Global Drug Diffusion and Innovation with the Medicines Patent Pool

Lucy Xiaolu Wang$^{1,2,3}$

$^1$University of Massachusetts Amherst, United States

$^2$Max Planck Institute for Innovation and Competition, Germany

$^3$Canadian Centre for Health Economics, Canada

Patent Protection vs. Access to Medicines

- Patents lead to high drug prices; then rising patent litigations
- More severe in developing countries and with drug bundling
- Branded-drug firms lack incentives to invest and sell in low- and middle-income countries (LMIC)
- Limited impact from policy interventions (not enough)
Can a patent pool spur global drug diffusion & innovation?
This Paper: the Medicines Patent Pool (MPP)

- Founded & funded by Unitaid in 2010.7, Geneva, Switzerland
- MPP aims to reduce coordination failures and benefit all players
Theoretical Predictions

**Patent Pools: Theoretical Impacts**

- Increase consumer welfare by reducing
  - Transaction costs: numerous searches and negotiations
  - Hold-up problem: one failed negotiation can deter innovation
  - Double markups: monopoly power in the vertical chain

- Effects on R&D investments depends on the net of
  - (+) reduce litigation costs and downstream infringement
  - (+) attract funds for contribution in access to medicine
  - (+) facilitate specialization in comparative advantages
  - (-) risks of price-fixing by pool participants
  - (-) restrictive licensing terms on product sales/development
Research Questions

Does the MPP spur global drug diffusion & innovation?

- Does the MPP spur affordable generic access in LMIC?
- How do firms react to the MPP in R&D inputs & outputs?
- Can the MPP balance diffusion (in LMIC) and innovation?

Goal: evaluate whether this novel institution can balance diffusion and innovation in a cost-effective manner.
MPP spurs generic access to HIV drugs in LMIC
- Increases % generic utilization for a drug by 7 p.p.

Firms react to MPP with more R&D inputs & outputs
- In clinical trials, firm participation, and product approvals

The MPP effectively balanced diffusion and innovation
- Insights into the Covid-19 technology access pool (C-TAP)
Literature Review & Contribution

- **Innovation and the Economy, esp. in Health Care**
  (Finkelstein 2004; Chaudhuri et al. 2006; Williams 2013; Kyle & Qian 2014; Cockburn et al. 2016; Duggan et al. 2016; Song et al. 2017; Sampat & Williams 2019)

- **Patent Pools on Competition and Innovation**
  (Lerner & Tirole 2004, 2015; Lemley & Shapiro 2005; Chiao et al. 2007; Lerner et al. 2007; Lampe & Moser 2013, 2015; Bekkers et al. 2017; Rey & Tirole 2019)

- Recent paper: Galasso & Schankerman (2021) focuses on diffusion: MPP increases drug licensing

- First empirical analysis on a biomedical patent pool; novel data on diffusion & innovation; implications to policy & future institutions
Institutional Background

Conceptual Framework (1/2): Generic Firms’ Perspective

- For generic firms that want to license a cocktail regimen
  - DTG (patented) failed to license
  - FTC (patented)
  - TAF (patented)

- Licensing the same set with the Medicines Patent Pool
  - bundled license

Note: Also apply to cases when a subset of compounds are patented within a regimen.
### Conceptual Framework (2/2): Cross-Firm Motives

- **Downstream generic firms**: profit & low-cost licensing
  - Increase licensed sales in developing countries

- **For research-oriented upstream firms outside the pool**
  - Increase diffusion-oriented innovation upstream

- **Branded firms in the MPP**: profit, costs, & social image
  - Gain sales in market with large volume and elastic demand
  - Lower administrative costs in licensing & legal costs
  - Possibility to license back follow-on innovation
MPP illustrative Example: New Cocktails Created & Sold

---

**Institutional Background**

**MPP license, 7/2014**

- **Dolutegravir (DTG):**
  - First approved in 8/2013;
  - Joined the MPP in 4/2014

- **Joint venture:**
  - GlaxoSmithKline,
  - Pfizer, Shionogi

- **TLD:** a single-pill once-daily cocktail
  - **FDA tentative approval: 8/2017**
  - Four other generic firms (MPP licensees) obtained approvals in 2018

- **MPP**

- **TDF (on patent) Gilead**

- **3TC (off-patent) ViiV**

- **DTG (on patent) ViiV**

- **bundle w/ other compounds**

---

**Low royalty rates:**
- 0% in 82 countries;
- <10% in 10 countries
Institutional Background

Background: MPP Geographical Coverage

- 10 HIV compounds are available for effective licensing, 2018
  - Comparable in/out: sales, avg. approval time, drug classes

- Generic firms worldwide can license drug bundles from the MPP to sell in territories defined in licensing contracts
Data: HIV Drug Sales, R&D Inputs & Outputs

- The complete HIV drug portfolio data: FDA & AIDSinfo
  - patent status in LMIC: MedsPaL & DrugPatentWatch
  - US drug patent data: Drug Bank via FDA Orange Book

- 40% of total HIV drug procurement in LMIC, 2007-2017
  - price & quality reporting by Global Fund-supported programs

  - from World Bank & Institute for Health Metrics & Evaluation

- R&D inputs: global clinical trials with HIV drugs, 2000-2017
  - global trials from US-registry & identifiers from AIDSinfo

- R&D outputs: all drug approvals for HIV treatment, 2005-2018
  - Drugs@FDA (tentative) approvals & WHO pre-qualification

▶ more details: diffusion data  ▶ more details: innovation data
<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>Institution &amp; Data</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Diffusion Analysis</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>Innovation Analysis</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Conclusion</td>
</tr>
</tbody>
</table>
1. Does the *Medicines Patent Pool* spur generic diffusion?

- Diffusion analysis: difference-in-differences & event studies
  - Sample: 103 countries, 29 drugs with 18 compounds

- Outcome variables: *generic efficiency & product variety*
  - % generic drug orders = \( \frac{\text{# purchases from generic firms}}{\text{# all purchases for the drug}} \)
  - % generic quantity ordered (% generic weighted by US adult dosing)
  - # distinct products purchased for a drug (-streng-dose-firm level)

**Drugs:**
- 3TC (single compound)
- ABC+3TC (multi-compound drug cocktail)

**Products:**
- 3TC 300mg tablet by Cipla
- 3TC 150mg tablet by Mylan
- 3TC 10mg/mL oral solution by Aurobindo
MPP on Drug Diffusion: Method

- Difference-in-Differences method: drug-country-year level
  \[ y_{dct} = \delta_{dc} + \delta_t + \beta MPP^{lic}_{dct} + \gamma X_{ct} + \eta X_{dct} + \varepsilon_{dct} \]
  \[ = 1 \text{ if } dc \text{ in pool at } t \]

- \( y_{dct} \): % generic orders, % generic quantity ordered, #products
- \( X_{ct} \): country-year controls: HIV prevalence & death rates, log(pop.), income, institutional factors (government effectiveness, regulatory quality, rule of law, control of corruption, voice & accountability, political stability & absence of violence)

- \( X_{dct} \): whether a drug is effectively patented in a country-year
- \( \delta_{dc} + \delta_t \): fixed effects for drug-country pairs and years
- Two-way cluster standard errors at the country & drug levels
Empirical Strategy

Threats to Identification & Justifications

- **Identification**: common trends (event study) & lack of common shocks (DGP)

- Which drugs are included in the pool, and how?
  - Perceived values, negotiation outcomes, voluntary contribution

- Which countries are covered in sales territory for a drug?
  - LMIC, HIV prevalence, public relations, prior voluntary licenses
  - Drug-region-year level variation & I use % generic measures

- How is the timing of drug-country inclusion determined?
  - Partly depends on scientific discovery & negotiation time
  - Cannot be predicted by country-year level observables

[^identification: timing reg.]
### Results

MPP increases generic diffusion at drug-country-year level

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) % generic orders (#)</th>
<th>(2) % generic orders (#)</th>
<th>(3) % generic orders (#)</th>
<th>(4) % generic quantities (patient-year)</th>
<th>(5) % generic quantities (patient-year)</th>
<th>(6) % generic quantities (patient-year)</th>
<th>(7) # products (strength-dose-firm)</th>
<th>(8) # products (strength-dose-firm)</th>
<th>(9) # products (strength-dose-firm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$MPP_{dct}$</td>
<td><strong>6.888</strong>* (3.178)</td>
<td><strong>7.223</strong>* (2.933)</td>
<td><strong>7.226</strong>* (2.932)</td>
<td><strong>6.653</strong>* (3.035)</td>
<td><strong>7.003</strong>* (2.802)</td>
<td><strong>7.010</strong>* (2.796)</td>
<td><strong>0.0739</strong></td>
<td><strong>0.0719</strong></td>
<td><strong>0.0717</strong></td>
</tr>
<tr>
<td>drug-country FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>year FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{ct}$ control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{dct}$ control</td>
<td>Y</td>
<td></td>
<td></td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>LHS mean</td>
<td>84.3</td>
<td>84.3</td>
<td>84.3</td>
<td>85.6</td>
<td>85.6</td>
<td>85.6</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Observations</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
</tr>
</tbody>
</table>

![Graph of % orders of generics](image1.png)

![Graph of % quantity of generics](image2.png)

![Graph of # products](image3.png)
Other Specifications & Robustness

- Use country-year fixed effects instead of observables
- Sensitivity analysis on country inclusion: robust
- Sensitivity analysis on drug comparisons: robust
- Subsample: in countries where a drug is not patented
- Debundle drugs at compound-level and re-analyze: robust
- Reduced form analyses on price/quantity channels
- DiD treatment heterogeneity: Bacon decomposition (De Chaisemartin and d'Haultfoeuille, 2020; Goodman-Bacon, 2021); Roth (2022) event studies (& Greenstone and Hanna (2014) and Dobkin et al. (2018), see manuscript & appendix for details)

- results: alternative specification
- sensitivity results: countries
- sensitivity results: drugs
- subsample: patent status
- robust results: debundle
- robust results: P, Q
- Bacon decomp. D
2. Does the *Medicines Patent Pool* foster innovation?

- Firms’ R&D decisions: from pipeline to market
- R&D inputs in clinical trials: Phases I-IV (waived for generics)
- R&D outputs in drug approvals: fast review for HIV drugs
Empirical Strategy

MPP on Drug Innovation: Method

- Exploit variation in the timing of when a compound enters the MPP
- Difference-in-differences model: at compound-year level
  \[ y_{at} = \delta_a + \delta_t + \beta MPP_{at} + \gamma X_{at} + \epsilon_{at} \]
  \[ = 1 \text{ if } a \text{ in pool at } t \]
- \( y_{at} \): # new clinical trials, # firms in trials, # new approvals
- \( X_{at} \): compound-year control on 1st FDA approval, US patents
- \( \delta_a + \delta_t \): compound FE and year FE, cluster at compound level
- Stratify outcomes by MPP-affiliation, phases, funders, etc.
- Timing is uncertain in theory (Rey & Tirole, 2019), data & interview

▶ more on innovation identification
MPP increases follow-on innovation: inputs & outputs

- R&D inputs (clinical trials) & outputs (approvals) increase
MPP increases trials, but more for outsiders than insiders

- \( MPP_{\text{insiders}} = MPP_{\text{branded firms}} \); outsiders = other entities
- Majority of the outsider firms are public/academic institutions

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) # trials</th>
<th>(2) # trials: MPP_{\text{insiders}}</th>
<th>(3) # trials: MPP_{\text{mix}}</th>
<th>(5) # trials: MPP_{\text{mix}}</th>
<th>(7) # trials: MPP_{\text{outsiders}}</th>
</tr>
</thead>
<tbody>
<tr>
<td>( MPP_{\text{at}} )</td>
<td>9.925** (4.534)</td>
<td>2.098** (0.883)</td>
<td>1.625* (0.859)</td>
<td>1.672</td>
<td>1.100</td>
</tr>
<tr>
<td>LHS mean</td>
<td>10.08</td>
<td>2.367</td>
<td>2.367</td>
<td>1.915</td>
<td>1.915</td>
</tr>
<tr>
<td>comp. &amp; year FEes</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>( X_{\text{at}} ) control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Observations</td>
<td>540</td>
<td>540</td>
<td>540</td>
<td>540</td>
<td>540</td>
</tr>
</tbody>
</table>

- The pattern of result is similar for \# firms involved
  - Demand-side policy can induce 2.5-fold increases in trials
Branded firms invest more in new compound development

- New compound development: pre-approval investigational trials
  - Explore new drugs, e.g., vaccines, gene therapy, cell therapy
  - Drug class-year unit; when a drug class is $1^{st}$ added to the pool
  - R&D input mainly increases in phase 3 by MPP insiders
MPP increases new (generic) HIV drug product approvals

- Generic firms’ comparative advantage: multi-firm bundling
  - 1st-ever drug cocktail and the status quo

- Increases in R&D outputs: new drug product approvals
  - Generic versions of: existing drugs, new combination/formulations

![Graph showing new approvals over time](image)

▼ drug approvals: DID results
Results Summary: MPP & Innovation

- Increases in **R&D inputs**: new trials & firm participation
  - Pool **outsiders** increase trials on **pooled compounds**
  - Pool **insiders** invest more in **new compound development**
  - **Post-market trials** are shifted from pool **insiders** to **outsiders**

- Increases in **R&D outputs**: mainly generic product approvals

- Others: duration analysis: shorter branded-to-generic time with MPP compounds; sensitivity analysis with count data models; Bacon decomposition; Roth (2022) event studies

  - histograms
  - duration analysis
  - sensitivity: count data model
  - Bacon decomp. 1

- Case studies: 1) **a pediatric cocktail** 2) **the TDF family** 3) **TLD revisit**
Outline

1. Introduction
2. Institution & Data
3. Diffusion Analysis
4. Innovation Analysis
5. Conclusion
Conclusion: MPP (Pre COVID-19)

- The MPP effectively spurs generic drug diffusion in LMIC
- Firms react to the MPP with more R&D inputs & outputs
- The MPP is effective in balancing diffusion & innovation
“Commitments to share knowledge, intellectual property and data
The COVID-19 Technology Access Pool (C-TAP) will compile, in one place, pledges of commitment made under the Solidarity Call to Action to voluntarily share COVID-19 health technology related knowledge, intellectual property and data. The Pool will draw on relevant data from existing mechanisms, such as the [Medicines Patent Pool](https://www.wipo.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool) and the UN Technology Bank-hosted Technology Access Partnership…”

Implementing partners

MPP’s active response to COVID-19 (https://medicinespatentpool.org/covid-19)

International Goals

The coronavirus pandemic presents an opportunity for the world to act in solidarity and turn this crisis into an impetus to achieve the UN Sustainable Development Goals.

MPP’s activities and contributions:

- In May 2022, WHO and MPP announced two agreements with NIH for 11 COVID-19 health technologies.
- In March 2022, 36 generic manufacturers signed agreements with MPP to produce generic versions of Pfizer’s oral COVID-19 treatment.
- In February 2022, WHO announced the establishment of a biomanufacturing training hub in the Republic of Korea along with 10 more countries to receive support from the mRNA hub in South Africa.
- In February 2022, Afrigen signed a grant agreement with MPP to establish a technology transfer hub for COVID-19 mRNA vaccines.
- In January 2022, 27 generic manufacturers signed agreements with MPP to produce COVID-19 antiviral medication molnupiravir for supply in 105 low- and middle-income countries.
- In November 2021, Pfizer and the Medicines Patent Pool signed a licence agreement to facilitate affordable access of Pfizer’s oral COVID-19 antiviral treatment candidate PF-07321332 in combination with low dose ritonavir in 95 countries.
- In October, MPP and MSD signed a voluntary licensing agreement to facilitate affordable access to molnupiravir in 105 low- and middle-income countries.
- On 21 September 2021, the Pan American Health Organization (PAHO) announced the selection of two centres in Argentina and Brazil for the development and production of mRNA-based vaccines in Latin America. MPP will be actively supporting this initiative through its expertise.
- On 8 June 2021, MPP launched VaxPatL, its new patents database devoted to COVID-19 vaccines.
- On 27 May 2021, MPP expanded its mandate into the licensing of technology with an initial focus on COVID-19 vaccines and pandemic preparedness.
- MPP is currently in discussions with a number of originator companies and research organisations for potential licences for COVID-19 health technologies, including with MSD for a potential licence for molnupiravir.
- In September 2020, MPP became part of the Access to COVID-19 Tool (ACT) Accelerator Therapeutics Pillar led by Unitaid and WHO.
- In May 2020, WHO called MPP to join the C-TAP (COVID-19 Technology Access Pool) initiative, a global collaboration to accelerate development, production and equitable access to COVID-19 tests, treatments, and vaccines.
- MPP’s experience in facilitating access through its voluntary licensing mechanism means that it could play a central role in applying its intellectual property and licensing expertise to patented products and technologies identified in the fight against COVID-19 to facilitate availability to those who need them most.
- On 31 March 2020, MPP temporarily expanded its mandate to include any health technology that could contribute to the global response to COVID-19.
Appendices

A1: Institutions
A2: Diffusion
A3: Innovation
A5: Others
Appendix Table of Content

- **Appendix 1: Institutions**: MPP compounds
- **Appendix 2: Diffusion**: diffusion sample: map
  - alternative specification
  - patent subsample
  - robust: P and Q
  - Bacon D
  - sensitivity: countries
  - sensitivity: drugs
- **Appendix 3: Innovation**: innovation ID
  - events: trials
    - events: ph. 3 trials
    - events: ph. 4 trials
  - duration analysis
  - count data model
  - Bacon I
  - case 1
  - case 3
- **Appendix 4: Others**: diffusion data
  - innovation data
  - pool design

Back to main sections: conclusion
Appendices

A1: Institutions

A2: Diffusion

A3: Innovation

A5: Others

Outline

6. Appendices

7. A1: Institutions

8. A2: Diffusion

9. A3: Innovation

10. A5: Others
MPP compounds comparison

- Comparison: sales, approval time, drug class, owners
  - Global top 200 drug sales 2012: 6 for HIV - 3 in MPP & 3 out
  - Average “age” of drugs are similar in & outside MPP (t-test)
  - Among all 6 drug classes for HIV: 4 for MPP drugs (outside: 4)
  - Among branded firms owns HIV drugs: 4 effectively in & 4 out
Diffusion Sample: MPP Geographic Coverage

# compound-years
- 1-10
- 11-20
- 21-25
- in MPP, no data
- outside MPP

[Map showing geographic coverage of MPP with color coding for compound-years]
## Diagnostic Regression

<table>
<thead>
<tr>
<th></th>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV death rate (age-adjusted, per 100k pop.)</td>
<td>-0.000137</td>
<td>-0.000139</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000228)</td>
<td>(0.000229)</td>
<td></td>
</tr>
<tr>
<td>HIV prevalence</td>
<td>4.10e-08</td>
<td>4.12e-08</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.20e-07)</td>
<td>(1.20e-07)</td>
<td></td>
</tr>
<tr>
<td>log(population)</td>
<td>0.193</td>
<td>0.196</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.420)</td>
<td>(0.425)</td>
<td></td>
</tr>
<tr>
<td>GDP per capita</td>
<td>7.16e-06</td>
<td>7.09e-06</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(6.02e-06)</td>
<td>(6.32e-06)</td>
<td></td>
</tr>
<tr>
<td>voice and accountability</td>
<td>0.000692</td>
<td>0.000715</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.00116)</td>
<td>(0.00126)</td>
<td></td>
</tr>
<tr>
<td>political stability and lack of violence</td>
<td>0.000450</td>
<td>0.000438</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000610)</td>
<td>(0.000636)</td>
<td></td>
</tr>
<tr>
<td>government effectiveness</td>
<td>-0.000310</td>
<td>-0.000305</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000790)</td>
<td>(0.000876)</td>
<td></td>
</tr>
<tr>
<td>regulatory quality rule of law</td>
<td>0.00126*</td>
<td>0.00125</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000740)</td>
<td>(0.000763)</td>
<td></td>
</tr>
<tr>
<td>control of corruption</td>
<td>-0.00105</td>
<td>-0.00106</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000632)</td>
<td>(0.000624)</td>
<td></td>
</tr>
<tr>
<td>patent$_{det}$</td>
<td>0.000653</td>
<td>0.000665</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.000677)</td>
<td>(0.000713)</td>
<td></td>
</tr>
<tr>
<td>country-drug &amp; year FE$s$</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{ct}$ controls</td>
<td>Y</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>$X_{det}$ controls</td>
<td></td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>$R^2$ (two-way s.e.)</td>
<td>0.820</td>
<td>0.821</td>
<td>0.821</td>
</tr>
<tr>
<td>$R^2$ (one-way s.e.)</td>
<td>0.827</td>
<td>0.828</td>
<td>0.828</td>
</tr>
</tbody>
</table>

*diffusion ID: timing*
Robustness Analyses

Diffusion Analysis: alternative specifications

- Use country-year FEs instead of observable controls

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) % generic orders</th>
<th>(2) % generic quantities</th>
<th>(3)</th>
<th>(4)</th>
<th>(5) # products</th>
<th>(6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$MPP_{dct}$</td>
<td>7.526**</td>
<td>7.535**</td>
<td>7.250**</td>
<td>7.254**</td>
<td>0.0623</td>
<td>0.0629</td>
</tr>
<tr>
<td></td>
<td>(3.355)</td>
<td>(3.347)</td>
<td>(3.123)</td>
<td>(3.122)</td>
<td>(0.113)</td>
<td>(0.113)</td>
</tr>
<tr>
<td>country-drug FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>country-year FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{dct}$ control</td>
<td>Y</td>
<td></td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LHS mean</td>
<td>84.3</td>
<td>84.3</td>
<td>85.6</td>
<td>85.6</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Observations</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
<td>7,084</td>
</tr>
</tbody>
</table>

- Robust and almost identical to main results

diffusion: robustness
Robustness Analyses

Robustness 1: compound-country-year analysis

- Debundle drugs at compound-level and re-analyze: robust
- Cluster at the country level: allow cross-compound correlation

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) % generic orders (#)</th>
<th>(2) % generic orders (#)</th>
<th>(3) % generic orders (#)</th>
<th>(4) % generic quantities (patient-year)</th>
<th>(5) % generic quantities (patient-year)</th>
<th>(6) % generic quantities (patient-year)</th>
<th>(7) # products (strength-dose-firm)</th>
<th>(8) # products (strength-dose-firm)</th>
<th>(9) # products (strength-dose-firm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>comp.-country FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>year FE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{ct}$ control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>$X_{act}$ control</td>
<td>Y</td>
<td></td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>LHS mean</td>
<td>79.8</td>
<td>79.8</td>
<td>79.8</td>
<td>82.1</td>
<td>82.1</td>
<td>82.1</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Observations</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
<td>6,485</td>
</tr>
</tbody>
</table>

diffusion: robustness
Robustness Analyses

Robustness 2: subsample analysis

- Subsample: in countries where a drug is not patented
  - Smaller magnitude (=>$\Rightarrow$ main channel: reduces licensing costs)

<table>
<thead>
<tr>
<th>Dept. Vars. Subsample</th>
<th>(1) % generic orders (#) $Pat.=1$</th>
<th>(2) % generic orders (#) $Pat.=0$</th>
<th>(3) % generic ordered (p.p.y) $Pat.=1$</th>
<th>(4) % generic ordered (p.p.y) $Pat.=0$</th>
<th>(5) # product-manufacturers $Pat.=1$</th>
<th>(6) # product-manufacturers $Pat.=0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panel A: drug-country-year subsamples</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$MPP_{act}$</td>
<td>20.65** (9.771)</td>
<td>4.360 (2.696)</td>
<td>18.03* (9.321)</td>
<td>4.675* (2.709)</td>
<td>-0.0122 (0.0886)</td>
<td>0.0887 (0.126)</td>
</tr>
<tr>
<td>LHS mean</td>
<td>83.73</td>
<td>84.54</td>
<td>84.42</td>
<td>86.12</td>
<td>1.75</td>
<td>1.70</td>
</tr>
<tr>
<td>Observations</td>
<td>2,029</td>
<td>5,055</td>
<td>2,029</td>
<td>5,055</td>
<td>2,029</td>
<td>5,055</td>
</tr>
<tr>
<td>Panel B: compound-country-year subsamples</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LHS mean</td>
<td>84.19</td>
<td>85.54</td>
<td>84.99</td>
<td>87.33</td>
<td>1.75</td>
<td>1.72</td>
</tr>
<tr>
<td>Observations</td>
<td>3,328</td>
<td>3,157</td>
<td>3,328</td>
<td>3,157</td>
<td>3,328</td>
<td>3,157</td>
</tr>
</tbody>
</table>
Robustness Analyses

Robustness 3: price and quantity channels

- Reduced form analysis of price and quantity regressions
  - Overall price effects are mostly driven by price reductions in generic drugs (35%), and the corresponding generic quantity supplied rises by 71% (i.e., more patient-years served).
  - Can't define a compound-country-year level counterpart

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) log(Prices (Per Patient Year))</th>
<th>(2) log(Prices (Per Patient Year))</th>
<th>(3) log(Prices (Per Patient Year))</th>
<th>(4) log(Quantity (Patient-Year Served))</th>
<th>(5) log(Quantity (Patient-Year Served))</th>
<th>(6) log(Quantity (Patient-Year Served))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall: -0.355*** 0.103 (0.0489)</td>
<td>Generic: -0.350*** 0.0798 (0.0335)</td>
<td>Branded: -0.0344 0.0653 (0.0887)</td>
<td>Overall: 0.523*** 0.171 (0.126)</td>
<td>Generic: 0.707*** 0.152 (0.149)</td>
<td>Branded: 0.0797 0.323 (0.352)</td>
</tr>
<tr>
<td>FErickers</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Xct control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Xdct control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>LHS mean</td>
<td>4.95</td>
<td>4.68</td>
<td>6.61</td>
<td>5.44</td>
<td>5.67</td>
<td>3.42</td>
</tr>
<tr>
<td># Obs.</td>
<td>7,084</td>
<td>6,167</td>
<td>1,351</td>
<td>7,084</td>
<td>6,167</td>
<td>1,351</td>
</tr>
</tbody>
</table>
Bacon Decomposition results in the diffusion sample (De Chaisemartin and d’Haultfoeuille, 2020; Goodman-Bacon, 2021)

<table>
<thead>
<tr>
<th>values/outcomes</th>
<th>coeff.</th>
<th>weight</th>
<th>coeff.</th>
<th>weight</th>
<th>coeff.</th>
<th>weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Panel A: diffusion sample</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(drug-country-year)</td>
<td>% generic orders</td>
<td>% quantity-adj. generic</td>
<td># prod. (within drug-country-year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing Groups</td>
<td>11.91</td>
<td>0.048</td>
<td>12.18</td>
<td>0.048</td>
<td>0.0001</td>
<td>0.048</td>
</tr>
<tr>
<td>Always vs timing</td>
<td>5.60</td>
<td>0.047</td>
<td>5.35</td>
<td>0.047</td>
<td>-0.04</td>
<td>0.047</td>
</tr>
<tr>
<td>Never vs Timing</td>
<td>6.79</td>
<td>0.901</td>
<td>6.66</td>
<td>0.901</td>
<td>0.09</td>
<td>0.901</td>
</tr>
<tr>
<td>Always vs never</td>
<td>50.92</td>
<td>0.001</td>
<td>38.31</td>
<td>0.001</td>
<td>-2.91</td>
<td>0.001</td>
</tr>
<tr>
<td>Within</td>
<td>76.23</td>
<td>0.003</td>
<td>82.28</td>
<td>0.003</td>
<td>0.10</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Panel B: competition sample</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(comp.-country-year)</td>
<td>% generic orders</td>
<td>% quantity-adj. generic</td>
<td># prod. (within comp.-country-year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing Groups</td>
<td>11.30</td>
<td>0.088</td>
<td>12.67</td>
<td>0.088</td>
<td>0.10</td>
<td>0.088</td>
</tr>
<tr>
<td>Always vs timing</td>
<td>5.73</td>
<td>0.019</td>
<td>7.51</td>
<td>0.019</td>
<td>0.11</td>
<td>0.019</td>
</tr>
<tr>
<td>Never vs Timing</td>
<td>8.89</td>
<td>0.878</td>
<td>9.60</td>
<td>0.878</td>
<td>0.16</td>
<td>0.878</td>
</tr>
<tr>
<td>Always vs never</td>
<td>4.09</td>
<td>0.006</td>
<td>1.74</td>
<td>0.006</td>
<td>-0.17</td>
<td>0.006</td>
</tr>
<tr>
<td>Within</td>
<td>25.99</td>
<td>0.009</td>
<td>18.50</td>
<td>0.009</td>
<td>-1.92</td>
<td>0.009</td>
</tr>
</tbody>
</table>
### Sensitivity Analysis 1: Countries

- Sensitivity analysis on territory inclusion: robust
  - MPP common territories: sub-Saharan Africa + Djibouti
  - Territories ever in MPP: countries in some drug’s territories

<table>
<thead>
<tr>
<th>Samples Dept. Vars.</th>
<th>(1) MPP common territories</th>
<th>(2) MPP ever-covered territories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% generic</td>
<td>%Q generic</td>
</tr>
<tr>
<td>( MPP_{dct} )</td>
<td>5.011*</td>
<td>5.312**</td>
</tr>
<tr>
<td></td>
<td>(2.851)</td>
<td>(2.553)</td>
</tr>
<tr>
<td>LHS mean</td>
<td>88.65</td>
<td>89.74</td>
</tr>
<tr>
<td># obs.</td>
<td>3,547</td>
<td>3,547</td>
</tr>
</tbody>
</table>

**diffusion: robustness**
Sensitivity Analysis 2: Drug Comparisons

(1) only 1st MPP drug addition and drugs in the same class; (2) drop drug classes without MPP inclusion; (3) drop drugs with US not recommended compounds; (4) drop drugs approved before 1996; (5) only drugs owned by MPP insiders; (6) by firms “all in” or “all out” MPP

<table>
<thead>
<tr>
<th>Samples</th>
<th>(1) drug class in 1st pool addition</th>
<th>(2) drop one drug class</th>
<th>(3) drop drug no longer U.S. recommended</th>
<th>(4) drugs approved 1996+</th>
<th>(5) drugs by MPP insider firms</th>
<th>(6) by firms “all in” or “all out” MPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPP_{act}</td>
<td>11.13***</td>
<td>7.030**</td>
<td>7.415**</td>
<td>6.848**</td>
<td>7.304**</td>
<td>8.087*</td>
</tr>
<tr>
<td></td>
<td>(3.586)</td>
<td>(2.951)</td>
<td>(2.967)</td>
<td>(2.938)</td>
<td>(2.842)</td>
<td>(3.787)</td>
</tr>
<tr>
<td></td>
<td>[3.471]</td>
<td>[2.773]</td>
<td>[2.687]</td>
<td>[2.705]</td>
<td>[2.706]</td>
<td>[3.633]</td>
</tr>
<tr>
<td>LHS mean</td>
<td>94.80</td>
<td>82.77</td>
<td>83.92</td>
<td>83.41</td>
<td>86.64</td>
<td>65.97</td>
</tr>
<tr>
<td># Obs.</td>
<td>4,463</td>
<td>5,828</td>
<td>6,316</td>
<td>5,786</td>
<td>6,127</td>
<td>3,196</td>
</tr>
</tbody>
</table>

Panel A: % generic orders as dependent variable

Panel B: % generic quantity ordered (patient year) as dependent variable

MPP_{act} | 10.32*** | 6.520** | 7.234** | 6.620** | 7.145** | 7.258* |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(3.366)</td>
<td>(2.874)</td>
<td>(2.838)</td>
<td>(2.823)</td>
<td>(2.727)</td>
<td>(3.648)</td>
</tr>
<tr>
<td></td>
<td>[3.335]</td>
<td>[2.781]</td>
<td>[2.693]</td>
<td>[2.702]</td>
<td>[2.709]</td>
<td>[3.973]</td>
</tr>
<tr>
<td>LHS mean</td>
<td>95.44</td>
<td>84.11</td>
<td>85.25</td>
<td>84.64</td>
<td>88.13</td>
<td>69.22</td>
</tr>
<tr>
<td># Obs.</td>
<td>4,463</td>
<td>5,828</td>
<td>6,316</td>
<td>5,786</td>
<td>6,127</td>
<td>3,196</td>
</tr>
</tbody>
</table>

diffusion: robustness
Outline

6 Appendices

7 A1: Institutions

8 A2: Diffusion

9 A3: Innovation

10 A5: Others
Identification Assumptions & Justifications

- **Identification**: common trends (event study) & lack of common shocks (DGP)
- Are compounds in MPP of higher values? w/ compound FE
  - Control for: US FDA approval status & US patent status
- Are firms strategically timing compound-level MPP entry?
  - Ambiguous in theory (Rey & Tirole, 2019); No, from data & interview

method: innovation
Event Studies: # new trials

- # new trials
- # new trials, MPP insiders
- # new trials, MPP in-out mix
- # new trials, MPP outsiders

 innov results: baseline
Firms further reallocate clinical trials across phases

- R&D reallocation cross-phase: esp/ phases 3 & 4 follow-on trials
  - 1: safety; 2: efficacy; 3: effectiveness; 4: post-market surveillance

- Large heterogeneity across phases and firm types
  - Follow-on trials on ph.3 trials mainly increases from outsiders
  - Post-market (ph.4) trials shifted from pool-insiders to outsiders
Overview of the Drug Approval Process

- Clinical trials from pipeline to market
- Increase ph.3 trials to push more products to the market

**Phase I**
- Safety & dosage
- 10-20 healthy volunteers

**Phase II**
- Efficacy & side effects
- A few hundreds patients

**Phase III**
- Efficacy & monitoring of adverse reactions (e.g., new cocktails)
- Hundreds to 1000+ people

**Phase IV**
- Post-market long-term safety & efficacy (in diverse patient groups)
- FDA approval (~6 mon. fast track)
- “Real life patients”

RnD reallocation
R&D input: phase 3 follow-on trials

- Phase 3: the large scale pre-approval human trial
  - Last stage before FDA review drugs for marketing
- MPP insiders increase ph.3 follow-on trials (new cocktails)
R&D input: phase 4 follow-on trials

- Phase 4: post-market surveillance trials monitoring safety
  Often mandatory to monitor the long-term impact for life-saving drugs
- MPP insiders reduce ph.4 trials & outsiders increase ph.4 trials

![Graphs showing R&D reallocation over time for MPP insiders, MPP mix, and MPP outsiders.](image)
R&D outputs: an overview of HIV drug approvals

- All approvals: branded & generic (innovation & imitation)
- Generic firms’ comparative advantage: multi-firm bundling
  - From the 1\textsuperscript{st}-ever drug cocktail to the status quo

<table>
<thead>
<tr>
<th>w/ new compounds</th>
<th>w/ existing compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 (50%)</td>
<td>30 (50%)</td>
</tr>
</tbody>
</table>

1\textsuperscript{st} approvals of HIV drugs

- Branded firms: 17, w/ 13 cocktails (bundles across 1.5 firms)
- Generic firms: 13, all cocktails (bundles across 2.3 firms)
### HIV Drug Approvals: DID results

- **Compound-year level** \# new drug product approvals

<table>
<thead>
<tr>
<th>Dept. Vars.</th>
<th>(1) # new approvals</th>
<th>(2) # new approvals</th>
<th>(3) # new approvals</th>
<th>(4) # new approvals</th>
<th>(5) # new approvals</th>
<th>(6) # new approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td>$MPP_{at}$</td>
<td>2.418** (0.908)</td>
<td>2.607** (0.993)</td>
<td>2.034** (0.961)</td>
<td>2.478** (0.980)</td>
<td>0.383** (0.143)</td>
<td>0.129 (0.140)</td>
</tr>
<tr>
<td>comp. &amp; year FE's</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>X_{at} control</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>LHS mean</td>
<td>2.28</td>
<td>2.28</td>
<td>2.01</td>
<td>2.01</td>
<td>0.27</td>
<td>0.27</td>
</tr>
<tr>
<td>Observations</td>
<td>378</td>
<td>378</td>
<td>378</td>
<td>378</td>
<td>378</td>
<td></td>
</tr>
</tbody>
</table>

- Branded firms react strongly with FDA approval, and generic firms react strongly w.r.t. the MPP net of FDA approval of a compound
Descriptive Analysis: “Time-to-1st Generic” Histograms

- w/o MPP compounds, 2005-2018
- w/ MPP compounds, 2005-2018
- w/o MPP compounds, 2010-2018
- w/ MPP compounds, 2010-2018

innovation results: summary
Duration Analysis: Time-to-Generic & the MPP

- Simple analysis of “time-to-generic”

<table>
<thead>
<tr>
<th></th>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
<th>(4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Panel A: Cox Proportional Hazard Model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPP</td>
<td>0.532**</td>
<td>0.647**</td>
<td>1.019**</td>
<td>0.371</td>
</tr>
<tr>
<td></td>
<td>(0.222)</td>
<td>(0.257)</td>
<td>(0.397)</td>
<td>(0.472)</td>
</tr>
<tr>
<td><strong>Panel B: Regression Analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPP</td>
<td>-3.204***</td>
<td>-3.727***</td>
<td>-1.827</td>
<td>-0.157</td>
</tr>
<tr>
<td></td>
<td>(1.117)</td>
<td>(1.317)</td>
<td>(1.102)</td>
<td>(1.738)</td>
</tr>
<tr>
<td>year FE</td>
<td></td>
<td></td>
<td><strong>Y</strong></td>
<td><strong>Y</strong></td>
</tr>
<tr>
<td>drug class FE</td>
<td></td>
<td></td>
<td><strong>Y</strong></td>
<td><strong>Y</strong></td>
</tr>
<tr>
<td>LHS mean</td>
<td>12.57</td>
<td>13.62</td>
<td>12.57</td>
<td>13.62</td>
</tr>
<tr>
<td>Observations</td>
<td>108</td>
<td>75</td>
<td>108</td>
<td>75</td>
</tr>
</tbody>
</table>
Alternative Method: Count Data Models

- Robustness results for the drug approval analyses

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

Robustness results for the drug approval analyses.
Bacon Decomposition results in the innovation sample (De Chaisemartin and d’Haultfoeuille, 2020; Goodman-Bacon, 2021)

<table>
<thead>
<tr>
<th>Panel B: innovation sample (compound-year level)</th>
<th># of new clinical trials</th>
<th># firms in clinical trials</th>
<th># drug product approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing Groups</td>
<td>6.96</td>
<td>11.05</td>
<td>1.06</td>
</tr>
<tr>
<td>Never vs Timing</td>
<td>10.08</td>
<td>21.56</td>
<td>2.78</td>
</tr>
<tr>
<td>Within</td>
<td>-44.06</td>
<td>-61.29</td>
<td>3.77</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># approvals, generic</th>
<th># approvals, branded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing Groups</td>
<td>0.80</td>
</tr>
<tr>
<td>Never vs Timing</td>
<td>2.44</td>
</tr>
<tr>
<td>Within</td>
<td>6.74</td>
</tr>
</tbody>
</table>

→ innovation results: summary
MPP Case 1: a Pediatric HIV Cocktail

- The lack of pediatric formulations reflect demand in high-income countries: most pregnant women are tested for HIV, and quick use of HIV drugs can prevent mother-to-children transmission.

- The first pediatric granules formulation for LPV/r was developed by Mylan with MPP licenses and marketed in 2018 (for sales in developing countries); and more to come (NYT 11/29/2019).

- If needed, branded firms can be granted back low-cost non-exclusive licenses for patents on this new formulation.

The New York Times

GLOBAL HEALTH

Nov. 29, 2019

New Strawberry-Flavored H.I.V. Drugs for Babies Are Offered at $1 a Day

Thousands of infants are doomed to early deaths each year, in part because pediatric medicines come in hard pills or bitter syrups that need refrigeration.

“… the more common ped. HIV treatment contains 40% alcohol and had a bitter metallic taste…” (4 syringes, twice a day)
MPP Case 2: the TDF family

- Case study: Gilead Sciences & TDF (prodrug of tenofovir)
- Gilead joined the MPP in 2011, put in drugs including TDF
- TAF (prodrug of TDF) enters MPP in 2014 (ph.3 starts in 2012, primary completion 2014, FDA approval 2015)
- Pipeline: tenofovir-based microbicides (ph.s 2+3 started in 2012, Gilead with partners; phase 1 finished in 2008)
MPP Case 3: TLD revisit (the illustrative example)

- TLD, the 3-compound daily cocktail 1\textsuperscript{st} created by Mylan
- TLD = TDF (Gilead) + DTG + 3TC (ViiV), 2017 approval
- ViiV started a clinical trial in 2017 on DTG+3TC (Dovato)
- FDA approval in 2019; same dose combo as TLD sub-dose
- The first, once-daily, single-pill, \textbf{two}-compound regimen
  - Comparable to some three-compound regimen
Data: HIV Drug Diffusion in LMIC

- The complete HIV drug portfolio data: FDA & AIDSinfo
  - Generic names, abbreviations, drug classes, branded firms
  - Information on US adult daily doses using FDA labeling

- HIV drug public procurement data in LMIC, 2007-2017
  - Price & quality reporting by Global Fund-supported programs

- MPP inclusion time & territories: MPP licensing contracts

- International patent status: MedsPaL & DrugPatentWatch

- Country-year controls: HIV death rate & prevalence, population, income, six institutional factors (worldwide governance indicators)
  - World Bank and Institute for Health Metrics & Evaluation
Data: R&D Inputs & Outputs on HIV Drugs

- **R&D inputs**: clinical trials with HIV compounds, 2000-2017
  - Global clinical trials from the US-registry clinicaltrials.gov
  - Compound-level trial identifiers from AIDSinfo

  - All FDA approvals and tentative approvals from Drugs@FDA
  - All WHO approvals from WHO pre-qualification program

- **US drug patent data**: Drug Bank via FDA Orange Book
Discussion: External Validity

- What can we learn beyond this case study of the MPP?
  - Combating HIV is important, yet it is still a special case

- External validity: beyond HIV and opportunistic infections
  - USPTO advocated patent pools for biotech, but no progress
  - CRISPR-Cas9 gene editing patent pools face many difficulties
  - MPP expands to cover all small molecule essential medicines
  - Business model innovation (Christensen et al., 2019).

“Prosperity paradox”: “market-creating innovations”; “It’s less about the actual product being sold, but more about the value networks and business model that innovators creates.”
Discussion: Pool Design

- Empirical evidence on patent pools is overall negative
  - Partly explained by the mechanism design features of pools
  - Measures matter: patent counts/citations vs. R&D activities

- Different from pools in ICT and the Eco-Patent Commons
  - No fragmented rights and clear value (closer to traditional pools)
  - Compound as the smallest licensing unit (not at patent level)
  - Highly skilled, passionate employees; active engagement

Esp. EcoPC: 1) lack of technology transfer; 2) firms are not specialized in energy/environment and file side-patents with limited values; 3) not much promotion of the EcoPC with unmotivated employees