Global Drug Diffusion and Innovation with the Medicines Patent Pool

Lucy Xiaolu Wang*

Oct. 2020

Abstract: I study the impact of the first joint licensing platform for patented drugs, the Medicines Patent Pool, on global drug diffusion and innovation. The pool allows generic firms worldwide to license drug bundles cheaply and conveniently for sales in a set of developing countries. I construct a novel dataset from licensing contracts, public procurement, clinical trials, and drug approvals. Using difference-in-differences methods, I find that the pool leads to substantial increases in the generic supply of drugs purchased. In addition, there are positive responses in R&D inputs and outputs. Finally, I estimate a simple structural model for a cost-benefit analysis.

Keywords: Patent pool, drug bundling, innovation and diffusion

JEL Code: O30, K20, I10

* Max Planck Institute for Innovation and Competition (email: xw377@cornell.edu). I am indebted to Sean Nicholson, Michael Waldman, Chris Forman, and Michael Lovenheim for valuable advice. For comments or discussions, I thank Panle Barwick, Charles Becker, Iain Cockburn, Wes Cohen, Jorge Contreras, Amanda Eng, Aija Leiponen, Josh Lerner, Ben Leyden, Doug Miller, Atul Nerkar, Chris Rider, David Ridley, Evan Riehl, Michael Roach, F.M. Scherer, Frank Sloan, Nahim Zahur, Rosemarie Ziedonis, and participants in CHITA 2018, IHS 2018, ISA 2019, CCC 2019, ASHEcon 2019, iHEA 2019, IPSC 2019, EPIP 2019, NEUDC 2019, WINDS 2019, INFORMS 2019, EGSC 2019, APPAM 2019, ESWM 2019, AEA 2020, CES 2020 and seminars at Cornell, the Medicines Patent Pool (MPP), NBER Productivity, Cornerstone Research, Charles River Associates, Berkeley Haas, Max Planck Institute for Innovation and Competition, UMass Amherst, UIC, RAND, the Melbourne Institute, National Univ of Singapore, Univ of Sydney, and the US Food and Drug Administration. Individuals from the MPP, WHO, and Janssen provided valuable insights, especially Charles Gore, Erika Dueñas, Maica Trabanco, Sébastien Morin, and Frank Daelemans. I thank Dalton Price for excellent research assistance. I gratefully acknowledge funding from Cornell University and the Institute for Humane Studies. All errors are mine.

1. Introduction

Intended to reward innovation, patents can also impede the diffusion of affordable generic drugs and the development of new formulations. A patent owner has the right to exclude others from using an invention and associated know-hows for roughly two decades. In principle, patent licensing allows a manufacturer to produce and sell a drug before patent expiration by paying royalties. In practice, firms ever-green patents (Hemphill and Sampat, 2012), making it costly to license when each drug can be covered by hundreds of patents.[1] This situation has more severe impacts in developing countries, where many drugs remain unaffordable and unavailable decades after their initial approvals (Kremer, 2002; Cockburn *et al*., 2016).[2] When such drugs are available, substantial welfare gains can be achieved (Azomahou *et al*., 2016).

The tradeoff between patent protection and access to medicines can result in negative consequences to both patients and firms. One notable illustration of the consequences is the distribution and development of drugs to treat acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV). Standard treatments require the bundling of multiple drugs (i.e., cocktails) taken daily, of which each drug can be owned by a different firm. As of 2017, only about 59% of the 37 million people living with HIV worldwide had access to HIV drugs.[3] The lack of a stable supply of drugs and fixed-dose cocktail pills make it difficult for patients to adhere to the course of medical treatment, which further accelerates antimicrobial resistance. In response, governments and generic drug firms in developing countries infringe on and invalidate patents, which can further reduce innovation incentives.

In this paper, I study the effects of patent pools, which are institutions designed to ameliorate the tension between patent protection and the diffusion of technologies. As depicted in Figure 1, patent pools are joint licensing platforms that typically gather complementary patents from many patent owners and provide "one-stop shopping" to manufacturers. Historically, patent pools were commonly used in many sectors, including aircraft, railways, and radio (Lerner and Tirole, 2004). Patent pools disappeared after World War II as a result of

[1] There is clear evidence of generic firms' comparative advantage in producing low-cost new cocktails. Before patent enforcement in developing countries, the first qualified single-pill HIV cocktail was created by generic firm Cipla in 2001 for $350 per patient-year, whereas the prices for the three standalone drugs were above $10,000. The cost dropped to about $140 per year after more generic entry (Hoen, 2016).
[2] Generic HIV drugs cost at least $200 per patient per year in the early 2000s, which was unaffordable in low-income countries that had average per capita health spending of $23 (Tirole, 2006).
[3] Source: https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics.

regulatory changes and were revived in the late 1990s to spur the development of information and communication technologies. Although there is growing interest among practitioners and the U.S. Patent and Trademark Office in creating biomedical patent pools (Clark *et al*., 2000; Van Overwalle, 2016), progress has been slow in the heavily regulated biomedical sector.

This paper investigates the first modern biomedical patent pool, the Medicines Patent Pool (MPP), which allows access to a set of HIV-related drug patents from multi-national firms with the goal of fostering the diffusion of generic drugs to developing countries and spurring cumulative innovation. Backed by the United Nations and founded in July 2010 in Geneva, Switzerland, the MPP is designed to facilitate generic licensing for drugs that typically treat infectious diseases that disproportionately affect resource limited countries. These MPP licenses do not apply to high-income countries. Although the MPP initially targeted HIV drugs only, it began to cover Hepatitis C and tuberculosis in 2015, further expanded its mandate to all small molecule drugs on the World Health Organization (WHO)'s essential medicine list, and it became part of the WHO's COVID-19 Technology Access Pool (C-TAP) on May 29, 2020.[4]

An illustrative example suggests that the MPP accelerates generic entry and new drug product development. A new compound, dolutegravir (DTG), was first approved in the U.S. in August 2013 and was added to the MPP in March 2014. Over a hundred patents on DTG were licensed from the pool by the generic firm Mylan in July 2014. The first DTG-based three-drug single-pill cocktail (TLD) made by Mylan was approved in 2017 for sales in developing countries; four other generic firms also obtained MPP licenses and drug approvals in 2018. Without the MPP, this process typically takes over a decade (Cockburn *et al*., 2016).

A biomedical patent pool can affect static efficiency (i.e., deadweight loss) and dynamic efficiency (i.e., innovation incentives) through different mechanisms. It can improve static welfare by addressing three problems: (1) transaction costs stemming from numerous patent negotiations with multiple drug owners; (2) hold-up problems where one failed negotiation is sufficient to prevent distribution of a generic cocktail; and (3) double-markup problems where downstream firms can also exert market power. The impact of a pool on dynamic efficiency is less clear. A pool can spur new drug product innovation from branded or generic firms by reducing transaction and litigation costs, increasing royalty revenue from underinvested markets

[4] Source: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool.

for branded firms which pool patents, and enabling generic firms to develop new products to meet the demand in poor countries. However, a pool can stifle innovation if licenses have price-fixing terms and restrict licensees in product development. Hence, the effect of a patent pool on innovation is ambiguous and depends on its design, underscoring the need for empirical analysis.

I examine the impact of the MPP on static and dynamic welfare. I study how the MPP affects generic shares in developing countries, the changes in R&D inputs and output associated with the pool, and the welfare gains compared to the pool's operating costs.

To examine how the MPP affects generic drug diffusion, I use the arguably exogenous variation of when a drug is included in the pool for generic licensing for a given territory. I construct a novel dataset of drug sales in developing countries and calculate the generic share of HIV drug purchases as the main outcome variable. The pool-inclusion timing is driven by factors independent of changes in the outcomes of interest, such as firms' attitudes and administrative efficiency, and are not frequently changed at drug-country level. Critically, I show that the timing is not determined by changes in demand-side factors such as HIV prevalence and death rates. I find that adding a drug in the MPP for a country increases generic drug share by about seven percentage points in that country, a result that is robust across various tests. I support the identifying assumptions using event studies, regression tests, and interviews which all indicate that the timing of entry to the MPP is exogenous to my outcomes of interest.

To further understand MPP-related changes of R&D on HIV drugs, I collect all U.S.-registered global clinical trials and drug product approvals by the two largest global approval agencies. With pro-competitive MPP license terms that emphasize diffusion-oriented innovation, I find increases in follow-on clinical trials that improve the use or bundling of a compound. Once an MPP compound enters the pool, there are more clinical trials and firm participation for drugs that include the compound. In particular, firms outside the pool increase late-stage trials for drug cocktails that include pooled compounds, and firms inside the pool invest more in new compound development. Post-approval trials that focus on long-term effects are shifted from pool insiders to pool outsiders. Furthermore, MPP-included compounds result in more new drug product approvals, especially of generic drugs approved for sales in developing countries. These new products can be licensed back to branded firms and thus also benefit developed countries.

Finally, I calculate the cost-effectiveness of the MPP. I use a simple structural model to estimate the benefit of the pool in comparison to its operating costs. Specifically, I use a nested

discrete choice demand model to capture the feature that compounds are more substitutable within the same drug class for cocktail treatments. I estimate two extreme cases for the supply side, competitive pricing and oligopolistic pricing, and simulate counterfactuals without the MPP. This exercise serves as a cost-benefit analysis instead of a sophisticated modeling exercise. I find that the MPP increases welfare substantially over its first seven years of establishment. Compared to no-MPP cases, there is a $0.7-1.4 billion (8.6-18.9%) increases in consumer surplus across assumptions, and producer surplus can also increase by up to $181 million (a 4.5%). The welfare gains far exceed the pool's total operating cost of $33 million during the same period.

This paper contributes to two strands of literature. First, I extend research on innovation and the economy by studying an institutional innovation designed to balance intellectual property protection and access to medicines. Prior studies find that innovation increases with market size (Acemoglu and Linn, 2004; Dubois *et al*., 2015).[5] In the global setting, *ex ante* analyses find patent enforcement can result in large welfare losses (Chaudhuri *et al*., 2006). *Ex post* studies are inconclusive, either finding little impact of drug patents on prices and sales (Duggan *et al*., 2016), or suggesting that patented drugs have higher prices and sales conditional on launch (Kyle and Qian, 2017). However, policies have limited impact to sustainably scale up drug diffusion and innovation for diseases primarily affecting low-income countries. The welfare effects of drug cocktails are ambiguous in merger simulations (Song *et al*., 2017), one of the inter-firm strategies closest to forming a patent pool. This paper provides the first evaluation of whether a novel institution can effectively balance diffusion and innovation.

Second, this paper contributes to the patent pool literature as the first empirical analysis of a biomedical patent pool. Theory papers emphasize the importance of pooling complements (Cournot, 1838; Shapiro, 2001; Lerner and Tirole, 2004) and discuss the complications for patent pools with both complementary and substitutable patents (Quint, 2014; Lerner and Tirole, 2015; Rey and Tirole, 2019). Many theoretical predictions are difficult to test empirically, especially when measuring the degree of substitutability by *ex post* prices or litigation, which can be endogenous to the pool. To overcome this difficulty, I use drug classification as an *ex ante* measure of substitutability to help better understand the pool design. In addition, most empirical studies on patent pools are either historical (Lampe and Moser, 2013, 2015) or on modern

[5] The impacts of patents on innovation are ambiguous in theoretical predictions (Green and Scotchmer, 1995; Bessen, 2004) and mixed in empirical analyses (Williams, 2013; Sampat and Williams, 2019).

software pools (Lerner *et al*., 2007; Bekkers *et al*., 2017) that both face challenges in data and measurement that limits its implication for other sectors.[6] I overcome these hurdles by utilizing the transparency of the MPP and rich institutional details from life sciences.

In addition, the experiences from the MPP provide valuable resources amid the current Covid-19 pandemic. Substantial concerns arise on the distribution of Covid-19 treatments and vaccines to developing countries that do not have local drug production capacity nor established markets. The ten-year experiences in licensing for drugs on infectious diseases makes the MPP a natural key implementing partner of the C-TAP, although it is early to conclude whether such a new institution will be effective for the current or future pandemics. The broad use of cocktail treatments in HIV, TB, hepatitis C, cancers, and trials of antibodies cocktails for Covid-19 all suggest value in building institutions that share features with the MPP.[7] While a patent pool cannot solve all the challenges in drug diffusion and innovation and cannot be applied to all contexts, my study on the MPP provides early insights on a new option to tackle such problems.

The paper proceeds as follows. Section 2 lays out background and the conceptual framework. Section 3 describes the data. Sections 4 and 5 present empirical strategies and results for diffusion and innovation analyses, respectively. Section 6 estimates a static structural model of demand and supply. Section 7 discusses and concludes.

2. Background and Conceptual Framework

2.1 HIV and Drug Cocktails

As one of the leading infectious diseases in history, AIDS/HIV has killed more than 35 million people and infected over 70 million people globally since 1980s. Today, AIDS remains a leading global cause of death, with almost two-thirds of the people living with HIV residing in Africa. Once a person is infected, HIV cannot be eliminated and can progress to AIDS that destroys the immune system and makes the patient vulnerable to opportunistic infections—a set of over 20 illnesses. AIDS remained a fatal disease and a leading cause of death until the mid-1990s when highly active antiretroviral therapy (HAART) was discovered. Death rates dropped

[6] The MPP is closer to traditional patent pools in history (i.e., with a small number of patent owners, not much ambiguity of who holds patent rights), compared to modern software patent pools.
[7] A discussion on antibodies cocktails for Covid-19: https://www.nature.com/articles/s41577-020-0365-7.

nearly 85% within a few years. Left untreated, AIDS patients survive three years on average, and life expectancy drops to one year if an opportunistic infection strikes.

Despite the lack of a cure, daily HAART can turn HIV from a fatal to a chronic disease. The HAART typically uses a bundle of antiretrovirals from multiple drug classes based on the mechanisms of action that target HIV at different stages of its life cycle. A patient who cannot maintain medication adherence and develops resistance to a drug will be resistant to all drugs within the same class, and a patient may switch to a different regimen once a side effect becomes intolerable. In sum, HIV compounds are complements due to bundling and substitutes due to side effect-induced switching. Therefore, both new single-pill cocktails and new compounds can improve current treatment. The cocktail feature and implications also apply to treatment for many other infectious diseases and certain cancers.

2.2 Patent Pools and the Medicines Patent Pool (MPP)

There is no universal design for patent pools. First used in 1856 to reduce litigations in the sewing machine industry, a typical patent pool is an institution in which patent holders share rights for joint licensing with members or firms outside of the pool. The specific licensing rules are case-specific. Patent pools were seen as exempt from regulatory scrutiny in the early twentieth century but almost disappeared after a 1945 U.S. Supreme Court decision on cartel behavior.[8] A patent pool expires when all pooled patents expire if the pool is not dissolved by the courts. Although not historically used in the biomedical sector, the prevalence and lack of cures for many infectious diseases and extensive patents associated with cocktail treatments provide a testing ground for the MPP to reduce intellectual property (IP) issues in global health.

The MPP aims to reduce coordination failure in the global medical supply chain, to spur generic licensing of patented drugs for sales in developing markets, and to avoid infringement or compulsory licensing.[9] The MPP negotiates with patent holders (branded firms) for drug licenses that enable generic firms to develop new treatments, including fixed-dose cocktails and pediatric

[8] *Hartford-Empire Co. v. United States*, 323 U.S. 386 (1945); a case in the glass container industry.
[9] With compulsory licensing, a government allows producing a patented product without the consent of the patent owner. The MPP has gained support from the WHO, the World Intellectual Property Organization (WIPO), and the World Trade Organization (WTO).

formulations (Figure 2).[10] Any improvements in production or formulation by licensees can be non-exclusively granted back to the original patent holders. Generic firms can license all territory patents on the set of drugs they needed from the pool. Royalty rates are typically set at no more than 5% of revenue.[11] The MPP receives quarterly drug development updates from licensees and encourages competition among generic firms can bring down prices and scale up access.

By the end of 2017, the MPP provided eligible licensing for 10 compounds covering four of the six HIV drug classes, and four out of the nine branded HIV drug providers had joined the MPP.[12] Figure 3 depicts the MPP sales territories; Appendix E reports a detailed summary of MPP license terms. Generic drug industries are heterogeneous across developing countries, with major generic firms based in India, China, Brazil, and South Africa; many sub-Saharan African countries lack local production and rely on imports. To assure branded firms that the intention of the MPP is to increase generic drug access in resource-limited countries, MPP licenses cannot be used for drug sales in high-income countries.

2.3 Conceptual Framework: Incentives to Participate Across Firms

Below, I discuss how three types of firms with different incentives interact with the MPP: generic firms, branded firms in the pool, and firms outside the pool. Generic firms can utilize the MPP to overcome IP-related barriers (e.g., patents and know-hows).[13] High royalties of patented compounds may deter generic firms from licensing and thus either exit the market or infringe patents and face costly litigations. If a generic firm has two compounds but needs a third, patent-protected compound to develop a new single-pill cocktail, this development can be held-up by the branded firm. In addition, downstream firms may not be willing to negotiate with several branded firms to license many patents on multiple new compounds for sales in different countries. The process of negotiating royalties can be costly for both branded and generic firms.

[10] The negotiation period can range from a few months to a few years. For instance, the MPP approached both Gilead and Janssen in 2010. Gilead joined the pool in 2011 and gradually licensed all of its HIV drugs, including two compounds that were not yet approved. In contrast, Janssen remained outside the MPP and agreed in 2015 to not enforce patent rights for the pediatric formulation of a drug it owns.
[11] Five percent implicit cap of MPP royalty rates is relatively low compared to the average licensing price (five to eight percent) in the U.S. (Author's calculation based on the drug licensing database BioSciDB).
[12] As of early 2019, nine patent holders have pooled thousands of patents on 17 drugs. I exclude from my analysis those that are not for HIV, pediatric-only licenses, and non-sue agreements.
[13] Although the discussion is mainly on patents, useful know-hows and data are also included in most licenses. Even for firms that try to sell in countries without issued patents, there can still be patents filed but pending grants. Licensing is always a safe option in the absence of complete information.

A generic firm that pays multiple royalties may use its downstream market power in the absence of multiple generic competitors. The MPP makes licensing easier, can reduce royalty rates, and avoid patent litigations.

At the same time, branded firms in the MPP can benefit. Besides easing the licensing and royalty negotiation process, branded firms can use the pool to monitor licensee compliance and have an option to license back patentable improvements developed by the licensees.[14] Many branded firms are proactive in advancing drug access in developing countries, but it is difficult to set up sales networks in those countries. In fact, branded firms can gain more profit from under-developed markets by generic licensing instead of selling at a loss.[15] As a result, branded firms may increase R&D in technically feasible trials that adapt to the needs of the emerging market. However, branded firms may charge a lower royalty rate from an individual firm and could lose out from IP sharing without prior evidence on MPP license compliances. A pool with price caps on royalty rates can be pro-competitive even with substitutable technologies, but how firms would behave is ambiguous in theory and requires more empirical work (Rey and Tirole, 2019).

In addition, a patent pool can generate spillover effects to upstream, research-oriented firms outside the pool (e.g., universities, public institutions). Employees at the MPP regularly present in medical conferences to disseminate information and communicate with scientists to encourage diffusion-oriented innovation. Inclusion in the MPP can indicate firms' openness to IP diffusion, and thus lower the litigation risks to research-oriented firms if a result enters the for-profit domain (Williams, 2013). This situation is similar to a patent commons (i.e., a pool with zero royalties) in open source software, where opening up IP can increase follow-on R&D and firm entry (Wen *et al.*, 2015). Often times, follow-on innovation by firms outside the pool can complement branded firms' R&D by discovering new or better use of approved drugs and by providing post-market surveillance. However, whether an access-oriented pool can effectively engage with the research community is an open empirical question.

[14] Grant back provision means the licensor has a right to use patentable technology made by the licensee as a result of the initial license, possible through either an agreement or reverse licensing.
[15] Gilead intended to license to the MPP the blockbuster hepatitis C drug—sofosbuvir. But the MPP was not allowed to cover hepatitis C then due to the initial company mandate. Gilead has to set up an access program to facilitate generic licensing of sofosbuvir in developing countries. [interview with the MPP] Harvard Business School cases (# 9-510-029 and #9-515-025) elaborate on Gilead's access programs.

3. Data

3.1 Data on HIV Drugs and MPP Licensing Contracts

I first collect data on all HIV drugs approved by the U.S. Food and Drug Administration (FDA), including both standalone compounds and multi-compound drug cocktails.[16] I obtain the data from the FDA and AIDS*info*.gov, which is a U.S. government agency providing information on HIV/AIDS. I convert branded names to generic names to standardize the coding, because the same drug can have different branded trade names in different countries. I then collect details about the MPP from its official website and the licensing contracts. The timing of a compound-country being included in the MPP is documented in the original contract and amendments.

Table 1 displays key information on all HIV compounds approved by 2018. There are six drug classes for HIV therapy, including 30 distinct compounds owned by nine branded entities from 11 firms. Among them, the market leaders are Gilead Science and ViiV Healthcare (i.e., a joint venture of GlaxoSmithKline, Pfizer, and Shionogi). I report the FDA approval dates for each compound and MPP addition dates for associated compounds by the end of 2018.

3.2 Drug Diffusion Data: Public Procurements, Patents, and Country-Year Controls

I use HIV drug purchase records from the Global Fund's Price and Quality Reporting, a large-scale public dataset that records procurement transactions made by Global Fund-supported programs. The non-profit Global Fund is the world's largest financier of health service programs for AIDS, tuberculosis, and malaria. Specifically, the Global Fund finances about 40 percent of all HIV drug purchases for low- and middle-income countries (LMIC).[17] The implementation relies on within-country partners such as ministries of health and country-specific committees, who report results to the Global Fund for monitoring purposes. My sample includes 29 HIV drugs involving 18 compounds purchased for 103 developing countries during 2007–2017. The raw data report the transaction date, the quantity of drugs purchased in various strengths and dosage forms, prices, selling firm, and destination country. I aggregate the raw data from purchasing records to create a country-drug-year level unbalanced panel dataset.

[16] All existing HIV drugs are approved in the most lucrative U.S. market. Similarly, all clinical trials on new drug development (for U.S. drug approval or academic publications) must be registered in the U.S.
[17] Source: Global Fund publication, 2016, available at https://tinyurl.com/y4dgwy3w.

To measure the diffusion of generic HIV drugs, I calculate the proportion of drug purchases for each given drug-country-year that is generic. Higher generic share is a sufficient but not necessary condition for lower prices, as the latter can be achieved by non-market strategies such as price ceiling and branded donations. The measure of generic share is also the most suitable normalized supply-side measure for practitioners and given the data availability.[18] Specifically, I divide the number of purchases made from generic firms by the total number of purchases for a drug within a country-year. I then convert each drug-purchase into a standardized quantity in units of per patient-day, and I calculate the percentage of generic drug quantity at the drug-country-year level.[19] I calculate the number of distinct drug products—as a drug-strength-dosage form-firm combination—at the drug-country-year level as a proxy measure of within-drug market competitiveness. During my sample period, the average shares of generic purchases and generic quantities are 84.3% and 85.6%, respectively (Table 2 Panel A).

I obtain HIV drug-country-specific international patent data from two sources. First, I use data from the MPP's own patent database, MedsPaL, which was created in collaboration with regional patent offices and provides the patent status (e.g., expiration date by country) of selected drugs. Second, I acquire data on all available international patents on HIV drugs from the Drug Patent Watch database, following Galasso and Schankerman (2014). A drug is covered by effective patents if there are any active patents for that drug in the country-year.[20]

I collect country-year level control variables from two sources. First, I use population and income (GDP per capita) provided by the World Bank. I also use the World Bank Worldwide Governance Indicators, which are six continuous measures of voice and accountability, political stability and absence of violence, government effectiveness, regulatory quality, rule of law, and control of corruption. Second, I obtain HIV prevalence and age-adjusted death rates from Global Burden of Disease Study Life Tables provided by the Institute for Health Metrics and Evaluation and curated by Our World in Data from Oxford University.

---

[18] Data was last accessed in 8/2018. The right truncation makes quantity outcomes inappropriate; prices are inconsistently recorded regarding whether to include shipping costs. The conversion of different strength-dosage forms to a per-unit price makes the interpretation difficult. Thus, I use U.S. adult dosing in the conversion to calculate prices only for a robustness check. Appendix A reports more details.

[19] The U.S. standard adult daily dosing information is from FDA labeling and AIDS*info* (Table D2). In the absence of dosing data for each country, this conversion provides a proxy. I use both the raw share of generics and the quantity-adjusted share to show that my results are not driven by idiosyncratic factors.

[20] Due to data availability reasons, I cannot distinguish which type of patents are in effect for each drug in each of the 103 countries. My empirical results suggest that this control does not affect my main results.

3.3 Drug Innovation Data: Clinical Trials, Drug Approvals, and Controls

I measure R&D inputs using clinical trials at the compound-year level from 2000–2017. I obtain clinical trials data from ClinicalTrials.gov, the U.S. registry of global trials and a most widely used source. The registry was first released in 2000 and was maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH).[21] I then obtain identifiers provided by AIDS*info* of trials related to each FDA-approved HIV drug and pre-approval investigational drug. AIDS*info,* another NLM service, offers access to the latest federally approved HIV/AIDS medical information. I convert all branded drug names to their generic names to unify the coding. Based on Table 2 Panel B, about 10 new trials involving a HIV compound are registered in a year, among which 4.4 trials are engaged by branded firms inside the MPP—2.4 trials in-house and two collaborated with firms outside the pool. About 21 firms are engaged in these trials each compound-year, with a similar distribution pattern.

I measure R&D outputs using HIV drug product approvals (branded and generic) during 2005–2018 by FDA and WHO, the two largest agencies whose approvals can expediate related registration in many developing countries. The FDA approves HIV drugs via either the regular channel or the international program. I extract all regularly-approved HIV drug products from Drugs@FDA; I obtain international program approvals via the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).[22] The two channels maintain the same safety, efficacy, and quality standards; the PEPFAR provides expedited reviews of generic drugs. The WHO pre-qualification program is the other main mechanism through which firms can fast register an approved, quality-assured drug in many low-income countries. There are 0.7 approval per drug-year and 2.3 approvals per compound-year (Table 2 Panel C), among which most approvals are for cocktails.

I obtain U.S. patent data from DrugBank, which is an online drug database widely used for peer-reviewed research. The U.S. patent status is closely tied with a drug's owner perceived value, given that U.S. is the largest drug market. The data provider obtains compound-specific

[21] Before 2000, the registry collected experimental drug trials on "serious or life-threatening diseases" (including HIV/AIDS). Now it includes all interventions: https://clinicaltrials.gov/ct2/about-site/history.
[22] Source: https://www.fda.gov/InternationalPrograms/PEPFAR/ucm119231.htm. PEPFAR began in 2004 and is for non-US marketed drugs. I use data from 2005–2018, after the establishment of the FDA's new initiative to expedite AIDS drug reviews in 2004 and the end of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement's grace period for Indian generic firms in 2005.

patent records from the FDA's Orange Book and further undertakes a manual curation process. I record the U.S. patent status based on the effective patent period for each compound (i.e., before the last granted patent expires), and I then assign drug-year level patent status accordingly.

4. Patent Pool and Global Diffusion of HIV Drugs

4.1 Empirical Strategy

To estimate the causal impact of the MPP on generic drug diffusion, I first define a drug "as it is"—either a standalone compound or a fixed-dose single-pill drug cocktail. Pool inclusion timing is coded based on compound-level inclusion into the pool, because a compound is the lowest-level unit for standalone and cocktail drugs alike. I exploit variation in the timing of drug-country additions to the pool and estimate the difference-in-differences model as follows.

$$y_{dct} = \delta_{dc} + \delta_t + \boldsymbol{\beta} MPP_{dct} + \tilde{\gamma}\tilde{X}_{ct} + \eta X_{dct} + \varepsilon_{dct} \qquad (1)$$

Here, y_{dct} is an outcome variable aggregated to the drug-country-year level, including the share of generic transactions of a drug, the quantity-adjusted generic shares, and the number of distinct products purchased for a drug in a country-year. MPP_{dct} is an indicator for whether a drug d has any compound included in the MPP in country c in year t. I also examine another MPP_{dct} measure using the share of MPP compounds in a drug for a country-year ct. The variable X_{dct} controls whether any effective patents on drug d exist in country c for a given year t.

Each regression contains fixed effects for drug-country pairs (δ_{dc}) and year (δ_t) to account for differences between drug-countries and years, respectively. The drug-country fixed effects capture differences in unobserved factors that correlate with the generic share of a drug in a country that are not recorded in observable data, such as response rate, resistance rate, and expected profit for each drug in each country. $\tilde{X}_{ct}$ contains a set of observed country-year level control variables, including institutional factors, HIV prevalence and death rates, log population, and GDP per capita.[23] Standard errors are two-way clustered at country and drug levels to allow for arbitrary autocorrelation within a country and a drug (Cameron *et al*., 2011).[24]

[23] The institutional factors are the six worldwide governance indicators described in the data section. I also use country-year fixed effects instead of observable controls as a specification test in section 4.3.
[24] Results are robust to alternative clustering methods at the country level or country-drug level.

There are two identifying assumptions: common trends and lack of common shocks. I test the former using an event study model, and I support the latter by elaborating on why the data generating process is driven by factors arguably orthogonal to the outcomes of interest.

I test the common trends assumption using an event study framework. This framework helps to assess the validity of the assumption that the trend in the control group that is outside the MPP (drug-country-years outside the MPP) is a valid counterfactual for the treated group (drug-country-years in the MPP). Differential trends of outcome variables between the treatment and control groups in the pre-treatment period would suggest endogeneity in drug-country inclusion or, potentially, correlation with other shocks. In addition, the event study measures the dynamic responses of outcomes to policies—whether the effects fade or build over time. The MPP impacts could gradually build up (because diffusion takes time) and diminish over time since the dependent variable is bounded by 100%. I estimate event study models as follows:

$$y_{dct} = \delta_{dc} + \delta_t + \sum_{j \in T} \boldsymbol{\beta_j} 1\begin{Bmatrix} MPP\ event \\ time_j \end{Bmatrix}_{dct} + \tilde{\gamma}\tilde{X}_{ct} + \eta X_{dct} + \varepsilon_{dct}. \qquad (2)$$

Here, β_j represents the difference between treatment and control units j years relative to when a drug-country was included in the MPP. For drug cocktails that have multiple compounds, I define the event time as years relative to when any compound was first included in the pool.

Next, I describe the data generating process to support the lack of common shocks assumption. First, which patented drugs are included in the pool results from perceived value and negotiation outcomes, and below I present evidence that drugs inside and outside the pool appear to be similar in quality and in initial approval year. In a learning-by-doing process, the MPP aims to target candidate drugs that are of high clinical and market values, but targeted drugs are not always added; firms can also voluntarily contribute other drugs to the pool. In principle, the MPP follows the WHO *Essential Medicine List* on marketed drugs that have demonstrated sufficient effectiveness.[25] In practice, the MPP also considers pre-approval drugs and aims to further speed up generic access. By the end of my sample period, patented drugs inside and outside the MPP are similar in terms of sales and approval time. Specifically, six HIV compounds are listed in the top 100 drugs by global sales in 2012, and three of the six HIV compounds are in the MPP (Table D3); the U.S. approval dates are similar for drugs in and outside the pool (Table 1).

[25] The WHO list includes all approved HIV drugs except three pre-2000 withdrawals. They are all of high market values. The MPP broadly target any HIV drugs in early years to demonstrate the business model.

Second, drug-specific MPP sales territories typically vary by the branded firm and always include sub-Saharan Africa and Djibouti; additional inclusion of countries roughly depends on income groups, prior voluntary licensing status, and exercises in public relations.[26] When initially adding a drug, branded firms typically include over 90 countries in the MPP territory, and rarely add more countries later. Thus, territory decisions are not likely driven by temporary country-specific demand shocks that can induce higher generic supply without the pool. In many cases, firms had already issued bilateral generic licensing and voluntary free licensing before the MPP was established, and countries in pre-existing licenses are typically also included in the initial MPP territory (Juneja *et al.*, 2017). This situation can bias my estimates towards zero. In addition, the control variables account for the country-year level differences over time in HIV death rates, HIV prevalence, population, income, and institutional factors that are related to the demand and distribution for the drug. The outcomes in percentages further account for supply-side factors, because overall demand increases will affect both generic and branded drugs.

Third, the timing of when a drug-country is eligible for MPP licensing is partly affected by negotiation time and scientific discovery. The negotiation time is affected by firms' attitude and administrative efficiency. For example, Gilead Sciences used generic licensing years before the MPP was established and has gradually put all of their HIV drugs into the pool, including two investigational drugs in late-stage clinical trials. In contrast, Janssen was approached by the MPP early on but has never officially joined the MPP.[27] While I cannot perfectly determine what drives entry and when it happens, it is unrelated to factors that are most likely to cause a bias. To show this, I regress the MPP indicator on observables related to demand, demographics, income, institutional factors, and fixed effects at drug-country and year levels. As shown in Table B1, none of the key observables are significant predictors of the timing, and the goodness of fit barely increases when adding observables to the regression.[28] Empirical tests and institutional knowledge indicate that the timing is driven by factors orthogonal to my outcomes of interest.

[26] Based on my discussions with MPP employees in Switzerland. A firm can follow the World Bank "low-income" definition or use its own cut-off value. A firm once split an island country name into two to boast public relations. Another firm once left a sub-Saharan African country outside the MPP territory unintentionally and added it once reminded. These factors are orthogonal to changes in my outcomes.
[27] Janssen agreed on a covenant not to sue without further commitment in technology transfer and formal licensing. Janssen is unsure whether the MPP model would work [interview with Frank Daelemans].
[28] Similar, Figure B1 depicts trends of HIV death rates and prevalence; neither show spikes during my sample period. Civil society advocacy and compulsory licensing threats for the inclusion of additional countries into the MPP are typically outside my sample periods and affecting the comparison group.

Furthermore, the smallest treatment unit is at the compound level, while each purchase is at the drug level: as a standalone compound or a drug cocktail. As a robustness check for measurement error, I estimate a compound-country-year level model where drug cocktails are converted into compounds. This model is estimated using equation (1) but on compound-country-year (y_{act}) aggregated data, with fixed effects at the compound-country and year levels.

4.2 Does the MPP Foster Diffusion of Affordable Generic Drugs?

The main results from the drug-country-year analysis indicate that the MPP increases generic shares (Table 3). Column (1) controls for fixed effects at drug-country and year levels; columns (2)–(3) adds controls at country-year and drug-country-year levels, respectively.[29] Coefficient estimates are stable across columns. The results indicate that adding a drug-country in the MPP increases the share of generic purchases of this drug in the country by about seven percentage points (Panel A) – a substantial increase given the already high generic coverage in developing countries (84% on average during my sample period). Columns (4)–(6) report results using the share of generic quantities purchased as outcomes. Estimates are similar in magnitude and precision to those in columns (1)–(3) and are stable across specifications. However, there is no statistically significant effect on the number of drug products purchased (columns 7–9). This result is consistent with the idea that countries may still purchase a subset of drug products when there are more options available and benefit from competition-induced price reductions.

The results are robust to using alternative measures of the treatment variable: the share of MPP compounds over total number of compounds for a drug in a country-year (Table 3 Panel B). The results are qualitatively similar to the indicator measure and slightly larger in magnitude. I mainly focus on the indicator measure below, because it captures the most salient changes at the extensive margin and favors simplicity in explanation.

The associated event studies support the main results discussed above (Figure 4). No pre-trends exist that violate the difference-in-differences assumptions. The lack of pre-trends is particularly clear for the outcomes of percentages of generic orders and generic quantities. The post-period trends for these outcomes rise from zero, consistent with the estimate of the significant positive average treatment effects, despite the lack of power to precisely estimate the

[29] Because comprehensive global patent data are hard to obtain (Lerner & Seru, 2017), I demonstrate the robustness of my results across specifications with and without the drug-country-year patent control.

impact for each post-period. The effects gradually build after a drug enters the MPP and stabilize over time, consistent with time varying treatment effects that take time to establish and then bounded by 100%. The event study for product variety demonstrates a similar pattern.

The compound-country-year analysis further supports my main results with more precise estimates, after converting drug cocktails into compounds (Table 3 Panel C). In the full sample, adding a compound in the pool increases the percentages of generic drug orders and generic drug quantities ordered by about 10% across specifications; all estimates are statistically significant at the 1% level. The estimates from the product variety regressions are larger in magnitude than those in the drug-country-year results, but similarly are not statistically significantly different from zero at conventional levels. Overall, there are no pre-trends from the event studies for the outcomes of interest (Figure 4 panel b). The post-period increases in the share of generic drug purchases and quantities are clear and significant.

4.3 Alternative Specification, Robustness Checks, Sensitivity Tests, and Heterogeneity

I test an alternative specification that includes a full set of country-year level fixed effects (Table B2). Country-year level observable controls are dropped in this specification due to collinearity. The country-year level fixed effects account for the differences between each country-year to capture unobserved demand or institutional shocks that occurred in a country-year not captured by the feasible observable controls. For example, changing legislative culture towards drugs, the overall likelihood of compulsory licensing, and activist activities – old country-specific channels that widely existed before the MPP's establishment but still have limited impact. All of the coefficient estimates are very similar in magnitude and statistical significance to those in my preferred main specification and thus strengthen my results.[30]

To demonstrate robustness regarding country territories included in the control group, I report a set of tests using alternative definitions. Some countries are more experienced in bringing generic drugs via traditional channels like patent invalidation and challenges that are independent and prior to the MPP's establishment, while others (e.g., sub-Saharan Africa) are waived from patent enforcement but lack local production capacity and rely on international

[30] I also test a specification that further includes a full set of drug-year fixed effects. The MPP coefficients are not statistically significant and are smaller in magnitudes. This lack of power with three set fixed effects is anticipated as MPP compounds enter 47 to 92 countries at the same time in my sample (e.g., see territory analyses in Table B3) and drug-year fixed effects would absorb treatment effects.

trade and other firms' incentives to sale in their territory. Although these concerns are addressed by the previous test, a subsample analysis further supports that the pool makes an impact even in areas with the most lenient access policies. Table B3 repeats the analyses in MPP-common territories for all drugs (47 countries: sub-Saharan Africa and Djibouti) and in the territories ever covered by any MPP drugs (92 countries). The results are similar to the main analysis.

Similar argument applies to a test using different drug samples and strengthen the main results (Table B4). Column (1) focuses on the first MPP addition of compounds and drugs in the same classes as these compounds. The first MPP addition is more likely to be unanticipated as this process is unprecedented. Column (2) drops drugs in the drug class without any MPP inclusion by the end of the sample period. Column (3) drops drugs with any of the four toxic compounds that are no longer recommended in the U.S., although they are still widely used in developing countries. Column (4) drops drugs approved before 1996, the year the oldest MPP compound was approved in the U.S. Column (5) keeps only drugs developed by branded firms inside the MPP. My results are robust in all cases.

I now show that the results in subsamples vary by patent status (Table B5). As discussed before, the MPP's impact is expected to be stronger in countries in which a drug is patented because a firm considering launching a generic drug in that country needs to secure a license (or licenses) or risk a lawsuit. Countries without patents can also benefit from the MPP through spillover effects, such as enhanced international trade. The results match the prediction: across specifications and measures, the share of generic drug orders increases more in countries where a drug placed in the MPP was patented. The MPP coefficient estimates are similar when using percentage of generic drug quantities purchased as the outcome variable. Similar to the baseline case, the impact of MPP inclusion on within-drug product varieties is statistically insignificant.

The above analyses all support the hypothesis that the MPP works as a novel institution to increase generic utilization. Here, I provide additional analyses using calculated fuzzy price and quantities measures (Table B6).[31] Overall price per patient-year reduces by about $87, mainly from a substantial reduction in generic prices, and quantities react correspondingly. A more solid analyses on prices and quantities would require much nuanced data and consider more factors such as market structure and demand in the presence of substitutes.

[31] In the main analysis, I use generic shares as main outcomes for reasons mentioned in section 3.2.

In sum, I find that the MPP increases the percentage of generic HIV drug purchases in developing countries. The result is robust to alternative specifications, measures, and subsamples consisting of different comparison groups. However, an increase in generic diffusion can occur at the cost of innovation, and it is *ex ante* unclear how firms may react to the MPP in R&D.

5. Patent Pool and Innovation in HIV Drugs

5.1 Drug Innovation Process: Clinical Trials and Drug Approvals

I use all trials initiated in 2000–2017 that include HIV drug compounds to measure R&D inputs. Before a new drug is marketed by a branded firm, it typically undergoes three phases of trials. Phase I usually tests drug safety in multiple doses on healthy volunteers. Phase II tests drugs on patients with the targeted disease to assess efficacy and side effects. Phase III evaluates a drug's efficacy and safety on a large scale *versus* a control therapy. For HIV/AIDS, trials often test a specific cocktail consisting of multiple compounds. Phase IV studies involve post-market surveillance to monitor drug use and determine a drug's long-term effects. Follow-on trials of drugs that have already been approved for the same or a different disease can skip phases I and II.[32] After a Phase III trial, a branded firm can submit a new drug application to the FDA, which decides whether to approve the drug and at what strength and dosage forms.[33] Generic drugs typically enter the market after the expiration of patents and market exclusivity, with a few exceptions.[34] Generic firms are not required to conduct trials for drug approvals as long as they provide sufficient evidence of the bioequivalence of their product to the reference drug.

5.2 R&D Reactions in Clinical Trials: Empirical Strategy & Results

5.2.1 Empirical Strategy

The identification argument is similar to that described in the diffusion analysis (section 4.1). As a diffusion-oriented pool, the MPP is not designed to change R&D except encouraging

[32] An indication is a symptom or condition that requires medical treatment. With toxic drugs, HIV trials often replace healthy volunteers with patients, combine three phases into two, and use surrogate endpoints (e.g., viral load) instead of mortality. A trial can take several months to years. About 10% of HIV trials do not record phases, when the main purposes are not applicable to phases or for behavioral trials.
[33] Drugs for life-threatening conditions (e.g., HIV/AIDS) are eligible for fast review to be approved within six months (the exact time taken is not always publicly available). The FDA posted a set of first approval time for HIV drugs: https://www.fda.gov/forpatients/illness/hivaids/treatment/ucm118915.htm.
[34] Generic firms can submit drug applications before the reference drug's patent expires through the FDA's tentative approval or international program, via a patent challenge, or via WHO pre-qualification.

incremental R&D to make better use of existing compounds, e.g., creating new formulation and single-pill cocktails that suit the market in LMIC. The timing of new compound additions is uncertain at the aggregate level. I discuss potential concerns and why this entry process is orthogonal to my outcomes of interest. I then examine R&D behaviors across firm types by MPP-affiliation. I mainly focus on reactions from firms outside the MPP and do not claim causality for MPP insiders, as I am not able to disentangle planned and reactive behaviors.

I estimate a difference-in-differences model that exploits when a compound is added to the MPP to examine changes in R&D activities involving that compound over time:[35]

$$y_{at} = \delta_a + \delta_t + \beta MPP_{at} + \gamma X_{at} + \varepsilon_{at} \,. \qquad (3)$$

Here, y_{at} is an outcome at the compound-year (at) level, including the number of new trials, the number of participating firms, and the previous two outcomes stratified by MPP-affiliation, phase, and funding source. MPP_{at} indicates whether a compound at time t was in the MPP. Each regression contains fixed effects for compound (δ_a) and year (δ_t). X_{at} controls for observed differences in compound-year levels, such as whether compound a was FDA-approved and whether the compound is U.S.-patented in year t. I cluster standard errors at the compound level.

The two identifying assumptions are similar to those in the diffusion analysis, common trends and lack of common shocks, with two minor differences. First, the unit of analysis is at the compound-level to match innovation measures. Second, factors affecting innovation likely differ from those affecting diffusion. To empirically justify the first identifying assumption regarding common trends, I estimate corresponding event studies using the following equation:

$$y_{at} = \delta_a + \delta_t + \sum_{j \in T} \beta_j \, 1\left\{ \begin{matrix} MPP\ event \\ time_j \end{matrix} \right\}_{at} + \gamma X_{at} + \varepsilon_{at} \,. \qquad (4)$$

Here, β_j represents the difference between treatment and control units j years relative to when a compound was included in the MPP. I specify the event window to be six years before and four years after the event; sample sizes are small outside of this range.

The process of innovation and the institution design of the MPP are inconsistent with the existence of common shocks that would bias my results. One concern is that the MPP may target and obtain compounds that are likely to generate substantial follow-on innovation. In practice,

[35] Following trial identifiers provided by AIDS*info*, trials covering multiple compounds are counted once for each compound. This logic is consistent with how Finkelstein (2004) defines disease-year trials.

the MPP is an institution with fewer than 20 employees, it mainly focuses on drug diffusion rather than innovation, and is not likely to have superior data on the value of a compound than HIV scientists and private firms. The clinical value of a compound is typically unclear until phase III completion, and the market value is further validated by FDA approval and U.S. patents. Most compounds in the pool are approved and have been marketed for years.[36] Overall, compounds in and out of the pool are roughly of similar quality as described in section 4.1.

Another concern is that firms may be making decisions regarding when to enter the pool compound-by-compound in response to expected future value. However, it is theoretically ambiguous how a non-profit patent pool with imperfectly complementary drugs would affect R&D (Rey and Tirole, 2019).[37] Empirically, the data and my interviews contradict with branded firms making sophisticated compound-level decisions. For example, Gilead contributed six MPP compounds by the end of 2018—all the HIV compounds that Gilead owned. The first four compounds were added to the MPP in 2011 shortly after the MPP approached Gilead, and the two other compounds were added as early as possible.[38] One firm almost contributed all its drugs but did not due to a CEO change.[39] These anecdotes indicate that compound-level unobserved characteristics that make R&D more attractive for a compound do not necessarily cause a firm to become more likely to add the compound into the pool. As the first patent pool to focus on drug access to resource-limited countries with large disease burden but little profit potentials, most of the negotiations between the MPP and branded firms are diffusion-oriented.

5.2.2 Do Firms Invest More in Compounds that are in the MPP?

I find that firms respond to the inclusion of a compound in the MPP with more follow-on clinical trials (Table 4 Panel A). Column (1) indicates that the number of new trials on drugs including a given compound increases by 9.9 trials after the compound is added to the MPP, close to the mean annual trial rate for a compound during my sample period. The initial estimate

[36] The results are similar when excluding two Gilead drugs entering the MPP pre-approval.
[37] The theoretical setting is closest to section 4.2.3 and Figure 4 in Rey and Tirole (2019). The impact of a pool (with complements, price caps, and licensing outside the pool) on firm behaviors is ambiguous.
[38] Although the first four compounds were added to the MPP in the same year (as a cocktail), the approval years for them are 2001, 2003, and 2012 (for 2), respectively. The fact that Gilead contributed compounds to the MPP as early as possible (for fast diffusion) and did not distinguish compounds by age, class, and other factors reduces the concern of endogenous timing for R&D and supports the key focus on diffusion.
[39] According to the MPP administrators, the timing of inclusion for other firms is mostly affected by firm leadership and administrative efficiency. Also see discussion and anecdotes in section 4.1.

is significant at the 5% level but loses statistical significance once I add observable controls. However, the coefficient magnitude remains close to the original specification. FDA approval has a significantly positive association with follow-on trials, while U.S. patent status does not have a significant coefficient. Results in column (4) indicate that branded firms inside the MPP collectively choose to initiate 1.6 more trials with MPP-associated compounds. However, the estimate is significant only at the 10% level. Similarly, column (8) indicates that MPP outsiders collectively increase new trials that include MPP-associated compounds, significant at the 10% level. The estimates from insider-outsider partnered trials are not statistically significant.

The results are qualitatively similar when using the number of firms that participated in trials as the outcome (Table 4 Panel B). Coefficient estimates are positive but not statistically significant at the 5% level in specifications that control for observables. Dividing coefficients from Panel A by their counterparts in Panel B provides a proxy for new clinical trials initiated per participating firm. The per-firm trial rate is about 0.9, 0.4, and 0.3 among insiders, outsiders, and mixed firms, respectively. The cross-column coefficient estimates are less stable among MPP insiders than outsiders, as branded firms react strongly to FDA approvals—when drugs can be marketed; in contrast, branded firms' decisions to join the MPP are less clear and more likely experimentation to use this new business model for diffusion. Outsiders react more strongly to the MPP in total new trials, as the increased openness that the pool provides creates additional incentives for follow-on innovation given the lower costs, and the per-firm trial is smaller as the outsiders are typically smaller in size compared to insiders. Overall, the results suggest that firms, on the margin, react positively to the MPP in terms of follow-on innovation.

The event studies support the effects estimated above (Figure 5). The event study for the number of new trials has no pre-trend but a clear post-period increase in new trial initiations, especially four years after MPP entry. The next three event studies display results for the number of new trials by MPP-affiliation status. The pre-trends for MPP insiders, despite not statistically different from zero, are noisier than those for outsiders and insider-outsider mixed trials. All event studies involving MPP outsiders demonstrate a pattern of post-period trial increases with a 3-4 years' lag. The event patterns are similar for the number of firms in new trials, and the post-period reactions are smoother and clearer in these cases, thus indicating that increases in post-MPP trials from MPP outsiders are primarily driven by more firm participation.

5.2.3 Heterogenous Effects on R&D Reallocation and by Funding Status

Across phases, firms respond to the MPP by starting more late-stage clinical trials, as reported in Table 5. One would not expect MPP addition to substantially affect phase I trials as these compounds are already tested for safety (except for new doses). Firms are more likely to invest more in phase III trials to create new or better drugs based on existing compounds. Panels A–D report results across phases I–IV. Results are not statistically significant for trials in phases I and II. The increases in new trials and firm participation for phase III trials are significant at the 1% level. Event studies in Figure B2 justify the results for phase III trials except fully in-house trials by MPP insiders. Notably, MPP insiders statistically significantly reduce phase IV post-market trials by about 0.4 per compound-year, with about 0.5 fewer firms participating, at 5% and 1% levels of significance, respectively. This reduction does not affect overall new phase IV trials, as the reduction is offset by firms outside the pool doing more phase IV trials (in-house or jointly with pool insiders). Event studies support this point.

Firms' responses to the MPP also vary by funding source, where firms with public-sector funding react more strongly with follow-on clinical trials (Table B7). Most firms outside the MPP are academic or public institutions. The increases are particularly strong among trials that are not fully funded by industry and in phase III that involve multiple compounds. In contrast, privately funded trials reallocated phase IV trials to pre-market development trials; this reduction is more than offset by increases in publicly funded phase IV trials. There are no pre-trends in the event studies for all cases except a pre-period shift in insider phase III trials (Figure B4).

These results extend prior findings in the literature. First, institutional innovation can generate results similar to those of policies, like those described in Finkelstein (2004)—policies that spur diffusion can spur technically feasible, follow-on clinical trials by 2.5-fold. My findings suggest that a public-private partnership institution can generate about 40% of that effect (1-fold). Second, my results complement Williams (2013) and Sampat and Williams (2019):[40] for small molecule drugs in LMIC, increased openness from privately owned IP (patents and know-how) can foster follow-on innovation from outsiders, particularly in non-private sectors.

5.2.4 Do Firms Invest More in New Compound Development?

[40] For gene technology, data restriction hinders follow-on innovation (Williams, 2013), but patents do not importantly affect follow-on innovation quantitatively (Sampat and Williams, 2019).

In previous sections, I analyzed clinical trials using approved compounds by the end of 2018 because trials on new compounds that had not been approved then would not have unified names (i.e., generic names). However, it is also important to understand the interaction of compounds' addition to the pool and firms' R&D activities in developing new compounds that have not been approved but can further complement existing drugs. To account for the fact that these pre-approved compounds would not have a unified name, I aggregate HIV investigational drug trials to the drug class-year level for this analysis. First, the trend in trials on investigational HIV drugs suggests no reduction in overall incentives to explore new drugs (Figure B5). Second, Table B8 and event studies (Figure 6) confirm the hypothesis that the MPP weakly increases overall R&D activity in investigational drugs. In addition, phase-specific event studies (Figure B6) justify that MPP insiders and industry-funded trials are increasing particularly for phase III trials. This result, together with previous results, indicates that MPP insiders and industry trial funders invest more in new compounds that can further complement existing drugs.

5.3 R&D Results in New Drug Approvals

5.3.1 Innovation and Imitation: Overview and Exploratory Analysis

I next use HIV drug approvals to analyze R&D outputs. All of the HIV drug approvals that I examine are original FDA and WHO approvals of a new product at the drug-strength-dosage form-firm level. These approvals are obtained by either branded or generic firms and include tentative generic approvals that only allow for sales in developing countries. At the drug level, a drug innovation is either an original approval of a new compound or the first approval of a cocktail that bundles different compounds, whereas a drug imitation is a follow-on product from the same drug at a chemical level but at a different strength-dosage form or by a different firm. At the drug product level (i.e., drug-strength-dosage form), a product innovation is the first approval of a drug in a formulation (strength-dosage form) by the first applicant, while product imitations include follow-on approvals of the same drug product by other firms. Not all approvals are U.S.-marketable, but all of them reflect the qualification of approved products.

Although branded drug makers are leaders in the development of new compounds, generic firms develop many new cocktails and products. As reported in Table B9, of the 30 first approvals of new drugs with already-approved compounds, twenty-seven are new drug cocktails. Among these 27, thirteen new cocktails were first created by generic firms. Moreover, all of the

new cocktails first created by generic firms have bundled compounds, owned by 2.31 branded firms on average. In contrast, new branded cocktails have bundled compounds owned by 1.47 branded firms on average, either via intra-firm bundling or cross-licensing between two firms. This pattern highlights the often-underappreciated role that generic firms play in drug innovation, particularly regarding the comparative advantage in cross-firm bundling. The overall pattern is similar at the drug product level, where generic firms capture a higher share of new drug products approved when strength and dosage forms are considered.

I analyze the association between MPP status and "time to first generic" using histograms, survival, and regression analyses. I focus on the sample where a drug product is first approved generically for a given drug-strength-dose after all of its underlying compounds are approved (i.e., it is technically feasible to produce a drug generically). Figure B7 reports histograms of the "time to first generic," with and without MPP compounds, in the full sample (2005–2018) and the sample since MPP establishment (2010–2018). In both samples, the average "time to first generic" product is smaller for drugs with MPP compounds: three to four years faster than the counterparts without MPP compounds. Table B10 reports Cox proportional hazard models and linear models that regress "time-to-generic" on an MPP indicator and fixed effects at year and drug class levels. The results suggest that products with MPP compounds have higher odds for an approval (positive coefficient in Panel A) than do the alternatives, and the "time-to-generic" is shorter for a drug with MPP compounds (negative coefficient in Panel B). These analyses provide evidence that the MPP is associated with faster generic approvals.

5.3.2 Does the Patent Pool Induce More Follow-on Drug Product Approvals?

The empirical strategy is identical to that used in the analysis of clinical trials except the outcomes are now the number of new approvals at the drug and compound levels.[41]

I find that firms have obtained more follow-on drug product approvals for compounds in the pool relative to those that enter the pool later or outside the pool (Table 6), including generic approvals of new cocktails (innovation) and more generic firms gain approvals to market existing drugs with pool-covered compounds (imitation). The MPP-induced increase in new drug product approvals is about 0.5 more approvals per year in pool-associated drugs and is robust

[41] I adjust the event windows to be five years before and after the event to account for the shorter sample periods 2005–2018, in contrast to 2000–2017 in the clinical trials sample.

across specifications (Panel A columns 1-2). The increased product approvals are primarily driven by generic firms, which create both new drug cocktails and existing products at lower costs. The results are consistent with the regulatory standards that exempt generic firms from conducting new clinical trials when the underlying compounds have been previously approved. The coefficient estimates are more precise statistically when the MPP treatment is measured at the percentage level to capture changes in both the extensive and intensive margins (Panel B).

These findings are robust to a sample where drugs are de-bundled to the compound level, and the coefficient estimates become larger (Table 6 Panel C). This result is expected as now the MPP effect captures the additional follow-on drug product approvals involving a compound in either standalone or cocktail form. These results are consistent with the hypothesis that follow-on approvals with pooled compounds are often developed as drug cocktails instead of as simple imitations at the compound-level, thereby suggesting higher social values derived through increased competition among new and more completed cocktail products.[42]

Event studies support the drug approval analyses (Figure 7). In both cases, there are no pre-trends in total new approvals and those by generic firms. For follow-on approvals by branded firms, the pre-trends do not significantly differ from zero but are noisy. Comparing graphs cross-column within panel, most of the new drug or compound-level approvals are driven by follow-on product approvals by generic firms, suggesting large imitation-based investment responses from generic firms. New approvals by branded firms do not substantially change in these figures once controlling for initial approvals. Across panels, the event study responses are larger when drug cocktails are de-bundled into compounds. Overall, the responses in trial initiation and firm participation suggest that firms outside the pool are responsive to increases in the expected return to technologically feasible products once barriers to entry are reduced.

In addition, I provided a few case studies to support the R&D analysis (Appendix F). Overall, results from the innovation analysis suggest that firms react to the MPP with higher R&D inputs and outputs. The increases in R&D inputs of new clinical trial initiations and firm participation come from both pool insiders and outsiders. While pool outsiders increase trials on drugs with pooled compounds, pool insiders invest more in new compound development and

[42] I also implement a count data model using conditional negative binomial to demonstrate robustness of the results (reported in Table B11), given that the mean dependent variable is small for drug approvals.

shift post-market trials to outsiders. The increases in R&D outputs of new drug product approvals are primarily driven by generic versions of existing drugs and new formulations.

6. Welfare Analysis

Quantifying the cost-effectiveness of a patent pool is difficult, as most products are sold globally despite relatively concentrated innovation activities. In my case, the MPP separates the market into sales territories and, based on my previous results, increases diffusion and R&D, so a welfare analysis for the LMICs in my diffusion sample is likely conservative. Another typical challenge is to categorize technologies with *ex ante* measures of their substitution patterns. My setting allows measuring substitutability by drug classes. The decision of HIV drug use follows sequential choices: first, choice of a drug class, and then choice of drugs within the chosen class. The MPP would not directly enter patients' preferences towards a drug but will make it cheaper to produce. Including the MPP as a marginal cost shifter is related to my previous findings and the conceptual framework that the pool lowers licensing and royalty costs (per-unit based).

Regardless of whether a drug purchased is a standalone compound or a cocktail, the treatment requires multi-compound bundling. I observe drug purchases but not how patients use them, which limits the richness of the demand model I can estimate. Besides, my sample period (2007-2017) is not sufficient to model new drug launches, as most of them have not entered my data, resulting in conservative welfare estimations. I also abstract away from branded-generic interactions with the drug-country-year level aggregate data. Thus, my exercise is best viewed as an empirical illustration of drug cocktails in the context of a patent pool.

6.1 Demand-Side: Nested Discrete Choice Model

Patients in each country choose whether to take drugs and choose among available choices following physicians' suggestions. The choice sets of drugs vary across countries and over time. Denote D_{ct} as the set of HIV drugs available from my data source in country c at year t, and index drug by j. Each patient-physician pair in a country in a given year decides whether to take a drug in the choice set $D_{ct} = \{1,2,..,d_{ct}\}$ or use outside options – taking no drugs or from other sources outside my sample. Each drug j belongs to drug class $g(j)$ based on its mechanism of action. Specifically, each patient-physician pair i in country c at year t chooses drug j from the $D_{ct} + 1$ options to maximize the conditional indirect utility function as below:

$$u_{ijct} = \underbrace{X_{jct}\beta - \alpha p_{jct} + \xi_{jct}}_{\delta_{jct}} + \zeta_{ig(j)ct} + (1-\sigma)\varepsilon_{ijct}. \quad (5)$$

Here, δ_{jct} is the mean utility of drug j in country-year market ct. X_{jct} is a vector of observables, including the number of compounds in a drug, number of distinct products for a drug in each country-year, HIV prevalence and death rates, income, log(population), institutional factors, and fixed effects at country and year levels. p_{jct} is the average price of drug j in country-year ct. ξ_{jct} is the unobserved quality of drug j for patients in country c in year t. ε_{ijct} is an independent taste shock following the extreme value distribution, $\zeta_{ig(j)ct}$ is a group specific taste of the patient-physician pair, and $(1-\sigma)$ measures the relative weight of idiosyncratic and group preferences.

Given the nested logit functional form, the market share of each product for any set of product qualities δ_j can be calculated à la Berry (1994).[43] The estimation equation is as follows:

$$\ln(s_j) - \ln(s_0) = \sigma \ln(s_{j|g(j)}) + \underbrace{X_j\beta - \alpha p_j + \xi_j}_{\delta_j - \delta_0}, \quad (6)$$

where $s_{j|g(j)}$ is drug j's share of its nest in a given country-year market ct. I estimate the model using two-stage least square with instruments for conditional market share $\ln(s_{j|g(j)})$ and price p_j. I include three instruments: patent status, the number of distinct manufacturers for a given drug in a country-year market, and the number of distinct competing products (i.e., drug product and manufacturer combinations for other drugs in the same drug class). The latter two are "BLP instruments" following Berry *et al.* (1995).[44] Standard errors are clustered at drug-country level. Using parameters from the demand estimation, the nested logit model allows researchers to calculate expected consumer surplus in each market using equation (7) below:

$$E(CS_{ct}) = \frac{1}{\alpha}\ln\left\{\Sigma_g\left[\Sigma_{j\in g}\exp\left(\frac{\delta_j}{1-\sigma}\right)\right]^{1-\sigma}\right\}. \quad (7)$$

[43] To explore the robustness of the results to the demand model specifications, I also implemented a plain logit model. In the empirical implementation, I define the market size as 30% of the population. I test the sensitivity of the results to other market size definitions and report those results in Table B14.

[44] The BLP instruments are valid as long as the drug characteristics are exogenous. The justification is that drug characteristics are determined at the time of trials, and once approved, firms cannot change the characteristics in the short-run. The instruments are relevant, as a drug that has close competitors (drugs within the same drug class work through the same mechanism of action) is likely to be priced lower.

Here, the choices among nests (i.e., drug classes) depend only on their mean utilities $\delta_j = X_j\beta - \alpha p_j + \xi_j$, as there are no nest-specific observables entering the utility function. The total consumer surplus during my sample period can be calculated as the summation of market-size weighted expected consumer surplus values across markets. Therefore, the baseline consumer surplus with the MPP can be calculated independent of the supply-side estimation.

6.2 Supply-Side: Competitive Pricing & Bertrand-Nash Game

In the absence of the universe of data and a proper model on oligopolistic pricing with a competitive fringe and threats of compulsory licensing in over a hundred of LMICs, I model two simple and conservative cases. The first case models supply using constant marginal cost pricing as in Bertrand competition. The second uses a Bertrand-Nash game in an oligopolistic setting. In both cases, the MPP affects pricing by lowering marginal costs as the MPP lowers royalty rates in joint licensing and injunctions are also typically calculated on a per-unit basis.[45]

In the first case, I estimate a marginal cost pricing scheme to capture the feature that generic firms produce at marginal costs and generic market shares are high in LMIC. My results from previous part support competitive pricing in that generic shares are high in base level and increases with the MPP. I use *j* to denote drug-country pair and estimate the following equation.

$$p_j = mc_j = X_j\gamma + \beta MPP_j + \omega_j \qquad (8)$$

Here, MPP indicates whether a drug-country is in the MPP in a year. X_j is a vector of drug-country-year level controls including whether a drug is effectively patented in a country-year, number of drug products and competitors for a drug in a country-year, country-year level HIV prevalence and age-adjusted death rates, population, income, institutional factors, country and year fixed effects. Quantity is not included in this baseline competitive case, because firms do not face capacity constraints in a competitive market with many generic firms. Once the pricing equation is estimated, counterfactual prices can be simulated by changing the MPP indicator.

In the second case, I estimate oligopolistic pricing in a static Bertrand–Nash game with differentiated products. Firms can have market power in the short-run before reaching the long-

[45] Due to the lack of complete HIV drug sales, I cannot back out the fixed costs and separately identify additional MPP-induced cost reduction. This suggests my cost results are conservative. In common with prior work (Song *et al*., 2017), I model drug pricing as a static game without sufficiently rich data.

run competitive equilibrium. Each firm acts as either a single-product or multi-product drug firm where each drug belongs to a nest (i.e., drug class). This design captures the feature that the brand ownership of a drug does not matter as much for generic drug makers, but the "business stealing effect" comes from drugs with similar characteristics (i.e., drug class). Each country-year is a market, and a firm maximizes profit from all drugs they produce using the equation:

$$\Pi = \Sigma_j(p_j - mc_j) \times s_j(p_j) \times M. \qquad (9)$$

Here, j indexes drug j in a country-year market, and M represents the same market size measure used in the demand estimation. Note that the substitution patterns between drugs j and k are affected by their corresponding drug classes g_j and g_k. The first-order condition yields

$$\mathrm{s_j}(p_j) + \Sigma_k(p_k - mc_k) \times \frac{\partial s_k(p)}{\partial p_j} = 0. \qquad (10)$$

I define the price derivative matrix as $\Delta_{jk} = -\frac{\partial s_k}{\partial p_j}$, following Berry *et al*. (1995). Here, f_j indicates that drug j is owned by firm f. I estimate two structures. First, I estimate a single product oligopoly, where each representative firm owns one product. Second, I estimate a multi-product oligopoly with drug-level ownership, where I assign a cross-firm cocktail owner to a separate entity. Derivation of Δ_{jk} and additional results are provided in Appendix C.

$$\Delta_{jk} = \begin{cases} \alpha s_j\left(\frac{1}{1-\sigma} - \frac{\sigma}{1-\sigma}s_{j|g} - s_j\right) & ,j = k \\ -\alpha s_j\left(\frac{\sigma}{1-\sigma}s_{k|g} + s_k\right) & ,j \neq k, g_j = g_k, f_j = f_k \\ -\alpha s_j s_k & ,j \neq k, g_j \neq g_k, f_j = f_k \\ 0 & ,o.w.(i.e., f_j \neq f_k) \end{cases} \qquad (11)$$

Rewrite the F.O.C as $s - \Delta[p - mc] = 0$; it then follows that $p = mc + \Delta^{-1}s$. The new estimation equation is as below, suppressing the country-year subscript and indexing drug with j:

$$mc_j = p_j - \Delta^{-1}s_j = X_j\gamma + \beta MPP_j + \eta q_j + \omega_j\ . \qquad (12)$$

Here, the covariate X_j specification is the same as that in equation (8), except I include quantity q in the regression to capture firms' capacity constraints in oligopolistic settings. I instrument q using the number of competing products in the same class (Berry *et al*., 1995; Song *et al*., 2017).

6.3 Results and Counterfactuals

Demand estimation results are consistent with model assumptions (Table B12). In the nested logit model, the coefficient estimate of within-group market share is 0.863 and statistically significant at the 1% level. This result supports the assumption that drugs are closer substitutes within a group than between groups. A comparison of the price coefficients between OLS and the nested logit model reveals that there is a positive correlation between price and demand shocks and that the instrumental variables mitigate the problem. The price coefficient increases in absolute value from -0.137 in the OLS model to -1.946 in the nested logit model, and in all models the price coefficients are significant at the 1% level.[46]

Supply-side estimates suggest that the MPP reduced drug costs and are robust to various assumptions concerning market structure. Results under constant marginal cost pricing are similar to these with oligopolistic pricing and indicate significant MPP-induced cost reductions at the 1% level (Table B13). Specifically, the MPP reduces cost by $0.6 per patient-day under competitive pricing and by $1.9 under oligopolistic pricing across ownership assumptions. The estimated quantity coefficients are positive yet small and are consistent with supply curves being upward sloping, as oligopolistic firms face some capacity constraint as quantity goes up. In cases where marginal costs are not independent of quantity, patent protection increases costs, and the number of competitors in the market reduces marginal costs. These results are robust to the inclusion of country-year level observable controls and to statistical tests on the BLP instrument.

I then use parameters from demand and supply estimation to simulate counterfactuals in which the MPP dot not exist or further expand. For example, I shut down the MPP parameters in the estimated oligopolistic marginal cost curve. I then simulate counterfactual equilibrium prices and quantities by solving the new first-order condition and update for each country-year market. New consumer and producer surpluses are computed accordingly (see Appendix C for details).

The welfare and counterfactual results quantify how much the MPP increases both consumer and producer surpluses (Table 7). Consumers benefit from cost savings induced by the MPP via joint licensing, and producers can benefit from market expansion in developing countries and increased sales via the generic network. The estimated current consumer surplus across all markets (country-year) during my sample period is $8.7 billion, on the same order of magnitude as the total revenue during my sample period ($4.3 billion) and consistent with

[46] The first-stage Kleibergen–Paap F-statistic for both endogenous variables is 19.30, and the Sanderson–Windmeijer multi-variate first-stage F-statistics for each endogenous variable are much larger.

demand being elastic. Compared to the counterfactual cases without a patent pool, the MPP results in $0.69-1.39 billion consumer surplus gains across market structure specifications. These are equivalent to 8.60-18.94% increases from the counterfactual consumer surpluses. Overall, the benchmark level of consumer welfare gains I estimate is similar to the MPP's estimates of cost savings ($1.06 billion).[47] The estimated producer surplus gains are up to $181 million and are consistent with theories in which producers can also benefit from cost-reducing technologies.

The costs of operating the patent pool can be incorporated using a back-of-the-envelope cost-benefit type analysis. There is typically little information on the costs for operating modern patent pools due to data availability issue. I overcome this issue with cost data from transparent, audited financial statements from the MPP (Table B15). The total operating cost of the MPP is about $33 million from its establishment in July 2010 to the end of 2017. This amount is small compared to the welfare gains estimated above. These counterfactual results, together with the diffusion and innovation analyses, suggest that the MPP is an effective business model in the LMIC setting with elastic demand to drugs for infectious diseases. Lower prices from generic licensing generate larger responses in terms of quantity increases, which can further increase profits. This calculation is conservative as both branded and generic firms also benefit from reduced administrative costs that are not incorporated here.

7. Discussion and Conclusion

I find that the MPP increases the diffusion of affordable generic versions of associated drugs by about seven percentage points. The results are stronger in countries where a drug has been patented and when drug cocktails are de-bundled to the compound level. The results are robust to a set of robustness and sensitivity tests. In addition, the pool also weakly increases R&D in follow-on clinical trials and drug product approvals. Branded firms inside the pool reallocate clinical trials to drugs close to the market and new compound development. Firms outside the pool increase trials with pooled compounds. And generic firms obtain more drug approvals with pool-associated compounds. Overall, the MPP increases welfare by lowering the costs of licensing and offers new channels of marketing in underdeveloped LMIC markets.

Although I focus on the MPP's initial work on HIV drug cocktails, the general original focus on infectious diseases and its continuous expansion deserve future work. The inclusion of

[47] They multiply quantities sold by the price differences between the lowest branded and generic prices.

hepatitis C and tuberculosis in 2015, the expanded mandate to all WHO's small molecule essential drugs in 2018, and the urgent partnership in the WHO's Covid-19 Technology Access Pool expose the MPP to different contexts, challenges and opportunities. The long-term impact of the MPP requires more research. As many diseases started from developing countries and became prevalent in the U.S., it is mutually beneficial to develop institutions to spur diffusion and innovation that can benefit all countries. Amid the Covid-19 pandemic and rising anti-microbial resistance, novel institutions such as the MPP offer new options and insights.

The MPP also provides insights from a mechanism design perspective. First, the MPP is a non-profit pool with for-profit patent holders. The public-private partnership makes it natural to consider diffusion and innovation in coordinated manners. This partnership is similar to the aircraft patent pool during WWI that spurred the growth of the U.S. aircraft industry. Second, the lowest licensing unit is at the compound level, and all relevant territory patents are included in the MPP licenses, eliminating concerns on selection in patents. Third, the pool segments the market to lower licensing costs for sales in LMICs while preserve high-income territories for branded firms. The geographic separation allows branded firms to maintain prior strategies in lucrative markets and to broaden well-compliant licensed sales in developing countries.

There are a few limitations given the context of the MPP. I take the pool design as given and cannot extrapolate if the pool design changes drastically or becomes fully profit driven. Despite substantial internal validity of the MPP on infectious diseases in LMICs, more research is needed to evaluate pools with complex biologic products in developed countries. Besides, because a patent pool is designed to reduce multiple frictions in the market for patent licensing, it is difficult to quantify the relative magnitude of each mechanism precisely.

This paper has multiple implications for policy and firm strategies. First, branded firms can use a patent pool to collaboratively expand market in LMIC and reduce costs. Second, effective technology diffusion involves licensing designs that allow for broad use of patents and the preservation of licensor's rights in preferred sales territory. Third, institutional innovation can align public and private interests to increase profits and improve welfare. Fourth, for diseases with heavy global burdens, technology diffusion can benefit both consumers and firms by leveraging comparative advantages across branded and generic firms in the global economy.

References

Acemoglu, D., & Linn, J. (2004). Market size in innovation: theory and evidence from the pharmaceutical industry. *The Quarterly Journal of Economics*, *119*(3), 1049-1090.

Aghion, P., Bloom, N., Blundell, R., Griffith, R., & Howitt, P. (2005). Competition and innovation: An inverted-U relationship. *The Quarterly Journal of Economics*, 120(2), 701-728.

Azomahou, T. T., Boucekkine, R., & Diene, B. (2016). HIV/AIDS and development: A reappraisal of the productivity and factor accumulation effects. *The American Economic Review*, *106*(5), 472-477.

Bekkers, R., Catalini, C., Martinelli, A., Righi, C., & Simcoe, T. (2017). Disclosure Rules and Declared Essential Patents (No. w23627). *National Bureau of Economic Research.*

Berry, S. T. (1994). Estimating discrete-choice models of product differentiation. *The RAND Journal of Economics*, 242-262.

Berry, S., Levinsohn, J., & Pakes, A. (1995). Automobile prices in market equilibrium. *Econometrica: Journal of the Econometric Society*, 841-890.

Bessen, J. (2004). Holdup and licensing of cumulative innovations with private information. *Economics Letters*, *82*(3), 321-326.

Cameron, A. C., Gelbach, J. B., & Miller, D. L. (2011). Robust inference with multiway clustering. *Journal of Business & Economic Statistics*, *29*(2), 238-249.

Clark, J., Piccolo, J., Stanton, B., Tyson, K., Critharis, M., & Kunin, S. (2000). *Patent pools: a solution to the problem of access in biotechnology patents?*. mimeo, USPTO.

Chaudhuri, S., Goldberg, P. K., & Jia, P. (2006). Estimating the effects of global patent protection in pharmaceuticals: a case study of quinolones in India. *The American Economic Review*, *96*(5), 1477-1514.

Cockburn, I. M., Lanjouw, J. O., & Schankerman, M. (2016). Patents and the global diffusion of new drugs. *The American Economic Review*, 106(1), 136-164.

Cournot, A., 1927, Researches into the Mathematical Principles of the Theory of Wealth, original published in French (1838), translated by N. Bacon, New York: Macmillan.

Dubois, P., De Mouzon, O., Scott-Morton, F., & Seabright, P. (2015). Market size and pharmaceutical innovation. *The RAND Journal of Economics*, *46*(4), 844-871.

Duggan, M., Garthwaite, C., & Goyal, A. (2016). The market impacts of pharmaceutical product patents in developing countries: Evidence from India. *The American Economic Review*, *106*(1), 99-135.

Finkelstein, A. (2004). Static and dynamic effects of health policy: Evidence from the vaccine industry. *The Quarterly Journal of Economics*, *119*(2), 527-564.

Galasso, A., & Schankerman, M. (2014). Patents and cumulative innovation: Causal evidence from the courts. *The Quarterly Journal of Economics*, *130*(1), 317-369.

Green, J. & Scotchmer, S. "On the division of profit in sequential innovation," *RAND Journal of Economics*, 1995, 26 (1), 20–33.

Hemphill, C. S., & Sampat, B. N. (2012). Evergreening, patent challenges, and effective market life in pharmaceuticals. *Journal of health economics*, *31*(2), 327-339.

Hoen, E. (2016). *Private Patents and Public Health: Changing intellectual property rules for access to medicines*. Health Action International.

Juneja, S., Gupta, A., Moon, S., & Resch, S. (2017). Projected savings through public health voluntary licences of HIV drugs negotiated by the Medicines Patent Pool (MPP). *PloS one*, *12*(5), e0177770.

Kremer, M. (2002). Pharmaceuticals and the developing world. *The Journal of Economic Perspectives*, *16*(4), 67-90.

Kyle, M., & Qian, Y. (2017). Intellectual property rights and access to innovation: evidence from TRIPS. *Working Paper*.

Lampe, R., & Moser, P. (2013). Patent pools and innovation in substitute technologies—evidence from the 19th-century sewing machine industry. *The RAND Journal of Economics*, *44*(4), 757-778.

Lampe, R., & Moser, P. (2015). Patent Pools, Competition, and Innovation—Evidence from 20 US Industries under the New Deal. *Journal of Law, Economics, and Organization*, *32*(1), 1-36.

Lerner, J., & Seru, A. (2017). *The use and misuse of patent data: Issues for corporate finance and beyond* (No. w24053). National Bureau of Economic Research.

Lerner, J., Strojwas, M., & Tirole, J. (2007). The design of patent pools: The determinants of licensing rules. *The RAND Journal of Economics*, *38*(3), 610-625.

Lerner, J., & Tirole, J. (2004). Efficient patent pools. *The American Economic Review*, *94*(3), 691-711.

Lerner, J., & Tirole, J. (2015). Standard-essential patents. *Journal of Political Economy*, *123*(3), 547-586.

Quint, D. (2014). Pooling with essential and nonessential patents. *American Economic Journal: Microeconomics*, *6*(1), 23-57.

Rey, P., & Tirole, J. (2019). Price caps as welfare-enhancing coopetition. *Journal of Political Economy*.

Sampat, B., & Williams, H. L. (2019). How do patents affect follow-on innovation? Evidence from the human genome. *American Economic Review*, *109*(1), 203-36.

Shapiro, C. (2001). Setting compatibility standards: cooperation or collusion. *Expanding the bounds of intellectual property. University Press, Oxford*, 8-0.

Song, M., Nicholson, S., & Lucarelli, C. (2017). Mergers with interfirm bundling: a case of pharmaceutical cocktails. *The RAND Journal of Economics*, *48*(3), 810-834.

Tirole, J. (2006). Intellectual property and health in developing countries. *Understanding poverty*, A. Banerjee, R. Benabou and D. Mookherjee, eds., *303*, 313.

Van Overwalle, G. (2016). Patent Pools and Clearinghouses in the Life Sciences: Back to the Future. *Research Handbook on IP and the Life Sciences, D. Matthews & H. Zech (eds.), Edward Elgar*

Wen, W., Ceccagnoli, M., & Forman, C. (2015). Opening up intellectual property strategy: Implications for open source software entry by start-up firms. *Management Science*, *62*(9), 2668-2691.

Williams, H. L. (2013). Intellectual property rights and innovation: Evidence from the human genome. *Journal of Political Economy*, *121*(1), 1-27.

Figures and Tables

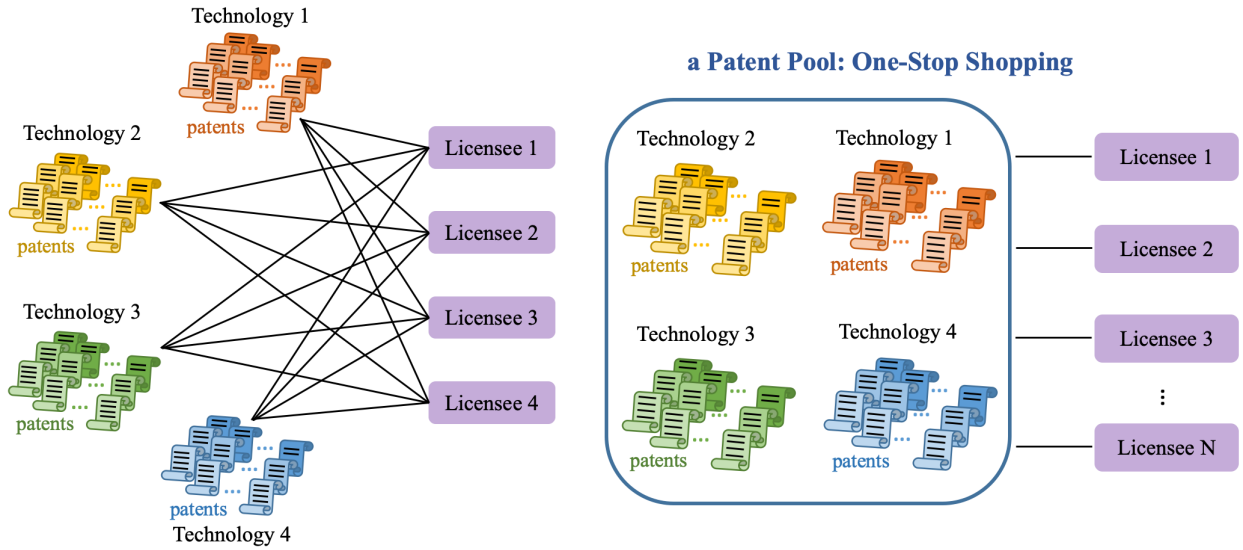


Figure 1: Graphical Structure of the Licensing Market without and with a Patent Pool

Notes: Author's graph. Each technology (e.g., a drug) has numerous underlying patents, and a complex technology (e.g., a drug cocktail) requires licensing multiple technologies for each licensee. The multiple patents involved and repeated negotiation with different patent owners (left). A patent pool provides a one-stop shopping through a joint licensing platform (right). Therefore, more licensees can enter the market to develop and sell new products (e.g., new cocktails or formulations).

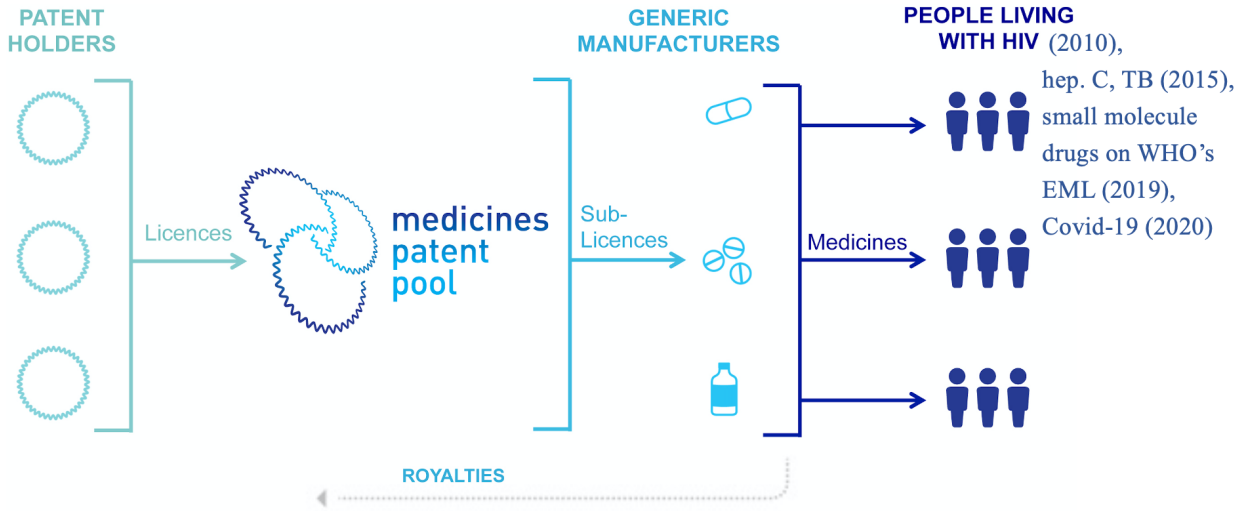
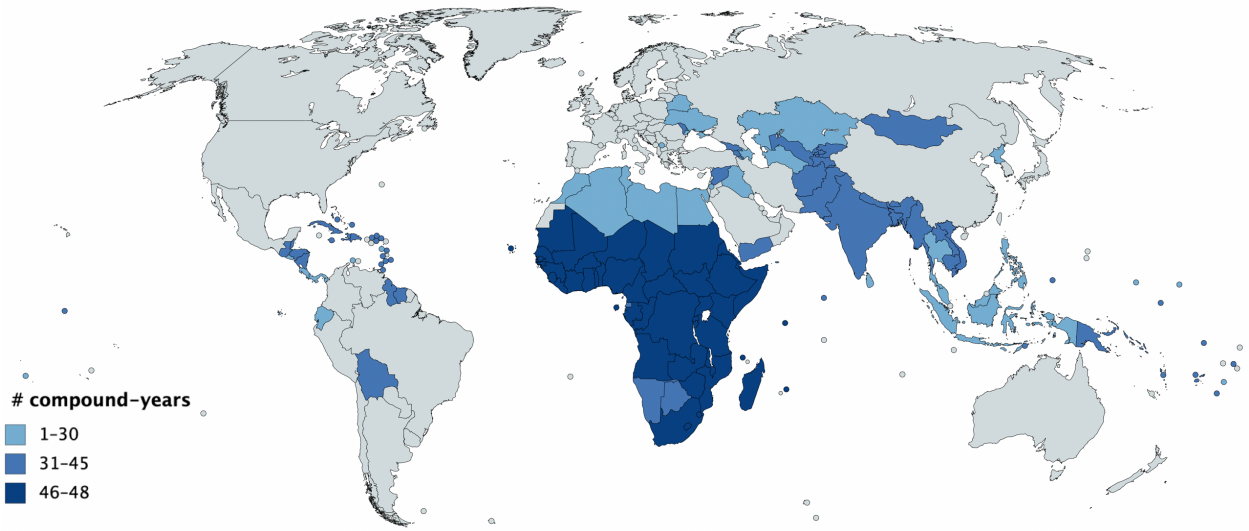
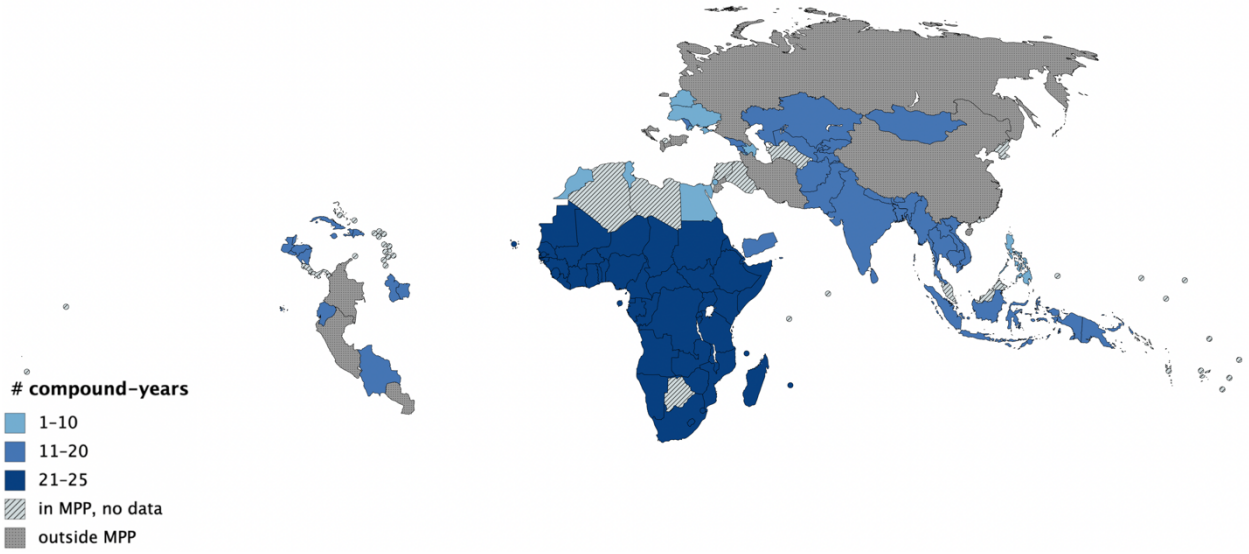


Figure 2: Licensing Structure for the Medicines Patent Pool

Notes: The figure depicts the basic structure of the MPP (edited form MPP official material). The MPP works as the intermediaries between branded drug firms and qualified generic licensees to help resource-limited countries. Royalties are typically capped at 5% of revenue and are free in many cases.



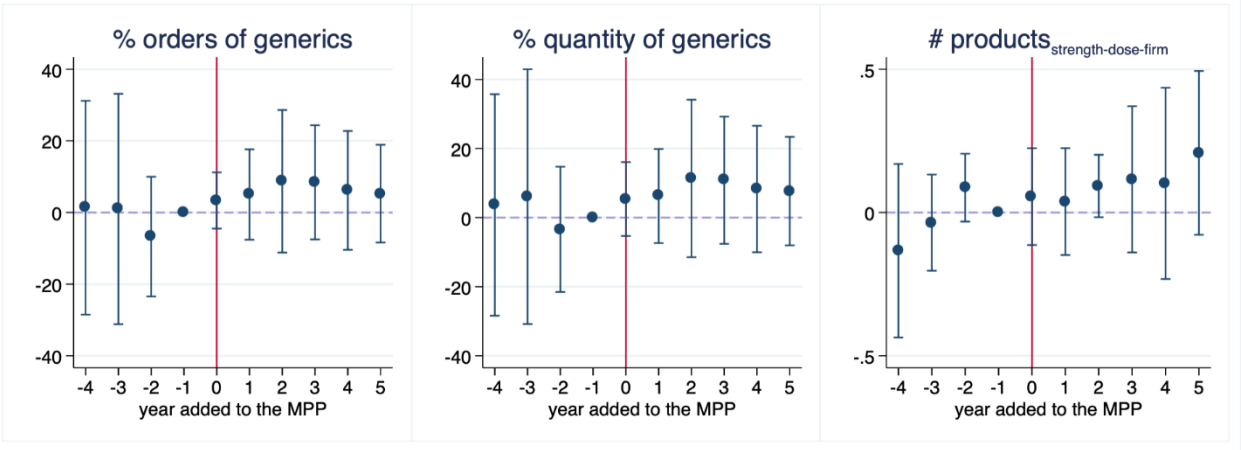
(a) MPP overall effective sales territory



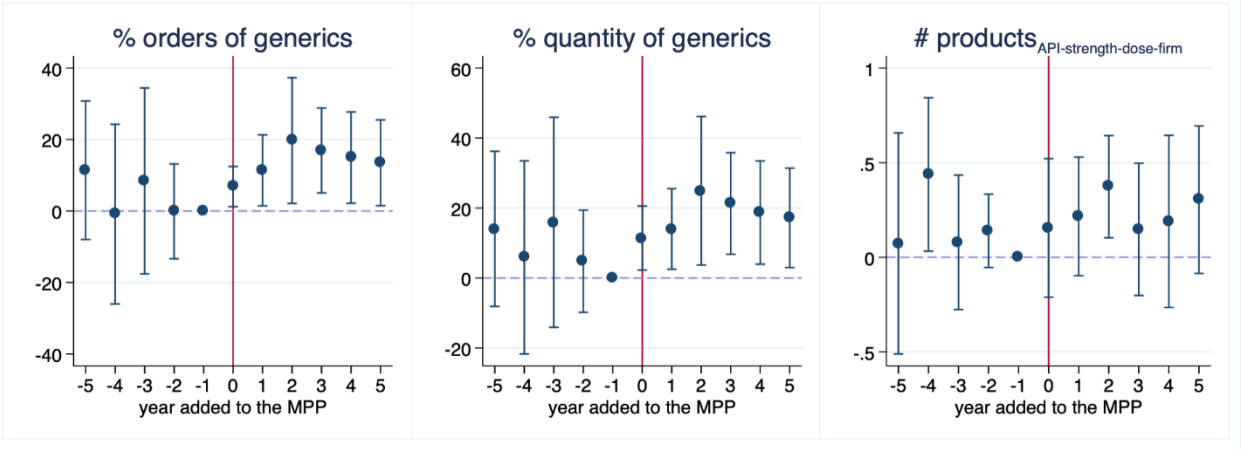
(b) MPP representation in the diffusion data

Figure 3: Geographic Penetration of the MPP: (a) Overall and (b) in the Diffusion Data

Notes: Color groups represent the compound-year weighted intensity of impact by the end of 2017. Panel (a) include all compound countries covered in the MPP sales territory, and panel (b) adapts the map to account for MPP compounds and countries in my datasets for the diffusion and structural analyses. Not all MPP-associated compounds appear in my data as many newer drugs need a couple of years to pass the production, registration, and distribution process.



(a) Drug-Country-Year Panel



(b) Compound-Country-Year Panel

Figure 4: Event Studies for Diffusion Analysis

Notes: These figures report event-study coefficient estimates using Equation (2). The units of observation for panel (a) and (b) are at drug-country-year (dct) and compound-country-year (act) levels, respectively. The dots are point estimates of differences in outcomes between treatment and control groups 4-5 years before MPP inclusion and 5 years after inclusion. The whiskers correspond to 95% confidence intervals.

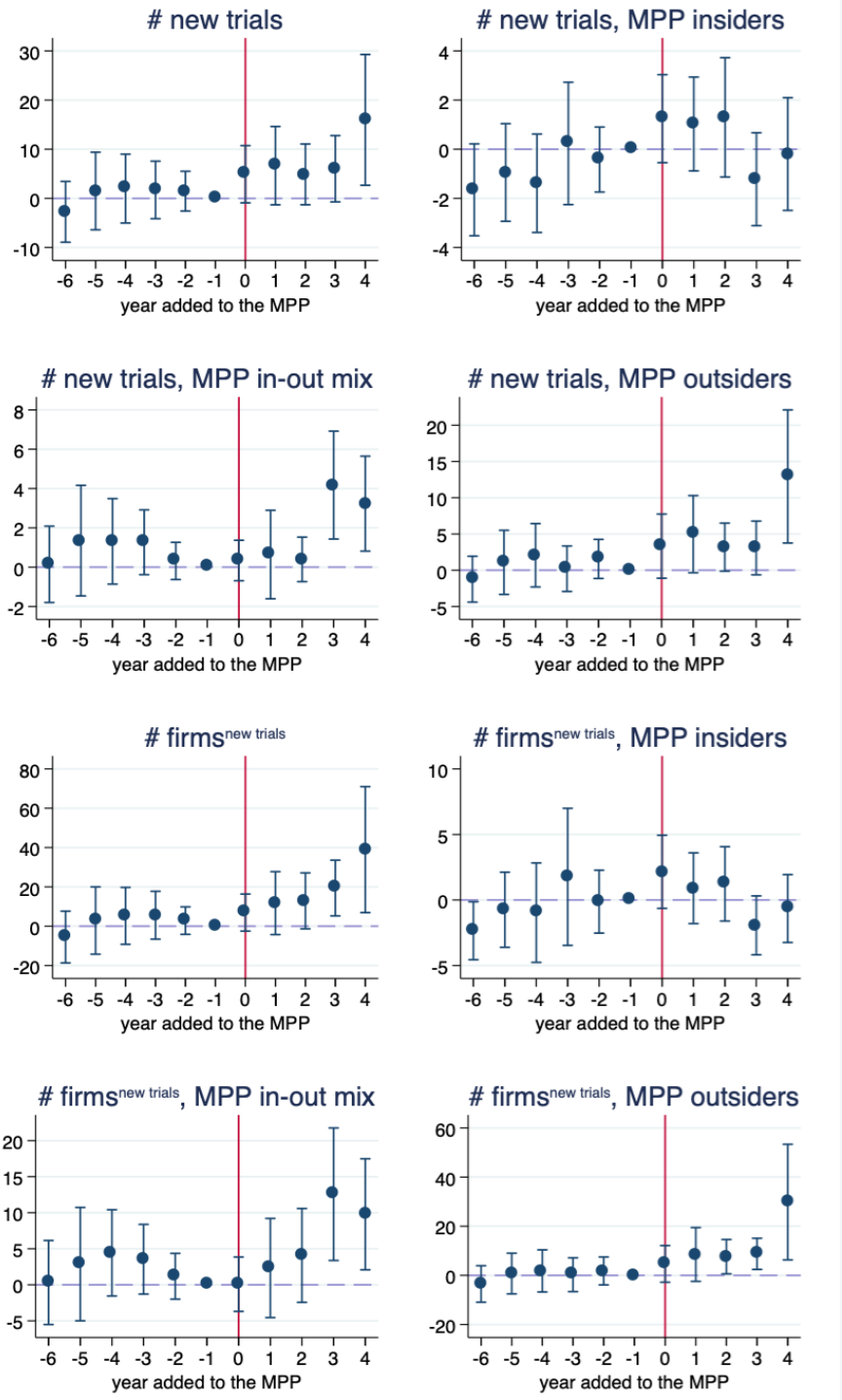


Figure 5: Event Studies for Innovation Analysis: New Clinical Trials and Firms Participated

Notes: These figures report event-study coefficient estimates using Equation (4). The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before MPP inclusion and 4 years after inclusion. The whiskers correspond to 95% confidence intervals.

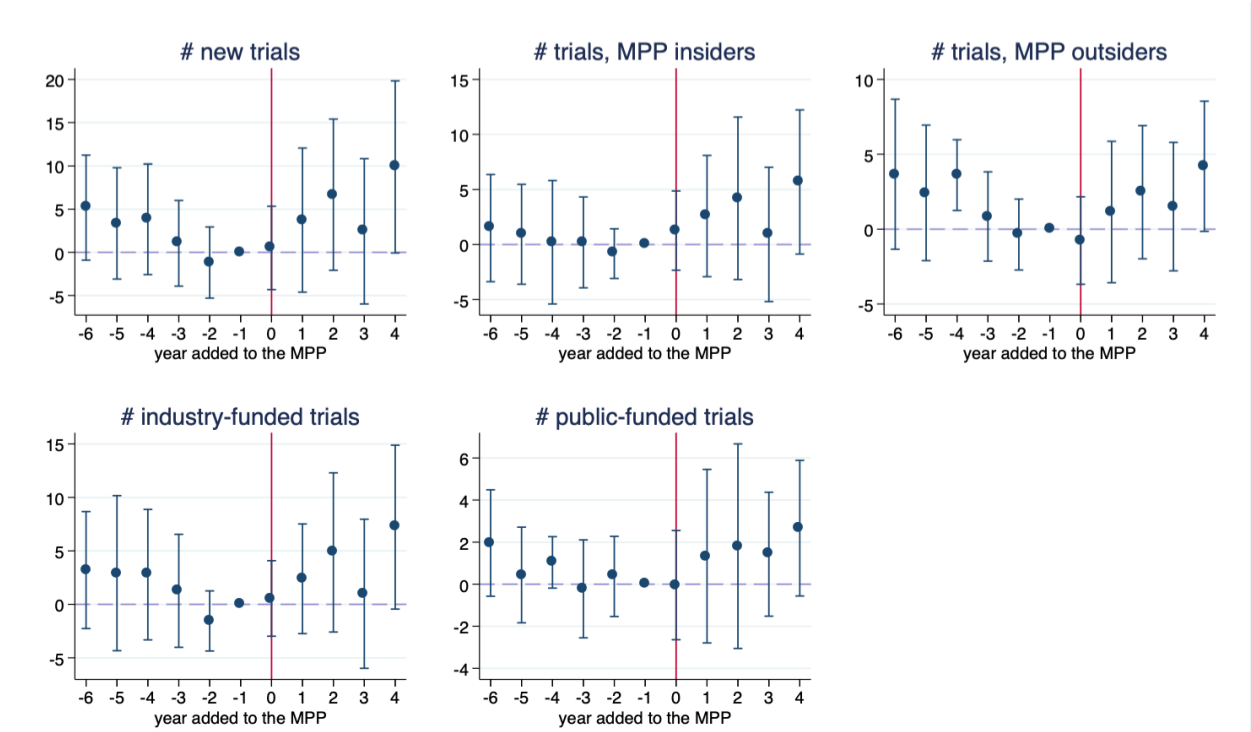
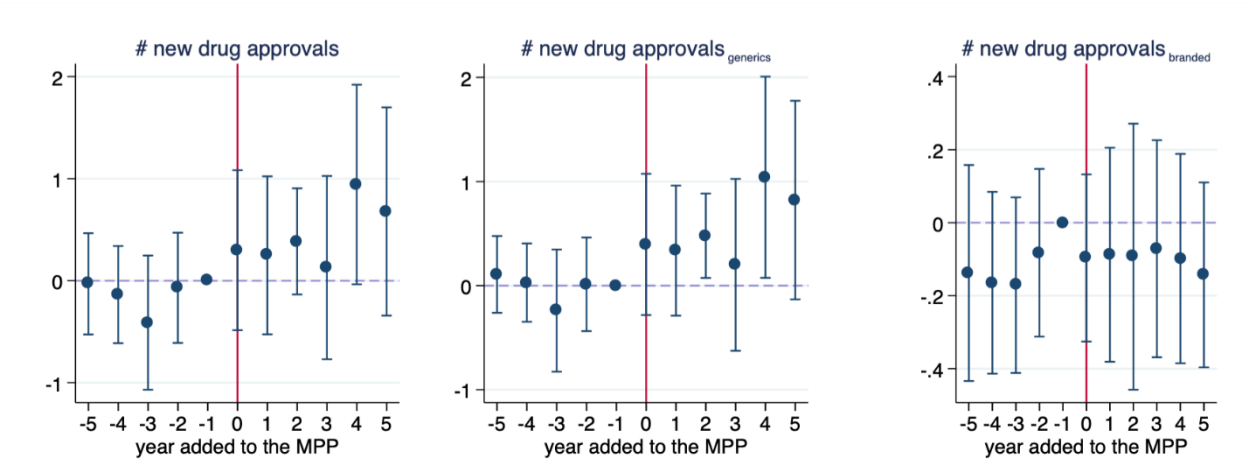
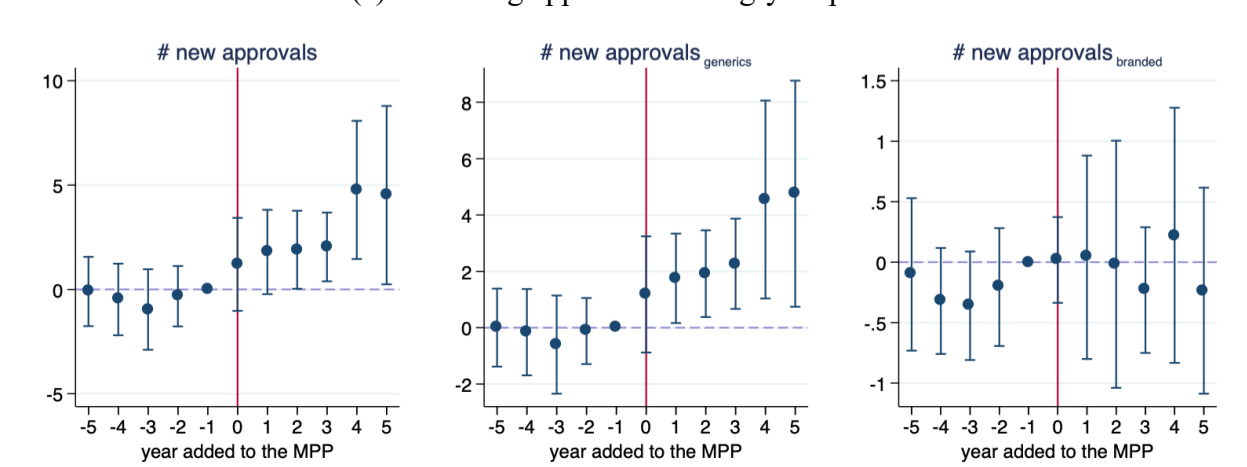


Figure 6: Event Studies for Innovation Analysis: Clinical Trials for HIV Investigational Drugs

Notes: These figures report event-study coefficient estimates using Equation (4), at drug class-year level. The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before and 4 years after MPP inclusion. The whiskers correspond to 95% confidence intervals.



(a): new drug approvals in drug-year panel



(b): new approvals in compound-year panel

Figure 7: Event Studies for Innovation Analysis: New Drug Product Approvals

Notes: These figures report event-study coefficient estimates using Equation (4). The dots are point estimates of differences in outcomes between treatment group and control groups 5 years before MPP inclusion and 5 years after inclusion. The whiskers correspond to 95% confidence intervals.

Table 1: Approved Active Pharmaceutical Ingredients (Compounds) Treating HIV
(generic names marked with * are compounds no longer recommended in the U.S.)

Drug class	Generic name	Abbr.	Brand drug holder	date: FDA approval	date: add to MPP
NRTIs	abacavir	ABC	ViiV Healthcare	1998.12.17	2013.02.13[ped]
	didanosine *	ddI	Bristol-Myers Squibb	1991.10.09	
	emtricitabine	FTC	Gilead Sciences, Inc.	2003.07.02	2011.07.11
	lamivudine	3TC	ViiV Healthcare	1995.11.17	
	stavudine *	d4T	Bristol-Myers Squibb	1994.06.24	
	tenofovir alafenamide	TAF	Gilead Sciences, Inc.	2015.11.05	2014.07.22
	tenofovir disoproxil fumarate	TDF	Gilead Sciences, Inc.	2001.10.26	2011.07.11
	zidovudine	ZDV	ViiV Healthcare	1987.03.19	
NNRTIs	doravirine	DOR	Merck & Co., Inc.	2018.08.30	
	efavirenz	EFV	Bristol-Myers Squibb	1998.09.17	
	etravirine	ETR	Janssen	2008.01.18	
	nevirapine	NVP	Boehringer Ingelheim	1996.06.21	
	rilpivirine	RPV	Janssen	2011.05.20	
PIs	atazanavir	ATV	Bristol-Myers Squibb	2003.06.20	2013.12.11
	darunavir	DRV	Janssen	2006.06.23	
	fosamprenavir	FPV	ViiV Healthcare	2003.10.20	
	indinavir *	IDV	Merck & Co., Inc.	1996.03.13	
	nelfinavir *	NFV	Agouron (ViiV)	1997.03.14	
	lopinavir	LPV	AbbVie Inc.	2000.09.15	2014.11.24[ped]; 2015.12.17[adult]
	ritonavir	r	AbbVie Inc.	1996.03.01	2014.11.24[ped]; 2015.12.17[adult]
	saquinavir	SQV	Hoffman-La Roche	1995.12.06	
	tipranavir	TPV	Boehringer Ingelheim	2005.06.22	
FIs	enfuvirtide	ENF	Hoffman-La Roche	2003.03.13	
EIs	Ibalizumab	IBA	TaiMed Biologics	2018.03.06	
	maraviroc	MVC	ViiV Healthcare	2007.08.06	
IIs	bictegravir	BIC	Gilead Sciences, Inc.	2018.02.07	2017.09.26
	dolutegravir	DTG	ViiV Healthcare	2013.08.12	2014.03.31[ped. & adult]
	elvitegravir	EVG	Gilead Sciences, Inc.	2012.08.27	2011.07.11
	raltegravir	RAL	Merck & Co., Inc.	2007.10.12	2015.02.20[ped]
Enhancers	cobicistat	COBI	Gilead Sciences, Inc.	2012.08.27	2011.07.11

Notes: (1) The table shows all drugs approved but not all in the diffusion sample (Table D2). E.g., the only monoclonal antibody, IBA, does not show up in any sales data. (2) I excluded 3 compounds withdraw from the market before 2000 (APV, ddC, DLV). EVG and COBI were first approved as part of a cocktail; standalone compounds were approved on 9/24/2014. Standalone TAF was approved on 2016.11.10 after cocktail approval on 2015.11.05. (3) MPP license for ABC and RAL restrict to pediatric formulation. I treat DRV as not in the pool, albeit NIH put in part of related patents but not those owned by Janssen, resulting in no technology transfer nor sub-licensing so far. (4) drug classes are groups by mechanisms of action (details in Table D1). (5) DTG was marked as 8/12/2013 in FDA raw data but as 8/13/2018 on FDA websites. DTG enters the MPP on 3/31/2014 with different territories for adult and pediatric products. (6) Agouron is a Pfizer subsidy since 1999 and Pfizer is part of the joint venture ViiV Healthcare (with GlaxoSmithKline and Shionogi).

Table 2: Summary Statistics of Outcome Variables

Variables	Unit of obs.	Obs.	Mean	Std. Dev.	Min	Max
Panel A: variables used in the diffusion analysis – cross-country panel analysis						
% generic orders (%)	drug-country-year	7,084	84.31	34.47	0	100
% generic quantity (%)	drug-country-year	7,084	85.63	34.16	0	100
# products	drug-country-year	7,084	1.72	1.04	1	10
% generic orders	comp.-country-year	6,485	79.82	36.94	0	100
% generic quantity	comp.-country-year	6,485	82.07	36.75	0	100
# products	comp.-country-year	6,485	2.53	1.94	1	21
Panel B1: variables used in the innovation analysis – clinical trials analysis						
# new trials	comp.-year	540	10.08	13.24	0	67
# firms in new trials	comp.-year	540	20.73	28.53	0	165
# new trials, MPP insiders	comp.-year	540	2.41	3.27	0	17
# new trials, MPP mix	comp.-year	540	1.99	3.49	0	23
# new trials, MPP outsiders	comp.-year	540	5.68	7.89	0	44
# firms in trials, MPP insiders	comp.-year	540	3.15	4.53	0	36
# firms in trials, MPP mix	comp.-year	540	5.92	10.52	0	69
# firms in trials, MPP outsiders	comp.-year	540	11.67	16.80	0	113
# new investigational trials	drug class-year	126	6.76	8.19	0	32
# firms in investigational trials	drug class-year	126	12.49	16.39	0	63
Panel B2: variables used in the innovation analysis – drug approval analysis						
# new approvals	drug-year	798	0.70	1.63	0	14
# new approvals, generic	drug-year	798	0.61	1.60	0	14
# new approvals, branded	drug-year	798	0.09	0.42	0	6
# new approvals	comp.-year	378	2.28	4.02	0	32
# new approvals, generic	comp.-year	378	2.01	3.97	0	31
# new approvals, branded	comp.-year	378	0.27	0.72	0	6

Notes: this table reports summary statistics for the main outcome variables used in the analysis. “Comp.” is short for compound, the smallest chemical units of a standalone drug. Panel A is for drug-country-year and compound-country-year level variables over the time period 2007-2017. Panel B1 is for compound-year level variables from HIV clinical trials during 2000-2017. MPP insiders refers to branded firms participated in the MPP, MPP outsiders refers to non-MPP firms, and MPP mix indicates trials by a mix of MPP insiders and outsiders. Panel B2 is for drug-year and compound-year level variables from FDA and WHO original drug approvals during 2005-2018.

Table 3: MPP and Generic HIV Drug Diffusion in LMICs

Dept. Vars.	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
	% generic orders (#)			% generic quantities (patient-year)			# products (strength-dose-firm)		
Panel A: Drug-Country-Year Analysis, MPP_{dct} as {0, 1} dummy									
MPP_{dct}	6.888**	7.223**	7.226**	6.653**	7.003**	7.010**	0.0739	0.0719	0.0717
	(3.178)	(2.933)	(2.932)	(3.035)	(2.802)	(2.796)	(0.113)	(0.104)	(0.104)
	[2.712]	[2.706]	[2.707]	[2.725]	[2.717]	[2.715]	[0.0812]	[0.0800]	[0.0798]
Panel B: Drug-Country-Year Analysis, MPP_{dct} as % of MPP compounds									
MPP_{dct}	7.154**	7.403**	7.409**	6.916**	7.183**	7.194**	0.0929	0.0939	0.0937
	(3.270)	(2.983)	(2.984)	(3.123)	(2.858)	(2.857)	(0.124)	(0.113)	(0.112)
	[2.870]	[2.851]	[2.853]	[2.870]	[2.858]	[2.859]	[0.0874]	[0.0850]	[0.0848]
drug-country FE	Y	Y	Y	Y	Y	Y	Y	Y	Y
year FE	Y	Y	Y	Y	Y	Y	Y	Y	Y
X_{ct} control		Y	Y		Y	Y		Y	Y
X_{dct} control			Y			Y			Y
LHS mean	84.3	84.3	84.3	85.6	85.6	85.6	1.7	1.7	1.7
Observations	7,084	7,084	7,084	7,084	7,084	7,084	7,084	7,084	7,084
Panel C: Compound-Country-Year Analysis									
MPP_{act}	9.576**	9.977**	10.12***	10.09***	10.42***	10.55***	0.156	0.140	0.132
	(3.708)	(3.493)	(3.487)	(3.369)	(3.248)	(3.261)	(0.193)	(0.185)	(0.186)
	[3.088]	[3.050]	[3.076]	[3.227]	[3.204]	[3.226]	[0.115]	[0.114]	[0.110]
comp.-country FE	Y	Y	Y	Y	Y	Y	Y	Y	Y
year FE	Y	Y	Y	Y	Y	Y	Y	Y	Y
X_{ct} control		Y	Y		Y	Y		Y	Y
X_{act} control			Y			Y			Y
LHS mean	79.8	79.8	79.8	82.1	82.1	82.1	2.5	2.5	2.5
Observations	6,485	6,485	6,485	6,485	6,485	6,485	6,485	6,485	6,485

Notes: This table reports the results of estimating equation (1). "Comp." is short for compound. Each cell reports the coefficient of interest from a separate regression. Coefficient estimates for the treatment variables $MPP_{d(a)ct}$ are reported across three measures across panels. The specification controls for drug (compound)-country-year level effective patent status and country-year level observables. Fixed effects for drug (compound)-country pairs and years are always included. Robust standard errors are clustered using two-way clustering at the drug (compound) and country levels and are reported in () parenthesis. Robust standard errors clustering at the country level is reported in []. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table 4: Innovation Analysis - Clinical Trials: New HIV Trials & Firms Participated

Panel A: # new HIV clinical trials								
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Dept. Vars.	# trials		# trials: $MPP_{insiders}$		# trials: MPP_{mix}		# trials: $MPP_{outsiders}$	
MPP_{at}	9.925**	8.093	2.098**	1.625*	1.672	1.100	6.155**	5.368*
	(4.534)	(4.831)	(0.883)	(0.859)	(1.025)	(1.051)	(2.848)	(3.084)
LHS mean	10.08	10.08	2.367	2.367	1.915	1.915	5.794	5.794
Panel B: # firms in new trials								
Dept. Vars.	# firms		# firms: $MPP_{insiders}$		# firms: MPP_{mix}		# firms: $MPP_{outsiders}$	
MPP_{at}	20.81**	17.75*	2.284**	1.747	5.366*	3.803	13.16**	12.20*
	(9.488)	(10.28)	(1.065)	(1.072)	(3.091)	(3.226)	(5.967)	(6.454)
LHS mean	20.73	20.73	3.104	3.104	5.754	5.754	11.87	11.87
comp. & year FEs	Y	Y	Y	Y	Y	Y	Y	Y
X_{at} control		Y		Y		Y		Y
Observations	540	540	540	540	540	540	540	540

Notes: This table reports the results of estimating equation (3) at the compound-year level. Each cell reports the coefficient of interest from a separate regression. $MPP_{insiders}$ means all the participants of a trial are branded firms contributed to the MPP, $MPP_{outsiders}$ are trials by firms outside the MPP, and MPP_{mix} denotes trials that are collaborated by MPP insiders and outsiders. Controls variables include FDA approval status, patent status, and fixed effects for compounds and years. Robust standard errors are clustered at the compound level. Robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table 5: Innovation Analysis - Clinical Trials: HIV Trials by Phase

Dept. Vars.	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	# New HIV clinical trials				# Firms in new HIV clinical trials			
	total	$MPP_{insiders}$	MPP_{mix}	$MPP_{outsiders}$	total	$MPP_{insiders}$	MPP_{mix}	$MPP_{outsiders}$
Panel A. Phase I								
MPP_{at}	1.114	-0.0388	0.168	0.986	2.314	-0.0325	0.525*	1.822
	(0.866)	(0.135)	(0.108)	(0.778)	(1.693)	(0.211)	(0.279)	(1.449)
LHS mean	1.352	0.331	0.144	0.876	2.306	0.539	0.363	1.404
Panel B. Phase II								
MPP_{at}	0.925	0.466	-0.134	0.593*	1.120	0.527	-0.524	1.117*
	(0.646)	(0.290)	(0.131)	(0.312)	(1.120)	(0.360)	(0.370)	(0.596)
LHS mean	1.909	0.530	0.261	1.119	3.704	0.672	0.889	2.143
Panel C. Phase III								
MPP_{at}	3.374***	1.945***	0.0680	1.361**	4.585**	2.122***	-0.132	2.594*
	(1.066)	(0.569)	(0.192)	(0.503)	(1.862)	(0.657)	(0.565)	(1.331)
LHS mean	2.885	1.141	0.446	1.298	5.970	1.376	1.402	3.193
Panel D. Phase IV								
MPP_{at}	1.325	-0.385**	0.614	1.096	4.539	-0.481***	2.435	2.585
	(1.151)	(0.152)	(0.491)	(0.797)	(2.971)	(0.165)	(1.634)	(1.564)
LHS mean	2.463	0.269	0.752	1.443	5.578	0.320	2.302	2.956

Notes: This table reports the results of estimating equation (3) at the compound-year level. The number of observations is always 540 in this balanced panel data. Each cell reports the coefficient of interest from a separate regression. $MPP_{insiders}$ means all the participants of a trial are branded firms contributed to the MPP, $MPP_{outsiders}$ are trials by firms outside the MPP, and MPP_{mix} denotes trials that are collaborated by MPP insiders and outsiders. Panels A to D report results by trial phase; phase IV is post-market surveillance. Controls variables include FDA approval status, patent status, and fixed effects for compounds and years. Robust standard errors are clustered at the compound level. Robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table 6: Innovation Analysis - Drug Approvals

Dept. Vars.	(1) # new approvals	(2) # new approvals	(3) # new approvals ^{generic}	(4) # new approvals ^{generic}	(5) # new approvals^{branded}	(6) # new approvals^{branded}
Panel A: Drug-Year Analysis, MPP_{dct} as {0, 1} dummy						
MPP_{dt}	0.555**	0.517*	0.445	0.508*	0.110**	0.00870
	(0.261)	(0.280)	(0.271)	(0.278)	(0.0482)	(0.0550)
Panel B: Drug-Year Analysis, MPP_{dct} as % compounds in the pool						
MPP_{dt}	0.749**	0.711**	0.616*	0.670*	0.133**	0.0410
	(0.321)	(0.341)	(0.338)	(0.341)	(0.0604)	(0.0641)
drug & year FEs	Y	Y	Y	Y	Y	Y
X_{dt} control		Y		Y		Y
LHS mean	0.70	0.70	0.61	0.61	0.09	0.09
Observations	798	798	798	798	798	798
Panel C: Compound-Year Analysis						
MPP_{at}	2.418**	2.607**	2.034**	2.478**	0.383**	0.129
	(0.908)	(0.993)	(0.961)	(0.980)	(0.143)	(0.140)
comp. & year FEs	Y	Y	Y	Y	Y	Y
X_{at} control		Y		Y		Y
LHS mean	2.28	2.28	2.01	2.01	0.27	0.27
Observations	378	378	378	378	378	378

Notes: This table reports the results of estimating equation (3). Each cell reports the coefficient of interest from a separate regression. Each adjacent two columns share the same dependent variable in different specifications. Panel A and Panel B differ in how the treatment variable is defined: as an indicator or percentage measure. Robust standard errors are clustered at the drug level. Robust p-value: *** p<0.01, ** p<0.05, * p<0.1.

Table 7: Welfare Estimation: Consumer & Producer Surpluses

welfare estimates ($ M)	MC pricing flat MC	Bertrand-Nash Oligopoly single-prod. firm	Bertrand-Nash Oligopoly multi-prod. firm
$\widehat{CS_0}$	7,354.5	8,055.1	8,025.8
$\widehat{CS}$	8,747.7	8,747.7	8,747.7
$\widehat{CS_1}$	8,883.3	8,821.5	8,816.4
Δ$: $\widehat{CS_0}$	1,393.2	692.6	721.9
Δ%: $\widehat{CS_0}$	18.94%	8.60%	8.99%
Δ$: $\widehat{CS_1}$	135.6	73.8	68.7
Δ%: $\widehat{CS_1}$	1.55%	0.84%	0.78%
$\widehat{PS_0}$	0	3,998.1	4,194.8
$\widehat{PS}$	0	4,179.5	4,309.6
$\widehat{PS_1}$	0	4,320.7	4,462.0
Δ$: $\widehat{PS_0}$	0	181.4	114.8
Δ%: $\widehat{PS_0}$	0	4.54%	2.74%
Δ$: $\widehat{PS_1}$	0	141.2	152.4
Δ%: $\widehat{PS_1}$	0	3.38%	3.54%

Notes: this table reports estimating the gains in consumer and producer surpluses with the MPP. Here, $\widehat{CS}$ denote the total consumer surplus cross-markets. $\widehat{CS_0}$ is the counterfactual consumer surplus without the MPP. Similarly, $\widehat{PS}$ and $\widehat{PS_0}$ denote the actual and counterfactual producer surpluses, respectively. $\widehat{CS_1}$ and $\widehat{PS_1}$ denote the counterfactual consumer and producer surpluses with a fully expanded MPP (covering all developing countries in my sample for a compound in the pool), respectively.

Online Appendix: Not for Publication

Global Drug Diffusion and Innovation with the Medicines Patent Pool

Online Appendix Table of Content

Appendix A: Data Construction 1
Appendix B: Figures and Tables 4
Appendix C: Mathematical Appendix 26
Appendix D: Medical Appendix 34
Appendix E: Legal Appendix 37
Appendix F: Case Studies on R&D 42

Appendix A: Data Construction

This appendix provides more details concerning how I construct the analytical samples. I describe the process of compiling the data for diffusion analysis and innovation analysis, respectively. For more information on certain generic data products generated in this process, I provide more detail in the supplementary online appendix.

A.1 Drug-country-year panel of HIV drug access

The *Price and Quality Reporting Data* provide information on procurement transactions made by Global Fund-supported programs.[1] Starting from the raw data, I follow the data caveats document and drop clearly duplicated transaction records. At the country-level, I construct a listing file with all countries in the dataset and assign the appropriate International Organization for Standardization (ISO) three-digit alphabetical country code. This procedure guarantees that a country will be consistently treated regardless of the variation in spelling (e.g., "Viet Nam" vs. "Vietnam"; "DR Congo" vs. "Congo (Democratic Republic)") and to facilitate data merging across different datasets. I also dropped the redundant regional-level summary data (e.g., "Western Asia" and "World").

At the firm level, I unify manufacturing firm names to correct inconsistency induced by different spellings (e.g., "Cipla" vs. "Cipla Ltd." vs. "Cipla Inc."). I assign a transaction-level indicator for generic drugs if the drug is purchased from a generic manufacturer. At the drug level, I focus on generic names (international names of compounds within a drug), as branded names vary across countries, depending partly on trademark registration. For drugs with multiple compounds, I unify the order of compounds within the drug to avoid over-counting of drug varieties; corresponding adjustments applied to all variables that are order-sensitive, such as milligram (mg) strength for each compound within a drug. For each drug in my database, I collected standard U.S. adult daily doses from FDA, AIDS*info*, and WHO, and I report the information in Appendix III (the medical appendix) Table A2.[2]

[1] Available at https://www.theglobalfund.org/en/sourcing-management/price-quality-reporting//. Data last accessed in 8/2018, when I request all available yearly data by 2017 from the online system. The data request system has been updated in 2019 and requires additional conversion from Tableau files.

[2] I focus on U.S. standard adult daily doses for two practical reasons. First, although it is ideal to collect country-specific dosing standards, it is practically impossible to collect this data across over 100 countries. Second, adult doses are more standard and comparable compared to pediatric doses that depend on age and weight. Realizing the caveats, I also use a quantity-free percentage of transaction measure.

I calculate the percentage of generic transactions by dividing the number of transactions made with generic manufacturers for a country and a given drug in a year by the total number of transactions made at the same country for the same drug in the same year. I then calculate the percentage of generic quantity purchases following the same idea. Since different drug products may have different strengths (e.g., "10mg/mL", "300 mg"), I calculate the effective strength for each smallest unit – stock keeping unit (SKU). I then calculate the total strength supplied in a transaction by multiplying strength per SKU with the number of SKU in a pack and the number of packs. The percentage of quantity ordered is calculated as the number of patient-years supplied by generic manufacturers for a drug-country-year to the total patient-years purchases for the same drug-country-year. Last, for product variety purchases, I count the number of unique drug-formulation (strength-dosage form)–manufacturer combinations in a country-year.

In the compound-country-year level analysis, I aggregate compound-specific information from multi-compound drugs into country-year levels. For example, I calculate the numbers of generic and total transactions related to a given compound in a country-year. I then reshape the data to the compound-country-year level and divide the two to get the percentage of generic transactions for a compound in a country-year. The same logic follows for other procedures.

A.2 Compound-year panel of HIV clinical trials

Clinical trials data are available from clinicaltrials.gov, the largest peer-reviewed clinical trials registry in the world and the most widely used by scientists. This U.S.-based trial registry accepts trial registration globally, particularly as multi-national companies typically conduct trials in multi-country clinical sites.[3] Each clinical trial has a unique identifier (i.e., an NCT number) and a set of data recorded and updated periodically.[4] Researchers can typically use Medical Subject Headings (MeSH) terms in the programming processes to pinpoint trials for specific disease conditions, but such processes are not always accurate to locate specific drugs. Therefore, I obtain compound-specific NCT numbers from AIDS*info* to identify HIV-related trials. I collect NCT numbers for all FDA-approved HIV drugs and investigational HIV drugs.

To keep a comprehensive record, I create a variable to store values for each trial based on the compound references in AIDS*info*. For trials referenced in AIDS*info* by brand names, I

[3] Researchers can retrieve a zipped file with all trials included in XML format or request certain trials with advanced search options. The site has been updated over time and users are recommended to check the latest XML schema and/or data request options (data last accessed: 11/2018).
[4] A descriptive webpage with data element definitions and mandatory information disclosure requirement in trials is available at: https://prsinfo.clinicaltrials.gov/definitions.html.

assign the associated generic name to unify the record. The number of new trials initiated for a compound-year is calculated based on the trial starting date reported and verified in the database. For each trial, I calculate the number of distinct firms collaborating in the trial. I then calculate the number of firms participated in a compound-year by computing the total number of firms collaborated in trials on a given compound in a year. This value captures the intensive margin of firms' trial participation on the compound-year level, including a firm's multiple participations across trials. For investigational trials, there are no generic names to facilitate unification, so I further collect the associated drug classes (mechanisms of action) for related aggregation.

A.3 Drug-year and compound-year panel of HIV drug product approvals

From the Drugs@FDA online database, I request "All Approvals by Month" (approvals, tentative approvals, and supplements) and append the data.[5] To pinpoint all approvals for HIV drugs, I convert the "active ingredients" variable all to lower-case and perform a text match: keep the record if the active ingredients of a drug include any compounds used in HIV treatment. Next, I subset the most relevant approvals—original approval of a drug product produced by a firm (submission code "ORIG-1") instead of supplements to approved applications (submission code including "SUPPL"). As a final check to avoid over-inclusion, I drop a few records of drugs approved for hepatitis C treatment with any antiretroviral compounds. In addition, the WHO pre-qualification program is the other largest drug approval and qualification agency.[6] The list is comprehensive and relatively clean. The other steps follow the same logic as described above.

One must be cautions in calculating the period between the first-ever approval of a drug and its follow-on approvals, either cumulative innovation or straightforward imitation. For standalone drugs with a single compound, each compound has a unique date for its first-ever approval. For drug cocktails, I calculated a first-ever technically feasible date as the date all the underlying compounds are approved in any format. I also record the first actual approval dates for cocktails with existing compounds. These approval dates can help us understand follow-on innovation in multiple respects: approvals of new cocktails and formulations *versus* imitations.

[5] Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Note there are other ways to obtain the underlying data that involve merging across segmented files. I use this conservative data request method due to the lack of detailed instruction concerning alternatives. Last accessed: 1/20/2019.
[6] Available at https://extranet.who.int/prequal/content/prequalified-lists/medicines.

Appendix B: Figures and Tables

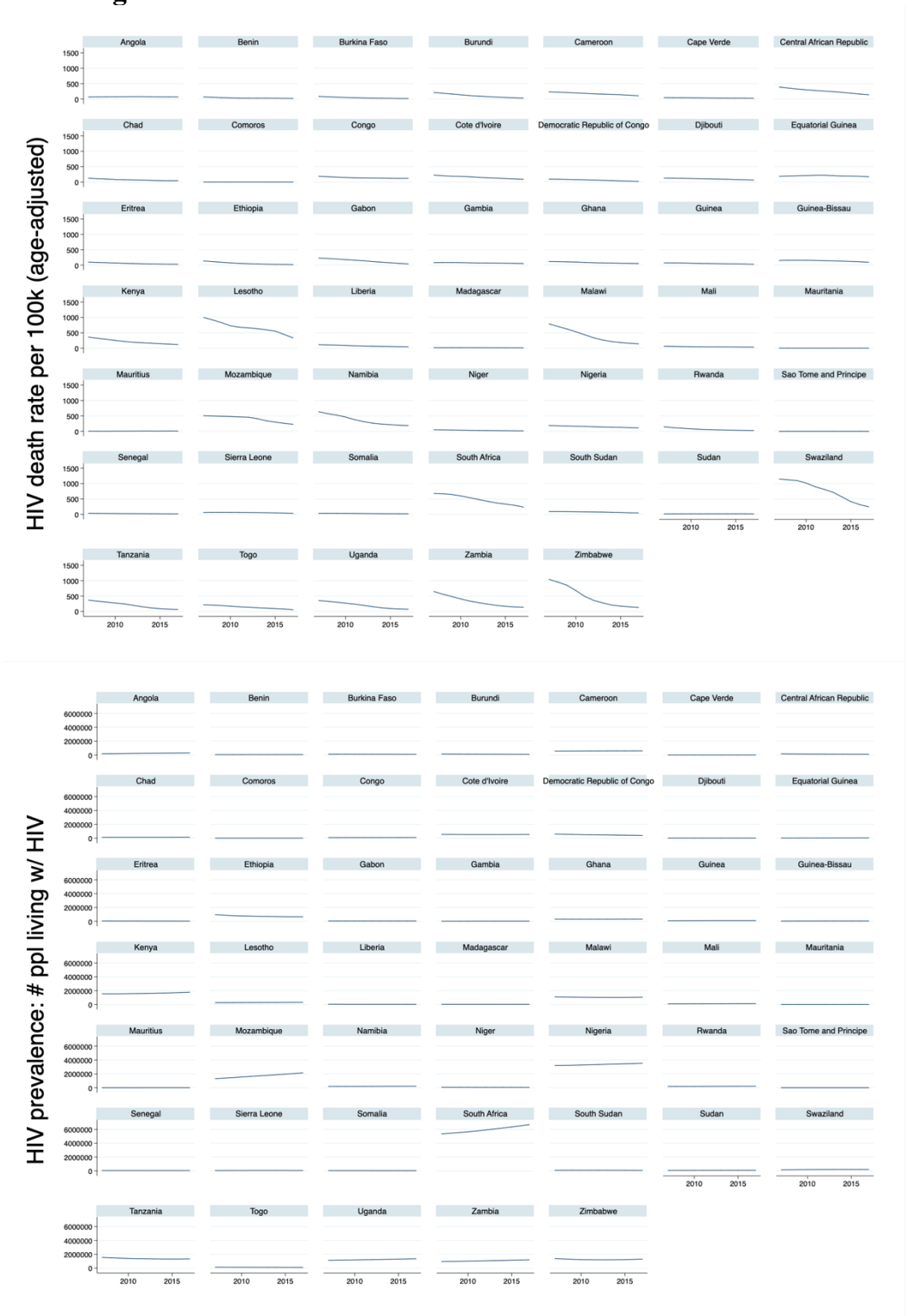


Figure B1: HIV death rate and prevalence, across MPP common territories

Notes: This figure visualize age-adjusted HIV death rate (per 100k population) and HIV prevalence in MPP common sales territory. In particular, there are no disease-related events generating exogenous shocks to HIV/AIDS mortality during the sample periods of my diffusion analysis.

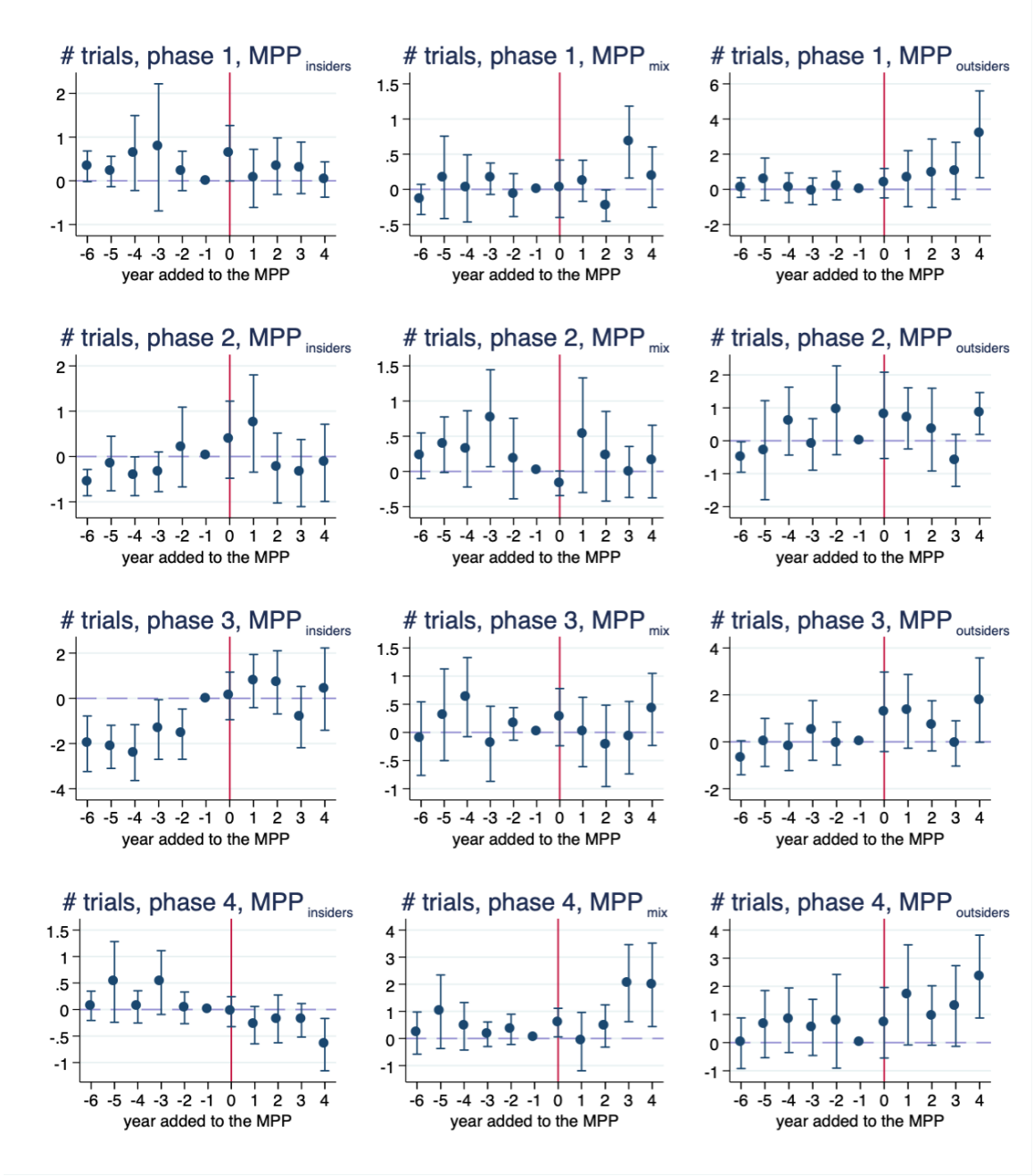


Figure B2: Event Studies for Innovation Analysis: Clinical Trials, by Firm and Phase

Notes: These figures report event-study coefficient estimates using Equation (4). The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before MPP inclusion and 4 years after inclusion. The whiskers correspond to 95% confidence intervals.

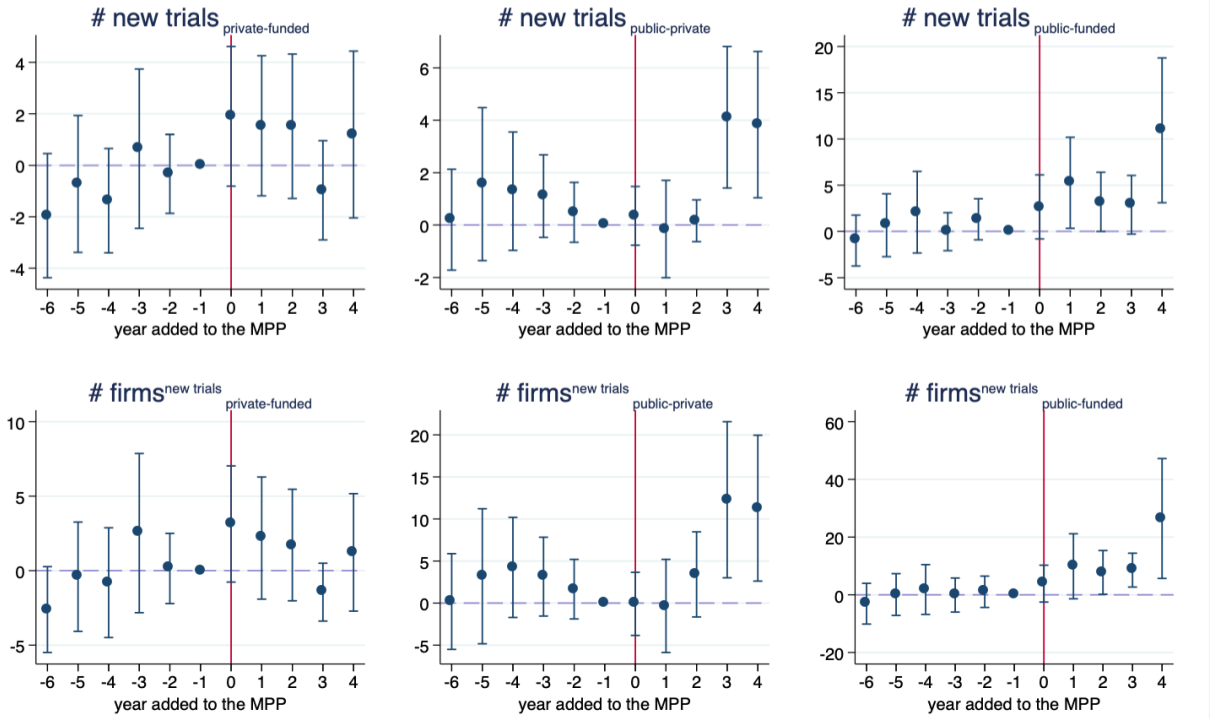


Figure B3: Event Studies for Innovation Analysis: Clinical Trials by Funding Type

Notes: These figures report event-study coefficient estimates using Equation (4). The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before MPP inclusion and 4 years after inclusion. The whiskers correspond to 95% confidence intervals.

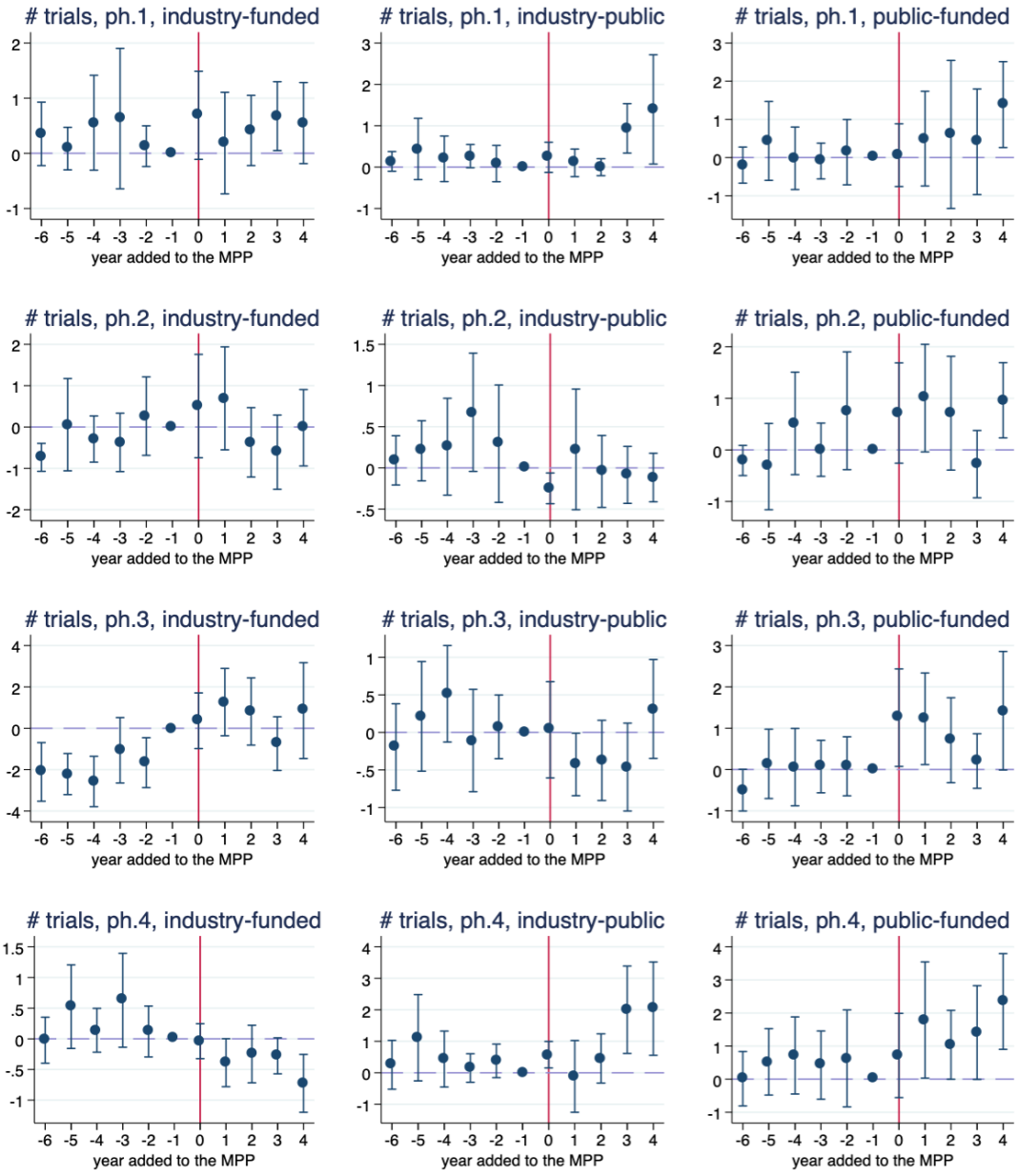
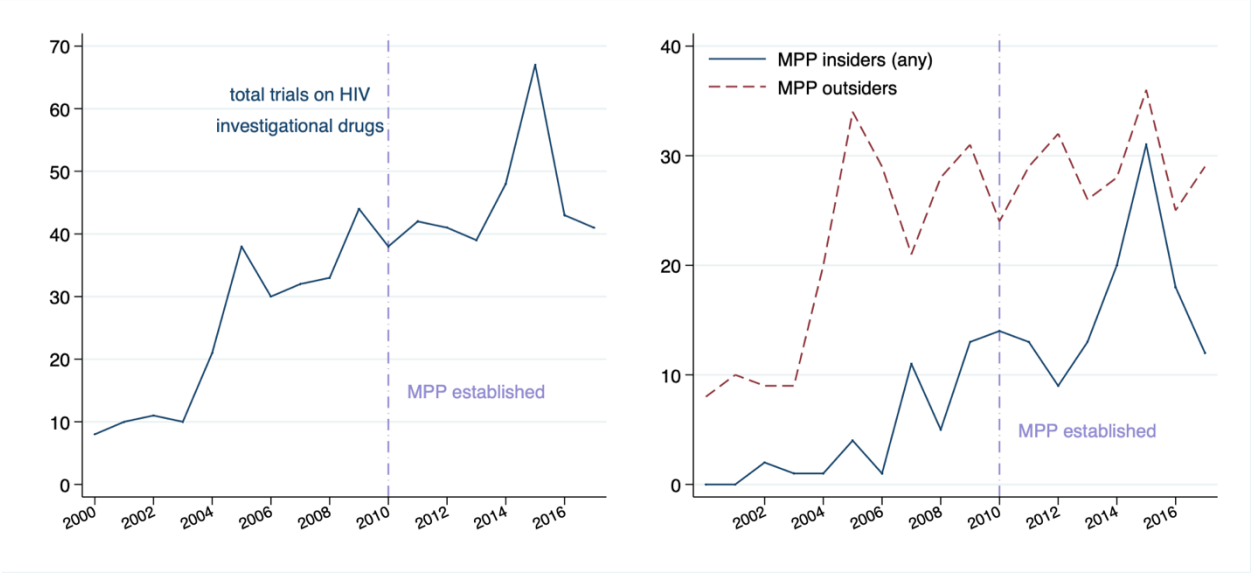
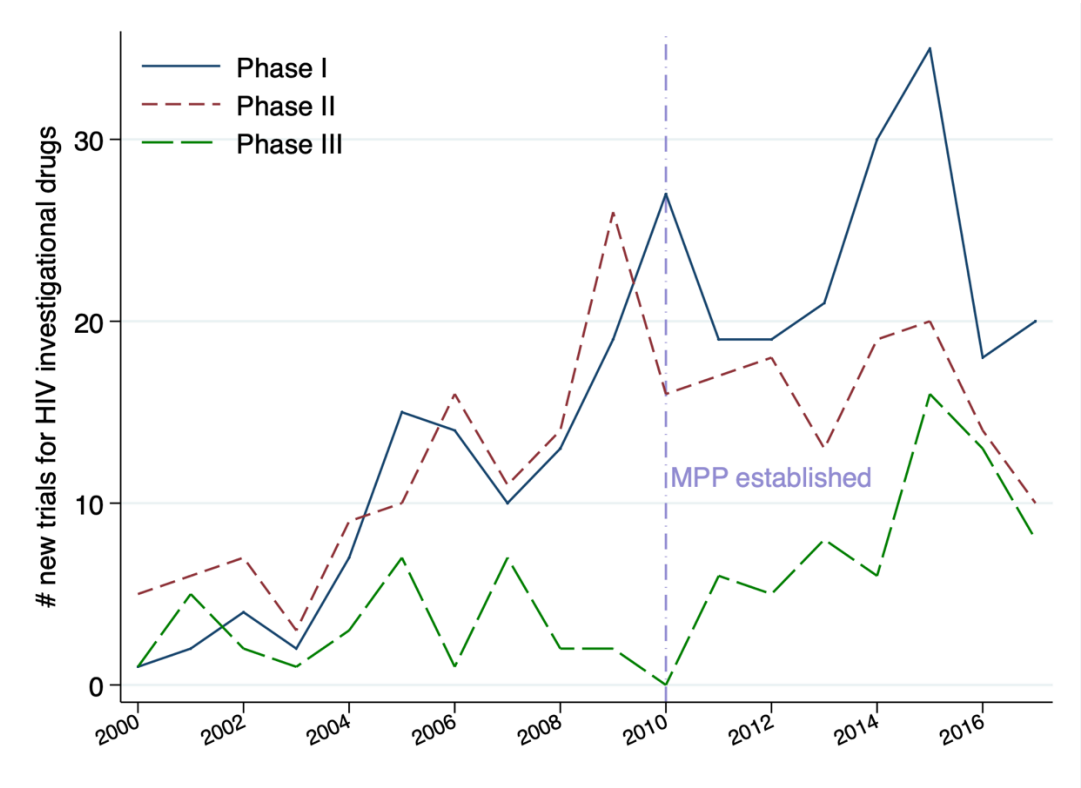


Figure B4: Event Studies for Innovation Analysis: Clinical Trials, by Funder and Phase

Notes: These figures report event-study coefficient estimates using Equation (4). The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before MPP inclusion and 4 years after inclusion. The whiskers correspond to 95% confidence intervals.



(a) Total Trials on HIV Investigational Drugs, and across MPP-affiliation



(b) Investigational Trials by Phases (I-III)

Figure B5: Descriptive Trends: # New Trials on HIV Investigational Drugs (pipeline)

Notes: This graph visualizes the trends of the number of new clinical trials initiated per year on HIV investigational drugs, i.e., new compounds that have not been approved (majority 90%, as in phases I-III) or investigational use of existing drugs (beyond approved antiretrovirals) for new HIV treatment purposes. The vertical dash line indicates the time when the Medicines Patent Pool established.

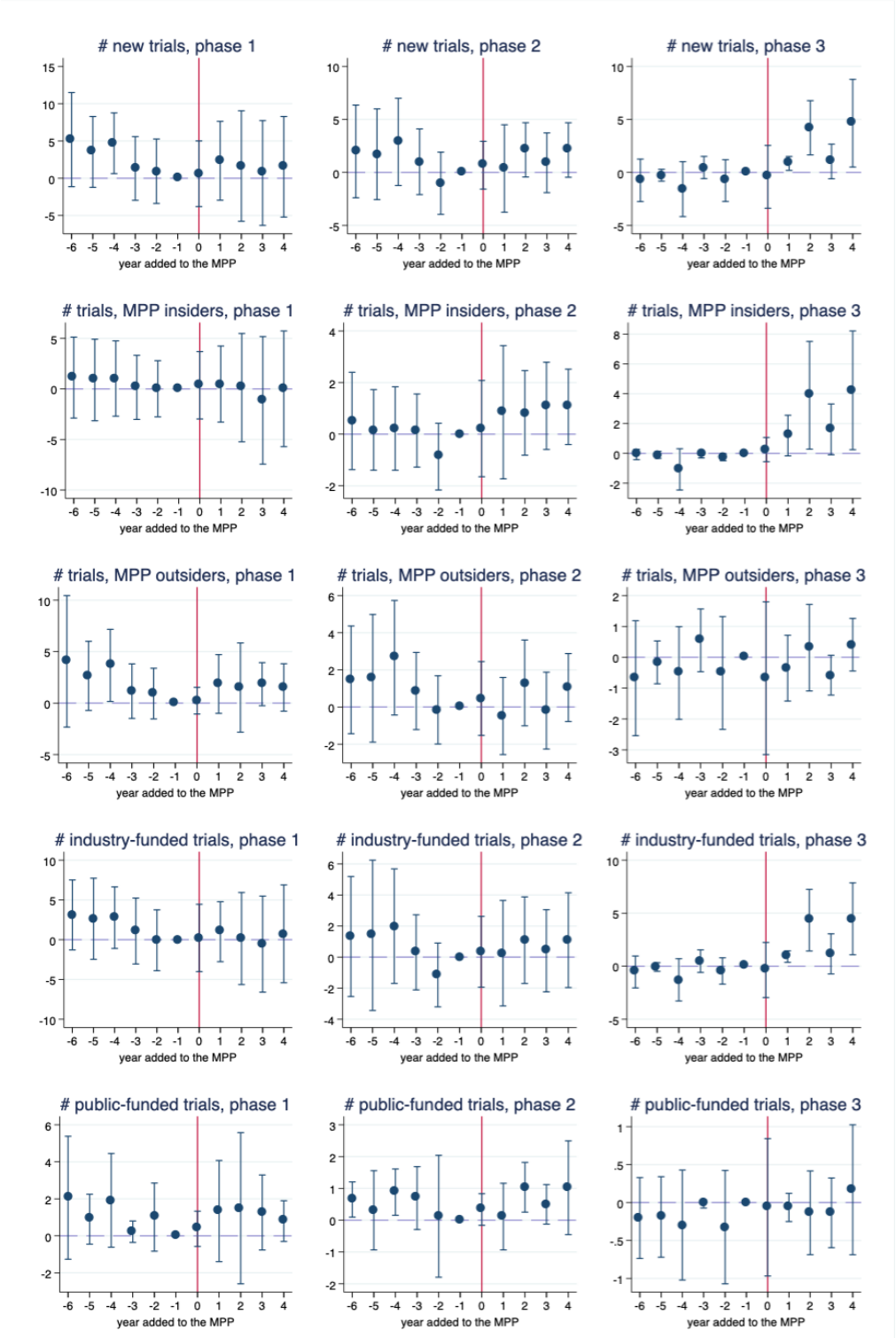


Figure B6: Event Studies: Clinical Trials for HIV Investigational Drugs, by Phase

Notes: These figures report event-study coefficient estimates using Equation (4), at drug class-year level. The dots are point estimates of differences in outcomes between treatment group and control groups 6 years before and 4 years after MPP inclusion. The whiskers correspond to 95% confidence intervals.

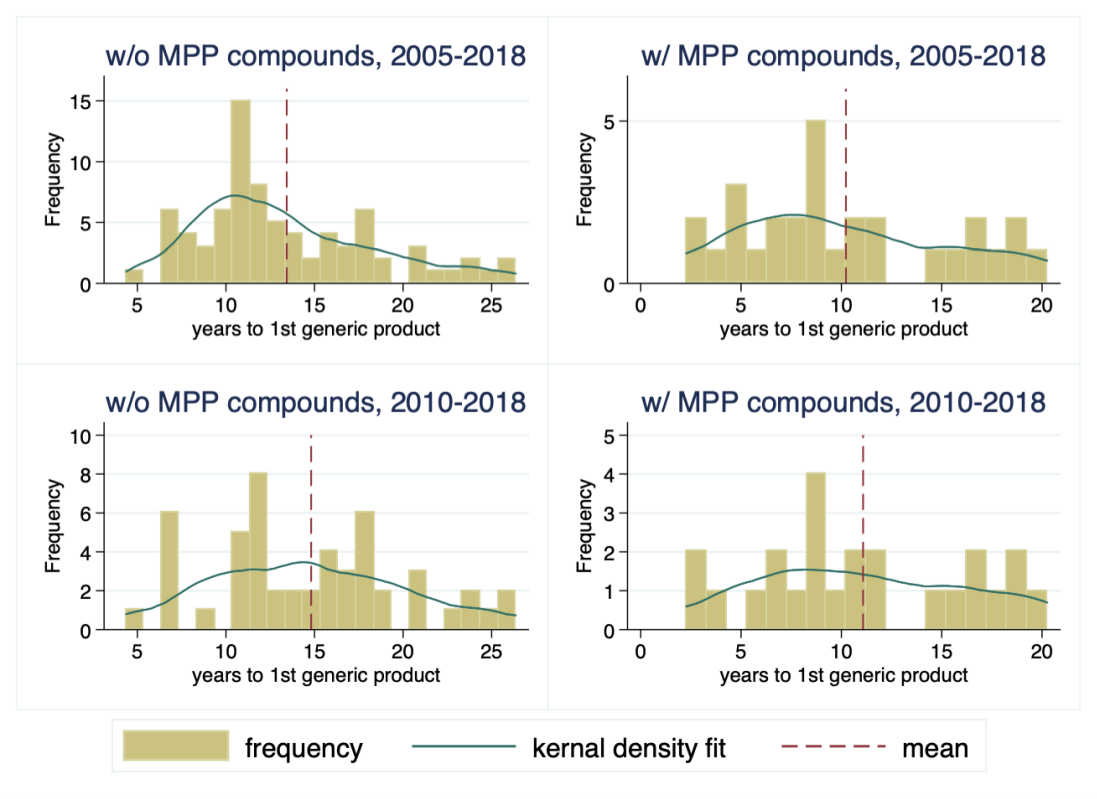


Figure B7: Histograms of Time-to-Generic by MPP Status

Notes: this set of figures pictures the association between time-to-generic and MPP status. Time-to-generic is measured as the years (continuous variable) between when all original compounds were approved and when the first generic (combination) of existing compounds is approved in a given strength-dosage form. The upper panel uses the full sample (2005-2018) and the bottom panel displays the sample where MPP has been established (2010-2018).

Table B1: Regressing MPP Indicator on Observables

	(1)	(2)	(3)
R^2 (two-way s.e.)	0.820	0.821	0.821
R^2 (one-way s.e.)	0.827	0.828	0.828
HIV death rate		-0.000137	-0.000139
(age-adjusted,		(0.000228)	(0.000229)
per 100k pop.)		[7.49e-05]	[7.56e-05]
HIV prevalence		4.10e-08	4.12e-08
		(1.20e-07)	(1.20e-07)
		[3.61e-08]	[3.63e-08]
log(population)		0.193	0.196
		(0.420)	(0.425)
		[0.153]	[0.153]
GDP per capita		7.16e-06	7.09e-06
		(6.02e-06)	(6.32e-06)
		[5.82e-06]	[5.86e-06]
voice and		0.000692	0.000715
accountability		(0.00116)	(0.00126)
		[0.00106]	[0.00106]
political stability		0.000450	0.000438
and lack of		(0.000610)	(0.000636)
violence		[0.000504]	[0.000503]
government		-0.000310	-0.000305
effectiveness		(0.000790)	(0.000876)
		[0.000721]	[0.000722]
regulatory		0.00126*	0.00125
quality		(0.000740)	(0.000763)
		[0.00102]	[0.00102]
rule of law		-0.00105	-0.00106
		(0.000632)	(0.000624)
		[0.000965]	[0.000964]
control of		0.000653	0.000665
corruption		(0.000677)	(0.000713)
		[0.000839]	[0.000835]
$patent_{dct}$			0.0139
			(0.0791)
			[0.0360]
country-drug & year FEs	Y	Y	Y
X_{ct} controls		Y	Y
X_{dct} controls			Y
Observations	7,084	7,084	7,084

Notes: this table reports a diagnostic regression on whether the MPP inclusion decision can be predicted by changes in observed characteristics during my sample period. As shown above, none of the observables are significant predictors of when a drug-country pair is added to the MPP and available for bundled licensing. In addition, the disease rate and prevalence, population, income, and institution-related factors do not effectively increase predictive power of the MPP inclusion indicator, net of fixed effects. Robust standard errors are two-way clustered at the drug and country levels and are reported in parenthesis (). Robust standard errors clustered at the country level is reported in []. Two-way robust p-values: * $p<0.1$.

Table B2: Diffusion Analysis in Alternative Specification

	(1)	(2)	(3)	(4)	(5)	(6)
Dept. Vars.	% generic orders		% generic quantities		# products	
MPP_{dct}	7.526**	7.535**	7.250**	7.254**	0.0623	0.0629
	(3.355)	(3.347)	(3.123)	(3.122)	(0.113)	(0.113)
	[2.700]	[2.700]	[2.734]	[2.736]	[0.0747]	[0.0746]
country-drug FE	Y	Y	Y	Y	Y	Y
country-year FE	Y	Y	Y	Y	Y	Y
X_{dct} control		Y		Y		Y
LHS mean	84.3	84.3	85.6	85.6	1.7	1.7
Observations	7,084	7,084	7,084	7,084	7,084	7,084

Notes: This table reports the results of estimating the MPP causal impact on drug-country-year level generic drug diffusion with an alternative specification. All the country-year level observables are replaced with a full set of country-year level fixed effects. Fixed effects for drug-country pairs are always included. Drug-country-year level effective patent status are included in the last set of columns to demonstrate coefficient stability. Each cell reports the coefficient-of-interest from a separate regression. Robust standard errors reported in () are clustered using two-way clustering at the drug and country levels. Robust standard errors reported in [] are clustered at the country level. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B3: Diffusion Analysis in Sample Territories

	(1)	(2)	(3)	(4)	(5)	(6)
Samples	MPP common territories			MPP ever-covered territories		
Dept. Vars.	% generic	%Q generic	# products	% generic	%Q generic	# products
Panel A: drug-country-year level analysis						
MPP_{dct}	5.011*	5.312**	0.115	7.528**	7.280**	0.0730
	(2.851)	(2.553)	(0.148)	(2.913)	(2.761)	(0.104)
	[3.318]	[3.423]	[0.121]	[2.690]	[2.699]	[0.0802]
LHS mean	88.65	89.74	1.77	85.68	87.00	1.73
# obs.	3,547	3,547	3,547	6,829	6,829	6,829
Panel B: compound-country-year level analysis						
MPP_{act}	8.378**	10.06**	0.228	10.54***	10.89***	0.129
	(3.922)	(3.546)	(0.266)	(3.593)	(3.334)	(0.190)
	[3.867]	[4.084]	[0.143]	[3.064]	[3.213]	[0.111]
LHS mean	84.34	86.33	2.77	81.29	83.53	2.57
# obs.	3,221	3,221	3,221	6,202	6,202	6,202
FEs	Y	Y	Y	Y	Y	Y
X_{ct} control	Y	Y	Y	Y	Y	Y
X_{dct} control	Y	Y	Y	Y	Y	Y

Notes: This table reports the results of estimating equation (1) in subsamples of MPP common territories (countries in every drug's territory) and MPP ever-covered territories (eligible for at least one drug). Each cell reports the coefficient-of-interest from a separate regression. Fixed effects for drug-country pairs (Panel A), compound-country pairs (Panel B), and years are always included. The specification also controls drug-country-year level effective patent status and country-year level observables. Robust standard errors reported in () are clustered using two-way clustering at the drug and country levels. Robust standard errors reported in [] are clustered at the country level. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B4: Diffusion Analysis in Sample Drugs

Samples	(1) drug class in 1st pool addition	(2) drop one drug class	(3) drop U.S. not recommended	(4) drugs approved since 1996	(5) drugs by MPP insider firms
Panel A: % generic orders as dependent variable					
MPP_{dct}	11.13***	7.030**	7.415**	6.848**	7.304**
	(3.586)	(2.951)	(2.967)	(2.938)	(2.842)
	[3.471]	[2.773]	[2.687]	[2.705]	[2.706]
LHS mean	94.80	82.77	83.92	83.41	86.64
# Obs.	4,463	5,828	6,316	5,786	6,127
Panel B: % generic quantity ordered (patient year) as dependent variable					
MPP_{dct}	10.32***	6.520**	7.234**	6.620**	7.145**
	(3.366)	(2.874)	(2.838)	(2.823)	(2.727)
	[3.335]	[2.781]	[2.693]	[2.702]	[2.709]
LHS mean	95.44	84.11	85.25	84.64	88.13
# Obs.	4,463	5,828	6,316	5,786	6,127

Notes: This table reports the results of estimating equation (1) in subsamples changing drugs in the comparison groups. Each cell reports the coefficient-of-interest from a separate regression. Fixed effects for drug-country pairs and years are always included. The specification also controls drug-country-year level effective patent status and country-year level observables. Robust standard errors reported in () are clustered using two-way clustering at the drug and country levels. Robust standard errors reported in [] are clustered at the country level. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B5: Subsample Diffusion Analysis: Ever vs Never Patented

	(1)	(2)	(3)	(4)	(5)	(6)
Dept. Vars.	% generic orders (#)		% generic ordered (p.p.y)		# product-manufacturers	
Subsample	$Pat.$=1	$Pat.$=0	$Pat.$=1	$Pat.$=0	$Pat.$=1	$Pat.$=0
Panel A: drug-country-year subsamples						
MPP_{dct}	20.65**	4.360	18.03*	4.675*	-0.0122	0.0887
	(9.771)	(2.696)	(9.321)	(2.709)	(0.0886)	(0.126)
	[7.667]	[2.678]	[7.079]	[2.770]	[0.118]	[0.0924]
LHS mean	83.73	84.54	84.42	86.12	1.75	1.70
Observations	2,029	5,055	2,029	5,055	2,029	5,055
Panel B: compound-country-year subsamples						
MPP_{act}	19.85***	4.601	17.29***	6.699	-0.193	0.372*
	(3.665)	(3.735)	(3.600)	(3.962)	(0.176)	(0.198)
	[4.321]	[3.537]	[4.351]	[3.941]	[0.152]	[0.176]
LHS mean	84.19	85.54	84.99	87.33	1.75	1.72
Observations	3,328	3,157	3,328	3,157	3,328	3,157
two sets of FEs	Y	Y	Y	Y	Y	Y
X_{ct} control	Y	Y	Y	Y	Y	Y
$X_{d(a)ct}$ control	Y		Y		Y	

Notes: This table reports the results of the model using equation (1), across subsamples in countries where a drug (Panel A) or compound (Panel B) is ever patented or never patented during my sample period. Each cell reports the coefficient-of-interest from a separate regression. The specification also controls effective patent status and country-year level observable factors. Fixed effects for drug(compound)-country pairs and years are always included. Robust standard errors are two-way clustered at the compound and country levels and are reported in parenthesis (). Robust standard errors clustered at the country level is reported in []. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B6: Diffusion Analysis: Reduced-form Price and Quantity Regressions

	(1)	(2)	(3)	(4)	(5)	(6)
	Prices (Per Patient Year)			Quantity (Patient-Year Served)		
Dept. Vars.	Overall	Generic	Branded	Overall	Generic	Branded
MPP_{dct}	-105.8	-86.73***	91.51	294.2	464.0	-169.8**
	(79.15)	(28.48)	(139.9)	(2,279)	(2,270)	(77.96)
	[46.09]	[23.82]	[202.0]	[1,000]	[1,042]	[134.2]
FEs	Y	Y	Y	Y	Y	Y
X_{ct} control	Y	Y	Y	Y	Y	Y
X_{dct} control	Y	Y	Y	Y	Y	Y
LHS mean	375.17	158.37	1696.03	6289.15	6198.92	90.23
# Obs.	7,084	6,167	1,351	7,084	7,084	7,084

Notes: This table reports the results of estimating equation (1) using prices and quantities as outcomes. The problems and measurement issues with direct price and quantity regressions are discussed in section 3.2 and footnotes 18-19. Each cell reports the coefficient-of-interest from a separate regression. Fixed effects for drug-country pairs and years are always included. The specification also controls drug-country-year level effective patent status and country-year level observables. The LHS mean for branded quantity is small because of the zeros exist in many units; the mean for non-zeros branded quantity is 473.12 instead. Robust standard errors reported in () are clustered using two-way clustering at the drug and country levels. Robust standard errors reported in [] are clustered at the country level. Two-way robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B7: Innovation Analysis - Clinical Trials: by Funding Types

	(1)	(2)	(3)	(4)	(5)	(6)
	# new HIV trials funded by			# firms in new HIV trials funded by		
Dept. Vars.	industry	ind.&pub.	public	industry	ind.&pub.	public
Total						
MPP_{at}	2.296*	0.898	4.899*	2.750*	3.231	11.77*
	(1.227)	(1.026)	(2.759)	(1.572)	(3.082)	(6.144)
LHS mean	3.417	1.996	4.663	4.494	5.880	10.36
Panel A. Phase I						
MPP_{at}	0.197	0.313	0.604	0.251	0.930	1.133
	(0.199)	(0.201)	(0.532)	(0.292)	(0.608)	(0.924)
LHS mean	0.546	0.209	0.596	0.774	0.546	0.985
Panel B. Phase II						
MPP_{at}	0.504	-0.244**	0.665**	0.556	-0.852**	1.416*
	(0.397)	(0.113)	(0.275)	(0.473)	(0.328)	(0.694)
LHS mean	0.806	0.291	0.813	1.007	0.941	1.756
Panel C. Phase III						
MPP_{at}	2.275***	-0.129	1.228***	2.743***	-0.664*	2.506*
	(0.721)	(0.0981)	(0.434)	(0.900)	(0.358)	(1.288)
LHS mean	1.524	0.393	0.969	1.943	1.256	2.772
Panel D. Phase IV						
MPP_{at}	-0.424**	0.574	1.174	-0.547***	2.352	2.735*
	(0.164)	(0.481)	(0.805)	(0.185)	(1.584)	(1.601)
LHS mean	0.354	0.796	1.313	0.444	2.402	2.731

Notes: This table reports the results of estimating equation (3). The number of observations is always 540 given the balanced panel data structure by design. Each cell reports the coefficient-of-interest from a separate regression. Industry-funded means the trial is 100% industry funded, while "ind.&pub." means the trial is private-public jointly funded. Controls variables include FDA approval status, patent status, and fixed effects for compounds and years. Robust standard errors are clustered at the compound level and are reported in parenthesis. Robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B8: Innovation Analysis - Clinical Trials on HIV Investigational Drugs

Dept. Vars.	(1) # new trials	(2) # trials, MPP insiders	(3) # trials, MPP outsider	(4) # industry-funded trials	(5) # public-funded trials
Total					
MPP_{at}	4.230	2.959	1.271	2.871*	1.360
	(2.254)	(1.529)	(1.071)	(1.229)	(1.072)
LHS mean	8.58	3.30	5.29	5.67	2.91
Panel A. Phase I					
MPP_{at}	-0.582	-0.440	-0.142	-0.823	0.241
	(1.305)	(0.855)	(0.762)	(0.918)	(0.605)
LHS mean	3.45	0.81	2.64	1.95	1.51
Panel B. Phase II					
MPP_{at}	0.553	0.888	-0.335	0.280	0.273
	(0.474)	(0.629)	(0.444)	(0.267)	(0.227)
LHS mean	3.23	1.18	2.06	2.34	0.89
Panel C. Phase III					
MPP_{at}	2.770*	2.504*	0.266	2.599**	0.170
	(1.230)	(1.097)	(0.284)	(1.051)	(0.195)
LHS mean	1.98	1.37	0.60	1.81	0.17

Notes: This table reports the results of estimating equation (3), at drug class-year level. The number of observations is always 91 with the balanced panel data structure. There are totally seven drug classes in the analysis, where six of them are drug classes with existing compounds approved and one drug class capturing the set of new drug classes without existing products for HIV treatment, such as gene therapy, biological antibody, etc. Each cell reports the coefficient-of-interest from a separate regression. Industry-funded means the trial at least partly funded by industry. Controls variables include FDA approval status, patent status, and fixed effects for compounds and years. Robust standard errors are clustered at the drug class level and are reported in parenthesis. Robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B9: 1st Time New HIV Drug Approvals with Existing Compounds

drug	firm	ymd	branded compound owners	#	type
Panel A: 1st Time New Drug Approvals by Branded Firms					
3tc+zdv	ViiV	1997.09.26	ViiV+ViiV	1	cocktail
abc+3tc+zdv	ViiV	2000.11.14	ViiV+ViiV+ViiV	1	cocktail
abc+3tc	ViiV	2004.08.02	ViiV+ViiV	1	cocktail
ftc+tdf	Gilead	2004.08.02	Gilead+Gilead	1	cocktail
efv+ftc+tdf	Gilead	2006.07.12	BMS+Gilead+Gilead	2	cocktail
ftc+rpv+tdf	Gilead	2011.08.10	Gilead+Janssen+Gilead	2	cocktail
abc+dtg+3tc	ViiV	2014.08.22	ViiV+ViiV+ViiV	1	cocktail
cobi	Gilead	2014.09.24	Gilead	1	standalone
evg	Gilead	2014.09.24	Gilead	1	standalone
atv+cobi	BMS	2015.01.29	BMS+Gilead	2	cocktail
cobi+drv	Janssen	2015.01.29	Gilead+Janssen	2	cocktail
3tc+ral	Merck	2015.02.06	ViiV+Merck	2	cocktail
ftc+rpv+taf	Gilead	2016.03.01	Gilead+Janssen+Gilead	2	cocktail
ftc+taf	Gilead	2016.04.04	Gilead+Gilead	1	cocktail
taf	Gilead	2016.11.10	Gilead	1	standalone
dtg+rpv	ViiV	2017.11.21	ViiV+Janssen	2	cocktail
cobi+drv+ftc+taf	Janssen	2018.07.17	Gilead+Janssen+Gilead+Gilead	2	cocktail
Panel B: 1st Time New Drug Approvals by Generics					
3tc+nvp+zdv	Pharmacare	2005.01.24	ViiV+BI+ViiV	2	cocktail
3tc+zdv+efv	Aurobindo	2006.03.06	ViiV+ViiV+BMS	2	cocktail
3tc+d4t+nvp	Cipla	2006.11.17	ViiV+BMS+BI	3	cocktail
3tc+d4t	Cipla	2007.01.19	ViiV+BMS	2	cocktail
d4t+3tc+efv	Strides	2007.06.01	BMS+ViiV+BMS	2	cocktail
3tc+tdf	Hetero	2009.11.05	ViiV+Gilead	2	cocktail
efv+3tc+tdf	Mylan	2010.10.25	BMS+ViiV+Gilead	3	cocktail
3tc+tdf+nvp	Matrix Labs	2011.09.08	ViiV+Gilead+BI	3	cocktail
atv+r	Matrix Labs	2011.11.18	BMS+AbbVie	2	cocktail
atv+r+3tc+zdv	Mylan	2014.09.04	BMS+AbbVie+ViiV+ViiV	3	cocktail
ftc+tdf+nvp	Mylan	2014.09.12	Gilead+Gilead+BI	2	cocktail
dtg+3tc+tdf	Mylan	2017.08.02	ViiV+ViiV+Gilead	2	cocktail
dtg+ftc+taf	Mylan	2018.02.09	ViiV+Gilead+Gilead	2	cocktail

Notes: This table summarizes the first approvals of HIV drugs based on existing compounds, reported for originators and generics in different panels and chronologically ordered within each panel. These first-time follow-on new approvals are typically for drug cocktails, except in three cases where the originators first created new compounds approved as part of a cocktail before the new standalone compound is approved. BI stands for Boehringer Ingelheim. The column of # count distinct brand owners of each underlying drug. Note that first-time new generic cocktails are not reported before 2005 because of a combination of international patent enforcement in India since then and new FDA approval initiatives. This table, together with Table 1, complete the list of first-approval information for all HIV drugs by end of 2018.

Table B10: Survival and Regression Analyses on Time-to-Generic

	(1)	(2)	(3)	(4)
Panel A: Cox Proportional Hazard Model				
MPP	0.532**	0.647**	1.019**	0.371
	(0.222)	(0.257)	(0.397)	(0.472)
Panel B: Regression Analysis				
MPP	-3.204***	-3.727***	-1.827	-0.157
	(1.117)	(1.317)	(1.102)	(1.738)
sample	2005-2018	2010-2018	2005-2018	2010-2018
year FE			Y	Y
drug class FE			Y	Y
LHS mean	12.57	13.62	12.57	13.62
Observations	108	75	108	75

Notes: this table reports results of analysis the association between time-to-generic and MPP status. Time-to-generic is measured as the years (continuous variable) between when all original compounds were approved and when the first generic (combination) of existing compounds is approved in a given strength-dosage form. The main variable of interest is an indicator variable of whether a first approved generic product has any MPP compound. Robust p-values: *** p<0.01, ** p<0.05, * p<0.1.

Table B11: Count Model Results for Innovation Analysis – Drug Approvals

	(1) # approvals	(2) # appr.^{generic}	(3) # appr.^{branded}
Panel A: drug-year new approvals			
MPP_{dt}	1.014***	1.212***	0.772
	(0.262)	(0.287)	(0.786)
LHS mean	0.70	13.22	1.95
Observations	798	518	518
Panel B: compound-year new approvals			
MPP_{at}	1.067***	1.115***	0.969**
	(0.227)	(0.259)	(0.477)
LHS mean	2.28	39.95	4.29
Observations	378	266	336
FEs	Y	Y	Y
controls	Y	Y	Y

Note: This table reports innovation results in drug approvals using conditional negative binomial regressions. Fixed effects are at drug and year levels for Panel A and at compound and year levels for Panel B. I run this exercise to test whether drug approval results in Table 6 (using linear models) are robust to using count data models. The number of observations dropped in columns (2) – (3) to adjust for different drug approved by generics and branded—drugs/compounds always have zero approvals by the corresponding firm type create no variation and dropped to account for different focus in actual investment areas.

Table B12: Results from the Demand Estimation

	(1) OLS	(2) Nested logit	(3) Logit
$\ln(s_{j\|g(j)})$	0.702***	0.862***	
	(0.0144)	(0.0814)	
p_j	-0.137***	-1.946***	-3.483***
	(0.0227)	(0.243)	(0.441)
drug age (U.S. appr.)	0.0119*	-0.196***	-0.449***
	(0.00637)	(0.0404)	(0.0838)
prod. variety	0.345***	-0.00503	0.434**
	(0.0335)	(0.122)	(0.179)
regulatory quality	0.00194	-0.0646***	-0.121***
	(0.00558)	(0.0208)	(0.0378)
rule of law	0.0226***	0.0507***	0.0532*
	(0.00546)	(0.0162)	(0.0291)
control of corruption	-0.00783*	0.0361**	0.0785***
	(0.00446)	(0.0148)	(0.0272)
Kleibergen-Paap F statistic		19.50	
1st stage $(s_{j\|g})$		104.42	
1st stage (p_j)		46.91	54.56
country FE	Y	Y	Y
year FE	Y	Y	Y
X_j controls	Y	Y	Y
Observations	7,084	7,084	7,084

Note: This table presents results of estimating the nested logit demand model as in equation (6) and compares it with OLS and plain logit. The instruments for conditional market share and price are: (1) whether a drug is effectively patented in the country-year, (2) the number of manufacturers for the same drug in a country-year, and (3) the number of competing products, i.e., drug product-firm combinations for other drugs in the same drug class. IVs for the plain logit do not include the second instrument to avoid over-identification. Only main parameters of interests are reported for simplicity. Observable controls, X_j include within-drug product variety in a country-year, number of compounds within a drug, number of years since a drug's U.S. approval, country-year level HIV prevalence and age-adjusted death rates, institutional factors (i.e., the six world governance indicators), log(population) and GDP per capita. The excluded instruments are at drug-country-year level: patent status, number of competitors and number of close competitors in the same drug class. The first-stage statistics displayed immediately under coefficients-of-interests are the Kleibergen-Paap F statistic that robust to heteroskedasticity. The first-stage F statistics for each endogenous variable is the Sanderson-Windmeijer multivariate F test of excluded instruments. Standard errors are clustered at drug-country level. Robust p-value: *** p<0.01, ** p<0.05, * p<0.1.

Table B13: Estimations of Pricing Equations

Dept. var: marginal cost ($)	(1) MC pricing flat MC	(2) Bertrand-Nash Oligopoly single-prod. firm	(3) Bertrand-Nash Oligopoly multi-prod. firm
MPP_j	-0.642***	-1.908***	-1.952***
	(0.112)	(0.524)	(0.539)
Q_j		3.60e-07***	3.83e-07***
		(1.27e-07)	(1.31e-07)
#variety	-0.209***	0.445*	0.495**
	(0.0616)	(0.234)	(0.244)
$\#firms_{dct}$	-0.310***	-1.584***	-1.662***
	(0.0398)	(0.480)	(0.494)
$Patent_{dct}$	-0.173	0.210	0.198
	(0.192)	(0.255)	(0.262)
year FE	Y	Y	Y
country FE	Y	Y	Y
X_j controls	Y	Y	Y
Kleibergen-Paap rk Wald F-stat		16.66	16.66
Observations	7,084	7,084	7,084

Notes: this table reports the results from estimating competitive marginal cost pricing and oligopolistic pricing on the drug-country-year diffusion sample using equations (8) and (12), respectively. Only main parameters of interests are reported for simplicity. X_j is a vector of drug-country-year level controls including whether a drug is effectively patented in a country-year, number of drug products and competitors for a drug in a country-year, country-year level HIV prevalence and age-adjusted death rates, population, GDP per capita, and institutional factors. Country and year fixed effects are always included. Quantity variable is instrumented by the number of competing products in the same drug class within a market (country-year). Standard errors are clustered at drug-country level to allow for arbitrary autocorrelation within a drug-country pair. The first-stage F-statistics reported are adjusted for heteroskedasticity clustering. Robust p-value: *** p<0.01, ** p<0.05, * p<0.1.

Table B14: Sensitivity Analysis of Demand Estimation to Market Size

	(1)	(2)	(3)	(4)	(5)
market size measures	10% population	30% population	50% population	70% population	pop*pr. HIV $death_{15to59}$
$\ln(s_{j\|g})$	0.862***	0.861***	0.861***	0.861***	0.863***
	(0.0826)	(0.0812)	(0.0810)	(0.0809)	(0.0811)
p_j	-1.968***	-1.942***	-1.938***	-1.937***	-1.941***
	(0.247)	(0.243)	(0.242)	(0.242)	(0.243)
1st stage joint	19.50	19.50	19.50	19.50	19.50
1st stage ($s_{j\|g}$)	104.42	104.42	104.42	104.42	104.42
1st stage (p_j)	46.91	46.91	46.91	46.91	46.91
country FE	Y	Y	Y	Y	Y
year FE	Y	Y	Y	Y	Y
X_j controls	Y	Y	Y	Y	Y
Observations	7,084	7,084	7,084	7,084	7,084

Note: This table presents results of estimating the nested logit demand model as in equation (6), and each column demonstrates robustness of the estimation to alternative market size measures. Observable controls, X_j include within drug product variety in a country-year, number of compounds within a drug, number of years since a drug's U.S. approval, country-year level HIV prevalence and age-adjusted death rates, institutional factors (i.e., the six world governance indicators), log(population) and GDP per capita. The excluded instruments are at drug-country-year level: patent status, number of competitors and number of close competitors in the same drug class. The first-stage statistics displayed immediately under coefficients-of-interests are the Kleibergen-Paap F statistic that robust to heteroskedasticity. The first-stage F statistics for each endogenous variable is the Sanderson-Windmeijer multivariate F test of excluded instruments. Each j denotes drug-country (dc) for simplicity in notations. Robust p-value: *** p<0.01, ** p<0.05, * p<0.1.

Table B15: Pool Operating Expenses from Financial Statement

time period	use of the funds (raw $/SFr.)	CHF/USD (annual)	MPP costs ($ current)
2010.7-2011.12	$ -4,254,666	NA	-4,254,666
2012.1-2012.12	SFr. -4,086,052	0.9377	-4,357,526
2013.1-2013.13	SFr. -4,271,467	0.9269	-4,608,336
2014.1-2014.12	SFr. -4,332,580	0.9147	-4,736,613
2015.1-2015.12	SFr. -4,759,073	0.9628	-4,942,951
2016.1-2016.12	SFr. -4,568,395	0.9848	-4,638,906
2017.1-2017.12	SFr. -4,974,406	0.9842	-5,054,263

Notes: I obtain the MPP operating costs from the financial statements in the "Annual Reports" from the MPP. Specifically, I use "use of the funds" within the "statement of changes in capital" to measure the costs of this platform. This calculation is similar to manually summing up the personnel and administrative costs (the two main categories of MPP expenditure). The annual foreign exchange rate of Swiss Francs to one U.S. Dollar is provided by the Federal Reserve Bank of St. Louis.

Appendix C: Mathematical Appendix

C.1 Derive price substitution matrix

I derive substitution matrix by taking partial derivatives of market share *k* w.r.t price *j*. Here, I derive the general expression for the price derivatives from the demand side. With information from the supply-side, the relevant elements from the matrix is the products owned by the same branded firm in a given market (i.e., subset products owned by the same firm).

Given that

$$\hat{s}_j = \frac{e^{\frac{\delta_j}{1-\sigma}}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma}}{\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}},\ \hat{s}_k = \frac{e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}}{\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}},\ \text{and}\ \hat{s}_{k|g} = \frac{e^{\frac{\delta_k}{1-\sigma}}}{\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}} = \frac{\hat{s}_k}{\hat{s}_g}$$

$$\frac{ds_k}{dp_j} = \frac{d}{dp_j}\left[\frac{e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}}{\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}}\right]$$

$$= \frac{\left(e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)'\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right] - e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]'}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]^2}$$

$$= \frac{\overbrace{\left(e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)'}^{\equiv A}}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} - \frac{e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\overbrace{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]'}^{\equiv B}}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]^2}$$

$$= \frac{A}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} - \hat{s}_k \times \frac{B}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]}, \quad \text{eqn. (III.1)}$$

where $A \equiv \left(e^{\frac{\delta_k}{1-\sigma}}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)' = \left(e^{\frac{\delta_k}{1-\sigma}}\right)'\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma} + e^{\frac{\delta_k}{1-\sigma}}\left(\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)'$

and $B = \left[\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]'\ if\ g(k) = g(j);\ = \left[\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]'\ if\ g(k) \neq g(j).$

In the following part, I derive the analytic forms of the price derivatives for three cases. In each case, I first derive the expressions for A and B and then plug them back into eqn. (III.1).

Simplification note: that $\left(e^{\frac{\delta_k}{1-\sigma}}\right)' = 0$ if $j \neq k$ and $\left(\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)' = 0$ if $g(j) \neq g(k)$.

Case 1: $j=k$ (diagonal elements)

$$A = \left(e^{\frac{\delta_j}{1-\sigma}}\right)' \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} + e^{\frac{\delta_j}{1-\sigma}} \left(\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma}\right)'$$

$$= -\frac{\alpha}{1-\sigma} e^{\frac{\delta_j}{1-\sigma}} \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} + e^{\frac{\delta_j}{1-\sigma}} \times \frac{\alpha\sigma}{(1-\sigma)} \times \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} \times \frac{\overbrace{e^{\frac{\delta_j}{1-\sigma}}}^{=\hat{s}_{j|g}}}{\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}}$$

$$= -\frac{\alpha}{1-\sigma} e^{\frac{\delta_j}{1-\sigma}} \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} \left(1-\sigma\hat{s}_{j|g}\right)$$

$$= -\frac{\alpha}{1-\sigma} \hat{s}_j \left(1-\sigma\hat{s}_{j|g}\right) \times \left[\sum_{g=0}^{G} \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]$$

$$B = \left[\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]' = (1-\sigma)\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} \left(e^{\frac{\delta_j}{1-\sigma}}\right)'$$

$$= -\alpha e^{\frac{\delta_j}{1-\sigma}} \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma} = -\alpha\hat{s}_j \times \left[\sum_{g=0}^{G} \left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]$$

Plug back to equation (III.1),

$$\frac{ds_j}{dp_j} = \frac{-\frac{\alpha}{1-\sigma}\hat{s}_j\left(1-\sigma\hat{s}_{j|g}\right)\times\left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} - \hat{s}_j \times \frac{-\alpha\hat{s}_j\times\left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]}$$

$$= -\frac{\alpha}{1-\sigma}\hat{s}_j\left(1-\sigma\hat{s}_{j|g}\right) - \alpha\hat{s}_j\hat{s}_j$$

$$= -\alpha\hat{s}_j\left(\frac{1}{1-\sigma} - \frac{\sigma}{1-\sigma}\hat{s}_{j|g} + \hat{s}_j\right)$$

Case 2: $j \neq k, g(j) = g(k)$ (different alternatives within the same nest)

$$A = \overbrace{\left(e^{\frac{\delta_k}{1-\sigma}}\right)'}^{=0} \left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma} + e^{\frac{\delta_k}{1-\sigma}} \left(\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)'$$

$$= e^{\frac{\delta_k}{1-\sigma}}(-\sigma)\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma-1} e^{\frac{\delta_j}{1-\sigma}} \times \frac{-\alpha}{1-\sigma}$$

$$= \frac{\alpha\sigma}{1-\sigma} \times \underbrace{\frac{e^{\frac{\delta_k}{1-\sigma}}}{\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}}}_{\hat{s}_{k|g}} \times \underbrace{e^{\frac{\delta_j}{1-\sigma}} \times \left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}}_{\hat{s}_j\times\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}} = \frac{\alpha\sigma}{1-\sigma}\hat{s}_{k|g}\hat{s}_j \times \sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}$$

$$B = \left[\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]' = (1-\sigma)\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\left(e^{\frac{\delta_j}{1-\sigma}}\right)'$$
$$= -\alpha\hat{s}_j \times \left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]$$

Plug back to equation (III.1),

$$\frac{ds_k}{dp_j} = \frac{\frac{\alpha\sigma}{1-\sigma}\hat{s}_{k|g}\hat{s}_j \times \sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} - \hat{s}_k \times \frac{-\alpha\hat{s}_j \times \left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} = \alpha\hat{s}_j\left(\frac{\sigma}{1-\sigma}\hat{s}_{k|g} + \hat{s}_k\right)$$

Case 3: $j \neq k, g(j) \neq g(k)$ (different alternatives in different nests)

$$A = \overbrace{\left(e^{\frac{\delta_k}{1-\sigma}}\right)'}^{=0}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma} + e^{\frac{\delta_k}{1-\sigma}}\overbrace{\left(\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{-\sigma}\right)'}^{=0} = 0$$

$$B = \left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]' = \left[\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]' = -\alpha\hat{s}_j \times \left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]$$

Plug back to equation (III.1),

$$\frac{ds_k}{dp_j} = -\hat{s}_k \times \frac{-\alpha\hat{s}_j \times \left[\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}\right]}{\left[\sum_{g=0}^{G}\left(\sum_{k\in g} e^{\frac{\delta_k}{1-\sigma}}\right)^{1-\sigma}\right]} = \alpha\hat{s}_j\hat{s}_k$$

Summary: Finally, I summarize the three cases together.

$$\frac{ds_k}{dp_j} = \begin{cases} -\alpha\hat{s}_j\left(\frac{1}{1-\sigma} - \frac{\sigma}{1-\sigma}\hat{s}_{j|g} + \hat{s}_j\right) & j = k \\ \alpha\hat{s}_j\left(\frac{\sigma}{1-\sigma}\hat{s}_{k|g} + \hat{s}_k\right) & j \neq k, g(j) = g(k) \\ \alpha\hat{s}_j\hat{s}_k & j \neq k, g(j) \neq g(k) \end{cases}$$

Notes: (1) here α is the absolute value of the price coefficient. (2) when calculating the $\widehat{\Delta}_{jk} = -\frac{ds_k}{dp_j}$, one also needs to put an extra condition $f_j = f_k$ in each case to index for drug ownership.

C.2 Counterfactual Estimation Procedures

Two counterfactual situations are evaluated: 1) without a patent pool; 2) with a fully expanded patent pool (once a compound enters, no geographic segmentation within my sample period). The goal is to use estimated demand and supply parameters to simulate counterfactual prices and quantities in each scenario (under different market structure assumptions) and compute changes in consumer and producer surpluses.

In section 6, I investigate two broad cases in the supply-side market structure: marginal cost pricing and Bertrand-Nash game. In the first case of marginal cost pricing, one can either assume marginal cost curves to be flat or increasing in quantity. Counterfactual regarding the case with flat marginal cost curves are fairly straightforward as counterfactual prices can be simulated by adjusting the counterfactual values of the MPP variable. In this case, consumers obtain all the social surplus. Alternatively, when assume marginal cost increases in quantity, a shift (down) in the supply curve will also affect equilibrium quantity. Regarding this case of competitive pricing with upward sloping marginal cost curve, I simulate counterfactuals using fixed point iterations.

In the second case of Bertrand-Nash game, I simulate counterfactual prices, quantities, and marginal costs by optimization in each country-year market. This case is then break down to three sub-cases: single product oligopoly and multi-product oligopoly. The major difference across three cases lays in how I define the ownership matrix. In the single product case, only the diagonal elements in the substitution matrix are relevant to a firm's pricing decision. In the multi-product case, I assign ownership based on branded-firm's drug ownership and treat cross-firm cocktail as owned by a separate firm.

In the following part, I described more details regarding how to use fixed point algorithm or optimization to solve for the equilibrium values in relevant scenarios.

Fixed point iteration: competitive pricing with upward sloping MC curve

$$\hat{q}_j = \Pr_j(\hat{p}_j) \times M = \hat{s}_j(\hat{p}_j) \times M \quad (1)$$

$$\hat{p}_j = mc_j(\hat{q}_j) = \beta MPP_j^{cf} + X_j\gamma + \eta\hat{q}_j + \omega_j \quad (2)$$

To fix ideas, I use $MPP_j^{cf} = 0, \forall j$ (counterfactual: without the MPP) to elaborate below. Note that the MPP only enters through supply side but not via the demand side. The analytical form for $\hat{s}_j$ in equation (1) is as below.[7]

$$\hat{s}_j = \frac{e^{\frac{\delta_j}{1-\sigma}}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma}}{\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}}, \text{ where } \delta_j(\hat{p}_j) = X_j\beta + \xi_j - \alpha\hat{p}_j$$

Now, obtain *counterfactual* equilibrium price and quantity using *fixed point algorithm*:

[7] More details are available from the book by Kenneth Train (2009) "Discrete Choice Methods with Simulation."

For each market (country-year), find $(\hat{p}_j, \hat{q}_j)$ $s.t.$ (1) and (2) hold. Start with a guess p_j^0 close to the true value with a random component, e.g., $p_j^0 = p_j(0.95 + 0.1 * uniform(1))$.

Iteration #1:

$$\hat{q}_j^1 = \hat{s}_j(\hat{p}_j) \times M$$
$$\hat{p}_j^1 = \underbrace{X_j\gamma + \omega_j}_{p_j - \eta q_j} + \eta\hat{q}_j^1$$

… iteration # $l+1$:

$$\hat{q}_j^{l+1} = \hat{s}_j(\hat{p}_j) \times M$$
$$\hat{p}_j^{l+1} = X_j\gamma + \omega_j + \eta\hat{q}_j^{l+1}$$

Continue until $\left\|p_j^{l+1} - p_j^l\right\| < \varepsilon$

Numerical optimization: oligopolistic pricing, with single/multi-product firms

$$\hat{p}_j = argmin_{p_j} \left\| \hat{p}_j - \widehat{mc}_j - \underbrace{\widehat{\Delta}_{jk}^{-1} \times \hat{s}_j}_{\widehat{makeup}_j} \right\|^2 \quad (1)$$

$$\hat{q}_j = \Pr_j(\hat{p}_j) \times M = \hat{s}_j(\hat{p}_j) \times M \quad (2)$$

$$mc_j(\hat{q}_j) = \beta MPP_j^{cf} + X_j\gamma + \eta\hat{q}_j + \omega_j \quad (3)$$

$$\hat{s}_j = \frac{e^{\frac{\delta_j}{1-\sigma}}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{-\sigma}}{\sum_{g=0}^{G}\left(\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}\right)^{1-\sigma}}, \text{ where } \delta_j(\hat{p}_j) = X_j\beta + \xi_j - \alpha\hat{p}_j \quad (4)$$

$$\widehat{\Delta}_{jk} = \begin{cases} \alpha\hat{s}_j\left(\frac{1}{1-\sigma} - \frac{\sigma}{1-\sigma}\hat{s}_{j|g} - \hat{s}_j\right) & ,j = k \\ -\alpha\hat{s}_j\left(\frac{\sigma}{1-\sigma}\hat{s}_{k|g} + \hat{s}_k\right) & ,j \neq k, g_j = g_k, f_j = f_k \\ -\alpha\hat{s}_j\hat{s}_k & ,j \neq k, g_j \neq g_k, f_j = f_k \\ 0 & ,o.w.(i.e., f_j \neq f_k) \end{cases} \quad (5)$$

$$\hat{s}_{j|g} = \frac{e^{\frac{\delta_j}{1-\sigma}}}{\sum_{j\in g} e^{\frac{\delta_j}{1-\sigma}}}, \text{ where } \delta_j(\hat{p}_j) = X_j\beta + \xi_j - \alpha\hat{p}_j \quad (6)$$

Here, for each market, a profit maximization decision is built within (1) to ensure that the counterfactual new price is generated from Bertrand-Nash game by minimizing the squared

distance between the price and the sum of marginal cost and markup. The latter two are simultaneously updated using (2) and (3) within the fmincon minimization within (1). I impose mild conditions that prices are positive and less than twice the actual non-counterfactual prices to ensure that price search is within a realistic range.

More specifically, the algorithm starts with an initial guess of $\hat{p}_j$ for each country-year market. It then calculates the objective function using $\hat{p}_j$, relevant demand and supply parameters, and the counterfactual marginal cost. The optimal new prices (from the first-order condition) is obtained using fmincon. The quantity and marginal cost are then updated with the above equation system.

Other counterfactuals

One can also obtain counterfactual estimations of oligopoly price setting with flat marginal cost curves. These results can be obtained with flexible adaptation to the above optimization code by revising the quantity part (set the quantity coefficients to zero) and use supply-side parameters from corresponding estimations (with flat marginal cost assumption).

Additional notes on alternative estimation approach

Alternatively, one can get the quantity equation (1) using a simulation approach (less efficient).

One can obtain equation (1) by simulating demand from the nested logit utility function.

$$u_{ijct} = \underbrace{X_{jct}\beta - \alpha p_{jct} + \xi_{jct}}_{\delta_{jct} = \ln(s_j) - \ln(s_0) - \sigma \ln(s_{j|g})} + \zeta_{ig(j)ct} + (1-\sigma)\varepsilon_{ijct}$$

Therefore, the utility from counterfactual prices for a given ct can be expressed as below. Where the $\zeta_{ig(j)} + (1-\sigma)\varepsilon_{ij}$ cannot be simulated with the independent GEV simulator in MATLAB but shall be simulated using the inverse CDF approach based on the nested logit CDF (Train book, p. 79, equation (4.1)).

$$u_{ij}(\hat{p}_j) = \underbrace{X_j\beta + \xi_j}_{\delta_j - \alpha p_j} + \alpha\,\hat{p}_j + \zeta_{ig(j)} + (1-\sigma)\varepsilon_{ij}$$

To simulate the utility for N_{sim} =100,000 consumers across drugs in a given market (country-year), draw $N_{sim} \times J$ nested logit errors from the Generalized Extreme Value (GEV) distribution. Here $j \in \{0,1,\dots,J\}$ indicates distinct drugs within a market, including the outside option 0. For each simulated consumer i, (1) calculate the $u_{ijct}, \forall j$, (2) find the j that maximizes utility for i, and (3) define the realized choices for person i as $z_j(i) = 1$ if i choses j.

With the realized choices, one can calculate $\hat{s}_j = \frac{\sum_i^{N_{sim}} z_j(i)}{N_{sim}}$ and $\hat{q}_j = M \times s_j$ for a single market. Then, repeat the process for each country-year market and save the results into a vector for (2).

C.3 Graphic representation of model fit, and additional results

To test the performance of the optimization and fixed-point algorithm, I use actual data instead of counterfactual values to test whether I can reproduce actual prices and quantities. In addition, I run the algorithm multiple times and confirmed the results are not sensitive to the initial guess. The numeric precision is about 99% in all these placebo tests. I report graphic representation below. In all cases, the placebo prices and quantities well fit with the 45-degree lines.[8]

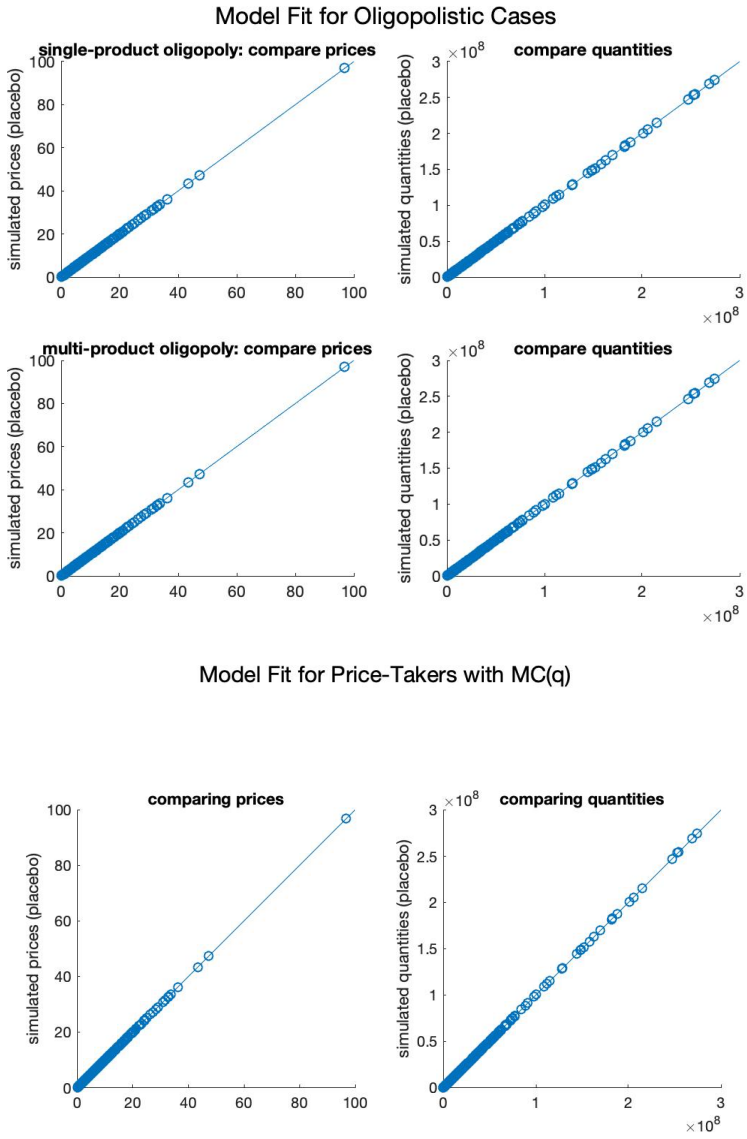


Figure C1: Graphical Demonstration of Model Fits

[8] I also produced corresponding graphs for "actual *vs.* counterfactual" and they are available upon request.

Additional results with alternative marginal cost assumptions

In the main analyses, I use flat marginal cost for competitive pricing and increasing marginal cost for oligopolistic pricing. These assumptions are good choices to capture the differences that compacity constraints matter in the two cases I study. This also provides more conservative estimates of the welfare gains from the MPP to consumers and producers.

As an additional exercise and comparison, I also produced the opponent counterfactuals. Specifically, price-taking firms with increasing marginal cost curves and oligopolistic pricing with flat marginal cost curves. From a realistic standpoint, the former case is more interesting as a transition stage of the two cases I discussed in the main text. However, it is worth noting that "price-takers with increasing marginal cost curve" is a typical case where the counterfactual producer surplus can explode. The reason is that when extrapolating the MC(q=0) point that is needed for calculating the producer surplus triangle, MC(q) curve would generate many negative prices with small quantities that would not be observed in the data. In other words, the in-sample fit can be fine, but the 0.5*beta(q)*q^2 provide overly large estimation for producer surplus (grey numbers), despite the still reasonable estimates of relative changes. The "oligopolistic pricing with flat MC" case uses strong assumptions that firms actively optimize and extract profit in LMICs without any capacity constraint, which contradicts reality and thus generate larger divisions in counterfactual cases. I report them below for a comparison.

Table C1: Welfare Re-Estimation: Alternative MC Assumptions

welfare estimates ($ M)	MC pricing MC(q)	Oligopolistic Pricing (w/ flat MC) single-prod. firm	multi-prod. firm
$E(\widehat{CS_0})$	8,112.5	6,409.2	6,246.4
$E(CS)$	8,747.7	8,747.7	8,747.7
$E(\widehat{CS_1})$	8,836.3	8,821.1	8,811.5
Δ$: CS_0	635.2	2,338.5	2,501.3
Δ%: CS_0	7.83%	36.49%	40.04%
Δ$: CS_1	88.6	73.4	63.8
Δ%: CS_1	1.01%	0.84%	0.73%
$E(\widehat{PS_0})$	252$B	3,071.3	3,315.2
$E(PS)$	266$B	4,179.5	4,309.6
$E(\widehat{PS_1})$	267$B	4,271.8	4,392.1
Δ$: PS_0	14.1$B	1,108.2	994.4
Δ%: PS_0	5.58%	36.08%	30.00%
Δ$: PS_1	338.4	92.3	82.5
Δ%: PS_1	0.13%	2.21%	1.91%

Additional graphs regarding these additional cases are available upon request.

Appendix D: Medical Appendix

Brief Explanation of the Background and Classes of Antiretroviral Therapy

Human immunodeficiency virus (HIV) infects the immune system's cells, resulting in the impairment or destruction of their functions. Such an infection leads to the progressive deterioration of the immune system, generating *immune deficiency*. This deficiency can be defined as the condition in which the immune system can no longer fight any infection or disease. Unlike certain other viruses, HIV does not allow the human body to disinfect itself completely. Once a patient infected with HIV, that patient will have it for life. Consequently, acquired immunodeficiency syndrome (AIDS) can develop when HIV is left untreated. This stage of infection occurs when one's immune system is badly damaged, making one vulnerable to *opportunistic infections* – infections that occur more frequently and severely among people with weakened immune system. Such infections include tuberculosis and several cancers. Although AIDS is the final stage of HIV infection, not everyone who has HIV advances to this stage. An HIV infection can be contracted through three main routes: (1) unprotected sexual intercourse; (2) the sharing of contaminated syringes, needles, surgical equipment or other sharp instruments and transfusion of contaminated blood; (3) from a mother to her infant during pregnancy, childbirth, and breastfeeding.

People with AIDS and left untreated typically survive about three years on average. Once dangerous opportunistic illnesses develop, an infected person's life expectancy without treatment falls to about one year. Although medical treatment is necessary to prevent the death of AIDS patients, no effective cure currently exist. However, with proper treatment, it is possible to control HIV. The medicine used for the treatment of HIV is antiretroviral therapy (ART). According to the WHO guidelines, standard ART consists of a combination of drugs to maximally suppress HIV and inhibit the disease's progression. In addition, this therapy prevents further transmission of HIV. As a result, huge reductions in death rates and infection rates have been documented when using a potent ART regimen, especially in the early stages of the disease. The WHO recommends that people with HIV undergo ART as soon as possible after diagnosis without restrictions of the CD4 counts (a type of immune cells greatly reduced in HIV patients). It also recommends pre-exposure prophylaxis for people at high risk of HIV infection as an additional option among other non-drug based comprehensive prevention plans.

Table D1: ART drug classes

Drug class (abbr.)	Simple description (mechanisms of action explanations)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	block reverse transcriptase, an enzyme HIV needs to make copies of itself.
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	bind to and later alter reverse transcriptase, an enzyme HIV needs to make copies of itself.
Protease Inhibitors (PIs)	block HIV protease, an enzyme HIV needs to make copies of itself.
Fusion inhibitor (FIs)	block HIV from entering the CD4 cells of the immune system, e.g., HR1.
Entry inhibitor (EIs)	block proteins on the CD4 cells that HIV needs to enter the cells, CCR5.
Integrase Inhibitors (IIs)	stop HIV from making copies of itself by blocking a key protein that allows the virus to put its DNA into the healthy cell's DNA.
Enhancers	help other ART work better by enhancing the blood levels.

Notes: (1) the distinctions between FIs and EIs are not substantial, mainly on which protein the drug binds to block HIV virus from entering the CD4 cells. In many cases they are grouped together into one broader class. (2) Entry inhibitors have multiple sub-classes, e.g., CCR5 inhibitor, post-attachment inhibitor (the new compound, IBA), etc.

Table D2: Clinical Guidelines on ART Standard Dosing (U.S. adult daily doses)

drug API code	adult daily dose	Notes
ABC	600 mg	
ATV	300 mg	
DRV; TCM	800 mg	
ddI	400 mg	250mg/d if weight <60kg
DTG	50 mg	
EFV	600 mg	
FTC	200 mg	
ENF; T20	180 mg	
ETR; ETV	400 mg	
FPV	1400 mg	
IDV	1600 mg	
3TC	300 mg	
MVC	600 mg	
NFV	2500 mg	2250 mg when taken 3 times/day
NVP	400 mg	Phase in: 200mg in the first 14 days
RAL	800 mg	
r; RTV	200 mg	The avg./mode: 100-400mg/d; depends on other compounds used
SQV	2000 mg	
d4T	80 mg	60mg if weight <60kg.
TDF	300 mg	
TPV	1000 mg	
ZDV; AZT	600 mg	FDA: 600mg; WHO 250-300mg
ABC+3TC	600+300 mg	
ABC+3TC+ZDV	600+300+600 mg	
ATV+r	300+100 mg	
EFV+FTC+TDF	600+200+300 mg	
EFV+3TC+TDF	600+300+300 mg	
EFV+3TC+ZDV	600+300+600 mg	
FTC+TDF	200+300 mg	
3TC+NVP+d4T	300+400+80 mg	if <60kg, then 300+400+60 mg
3TC+NVP+ZDV	300+400+600 mg	
3TC+d4T	300+80 mg	
3TC+TDF	300+300 mg	
3TC+TDF+NVP	300+300+400 mg	
3TC+ZDV	300+600 mg	
LPV+r	800+200 mg	

Notes: This table is used to convert active pharmaceutical ingredients (API) into standardized U.S. adult drug daily doses as a quantity-adjusted measure. Five observations in grey are dropped from the sample as they only appear in the data for a handful of times. I checked drug dosing guidelines using AIDS*info* and FDA labeling, and consulted WHO guidelines for global standards. The above measures are recorded as adult daily dosing for a representative patient weighted over 60 kg (the average adult weights are above 60 kg in most countries but can be smaller in low-income and developing countries). The localized doses can be smaller than the U.S. guideline in resource-limited developing countries. In the absence of country-specific clinical guidelines, I use this U.S. adult-based conversion as one outcome of interest.

Table D3: 2017 and 2012 top selling HIV drugs and MPP status

The two tables here are used to demonstrate top-selling HIV drugs.

Table D3.1: HIV drugs among 2017 top 200 drugs by global sales

rank 2017	HIV drugs among top 200 drugs by global sales, 2017	generic abbreviations	MPP status (by 12/31/2017)	sales ($M)
24	Genvoya	EVG+TAF+FTC+COBI	all in	3,730
31	Triumeq	ABC+DTG+3TC	out*+in+out	3,172
32	Truvada	FTC+TDF	all in	3,169
72	Prezista/Prezcobix/Rezolsta	[Prezista]: DRV; [Prezcobix/Rezolsta for US/Europe]:DRV+COBI	out$; out$+in	1,821
74	Tivicay	DTG	in	1,810
75	Atripla	EFV+FTC+TDF	out+in+in	1,806
100	Descovy	FTC+TAF	in	1,300
109	Isentress and Isentress HD	RAL	out*	1,204
120	Odefsey	FTC+RPV+TAF	out+in	1,106
126	Stribild	EVG+COBI+FTC+TDF	all in	1,054
129	Viread	TDF	in	1,046
139	Complera/Eviplera	[US/European]: RPV+FTC+TDF	out+in+in	966
191	Sustiva franchise (includes sales of bulk efavirenz)	EFV	out	729
196	Edurant/rilpivirine	RPV	out	714

Table D3.2: HIV drugs among 2012 top 100 drugs by global sales

rank 2012	HIV drugs among top 100 drugs by global sales, 2012	generic abbreviations	MPP status (by 12/31/2017)	sales ($M)
26	Atripla	EFV+FTC+TDF	out+in+in	3574
29	Truvada	FTC+TDF	all in	3,303
67	Sustiva franchise (includes sales of bulk efavirenz)	EFV	out	1,527
68	Reyataz	ATV	in	1521
71	Isentress	RAL	out*	1515
76	Prezista	DRV	out$	1414

Notes: out* means restrictive MPP licenses (pediatric-only) and treated as outside the pool for conservative estimates. out$ means the corresponding drug is not officially in the pool but have price arrangements with the MPP. The top selling drug list is obtained from Med Ad News report and has been used in previous studies. For more details regarding the source, see Duggan and Scott Morton (2006).

Reference: Duggan, M., & Scott Morton, F. M. (2006). The distortionary effects of government procurement: evidence from Medicaid prescription drug purchasing. *The Quarterly Journal of Economics*, *121*(1), 1-30.

Appendix E: Legal Appendix

Table E1: Key MPP license contract terms
(Simple explanations of abbreviations are listed at the end of the table)

API code	firm	eligibility for sublicenses (manufacturing)	sales scope: # countries	sales outside territory	royalty rates (in territory)	technology transfer	additional flexibilities
ABC (ped.)	ViiV	worldwide	121	permitted if no granted patents or non-infringing	0%	n/a	challenge
ATV	BMS	worldwide	122	enables those not relying on BMS tech to sell if not infringe granted patents	3%: adult forms in countries w/ patents; 0%: ped., or sub-Saharan/ India sales	provided to all sublicensees, no obligation to use	n/a
BIC	Gilead	China, India, South Africa	116	permitted if compulsory license issued	5% of FP net sales. 0% on API/ped. formulation.	one time for Indian & South-African sub-licensees	terminate; challenge
COBI	Gilead	China, India, South Africa	116	permitted if compulsory license issued	5% of FP net sales. 0% on API/ped. forms.	one time for Indian & South-African sub-licensees	terminate; challenge
DTG (adult; ped.)	ViiV	worldwide	adult: 94; ped.: 121	permitted if no granted patents or non-infringing	0%: all ped. & adults in 82 countries; 5%: Philippines, India, Vietnam, Moldova; 7.5%: Egypt, Indonesia, Morocco, Armenia, Ukraine, Mongolia, Tunisia; 10%: Turkmenistan	n/a	challenge
EVG	Gilead	China, India, South Africa	109	permitted if compulsory license issued	5% of FP net sales. 0% on API/ped. sales	one time for Indian sub-licensees	terminate; challenge
FTC	Gilead	China, India, South Africa, & licensed on TDF, TAF, COBI, EVG, even if terminated	116	possible if not infringe any granted patents	0%; there may be royalties on other components of any specific combination	n/a	licensees terminated TDF can still benefit from no-sue on tdf/ftc, taf/ftc, & tdf/ftc/efv
LPV/r (adult; ped.)	AbbVie	worldwide	adult: all 54 African; ped.: 102	permitted if not infringe granted patents	0%	n/a	challenge
RAL (ped.)	MSD	worldwide	92	permitted if not infringe granted patents	0%	n/a	challenge
TAF	Gilead	China, India, South Africa	116	permitted if compulsory license issued	5% of FP net sales. 0% on API/ped. sales	one time for Indian sub-licensees	terminate; challenge
TDF	Gilead	China, India, South Africa	116	permitted if compulsory license issued	3-5% of FP net sales. 0% on API/ped. sales.	one time for Indian & South-African sub-licensees	terminate

Notes: (1) common information omitted in the table: all of these licenses allow flexible compound combinations, all waive data exclusivity, all agree patents pooled include all pending and granted patents, and all agree to let WHO or a stringent regulatory authority (SRA), such as U.S. FDA, to help with quality-assurance. (2) A typical example for sales outside of territory when non-infringing is in the presence of compulsory license. (3) the sublicensing territory defines the manufacturing territory and the sales scope defined the countries available for sales using MPP licenses. (4) The "countries" defined in the sale scope (geographic territory) are economy/countries as in the World Bank/United Nations definition, but not necessarily a sovereign state (e.g., certain commonwealths are treated as an independent "country" in measures of economics/development). (5) API = Active Pharmaceutical Ingredient (i.e., compound, for small molecule drugs). FP = finished products. (6) Contracts regarding "manufacturing" in the MPP typically do not distinguish between API vs. FP manufacturers. (7) In the last column, "challenge" = allow patent challenges; "terminate" = allow termination of licensing agreements.

Source: The Medicines Patent Pool official website product page (https://medicinespatentpool.org/what-we-do/global-licence-overview/licences-in-the-mpp/), collected from each compound's key features and detailed/corrected a few incidences with raw information from the MPP (sub-)licensing contracts. Last updated: December 31, 2018.

Panel E2: Drug-Territory Coverage Final Panel (by end of 2018)

Country names	code	ldc	atv	bic	cobi	dtg	evg	ftc	lpv/r	taf	tdf
Afghanistan	AFG	1	2013	2017	2011	2014	2011	2011		2014	2011
Algeria	DZA	0	2017						2015		
Angola	AGO	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Anguilla	AIA	0		2017	2011		2011	2011		2014	2011
Antigua and Barbuda	ATG	0	2013	2017	2011		2011	2011		2014	2011
Armenia	ARM	0	2013	2017	2011	2016	2011	2011		2014	2011
Aruba	ABW	0		2017	2011			2011		2014	2011
Azerbaijan	AZE	0	2013								
Bahamas	BHS	0		2017	2011		2011	2011		2014	2011
Bangladesh	BGD	1	2013	2017	2011	2014	2011	2011		2014	2011
Barbados	BRB	0		2017	2011		2011	2011		2014	2011
Belarus	BLR	0	2013	2017	2017			2017		2017	2017
Belize	BLZ	0	2013	2017	2011		2011	2011		2014	2011
Benin	BEN	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Bhutan	BTN	1	2013	2017	2011	2014	2011	2011		2014	2011
Bolivia	BOL	0	2013	2017	2011	2014	2011	2011		2014	2011
Botswana	BWA	0	2013	2017	2017	2014	2017	2011	2015	2014	2011
British Virgin Islands	VGB	0		2017	2011		2011	2011		2014	2011
Burkina Faso	BFA	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Burundi	BDI	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Cambodia	KHM	1	2013	2017	2011	2014	2011	2011		2014	2011
Cameroon	CMR	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Cape Verde	CPV	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Central African Republic	CAF	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Chad	TCD	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Comoros	COM	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Cook Islands	COK	0	2017								
Costa Rica	CRI	0	2013								

Côte d'Ivoire	CIV	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Cuba	CUB	0	2013	2017	2011		2011	2011		2014	2011
Dem. Republic of the Congo	COD	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Djibouti	DJI	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Dominica	DMA	0	2013	2017	2011		2011	2011		2014	2011
Dominican Republic	DOM	0	2013	2017	2011			2011		2014	2011
Ecuador	ECU	0	2013	2017	2017		2017	2011		2014	2011
Egypt	EGY	0	2017			2014			2015		
El Salvador	SLV	0	2013	2017	2017	2014	2017	2011		2014	2011
Equatorial Guinea	GNQ	0	2017	2017	2011	2014	2011	2011	2015	2014	2011
Eritrea	ERI	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Ethiopia	ETH	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Fiji	FJI	0	2013	2017	2011		2011	2011		2014	2011
Gabon	GAB	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Gambia	GMB	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Georgia	GEO	0	2013	2017	2011	2014	2011	2011		2014	2011
Ghana	GHA	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Grenada	GRD	0	2013	2017	2011		2011	2011		2014	2011
Guatemala	GTM	0	2013	2017	2011	2014	2011	2011		2014	2011
Guinea	GIN	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Guinea-Bissau	GNB	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Guyana	GUY	0	2013	2017	2011	2014	2011	2011		2014	2011
Haiti	HTI	1	2013	2017	2011	2014	2011	2011		2014	2011
Honduras	HND	0	2013	2017	2011	2014	2011	2011		2014	2011
India	IND	0	2013	2017	2011	2014	2011	2011		2014	2011
Indonesia	IDN	0	2017	2017	2017	2014	2017	2011		2014	2011
Iraq	IRQ	0	2013								
Jamaica	JAM	0	2013	2017	2011		2011	2011		2014	2011
Kazakhstan	KAZ	0	2013	2017	2017		2017	2011		2014	2011
Kenya	KEN	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Kiribati	KIR	1	2013	2017	2011	2014	2011	2011		2014	2011
Korea Dem. Republic	PRK	0	2013			2014					
Kosovo	XKX	0				2014					
Kyrgyzstan	KGZ	0	2013	2017	2011	2014	2011	2011		2014	2011
Lao PDR	LAO	1	2013	2017	2011	2014	2011	2011		2014	2011
Lebanon	LBN	0									
Lesotho	LSO	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Liberia	LBR	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Libya	LBY	0	2013						2015		
Madagascar	MDG	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Malawi	MWI	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Malaysia	MYS	0	2017	2017	2017			2017		2017	2017
Maldives	MDV	0	2013	2017	2011		2011	2011		2014	2011
Mali	MLI	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Marshall Islands	MHL	0	2013								
Mauritania	MRT	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Mauritius	MUS	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Micronesia	FSM	0	2013			2014					

Moldova	MDA	0	2013	2017	2011	2016	2011	2011		2014	2011
Mongolia	MNG	0	2013	2017	2011	2014	2011	2011		2014	2011
Montserrat	MSR	0		2017	2011			2011		2014	2011
Morocco	MAR	0	2017			2016			2015		
Mozambique	MOZ	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Myanmar	MMR	1	2013	2017	2011	2014	2011	2011		2014	2011
Namibia	NAM	0	2013	2017	2017	2014	2017	2011	2015	2014	2011
Nauru	NRU	0	2013	2017	2011		2011	2011		2014	2011
Nepal	NPL	1	2013	2017	2011	2014	2011	2011		2014	2011
Nicaragua	NIC	0	2013	2017	2011	2014	2011	2011		2014	2011
Niger	NER	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Nigeria	NGA	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Niue	NIU	0	2017								
Pakistan	PAK	0	2013	2017	2011	2014	2011	2011		2014	2011
Palau	PLW	0	2013	2017	2011		2011	2011		2014	2011
Palestine	PSE	0	2013			2014					
Panama	PAN	0	2013								
Papua New Guinea	PNG	0	2013	2017	2011	2014	2011	2011		2014	2011
Philippines	PHL	0	2017	2017	2017	2014		2017		2017	2017
Republic of the Congo	COG	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Rwanda	RWA	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Samoa	WSM	0	2013	2017	2011	2014	2011	2011		2014	2011
Sao Tome and Principe	STP	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Senegal	SEN	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Seychelles	SYC	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Sierra Leone	SLE	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Solomon Islands	SLB	1	2013	2017	2011	2014	2011	2011		2014	2011
Somalia	SOM	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
South Africa	ZAF	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
South Sudan	SSD	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Sri Lanka	LKA	0	2013	2017	2017	2014	2017	2011		2014	2011
St Lucia	LCA	0	2013	2017	2011		2011	2011		2014	2011
St. Kitts and Nevis	KNA	0	2013	2017	2011		2011	2011		2014	2011
St. Vincent & the Grenadines	VCT	0	2013	2017	2011		2011	2011		2014	2011
Sudan	SDN	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Suriname	SUR	0	2013	2017	2011		2011	2011		2014	2011
Swaziland	SWZ	0	2013	2017	2011	2014	2011	2011	2015	2014	2011
Syrian Arab Republic	SYR	0	2013	2017	2011	2014	2011	2011		2014	2011
Tajikistan	TJK	0	2013	2017	2011	2014	2011	2011		2014	2011
Tanzania	TZA	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Thailand	THA	0		2017	2017		2017	2011		2014	2011
Timor-Leste	TLS	1	2013	2017	2011	2014	2011	2011		2014	2011
Togo	TGO	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Tonga	TON	0	2013	2017	2011		2011	2011		2014	2011
Trinidad and Tobago	TTO	0		2017	2011		2011	2011		2014	2011
Tunisia	TUN	0	2017			2014			2015		
Turkmenistan	TKM	0	2013	2017	2017	2014	2017	2011		2014	2011
Turks and Caicos Islands	TCA	0		2017	2011		2011	2011		2014	2011

Tuvalu	TUV	1	2013	2017	2011	2014	2011	2011		2014	2011
Uganda	UGA	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Ukraine	UKR	0	2017	2017	2017	2016		2017		2017	2017
Uzbekistan	UZB	0	2013	2017	2011	2014	2011	2011		2014	2011
Vanuatu	VUT	1	2013	2017	2011	2014	2011	2011		2014	2011
Vietnam	VNM	0	2017	2017	2011	2014	2011	2011		2014	2011
Yemen	YEM	1	2013	2017	2011	2014	2011	2011		2014	2011
Zambia	ZMB	1	2013	2017	2011	2014	2011	2011	2015	2014	2011
Zimbabwe	ZWE	0	2013	2017	2011	2014	2011	2011	2015	2014	2011

Notes: The above table include the complete licensing territories for adult formulations specified in MPP contracts by end of 2018. Among all the countries that ever covered in the MPP territory, only three are not developing countries by the World Bank 2018 classifications: Belarus, Moldova, and Ukraine. The country code reported in the table and used in the analysis is the ISO three-digit alphabetical code that uniquely identify a country. Given the multiple ways of country name spellings and historical country name changes (e.g., most recently in Apr. 2018, Swaziland to eSwatini), the most rigorous way is to merge any country-involved data set using country code instead of country names.

List of the 103 countries (and code) covered in the Global Fund data in the Diffusion Analysis:

Afghanistan (AFG), Albania (ALB), Angola (AGO), Armenia (ARM), Azerbaijan (AZE), Bangladesh (BGD), Belarus (BLR), Belize (BLZ), Benin (BEN), Bhutan (BTN), Bolivia (Plurinational State) (BOL), Bulgaria (BGR), Burkina Faso (BFA), Burundi (BDI), Cambodia (KHM), Cameroon (CMR), Cape Verde (CPV), Central African Republic (CAF), Chad (TCD), China (CHN), Colombia (COL), Comoros (COM), Congo (COG), Congo (Democratic Republic) (COD), Croatia (HRV), Cuba (CUB), CÃ´te d'Ivoire (CIV), Djibouti (DJI), Dominican Republic (DOM), Ecuador (ECU), Egypt (EGY), El Salvador (SLV), Equatorial Guinea (GNQ), Eritrea (ERI), Ethiopia (ETH), Gabon (GAB), Gambia (GMB), Georgia (GEO), Ghana (GHA), Guatemala (GTM), Guinea (GIN), Guinea-Bissau (GNB), Guyana (GUY), Haiti (HTI), Honduras (HND), India (IND), Indonesia (IDN), Iran (Islamic Republic) (IRN), Jamaica (JAM), Jordan (JOR), Kazakhstan (KAZ), Kenya (KEN), Kyrgyzstan (KGZ), Lao (Peoples Democratic Republic) (LAO), Lesotho (LSO), Liberia (LBR), Macedonia (Former Yugoslav Republic) (MKD), Madagascar (MDG), Malawi (MWI), Mali (MLI), Mauritania (MRT), Mauritius (MUS), Moldova (MDA), Mongolia (MNG), Morocco (MAR), Mozambique (MOZ), Myanmar (MMR), Namibia (NAM), Nepal (NPL), Nicaragua (NIC), Niger (NER), Nigeria (NGA), Pakistan (PAK), Palestine (PSE), Papua New Guinea (PNG), Paraguay (PRY), Peru (PER), Philippines (PHL), Russian Federation (RUS), Rwanda (RWA), Sao Tome and Principe (STP), Senegal (SEN), Sierra Leone (SLE), Somalia (SOM), South Africa (ZAF), South Sudan (SSD), Sri Lanka (LKA), Sudan (SDN), Suriname (SUR), Swaziland (SWZ), Tajikistan (TJK), Tanzania (United Republic) (TZA), Thailand (THA), Timor-Leste (TLS), Togo (TGO), Tunisia (TUN), Uganda (UGA), Ukraine (UKR), Uzbekistan (UZB), Viet Nam (VNM), Yemen (YEM), Zambia (ZMB), Zimbabwe (ZWE)

Appendix F: Case Studies on R&D

To supplement the innovation results, I provide a few qualitative cases on new generic drugs that have stemmed from the MPP and firms' decisions or reactions during the process. Although ex ante unclear, new products created by MPP generic licensees can benefit branded firms by offering a higher market value in developing countries outside the MPP territories. For example, the new single-pill once-daily cocktail TLD was first approved by a generic firm in 2018 and recommended by the WHO as a starting therapy for treatment naïve patients in the same year. This WHO recommendation can potentially increase branded sales in other middle-income countries that are not covered by the pool.

Branded firms are not active in developing pediatric formulations, partly because most pregnant women in the U.S. are tested for HIV. Mother-to-children transmission can then be prevented by suppressing the viral load during pregnancy with HIV drugs. The lack of a pediatric version mainly affects developing countries and low-income populations in developed countries. Under such a circumstance, pooled licensing can induce socially beneficial innovation by allowing generic firms to develop localized solutions. For example, the first pediatric granules formulation for lopinavir/ritonavir (LPV/r) was developed by generic firms with MPP licenses and gained FDA approvals in 2018. If needed, branded firms can be granted back low-cost non-exclusive licenses for patents on this new formulation.

Once participating in the pool, branded firms may adjust R&D strategies accordingly. The case of Gilead's pool participation and R&D decisions illustrate this point. Gilead joined the MPP in July 2011 and contributed several approved drugs, including tenofovir disoproxil fumarate (i.e., TDF, a prodrug of tenofovir).[9] Gilead then started phase II trials of tenofovir alafenamide fumarate (i.e., TAF, a prodrug of TDF) in December 2011, collected primary results in October 2012, and started phase III trials in December 2012. The phase III trials on a TAF cocktail were completed with main results in 2014, and TAF was licensed to the MPP in the same year, before the 2015 FDA approval. It is worth noting that the earliest clinical trial of TAF was completed in 2003. Although a firm's phase III trial decision can be affected by many factors, the timeline suggests that Gilead is at least not reducing R&D after MPP participation.[10]

In addition, discussions with practitioners suggest that drug access programs can benefit branded firms by improving corporate image. This change can increase employee retention and attract institutional investors (e.g., pension funds) who would invest in firms that actively make a social impact. Generic licensing via the MPP can be a cost-effective way to reach these goals.

[9] Prodrug is an inactive compound that can be metabolized into a pharmacologically active form within the body. In many cases, prodrug can improve the absorption of a drug with lower dose and side-effects.
[10] Furthermore, Gilead started phases II/III trials on tenofovir-based microbicides in 2012, while the phase I trials were finished in 2008. Those trials are joint with partners in the public sector from South Africa. Because microbicides belong to a new drug class that is more valuable to developing countries, Gilead's decision may reflect a combination of factors, among which can be its engagement with the MPP.