level applications. The regression results are quantitatively very similar with this alternative control variable.

[15] Including the decline in approval time for the U.S. applications reduces the amount of observations, because this variable is only available for a few ATC drug categories. We find that the regression results are very similar regardless of whether we incorporate the decline in approval time for the U.S. applications or not.

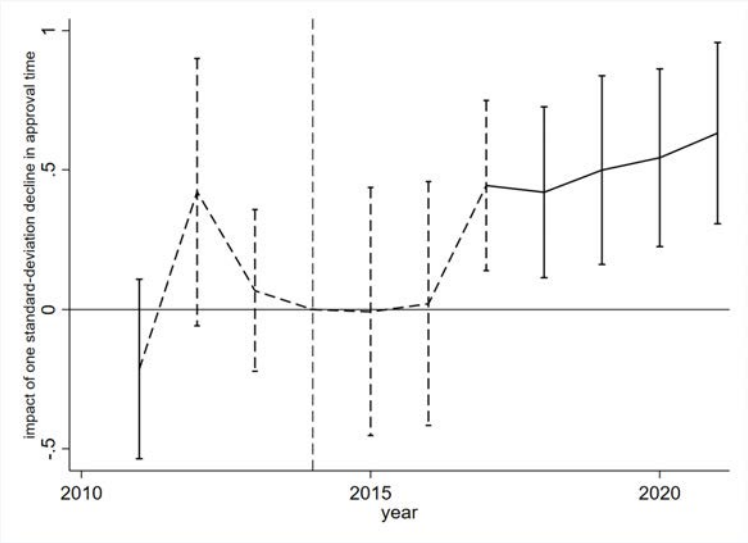


Figure 5: Impact of Decline in Approval Time on Number of IND Applications

Notes: This graph shows the β_t parameters estimated by equation (2), with the corresponding 90% confidence intervals. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the ATC category level.

Table 1: Difference-in-Difference Estimates

	# IND Apps		# IND Apps (Incumbents)		# IND Apps (entrants)	
	(1)	(2)	(3)	(4)	(5)	(6)
	Poisson	Poisson	Poisson	Poisson	Poisson	Poisson
decline$\times$post$_{2015-2017}$	.33*	.14	.38**	.24*	.56	.56
	(.20)	(.15)	(.18)	(.13)	(.58)	(.58)
decline$\times$post$_{2018-2021}$	.68**	.51***	.67**	.54***	1.38**	1.38**
	(.30)	(.19)	(.29)	(.17)	(.60)	(.60)
Drug and Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Controls	No	Yes	No	Yes	No	Yes
Obs	1,199	1,199	1,199	1,199	413	413
R-squared	0.84	0.85	0.80	0.81	0.87	0.87
Mean	8.31	8.31	5.20	5.20	2.23	2.23

Notes: We perform a simplified difference-in-difference version of equation (2): $y_{jt} = \exp(\beta_1 decline_j \times post_{2015-2017} + \beta_2 decline_j \times post_{2018-2021} + \alpha_t + \gamma_j + \mathbf{X}_j \times \alpha_t) + \epsilon_{jt}$, where $post_{2015-2017}$ and $post_{2018-2021}$ indexes the 2015–2017 and 2018–2021 periods, respectively. For new firms, because the data starts from 2015 and we use 2015 as the baseline year in our event study, we construct $post_{2015-2017}$ as an indicator for the 2016–2017 period. In Columns (1)–(2), the dependent variable is the number of IND applications. In Columns (3)–(4), the dependent variable is the number of IND applications by incumbent firms, and in Columns (5)–(6), the dependent variable is the number of IND applications by new entrants. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. Standard errors are clustered at the ATC category level. We compute * $p < .10$, ** $p < .05$, *** $p < .01$.

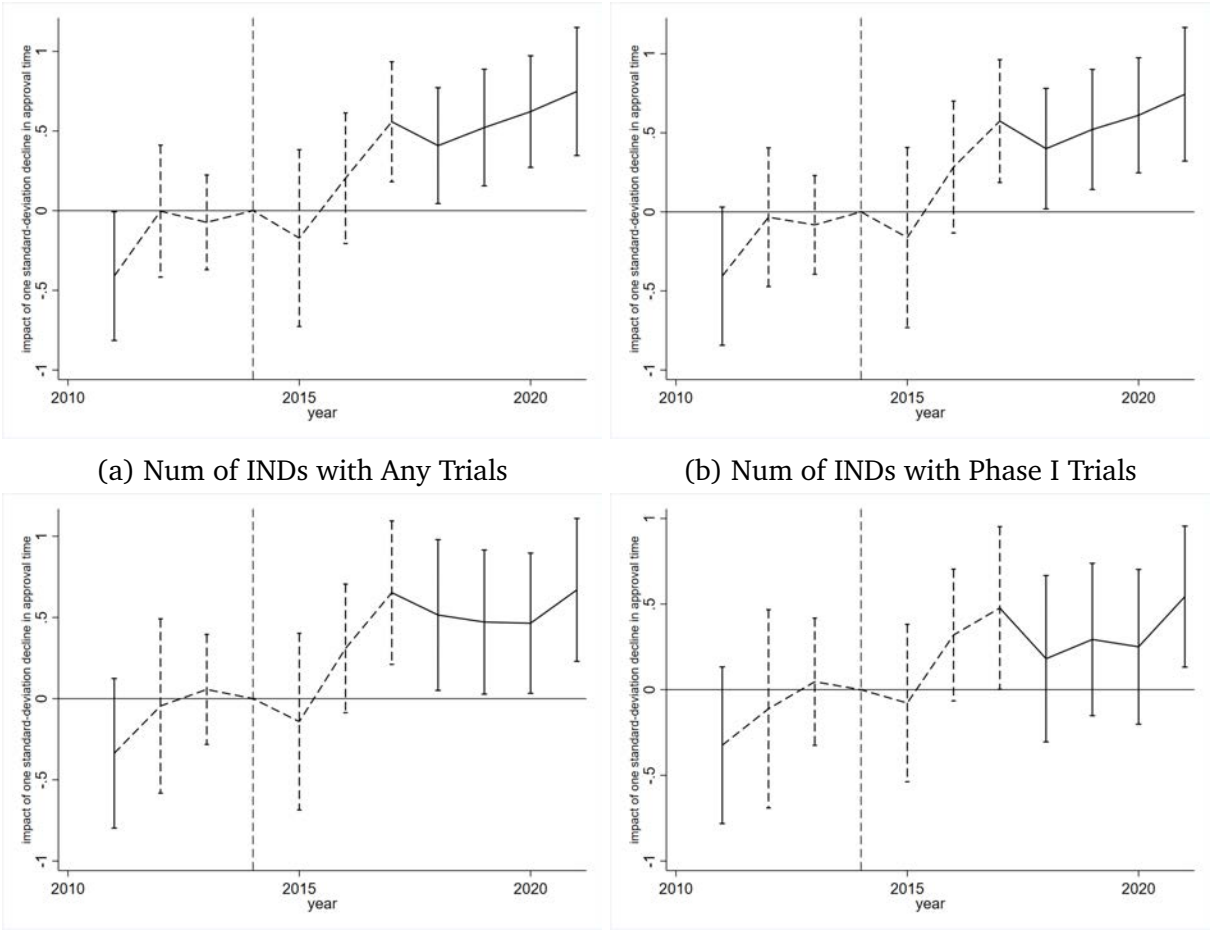
found in the clinical trial data, whereas in the post-reform period, this figure increased to 79%, indicating that the concern may not be valid. We also perform an additional test in which we replace the dependent variable in equation (2) with the number of INDs that resulted in any clinical trials, Phase I clinical trials, Phase II clinical trials, and Phase III clinical trials, respectively. The results, presented in Figure 6, indicate that a decrease in approval time always led to an increased number of INDs associated with clinical trials of all stages, supporting the notion that firms genuinely made efforts in relation to their submitted INDs.[16]

Robustness Checks We conduct robustness checks on our reform measurement and assess the potential influence of other reforms implemented post-2015. The detailed results of these checks can be found in Appendix D.3. First, our results remain consistent when we employ the pre-reform share of backlogs at the drug level as an alternative measure for the reform's intensity in regression equation (2), as illustrated by Appendix Figure D.3.

Second, our findings are not driven by another significant medical reform that occurred during the same period, namely, the modification of the drug reimbursement list for public health insurance. To challenge our findings, any other policies would need to be correlated with reductions in approval times at the drug level. However, as reported by Appendix Table D.3, our analysis reveals no significant correlation between the reduction in approval times and the number of drugs covered by insurance at the drug level.

A Decomposition of the Drug-level Effect: Entry and Incumbents We investigate whether the change in IND applications after the reform was driven by new firms or incumbent firms. As mentioned earlier, to identify new firms, we match our data with China's Business Registration Data for 2021, which contains information on the year of establishment for all firms established before 2021. We define a firm as new if it was established during the post-reform period (after 2015). Overall, new firms made up 36% of all innovative firms in the post-reform period.

[16] As mentioned above, the probability of post-2015 approved IND passing the NDA is still low (15%). Due to this data limitation, we have not yet found a strong impact of the regulation on NDAs.



(a) Num of INDs with Any Trials

(b) Num of INDs with Phase I Trials

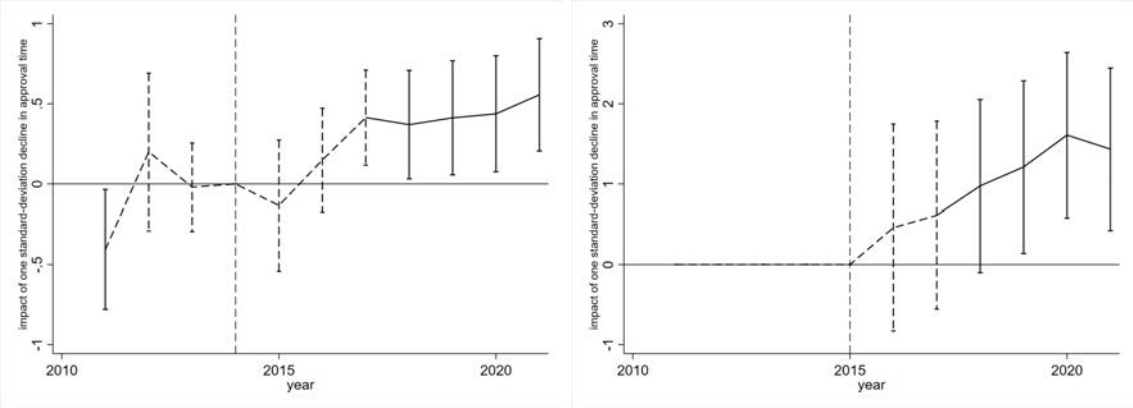
(c) Num of INDs with Phase II Trials

(d) Num of INDs with Phase III Trials

Figure 6: Impact on the Number of INDs with Clinical Trials

Notes: This graph shows the β_t parameters estimated by equation (2), with the corresponding 90% confidence intervals, for the number of INDs that resulted in any clinical trials, Phase I clinical trials, Phase II clinical trials, and Phase III clinical trials, respectively. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, as well as the decline in approval time for the U.S. applications after 2015, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the ATC category level.

We then evaluate how the decline in approval time affected both incumbents' and new firms' innovative activities. We thus replace the dependent variable in equation (2) with the amount of incumbents' and new firms' IND applications, respectively. Figure 7 shows that the decline in approval time had a positive impact on both incumbents' and new firms' innovative activities. (See Appendix Table D.2 for the estimation results). Columns (3)–(6) of Table 1 summarize the difference-in-difference estimates.



(a) Number of IND by Incumbents (b) Number of IND by New Firms

Figure 7: Impact of Decline in Approval Time on Incumbents' and New Firms' Innovation

Notes: This graph shows the β_t parameters estimated by equation (2), with the corresponding 90% confidence intervals. New firms barely had innovations before 2015: few firms appeared to apply for IND before being formally established. Thus, for regressions regarding new firms' IND applications, we set $\beta_{2015} = 0$, and therefore β_t in other years corresponds to changes in β_t relative to year 2015. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the ATC category level.

Together, we find that the proportional increase in the amount of IND applications due to declines in approval time was stronger for new firms than incumbents, especially in the 2018–2021 period: the magnitude for new firms more than doubles that for incumbents. However, as the new firms were generally smaller, their overall contribution to innovation due to declines in approval time was similar to that of the incumbents at the aggregate level: for the quantity increase in INDs, the incumbents and new entrants accounted for 56% and 44%, respectively.

Who invested in these new firms? Has the reform attracted new investment from regions with advanced pharmaceutical technologies to China? In Appendix Figure D.4, we use detailed investors' information for medical firms to investigate the presence of foreign investment in China's pharmaceutical innovation. Our findings indicate that the average share of equity held by foreign investors (including Hong Kong, Taiwan, and Macau) among newly established firms was approximately 30% during the 2011–2021 period, highlighting a significant foreign investment presence. Furthermore, following the regulatory reforms in 2015, the average share of equity held by foreign investors among newly established firms increased from 23.6% in the pre-reform period to 35.0% in the post-reform period. Additionally, our analysis reveals that the main regions of origin for foreign equity are Hong Kong and the U.S., which are associated with advanced pharmaceutical technologies.

Interpretation In sum, these findings are consistent with our conceptual framework. Expecting a higher return for innovation, both incumbents and new firms increased their innovation quantities. Moreover, increased firm entry led to larger proportional responses from new firms compared with incumbents. In Appendix Figure D.5, we further contrast the yearly responses of the number of new firms with those of the number of new firms' IND (derived from Panel (b) of Figure 7) to the decrease in approval time. We find that the difference in responses between the number of new firms' IND and the number of new firms is similar in magnitude to the response of the number of incumbents' IND (Panel (a) of Figure 7). This is in accordance with our conceptual framework, which demonstrates that the difference in responses to regulatory policy changes between new firms and incumbents is attributable to the increased entry of new firms.

5.3 Firm-level Evidence

Since drug innovation and applications are undertaken by firms, it is useful to directly understand firms' responses to regulations, which complements our drug-level analyses.

Similar to the ATC-level regression, we adopt the following regression equation:

$$y_{it} = \exp(\beta_t decline_i + \gamma_i + \alpha_t + \mathbf{X}_i \times \alpha_t) + \epsilon_{it} \tag{3}$$

where $decline_i$ is the decline in approval time between the 2012–2014 period and the 2015–2017 period for firm i's IND applications. As we require information on approval time for both the pre-reform and post-reform periods, we can construct $decline_i$ for 166 firms, which were incumbent firms according to our definitions in the previous subsection and accounted for around 40% of all IND applications in the 2011–2021 period. The rest of IND applications are from incumbent firms that did not innovate in either the 2012–2014 period or the 2015–2017 period, and new firms that were established after the reform.

$\mathbf{X}_i$ is a set of pre-reform firm characteristics, including the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period. As the controls are initially computed based on ATC categories, we aggregate them into firm-level variables based on the firm's pre-reform composition of applications across ATC categories.

The error term ϵ_{it} may be correlated with $decline_i$, as firms may select into research on drugs that experienced larger decreases in the application time, which suggests a positive correlation between ϵ_{it} and $decline_i$ and an upward bias of OLS coefficients. There could also be measurement errors in the construction of $decline_i$, which suggests a downward bias of OLS coefficients. Thus, we construct a Bartik-type instrument based on the firm's pre-reform composition of applications:

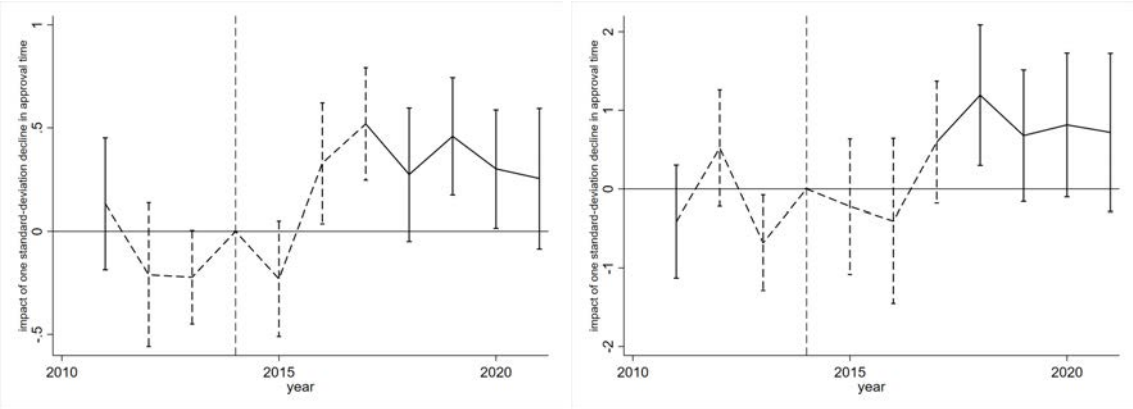
$$x_i = \sum_j s_{ij} decline_j \tag{4}$$

where s_{ij} is the share of firm i's IND applications in ATC category j in the pre-reform period, and $decline_j$ is the ATC-level decline in approval time within three years in the post-reform period relative to that within three years in the pre-reform period.

Our instrument aims to capture plausibly exogenous variation in the decline of approval

time that is uncorrelated with firm i's error term. The identification of such shift-share instrument relies on the orthogonality of the shifts or the shares (Goldsmith-Pinkham, Sorkin and Swift, 2020; Borusyak, Hull and Jaravel, 2022). Our identification tends to hold because each firm is relatively small and unlikely drives the policy reform.

Figure 8 plots the coefficients from the OLS and IV regressions. We find that the OLS and IV results both suggest a significantly positive effect of the decline in approval time on the number of firm-level IND applications. The IV coefficients are slightly larger than the OLS coefficients, suggesting a potentially downward bias of the OLS coefficients due to the measurement errors. Nevertheless, the magnitude of the OLS and IV coefficients are similar to our previous results based on ATC-level regressions (Figure 5).



(a) OLS (b) IV

Figure 8: Impact of Decline in Approval Time on Firm-level Innovation

Notes: This graph shows the β_t parameters estimated by equation (3) using the OLS and the instrument constructed in equation (4), with the corresponding 90% confidence intervals. We control the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, as well as the decline in approval time for the U.S. applications after 2015. As the controls are initially ATC-level, we aggregate them into firm-level variables based on the firm's pre-reform composition of applications across ATC categories. We also add the interaction of the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the firm level.

6 Implications on Innovation Novelty

Using drug-level and firm-level data, we have demonstrated that the regulatory reform increased IND applications. What is the implication of these findings on innovation novelty of China's pharmaceutical industry? To answer this question, we employ a novel measure of innovativeness—whether the drug applications adopt the targets already used in the U.S.–and conduct a few robustness checks around this measure.

In Figure 9, we plot the share of drug applications adopting the targets already used in the U.S., which declined by 12 percentage points (from 86% to 74%) between 2011 and 2021, suggesting a large increase in the informativeness of China's drug applications. It is useful to have two benchmarks to better understand the magnitude of this improvement in drug novelty. First, China's progress is even more visible against a global trend. In Figure E.1, we exploit global trial data (as we lack drug application data for other countries) and compare the innovativeness of Phase I clinical trials (the step following IND) in both China and the U.S.. We find that between 2011 and 2021, the share of Phase I clinical trials adopting the targets already used in the U.S. remained largely unchanged in the U.S., but experienced a sharp decline by 15 percentage points from 97% to 82% in China, the magnitude of which echos our finding in Figure 9. Second, in the U.S. in year 2021, 79% of Phase I clinical trials adopted the existing targets. These comparisons suggest that China has been moving toward the frontier during the past decade.

Importantly, aggregate innovation novelty can be affected by both within-drug change and across-drug change. We denote the yearly share of drugs with targets already used in the U.S. registration as Z_t and formalize these two channels as follows:

$$Z_t = \sum_j \frac{y_{jt}^{inc}}{\sum_j y_{jt}^{inc} + y_{jt}^{new}} h_{jt}^{inc} + \frac{y_{jt}^{new}}{\sum_j y_{jt}^{inc} + y_{jt}^{new}} h_{jt}^{new}, \tag{5}$$

where y_{jt}^{inc} and y_{jt}^{new} are the numbers of ATC category j's IND applications in year t by incumbent and new firms, respectively. Thus, $\frac{y_{jt}^{inc}}{\sum_j y_{jt}^{inc}+y_{jt}^{new}}$ and $\frac{y_{jt}^{new}}{\sum_j y_{jt}^{inc}+y_{jt}^{new}}$ represent the

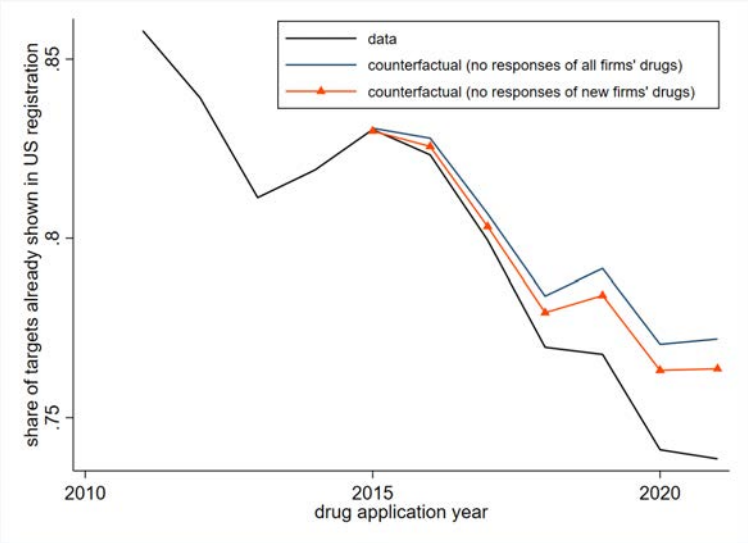


Figure 9: Impact of Changes in Approval Time on Drug Applications' Innovativeness through Changes in Composition

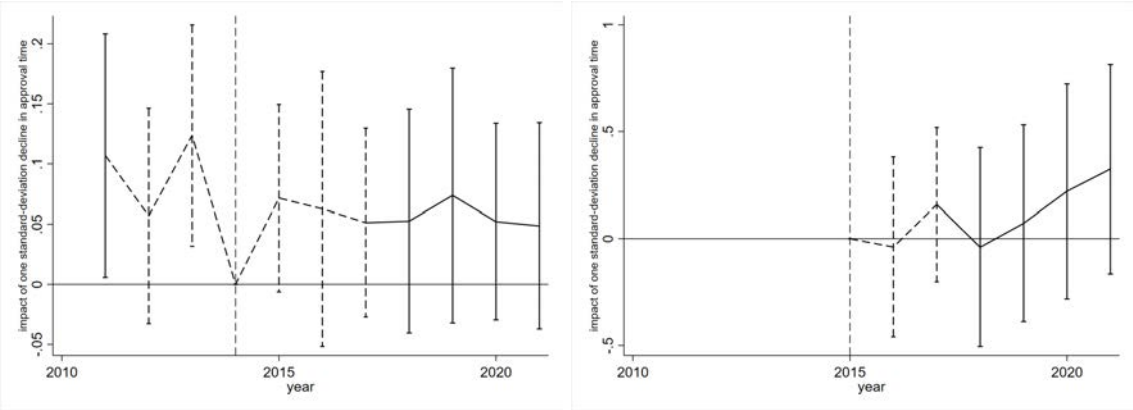
Notes: In this graph, for Chinese drugs that have information available on their targets, we illustrate the percentage of Chinese drugs that have adopted targets already demonstrated in U.S. registered drugs.

shares of ATC category j's IND applications in overall IND applications for incumbent and new firms, respectively. h_{jt}^{inc} and h_{jt}^{new} are the shares of ATC category j's drugs with targets already used in the U.S. in year t for incumbent and new firms, respectively.

Equation (5) illustrates that the regulatory reform can affect innovation novelty via two channels: a within-drug innovativeness channel h_{jt}^{inc} and h_{jt}^{new}, and the composition channel y_{jt}^{inc} and y_{jt}^{new}. Next, we examine them separately.

The Within-drug Innovativeness Channel h_{jt}^{inc} and h_{jt}^{new} Using a specification similar to equation (2), we examine innovatiness as the outcome. Specifically, Figure 10 plots the the β_t parameters estimated by equation $y_{it} = \beta_t decline_i + \gamma_i + \alpha_t + \mathbf{X}_i \times \alpha_t + \epsilon_{it}$, with the corresponding 90% confidence intervals, where y_{it} is one minus the share of targets already shown in U.S. registration for each ATC category and each year, which measures the share of innovative targets and thus proxies the drug innovativeness. New firms barely had innovations before 2015: few firms appeared to apply for IND before being formally established. Thus, for regressions regarding new firms' innovativeness, we set $\beta_{2015} = 0$,

and therefore β_t in other years corresponds to changes in β_t relative to year 2015 (for incumbents, we set $\beta_{2014} = 0$). As shown, there are no statistically significant effects observed across all years. Thus, it appears that the regulatory reform does not lead to noticeable improvements in within-drug innovativeness (i.e., h_{jt}^{inc} and h_{jt}^{new}) in our studied period.



(a) Incumbents' Innovativeness (b) New Firms' Innovativeness

Figure 10: Impact of Decline in Approval Time on Incumbents' and New Firms' Drug Innovativeness (ATC-level)

Notes: This figure shows the β_t parameters estimated by equation $y_{it} = \beta_t decline_i + \gamma_i + \alpha_t + \mathbf{X}_i \times \alpha_t + \epsilon_{it}$, with the corresponding 90% confidence intervals, where y_{it} is one minus the share of targets already shown in U.S. registration for each ATC category and each year, which measures the share of innovative targets and thus proxies the drug innovativeness. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, as well as the decline in approval time for the U.S. applications after 2015, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the ATC category level.

The Composition Channel y_{jt}^{inc} and y_{jt}^{new} In Section 5, we showed that the policy reform significantly impacted the quantity of new drug applications, and the impact differed across ATC categories with different declines in approval time after the reform. We then use the estimated policy impact to construct y_{jt}^{inc} or y_{jt}^{new} in the counterfactual scenario with no medical reform being implemented. The corresponding overall novelty based on

this counterfactual scenario is

$$Z'_t = \sum_j \frac{y_{jt}^{inc} \exp(-\beta_t^{inc} decline_j) h_{jt}^{inc} + y_{jt}^{new} \exp(-\beta_t^{new} decline_j) h_{jt}^{new}}{\sum_j y_{jt}^{inc} \exp(-\beta_t^{inc} decline_j) + \sum_j y_{jt}^{new} \exp(-\beta_t^{new} decline_j)}.$$

β_t^{inc} and β_t^{new} denote the estimated responses of the number of IND applications to the decline in approval time for incumbent and new firms, respectively, as shown in Figure 7.

As shown by the blue line in Figure 9, without the policy reform, the counterfactual composition would imply a larger share of Chinese drugs adopting mature U.S. targets. Quantitatively, we find that the policy reform reduced the share of Chinese drug applications adopting mature U.S. targets by 3.3 percentage points and can explain 36% of the post-reform decline (9.2 percentage points) in the share of Chinese new drugs adopting mature U.S. targets through changes in the composition of new drug applications.

It is worth noting that new entrants are more innovative than incumbents. In Appendix Figure E.2, we plot the share of targets that had been explored in the U.S. by incumbents and new entrants. For the incumbents, the share gradually declined from 85% in 2012 to 80% in 2020. For the new entrants, the share change was from 80% in 2015 to 67% in 2020. The fact that new entrants are more innovative and the previous finding that new firms' innovative quantity responds more to the policy reform (Figure 7) have important implications on the aggregate change on innovation novelty.

Specifically, in Figure 9, we plot the orange line representing the counterfactual novelty when we only consider responses of the number of new firms' drugs to the policy reform. We find that 80% of the improved innovativeness due to the policy reform was driven by the responses of the number of new firms' drug applications. We summarize the quantitative channels in Table 2. During 2015–2021, the share of targets already shown in the U.S. declined by 9.2 percentage points, out of which the decline of approval time can explain 35.8% (3.3 percent points). Within this improvement due to regulatory reforms, new firms contributed to 78.8%, due to their higher innovativness and more responses to the reform. These findings offer an interesting contrast between quantity and novelty in innovation: new firms' contribution to innovative quantity change is sizable but not dominant, but

Table 2: Impact of Changes in Approval Time on Drug Applications' Innovativeness through Changes in Composition

	Δ Share of Targets Already Shown in U.S. Registration, 2015–21
Actual decline	-9.2 p.p.
Due to responses of all firms' IND to changes in approval time	-3.3 p.p.
Due to responses of new firms' IND to changes in approval time	-2.6 p.p.

their contribution in terms of novelty appears even more important.

Robustness Checks As a robustness check, we construct the innovativeness measure based on European drug registration data, which is collected from the European Medicines Agency and the Head of Medicines Agency. Appendix E.3 depicts the share of drug applications adopting the targets already used in Europe. We notice an 8.6-percentage-point decrease in the share in the post-reform period (after 2015). Using equation (5), we determine that the policy reform lowered the share of Chinese drug applications adopting established European targets by 2.9 percentage points and accounts for 34% of the post-reform reduction. Additionally, we find that 76% of the enhanced innovativeness owing to the policy reform was propelled by the responses regarding the quantity of new firms' drug applications.

An additional concern is that if Chinese drugs' targets do not align with those of mature drugs in the U.S. or EU, they may be specific to China and of inferior novelty. To address this concern, we remove all Chinese drugs with targets that have never appeared in U.S. clinical trials. As a result, the remaining targets have been or are being investigated in the U.S., and we utilize this subset of targets to determine the percentage of Chinese drugs adopting mature targets found in registered U.S. medicines. Appendix Figure E.4 replicates Figure 9 with this constraint and demonstrates that the findings are very similar quantitatively.

Interpretation Our conceptual framework predicts an increase in incumbents' novelty and an ambiguous change in new firms' novelty in response to the reform. In our empirical analysis, we observe that the reform has attracted a large number of innovative new firms to enter the market, and this shift in the composition of market players accounts for a significant portion of the overall enhancement in drug novelty. These empirical findings highlight the fact that inadequate regulatory practices can discourage the participation of innovative newcomers, ultimately hindering progress in the industry.

7 Further Evidence: Stock Market Responses

As further evidence to examine whether the reform leads to a better innovation environment, we study how a firm's stock price reacts to NDAs. In the previous section, we use the number of INDs to quantify medical innovation. However, since INDs represent the early stage of drug development, significant uncertainty surrounds their success, making it difficult to generate significant stock market responses. To more accurately assess the market response to medical innovation and its change after the regulatory reform, this section focuses on the final approval of new drugs, which marks the end of the new drug application process and allows the drug to be sold in the market.

As emphasized above, the majority of the NDAs we study started their IND applications before the reform. Thus, the exercise here is not to directly evaluate the value of INDs in our main analysis. Instead, it offers suggestive evidence on how the market perceives the reform.

There are anecdotal instances indicating that, in recent years, the stock market has responded favorably to the sanctioning of new drug applications, hinting at an enhancement in the novelty of innovation. Take, for example, when Fuzuloparib, an orally active PARP inhibitor, devised by Jiangsu Hengrui Pharmaceuticals Co., Ltd., received the nod from the CFDA on December 16th, 2020. The ensuing day witnessed a 5.5% surge in Hengrui's stock price, an ascent that stood 4.2 percentage points above the market's aver-

age.[17] Though there are similar cases associated with other new drugs, skepticism persists regarding the significance of new drug approvals. Therefore, discerning the consistency of the positive stock market response pre and post the reform can shed lights on the caliber of innovation.

7.1 Motivational Evidence and Research Design

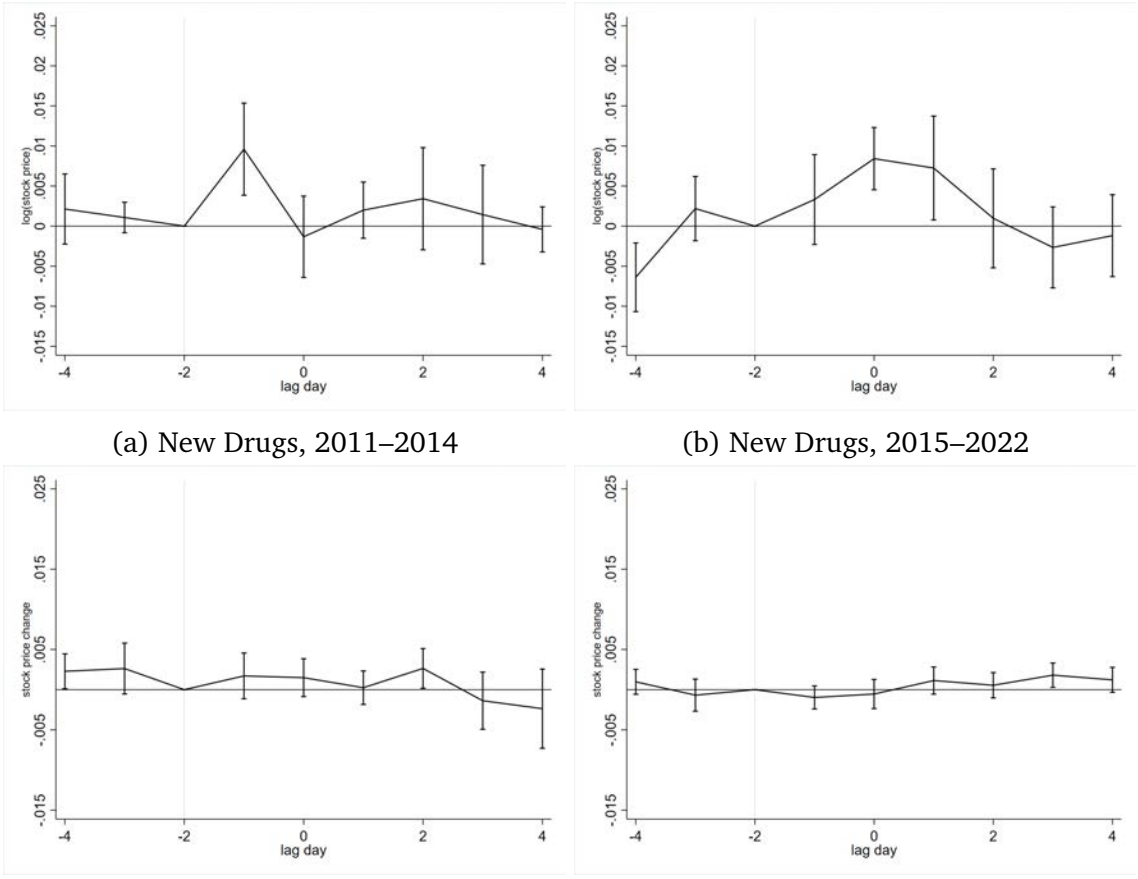
We are interested in how the stock market responded to new drug approval before and after the reform. To see these patterns, we present the results of our event-study designs in Figure 11, focusing on examining stock returns as the outcome. In order to address concerns related to insider trading problems in China, we selected two days before the approval as the reference date. This choice is in line with previous research by Qiu, He and Xiao (2018) and He, Wang and Zhu (2023), who have highlighted the possibility of insiders with favorable information engaging in buying or selling stocks ahead of time. In these specifications, we control for firm fixed effects and day fixed effects. As shown in Panels (a) and (b), while there was no clear market response before the reform, the market responded positively to NDAs in the days following the news. In addition, we plot the estimates using generic drug approvals in Panels (c) and (d), which can be considered as placebo tests: the market response is not driven by time trend but is specific to new drugs.

Motivated by these patterns, we employ a triple-difference design to estimate the impact of the reform on stock market responses:

$$\begin{aligned} R_{i,g,t} =& \alpha_0 + \beta_1 PostApproval_{g,t} + \beta_2 PostApproval_{g,t} \times Treat_{i,g} \\ &+ \beta_3 PostApproval_{g,t} \times PostReform_t + \beta_4 PostReform_t \times Treat_{i,g} \\ &+ \beta_5 Treat_{i,g} \times PostApproval_{g,t} \times PostReform_t + \gamma_{i,g} + \gamma_{g,t} + \gamma_{markettype,g} + \epsilon_{i,g,t} \end{aligned} \tag{6}$$

Following Cengiz et al. (2019), we consider each grant of a new drug as a distinct event

[17] Fuzuloparib is distinguished as the inaugural PARP inhibitor pioneered by a Chinese enterprise. Presently, the global market acknowledges four other PARP inhibitors, the brainchildren of renowned corporations like AstraZeneca, Pfizer, Clovis, and Zai Lab.



(a) New Drugs, 2011–2014

(b) New Drugs, 2015–2022

(c) Generic Drugs, 2011–2014

(d) Generic Drugs, 2015–2022

Figure 11: Dependent Variable: Stock Returns (Daily)

Notes: This graph shows the β_τ parameters estimated from event studies for new drugs and generic drugs, with the corresponding 90% confidence intervals. The standard errors are clustered at the event-firm level.

(denoted by g) and create separate treatment and control groups based on these events. The control group consists of all firms that did not receive any grants for new drugs during the event period. We define the daily stock return of firm i at time t during event g as $R_{i,g,t} = log(p_{i,t}) - log(p_{i,t-1})$, where $p_{i,t}$ is the stock price of stock i at time t. The variable $PostApproval_{g,t}$ is a dummy variable that indicates whether the time t is before or after the two periods before the approval of a new drug for event g. Similarly, $PostReform_t$ is a dummy variable that indicates whether the year of date t is before or after the drug reform. $Treat_{i,g}$ is a dummy variable indicating whether firm i is treated during event g.

In order to account for the overall patterns in stock returns during specific event periods or in certain stock markets in China, we introduce event-firm fixed effect ($\gamma_{i,g}$), event-date fixed effect ($\gamma_{g,t}$) and event-market fixed effect($\gamma_{markettype,g}$) into the regression analysis.[18] To capture these trends, we include changes in stock prices (during the same time period as the events) for medical firms that did not have any new drug approvals during our sample period.

7.2 Results

We draw stock price data from CSMAR Database. There are totally 467 medical listed firms that have ever existed between 2010 and 2022. Among all these firms, there were 139 new drugs granted between 2010 and 2022 owned by 58 firms.[19] Since the listing process for new firms takes time, only six firms were established and listed after 2015 and had no record of approved drugs before 2022. As a placebo test, we also perform the event study for the reaction of the stock returns to the grant of generic drugs, which use the same active ingredients as brand-name medicines after the patents on the original drugs expire and are thus generally less profitable and innovative than new drugs. Among

[18]The medical firms that have been sampled for our study are listed across various markets, including A-share market (in Shanghai, Shenzhen, and Beijing), B-share market (in Shanghai and Shenzhen), Growth Enterprise Market, and Sci-Tech Innovation Board.

[19]We define the medical firm as the firm of which the industry is the pharmaceutical based on the Guidelines for the Industry Classification of Listed Companies (2012 Revision), or the firm of which the name contains the "medical" (yi in Chinese) or "pharmaceutical" (yao in Chinese).

Table 3: Dependent Variable: Stock Returns (Daily)

	Pre-reform Period DID		Post-reform Period DID		All Period Triple DID	
	(1)	(2)	(3)	(4)	(5)	(6)
			Panel A: New Drug			
Treat×PostApproval	0.0001		0.0042		0.0001	
(window=2 days)	(0.0035)		(0.0036)		(0.0035)	
Treat×PostApproval		0.0014		0.0080***		0.0014
(window=3 days)		(0.0026)		(0.0030)		(0.0026)
Treat×PostApproval×PostReform					0.0042	
(window=2 days)					(0.0050)	
Treat×PostApproval×PostReform						0.0066*
(window=3 days)						(0.0039)
Obs	16,756	25,640	68,022	102,091	84,778	127,731
R-square	0.2480	0.2480	0.2935	0.2548	0.2837	0.2536
			Panel B: Generic Drug			
Treat×PostApproval	-0.0021		-0.0001		-0.0021	
(window=2 days)	(0.0015)		(0.0014)		(0.0015)	
Treat×PostApproval		-0.0026		-0.0001		-0.0026*
(window=3 days)		(0.0014)		(0.0011)		(0.0014)
Treat×PostApproval×PostReform					0.0019	
(window=2 days)					(0.0019)	
Treat×PostApproval×PostReform						0.0024
(window=3 days)						(0.0015)
Obs	71579	109860	292759	425127	3364338	535372
R-square	0.3905	0.3603	0.2909	0.2665	0.3164	0.2913

Notes: The dependent variable in each column is the daily stock return. In Panel A, we focus on the event of the grant of the new drug. As a placebo test, we analyze the event of the grant of the generic drug in Panel B. For each event of the drug grant, we perform the difference-in-difference analysis to explore the effect of that event. We set the observation window as ± 2 days in odd columns and ± 3 days in even columns around two days before the approval (consistent with our event study), respectively. We control for event-firm fixed effects, event-date fixed effects, and event-market fixed effects. Standard errors are clustered at the firm-date level. Significance levels: 10% *, 5% **, 1% ***.

listed medical firms, 120 listed firms had 784 generic drugs granted between 2010 and 2022.

Before reporting the triple-difference estimates, we present the DID estimates for the periods before and after the reform in Columns (1)–(4) of Table 3. As shown, before the reform, the stock market response to NDAs was positive but not always significant. After the reform, however, the positive response more than doubled in magnitude and became significant.

Columns (5)–(6) present the triple-difference estimates. According to these estimates, the stock returns to new drugs after the reform are statistically and economically meaningful. According to Column (6), in the post-reform period, there was a cumulative stock

return of approximately 1.9% over the three days starting from one day before the approval announcement ($\tau = -1, 0, 1$). To assess the market evaluation of new drugs in absolute terms, we take into account the market value of the treated firms on the event date, which had an average value of 85.6 billion RMB. Based on this analysis, we can observe that the market has assigned an average value of 1.63 billion RMB (approximately 0.23 billion dollars) to each approved new drug, which is sizable economically.

Interpretation Again, we should note that most of firms in this analysis are established incumbents, and most of the NDAs started their IND applications prior to the reform. We interpret these findings as an indication that the market perceives an enhancement in drug innovation novelty post-reform, rather than as a comprehensive assessment of the value of drug innovation following the reform. These results are consistent with how we interpret the reform in our conceptual framework: the improvement in regulation increases expected returns from innovation.

8 Conclusion

This paper examines the impact of adopting specific regulatory practices in frontier countries on fostering innovation in emerging markets. Although China is just one of several economies that have implemented such regulatory reforms, this pivotal policy research question has not been extensively investigated prior to this study. [20]

Our paper makes three main findings. First, regulatory reform plays a constructive role in bolstering the volume of innovation. Second, the reform's influence extends beyond mere quantity. It acts as a catalyst for the infusion of novel, forward-thinking enterprises into the market and triggers a transformative shift in the composition of firms. This recalibration significantly impacts the overall innovativeness of the pharmaceutical industry.

[20] For example, in 2012, Mexico streamlined its review process for applications pre-reviewed by certified external entities, leading to a notable decrease in median review durations (Patel, McAuslane and Liberti, 2019). In a similar vein, Malaysia's regulatory authority took strides in 2013 to align with international standards, minimizing repetitive testing and hastening the market entry of new products.

Third, the stock market responses appear to support a novelty improvement in new drugs after the reform.

Our findings can be interpreted through a straightforward framework, in which the regulatory reform increased the anticipated returns from innovation by reducing waiting time, leading to an uptick in innovation efforts and prompting the entry of new firms. Importantly, we find that these new firms deterred by the old regulatory regime could be more innovative than the incumbent firms.

Evidently, a pronounced discrepancy in innovation prowess persists between burgeoning economies and their developed counterparts. This gap, stemming from a complex interplay of factors, implies the ongoing challenges. Despite the efforts to enact regulatory reforms and elevate the standards of innovation, China's pharmaceutical sector remains in the nascent stages of its innovation journey. Zooming in on the regulatory landscape, it becomes apparent that many critical junctures merit consideration. These range from fine-tuning the regulations governing the distribution of pharmaceuticals from manufacturers to medical institutions, to the pivotal matter of regulating physicians' prescriptions to patients. Our investigation indicates that, rather than advocating for more or fewer regulations or wholesale adoption of regulatory approaches, identifying and adopting specific effective regulatory practices can yield useful insights.

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A 2015 Regulatory Reform in China

The National Center for Drug Evaluation (CDE), a subsidiary of the National Medical Products Administration (NMPA),[21] is responsible for reviewing applicants' information on drug efficacy and safety, approving clinical studies, and evaluating clinical results. In 2014 and 2015, the CDE faced a backlog of 18,597 and over 21,000 applications, respectively, resulting in delays in drug access for patients and increased costs and uncertainty for pharmaceutical companies (Zhou et al., 2017). These issues led to widespread industry complaints and demands for change. A series of reforms were initiated in 2015 to address the challenges faced by the system, marked by "The Opinions on Reforming Review and Approval Process for Drugs and Medical Devices" (hereafter, "The Opinions") submitted by the CFDA to the State Council.[22]

The implementation of the series of reforms involved several steps. After the publication of "The Opinion" in August 2015, numerous other policy documents were issued to address various aspects of the issue. For instance, on November 11th, 2015, the NMPA released the "Announcement of the State Administration for Several Policies concerning Drug Registration Review and Approval."[23] This document mandated that generic drugs must pass the "Generic Quality Consistency Evaluation (GQCE)" before submitting an application. The evaluation's objective is to ensure that the original brand-name drug and its generic counterpart are essentially bioequivalent, a standard practice in the global pharmaceutical market for decades but not previously required in China. Additionally, this document introduces new punishment standards for under-qualified applications and detected data falsification, allowing applicants to withdraw their already submitted applications to avoid potential penalties.

Achieving a reduction in process time was a gradual process. In August 2016 and

[21] Previously, the center was named the China Food and Drug Administration (CFDA). The CFDA changed its name to NMPA in March 2018.

[22] Guo Fa [2015] No. 44: http://www.gov.cn/zhengce/content/2015-08/18/content_10101.htm

[23] https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/ggtg/qtggtg/20151111120001229.html

October 2017, the NMPA published two revised versions of "Measures for the Administration of Drug Registration" to solicit public opinion.[24] The 2017 draft version explicitly set time limits for drug approval applications—60 working days for IND applications and 100 working days for New Drug Applications (NDAs). In October 2017 and October 2018, these time limits were incorporated into two revised drafts of "The Medicinal Product Administration Law of the People's Republic of China," which was eventually adopted at the 12th Session of the Standing Committee of the Thirteenth National People's Congress of the People's Republic of China on August 26, 2019.[25] As shown in Figure 3, we notice a steady decrease in the average process time since 2015, stabilizing in 2019 at around fewer than 100 calendar days. This informs our identification strategy of measuring the reduction in approval time during the transition period from 2015 to 2017 compared to the pre-reform years.

B A Simple Framework

We develop a parsimonious model to motivate our analysis. Our model allows for endogenous firm entry and novelty choices, augmented by taking into account product quantities and regulatory time lags.

B.1 Model Setup

We consider two types of goods as in Acemoglu and Linn (2004). First, there is a basic good, which can be consumed, or used for the production of drugs, or for research inputs. We treat the basic good as the numeraire with its price normalized to one. Second, there is a drug with many varieties that can be potentially supplied by many producers.

[24] 2016: https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/zhqyj/zhqyjyp/20160725154601588.html; 2017: https://www.nmpa.gov.cn/directory/web/nmpa/zhuanti/ypqxgg/ggzhqyj/20171023174301598.html

[25] https://gkml.samr.gov.cn/nsjg/fgs/201909/t20190917_306828.html

Medical Demand Suppose that the economy is inhabited by a representative household with a fixed endowment of the basic good, Y. This representative household can be thought of as aggregating all the demand for basic goods and drugs across all the individuals with different income levels and diseases in the economy. The utility function is expressed as:

$$\begin{aligned} &U = Z^{\delta} X^{1-\delta}, \\ &\text{s.t. } Z + PX = Y. \end{aligned} \tag{2.7}$$

Z represents the consumption of the basic good, and δ denotes the share of expenses dedicated to the basic good. X is an aggregate quantity of the drug comprising the quantities demanded for various varieties manufactured by different producers, as described by the following function:

$$X = \left(\int u(\omega)^{\frac{1}{\sigma}} x(\omega)^{\frac{\sigma-1}{\sigma}} d\omega \right)^{\frac{\sigma}{\sigma-1}}, \tag{2.8}$$

where we employ ω to index each variety. As a drug's effectiveness depends on its novelty, we consider $u(\omega)$ to be the novelty of variety ω, and $x(\omega)$ to be the quantity. The elasticity of substitution among different varieties, $\sigma > 1$, conveys the idea that multiple varieties may serve as imperfect substitutes due to aspects like brand and taste, reflecting the real-world coexistence of numerous drug varieties in the market. The quantity demanded for each variety ω is given by $x(\omega) = u(\omega)p(\omega)^{-\sigma} P^{\sigma} X$, where $P = \left(\int u(\omega) p(\omega)^{1-\sigma} d\omega \right)^{1/(1-\sigma)}$ is the aggregate price index for the drug. Given that there is a continuum of varieties, the drug market is under monopolistic competition.

Regulatory Policy For the sake of analytical simplicity, we assume consumption occurs at time $t = 0$. Drug varieties result from producers' innovation efforts, as we will describe below. Nonetheless, to effectively serve the market at $t = 0$, a prospective drug producer must also await approval from the government regulatory bureau for drug innovation procedures, such as clinical trials. We presume the waiting time to be g. Consequently, a potential producer must initiate the innovation process at $t = -g$ to cater to the market.

Innovation and Novelty Choices Firms are heterogeneous in their innovation capabilities, denoted by $\theta_i > 0$. They decide on their innovation intensity, k_i, where higher intensities correspond to a greater number of drug applications. Each application corresponds to one drug variety. The innovation costs are represented by $\psi_k(k_i)^\gamma$, with $\gamma > 1$ signifying a convex function, as often assumed in the literature (e.g., Klette and Kortum, 2004; Lentz and Mortensen, 2008). For the sake of simplicity, we assume that the expected number of new applications approved is given by $\theta_i k_i$. By multiplying θ_i, we posit that more innovative firms are likely to successfully generate more innovation outcomes given the same innovation intensity.[26]

We assume that, in addition to selecting innovation quantities, firms can also choose the novelty of their drug applications. A higher novelty u will proportionally increase drug profits; however, enhancing novelty would necessitate costs $\psi_u u^\phi$ per unit of drug application, where $\phi > 1$ indicates that the costs are convex in novelty u.

Firm Types There exist two separate categories of producers: incumbents and potential entrants (new firms). The measure of incumbents and potential entrants is denoted by M and M_e, respectively, both with innovation capacity distributions represented by $F(\theta)$. In order to initiate innovation and apply for drug approvals, potential entrants must bear an extra fixed entry cost f. These fixed costs might include expenditures such as registration fees, which are not applicable to incumbents since they are already registered and may produce some established drugs concurrently. We assume that the fixed cost f for each firm is a random variable drawn from the distribution $G(f|\theta)$, which allows for the possibility of more innovative firms having distinct fixed cost distributions, as they may have the need to recruit highly educated individuals, which can entail significant expenses. Lastly, the production cost per unit of drug variety is identical (denoted by $c > 0$) for all firms.

[26] We could also assume that, with the same innovation intensity, more innovative firms incur lower innovation costs. Such an alternative assumption would lead to very similar analytical predictions about how the regulatory policy change affects the number of drug applications by incumbents and new firms.

B.2 Solving the Model

Incumbents' Problem We now solve the incumbent's innovation decisions by backward induction. First, given the choice of innovation intensity k and choice of novelty u, incumbent i chooses the optimal price to maximize the profits at $t = 0$:

$$\begin{aligned} &\max_{p_i} \ \theta_i k(p_i - c)x_i \\ &\text{s.t. } x_i = u\left(p_i\right)^{-\sigma} P^{\sigma} X. \end{aligned} \tag{2.9}$$

According to the first-order condition, we can obtain $p_i = \tilde{\sigma}c$, where $\tilde{\sigma} = \sigma/(\sigma - 1)$. Due to the waiting time of regulatory bureaus, the producer needs to initiate innovations at $t = -g$. For ease of notation, we define $\pi = (1 + r)^{-g}(\tilde{\sigma}c)^{1-\sigma}P^{\sigma}X/\sigma$ as the present value of profits per approved application (when novelty $u = 1$) at the time of initiating innovations, where r is the interest rate. Thus, the producer's problem at the time of initiating innovations is:

$$\max_{\{k,u\}} \ k\left[\theta_i u\pi - \psi_u u^{\phi}\right] - \psi_k k^{\gamma}. \tag{2.10}$$

As the drug applications are homogeneous, the firm will choose the same novelty u for its all drug varieties. According to the first-order conditions, we find that besides variables and parameters common to every firm, the optimal innovation quantity and novelty of firm i depend on its innovation capability θ_i:

$$u(\theta_i) = \left(\frac{\theta_i \pi}{\phi \psi_u}\right)^{\frac{1}{\phi - 1}}, \tag{2.11}$$

$$k(\theta_i) = \left(\frac{(\phi - 1)\left(\theta_i \pi\right)^{\frac{\phi}{\phi - 1}}}{\phi^{\frac{\phi}{\phi - 1}} \psi_u^{\frac{1}{\phi - 1}} \psi_k \gamma}\right)^{\frac{1}{\gamma - 1}}. \tag{2.12}$$

The optimal quantity and novelty of innovation increases with the firm's innovation efficiency θ_i and the potential profits π. The total number of drug applications by incumbents is $N = M \int_0^{\infty} k(\theta) dF(\theta)$.

New Firms' Problem We also solve new firms' innovation decisions by backward induction. Similar to incumbents' problem in equation (2.9), each new firm i's optimal pricing strategy in the drug market is also $p_i = \tilde{\sigma}c$. Then, the new firm's problem at the time of initiating innovations is:

$$\max_{\{k,u,\mathcal{I}\}} \mathcal{I}\Big\{k\left[\theta_i \pi u - \psi_u u^{\phi}\right] - \psi_k k^{\gamma} - f\Big\}. \tag{2.13}$$

where $\mathcal{I} \in \{0, 1\}$ indexes whether the new firm chooses to actively innovate. Given active innovation status $\mathcal{I} = 1$, we can solve new firm i's innovation intensity and novelty choices, which are identical to equations (2.11)–(2.12).

A new firm will engage in innovation if and only if the profits from innovation net of entry costs are positive, and these profits decrease with the fixed cost f. Consequently, we can determine the threshold of the fixed cost for new firms with innovation capacity θ to participate in innovation as follows:

$$\bar{f}(\theta) = (\gamma - 1)\psi_k \left(\frac{(\phi - 1)\left(\theta_i \pi\right)^{\frac{\phi}{\phi-1}}}{\phi^{\frac{\phi}{\phi-1}} \psi_u^{\frac{1}{\phi-1}} \psi_k \gamma} \right)^{\frac{\gamma}{\gamma-1}}. \tag{2.14}$$

Hence, for new firms that must incur fixed entry costs, only those with lower fixed costs than $\bar{f}(\theta)$ will participate in the innovation process. The total number of drug applications by new firms is $N_e = M_e \int_0^{\infty} k(\theta) G(\bar{f}(\theta)|\theta) dF(\theta)$. The average innovation capacity of new firms is given by $\int_0^{\infty} \theta G(\bar{f}(\theta)|\theta) dF(\theta) / \int_0^{\infty} G(\bar{f}(\theta)|\theta) dF(\theta)$.

B.3 Model Predictions on Regulatory Policy Changes

We now examine a regulatory policy change that reduces the waiting time for government decisions from g to g', where $g' < g$. The subsequent proposition encapsulates the findings.

Proposition 1 (Regulatory Policy Change and Innovation)**.** *In the event that the waiting time for government decisions decreases from g to $g' < g$, we can derive the following results: (i) The present value of profits per approved application increases, $\pi' > \pi$.*

(ii) The proportional change in the number of drug applications by incumbents is:

$$\frac{N'}{N} = \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > 1. \tag{2.15}$$

(iii) The proportional change in the number of drug applications by new firms is:

$$\frac{N'_e}{N_e} = \frac{\int_0^\infty \theta^{\frac{\phi}{(\phi-1)(\gamma-1)}} G(\bar{f}'(\theta)|\theta) dF(\theta)}{\int_0^\infty \theta^{\frac{\phi}{(\phi-1)(\gamma-1)}} G(\bar{f}(\theta)|\theta) dF(\theta)} \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > 1. \tag{2.16}$$

where the change in the cost threshold is given by $\bar{f}'(\theta)/\bar{f}(\theta) = (\pi'/\pi)^{\frac{\phi\gamma}{(\phi-1)(\gamma-1)}} > 1$*, which implies that conditional on innovation capacity* θ*, a greater proportion of new firms initiate innovation following the decrease in waiting time.*

(iv) The proportional change in novelty for incumbents is as follows:

$$\frac{u'(\theta_i)}{u(\theta_i)} = \left(\frac{\pi'}{\pi}\right)^{\frac{1}{\phi-1}} > 1. \tag{2.17}$$

The change in novelty is ambiguous for new firms due to the ambiguous impact on the composition of new firms' innovation capacities.

(v) With more innovations and better novelty, the drug's aggregate price index $P' < P$*.*

Proof: See Appendix B.4.

In response to a regulatory policy change that reduces the waiting time for government decisions, our model expects an increase in the expected profits of drug applications, even in the face of heightened competition brought about by this change. Results (ii) and (iii) demonstrate that the rise in expected profits stimulates innovation for both incumbents and new firms. Additionally, when comparing these two outcomes, our model forecasts a more substantial innovation response from new firms relative to incumbents. The discrepancy in responses between new firms and incumbents is solely due to the extensive margin of new firms (weighted by their innovation capacities), as higher innovation profits also drive increased entry by these firms. Result (iv) suggests an improvement in the novelty

of drug applications for existing incumbents. However, the average change in new firms' novelty is ambiguous, as the reform has an ambiguous impact on the composition of new firms' innovation capacities. Lastly, Result (v) reveals that, as a consequence of increased innovations and enhanced drug innovativeness, the aggregate price index of the drug market would decrease, indicating more competition in the drug market and an equilibrium that is more favorable for consumers.

B.4 Proof of Proposition 1

We first prove Result (i) by contradiction. Suppose that the present value of profits π' declines. According to equations (2.11), (2.12), and (2.14), this would imply that for each firm i, its quantity and novelty of innovation declines, and the capability threshold for new firms increases. Thus, this would indicate a higher level of aggregate price, $P' > P$. We also note that:

$$\pi' = \frac{(1+t)^{-g'}}{\sigma}(\tilde{\sigma}c)^{1-\sigma}(P')^{\sigma}X' = \frac{(1+t)^{-g'}}{\sigma}(\tilde{\sigma}c)^{1-\sigma}(P')^{\sigma-1}(1-\delta)Y \tag{2.18}$$

where $P'X' = (1-\delta)Y$ is the total expenditures on drugs according to Cobb-Douglas preferences. Thus, we would have $\pi'/\pi = (1+r)^{g-g'}(P'/P)^{\sigma-1}$, which is strictly larger than 1 if $P' > P$. This violates the assumption that the present value of profits π' declines. Similarly, we can prove that π' cannot be equal to π. Thus, it must be that $\pi' > \pi$.

To prove Result (ii), we note that $N = M\int_0^{\infty} k(\theta)dF(\theta)$. Thus,

$$\frac{N'}{N} = \frac{\int_0^{\infty} k'(\theta)dF(\theta)}{\int_0^{\infty} k(\theta)dF(\theta)} = \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > 1, \tag{2.19}$$

where the second equality uses the solution for $k(\theta)$ in equation (2.12).

For Result (iii), we notice that $N_e = M_e \int_0^\infty G(\bar{f}(\theta)|\theta)dF(\theta)$. Thus,

$$\frac{N_e'}{N_e} = \frac{\int_0^\infty k'(\theta)G(\bar{f}'(\theta)|\theta)dF(\theta)}{\int_0^\infty k(\theta)G(\bar{f}(\theta)|\theta)dF(\theta)} = \frac{\int_0^\infty \theta^{\frac{\phi}{(\phi-1)(\gamma-1)}} G(\bar{f}'(\theta)|\theta)dF(\theta)}{\int_0^\infty \theta^{\frac{\phi}{(\phi-1)(\gamma-1)}} G(\bar{f}(\theta)|\theta)dF(\theta)} \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > \left(\frac{\pi'}{\pi}\right)^{\frac{\phi}{(\phi-1)(\gamma-1)}} > 1. \tag{2.20}$$

where the second equality uses the solution for $k(\theta)$ in equation (2.12), and the first inequality uses $\bar{f}'(\theta)/\bar{f}(\theta) > 1$ according to equation (2.14) when $\pi' > \pi$. Result (iv) can be directly proved using the formula for novelty in equation (2.11). However, the reform has an ambiguous impact on the composition of new firms' innovation capacities and the average innovation capacity of new firms ($\int_0^\infty \theta G(\bar{f}(\theta)|\theta)dF(\theta)/\int_0^\infty G(\bar{f}(\theta)|\theta)dF(\theta)$).

Finally, given that each firm's quantity and novelty of innovation increases, and the fixed cost threshold for new firms increases (more entry), this would indicate a lower level of aggregate price for the household, $P' < P$, as reported in Result (v).

C Additional Results for Section 4

C.1 IND Approval Time vs. IND-Final Approval Time

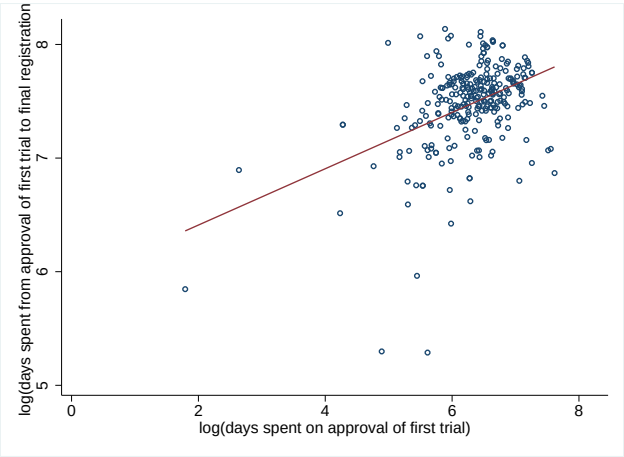


Figure C.1: Correlation between Approval Times

Notes: This graph shows the correlation between IND approval time and the time spent from IND approval to final registration, for each drug application with available data.

C.2 Decline in Approval Time vs Drug Characteristics

Table C.2: Correlation between Decline in Approval Time and Characteristics

	Dependent Variable: Decline in Approval Time					
	(1)	(2)	(3)	(4)	(5)	(6)
Num of applications 12–14	0.52					
	(1.68)					
HHI innovation 12–14		62.43				
		(97.35)				
Share of targets shown in U.S. 12–14			-24.89			
			(132.72)			
Share of IND Applications 12–14				-126.97		
				(209.93)		
U.S. approval time before 2015					.13	
					(.10)	
Decline in U.S. approval time after 2015						.12
						(.12)
Constant	179.85***	168.57***	209.53**	215.93***	117.75**	200.58***
	(49.80)	(33.91)	(98.10)	(50.22)	(54.66)	(33.35)
Obs	109	109	109	109	92	80
R-squared	0.00	0.00	0.00	0.00	0.02	0.02
Mean	190.59	190.59	190.59	190.59	190.59	190.59

Notes: "HHI" is short for the Herfindahl-Hirschman index. Standard errors are clustered at the ATC category level. * $p < .10$, ** $p < .05$, *** $p < .01$

C.3 Approval Decline vs. Pre-reform Approval Time

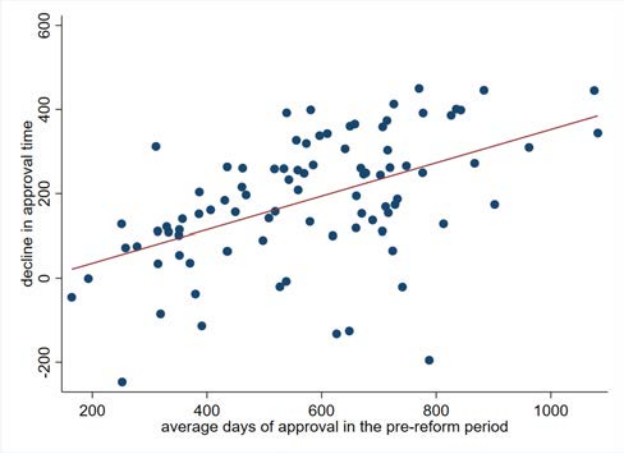


Figure C.3: Relation to Previous Approval Time

Notes: This graph shows the decline in approval time between 2015–2017 and 2012–2014 (y-axis) on the average days of approval in 2012–2014 (x-axis), across 4-digit ATC categories. We truncate 5% of the decline in approval time to avoid extreme values in the graph.

C.4 Approval Decline vs. Backlogs

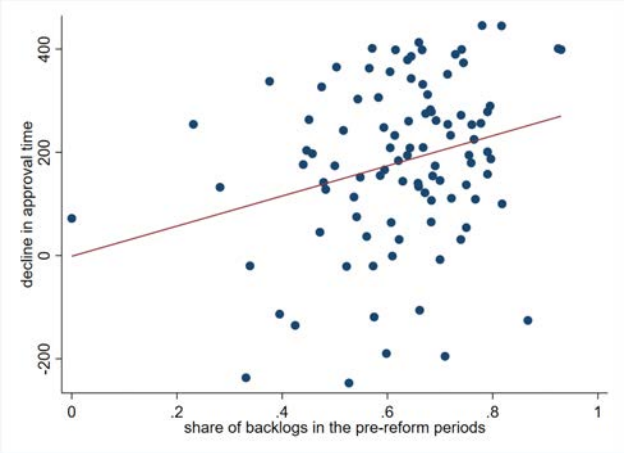


Figure C.4: Relation to Pre-reform Share of Backlogs

Notes: This graph shows the decline in approval time between 2015–2017 and 2012–2014 (y-axis) on the pre-reform share of backlogs (x-axis), across 4-digit ATC categories. We compute the pre-reform share of backlogs as: among all the IND applications that were submitted in 2012–2014, the share of applications that had not been approved by the end of 2014. We truncate 5% of the decline in approval time to avoid extreme values in the graph.

D Additional Results for Section 5

D.1 Summary Statistics

Table D.1: Summary Characteristics

Variable	N	Mean	Std
ATC Drug Level			
Number of IND apps (yearly)	1,199	8.31	60.10
Number of applying firms in each year	1,199	2.54	15.19
Decline in approval time (days)	109	197.40	228.45
HHI in innovation 12–14	109	0.35	0.22
Share of targets already shown in the U.S. 12–14	109	0.76	0.16
U.S. approval time (NDA) before 2015	92	615.05	274.58
Decline in U.S. approval time after 2015	80	232.48	242.07
Firm Level			
Number of IND apps (yearly)	1,826	2.30	5.29
Decline in approval time 12–14	166	218.89	261.73
HHI in innovation 12–14	166	0.24	0.18
Share of targets already shown in the U.S.	166	0.74	0.11
U.S. approval time (NDA) before 2015	158	515.50	162.33
Decline in U.S. approval time after 2015	151	177.43	133.21

Notes: This table reports the summary statistics for variables used in the regressions. We compute the number of applications, the Herfindahl-Hirschman index (HHI), the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications for each ATC category in the 2012–2014 period, using our medical registration data. In drug-level regressions, where applications may have multiple applicants, we handle these applications by treating them as if each applicant applied separately. This approach helps us analyze incumbents and new firms separately. Notably, the regression results presented in Figure 5 remain very similar even when considering applications with multiple applicants as a single application. We compute the approval time for the U.S. drug applications using the drug data from the U.S. Food and Drug Administration (FDA), and the data is only available for NDA applications of approved drugs. We then assign the ATC category for each drug application, according to each drug's main ingredient and the WHO database. We can therefore compute the decline in approval time for the U.S. applications that were received after 2015 relative to the applications that were received before 2014, for each ATC category.

D.2 The Impact on IND Applications: Event-study Estimates

Table D.2: The Impact of Decline in Approval Time on the Number of IND Applications

	# IND Apps		# IND Apps (Incumbents)		# IND Apps (entrants)	
	(1)	(2)	(3)	(4)	(5)	(6)
	Poisson	Poisson	Poisson	Poisson	Poisson	Poisson
β_{2011}	-.25	-.21	-.47*	-.41*	.00	.00
	(.24)	(.19)	(.28)	(.23)	(.)	(.)
β_{2012}	.59	.42	.26	.20	.00	.00
	(.50)	(.29)	(.42)	(.30)	(.)	(.)
β_{2013}	.08	.07	-.02	-.02	.00	.00
	(.22)	(.18)	(.21)	(.17)	(.)	(.)
β_{2015}	.20	-.01	.01	-.13	.00	.00
	(.26)	(.27)	(.26)	(.25)	(.)	(.)
β_{2016}	.23	.02	.28	.15	.46	.46
	(.29)	(.26)	(.28)	(.20)	(.78)	(.78)
β_{2017}	.63**	.44**	.53**	.41**	.61	.61
	(.28)	(.19)	(.26)	(.18)	(.71)	(.71)
β_{2018}	.61**	.42**	.49*	.37*	.98	.98
	(.29)	(.19)	(.30)	(.21)	(.65)	(.65)
β_{2019}	.68**	.50**	.53	.41*	1.21*	1.21*
	(.34)	(.21)	(.34)	(.22)	(.65)	(.65)
β_{2020}	.72**	.54***	.55	.44**	1.61***	1.61***
	(.33)	(.19)	(.35)	(.22)	(.62)	(.62)
β_{2021}	.80***	.63***	.66**	.56***	1.43**	1.43**
	(.30)	(.20)	(.33)	(.21)	(.61)	(.61)
Controls	No	Yes	No	Yes	No	Yes
Obs	1,199	1,199	1,199	1,199	413	413
R-squared	0.86	0.87	0.82	0.83	0.91	0.91
Mean	8.31	8.31	5.20	5.20	2.23	2.23

Notes: We always include firm and year fixed effects in all regressions. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. Standard errors are clustered at the ATC category level. * $p < .10$, ** $p < .05$, *** $p < .01$.

D.3 Robustness Checks for Section 5.2

Alternative Measure of the Reform's Strength. As discussed in Section 4, drug-level approval time change is affected by pre-reform backlogs. Thus, we also use the drug-level pre-reform share of backlogs as an alternative measure for the strength of the reform, as the reform was driven by the need to tackle the backlogs. We thus perform equation (2) but substitute the independent variable $decline_j$ with the share of backlogs in the pre-reform period. Appendix Figure D.3 shows that after 2015, an increase in the pre-reform share of backlogs had a significantly positive impact on innovation levels, which aligns with our evidence that drugs with a large share of backlogs in the pre-reform period could experience a more substantial decline in approval time afterward (Appendix Figure C.4).

Other Reforms During the Same Period. During the same period, another major reform was initiated in the Chinese healthcare system, involving the negotiation of the public health insurance drug reimbursement list. Prior to this reform, the most recent national drug formulary dated back to 2009 and had not been updated. In November 2015, the National Health Commission officially started the national drug price negotiation pilot. Consequently, the 4th version of the national public health insurance drug formulary was released in 2017.[27] Since then, the formulary has been annually updated. This negotiation primarily targets newly marketed innovative drugs, aiming to enhance patient affordability and stimulate innovation within the pharmaceutical industry.

We considered the possibility that drug categories with a substantial reduction in approval times might also receive more extensive coverage under public insurance during the formulary adjustment. Such a scenario would necessitate a reevaluation of our parameters. To address potential confounding factors from the demand side, we analyzed the relationship between the decrease in approval times and the number of drugs covered by insurance at the ATC level, as presented in Appendix Table D.3. The coverage is categorized into two tiers, with Tier 1 offering more comprehensive benefits. Consequently,

[27] Ministry of Human Resources and Social Security Issues the 2017 Edition of the Drug Formulary https://www.gov.cn/xinwen/2017-02/23/content_5170392.htm

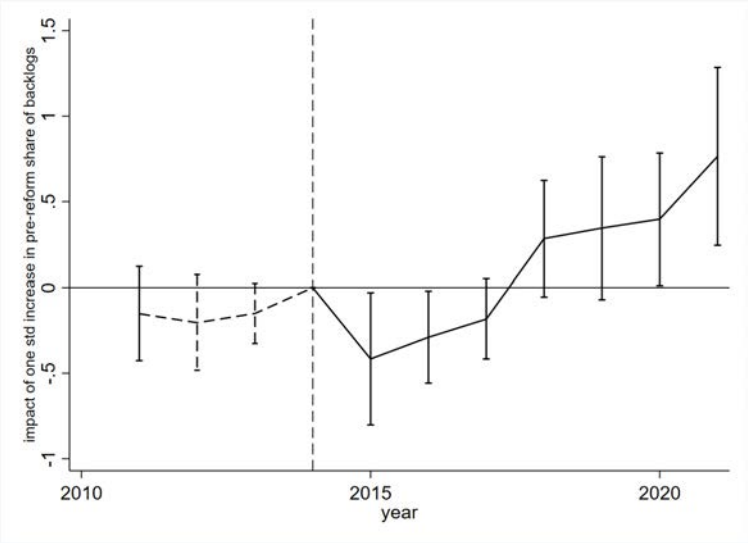


Figure D.3: Impact of Pre-reform Share of Backlogs on IND Applications

Notes: This graph shows the β_t parameters estimated by equation (2), using the share of backlogs in the pre-reform period as the measure of the reform, with the corresponding 90% confidence intervals. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012–2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. The standard errors are clustered at the ATC category level.

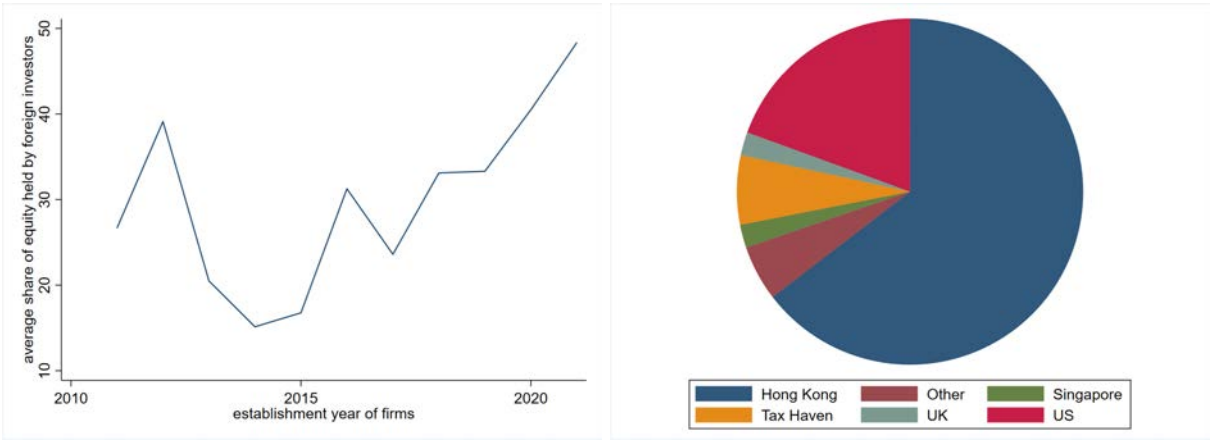
we separately investigated the correlation between our primary explanatory variable and the number of drugs in each tier. Our findings do not reveal any significant correlations, suggesting that the regulatory reforms impacting the supply side are independent of the insurance policy changes targeting the demand side.

Table D.3: Correlation between Decline in Approval Time and Insurance Coverage

	(1)	(2)	(3)
#Drugs	.87		
	(2.50)		
#Drugs in Tier 1		23.42	
		(19.57)	
#Drugs in Tier2			.59
			(2.74)
Constant	171.56***	160.26***	175.35***
	(37.14)	(28.95)	(37.42)
N	102	102	102

Standard errors in parentheses
* $p < .10$, ** $p < .05$, *** $p < .01$

D.4 Foreign Investment in Firm Entry



(a) Equity by Foreign Investors (b) Sources of Foreign Equity

Figure D.4: Foreign Equity of Newly Established Firms

D.5 The Impact on the Number of New Firms

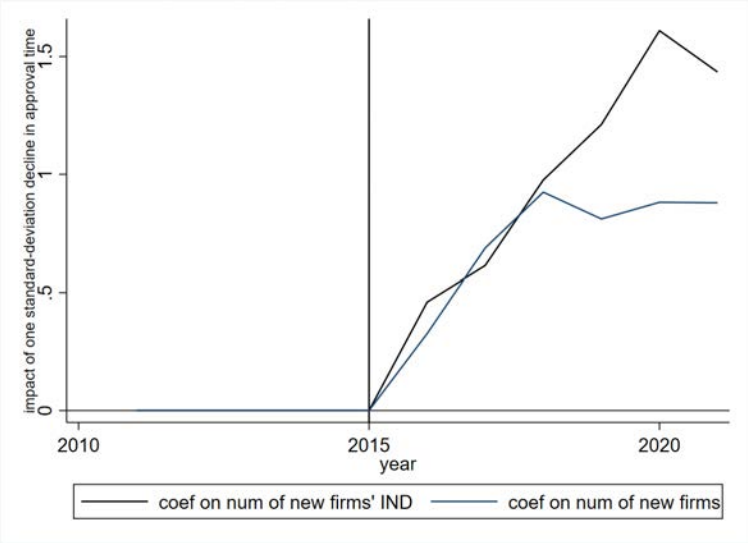


Figure D.5: Impact of Decline in Approval Time on New Firms

Notes: This graph shows the β_t parameters estimated by equation (2). New firms barely had innovations before 2015: few firms appeared to apply for IND before being formally established. Thus, for regressions regarding new firms, we set $\beta_{2015} = 0$, and therefore β_t in other years corresponds to changes in β_t relative to year 2015. Controls include the Herfindahl-Hirschman index, the share of targets already shown in the U.S., and the share of IND applications in total ATC-level applications in the 2012-2014 period, for each ATC category. As the controls are time-invariant and absorbed by ATC-level fixed effects, we interact the control variables with the dummy indicating the post-reform period. To avoid ambiguity, we do not display the confidence intervals on this graph.

E Additional Results for Section 6

E.1 Innovativeness of Phase I Clinical Trials in China and the U.S.

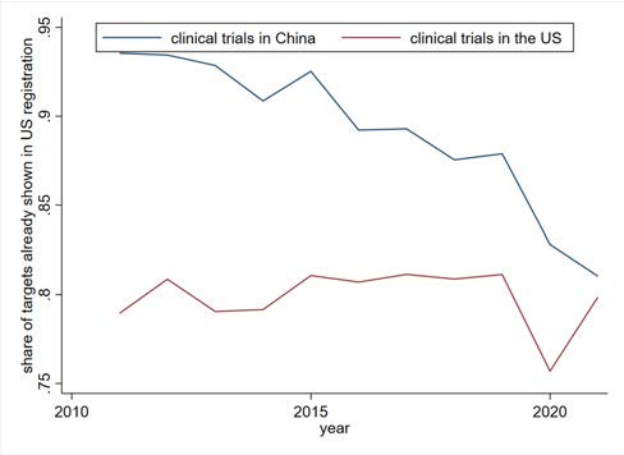


Figure E.1: Innovativeness of Phase I Clinical Trials in China and the U.S.

Notes: For China, we gather information from the Chinese Clinical Trial Database provided by China's Bureau of Medicine and the WTO Database. For the U.S., we rely on the PharmaGO Global Clinical Trial Database. This database is sourced from the U.S. ClinicalTrials.gov database and encompasses clinical trials with public or private funding from over 220 countries.

E.2 Innovativeness of Drug Applications by New and Incumbent Firms

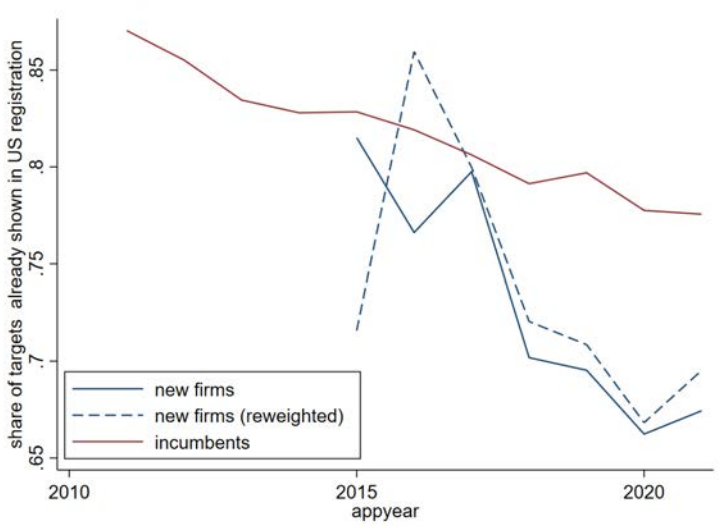


Figure E.2: Innovativeness of Drug Applications by New and Incumbent Firms

Notes: This graph depicts the proportion of drugs adopting targets that have already been demonstrated in U.S. registration for both incumbents and new firms. To account for drug composition across ATC categories, we implement the following procedure: (1) we calculate the share of new firms' drugs adopting targets already demonstrated in U.S. registration for each ATC category per year; and (2) we then utilize the number of incumbents' IND applications across ATC categories in the corresponding year as weights to compute the reweighted aggregate share of drugs adopting targets already demonstrated in the U.S. registration for new firms. The reweighted share is illustrated by the blue dash line.

E.3 Taragets in the EU Drugs

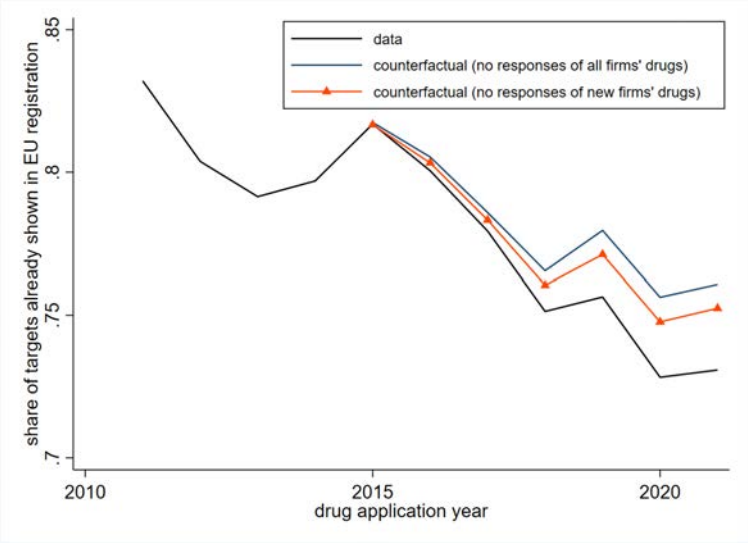


Figure E.3: Impact of Changes in Approval Time on Drug Applications' Innovativeness through Changes in Composition

E.4 New Targets Also Explored by the U.S. in Clinical Trials

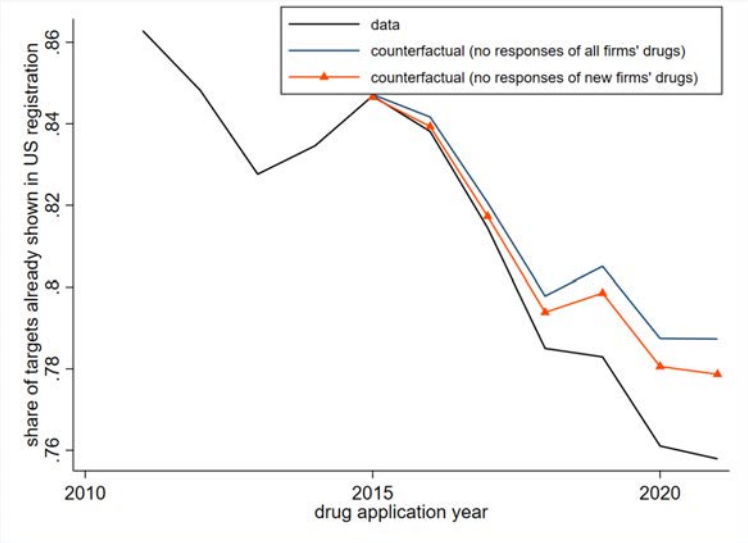


Figure E.4: Impact of Changes in Approval Time on Drug Applications' Innovativeness through Changes in Composition