

Policy Incentives for Pharmaceutical Innovation

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JOB MARKET PAPER



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Incentives for drug innovation

Pharmaceutical interventions are responsible for huge mortality and morbidity gains since the 20th century.

- Accounts for ~1/3 of life expectancy increases in recent decades (Buxbaum et al, 2022)

R&D in this industry is notoriously expensive and risky.

- On the order of ~\$1.5-2 billion per approved new compound (DiMasi et al, 2016)
- Rule of thumb estimate that <10% of new drugs reach market

Once on the market, drug products are easily replicable.

Policy solution: FDA-granted market exclusivity and patents

- New Chemical Entities receive 5 years of exclusivity before generic entry

Incentives for *certain types of* drug innovation

Policy typically offers increased incentives where discrepancies between private and social value of innovation may lead to suboptimal innovation.

- Orphan drugs (7 years), biologics (12 years)

Can market exclusivity more efficiently “target” drug innovation compared to patents?

- Rivals cannot legally challenge market exclusivity
- Specific to pharmaceuticals and FDA’s authority
- Precedent for tailoring term lengths

Research question

Key economic and policy question:

How does extending exclusivity affect innovation?

Today:

Evaluate effects of a 2012 policy (Generating Antibiotic Incentives Now Act, “GAIN Act”) that extended market exclusivity for antibiotics by an additional 5 years.

Preview of reduced form results

Difference-in-differences approach compares antibiotics to non-GAIN-eligible infectious disease products

The GAIN Act increased antibiotics innovation across a range of outcomes, including:

- Patent filings ↑ 47%
 - Related to drugs as well as diagnostics
- Preclinical studies increase (with a delay)
- Clinical studies (phase 3 only) increase
 - Drugs with product patents (more novel) and older patents (larger benefit from GAIN) drive response

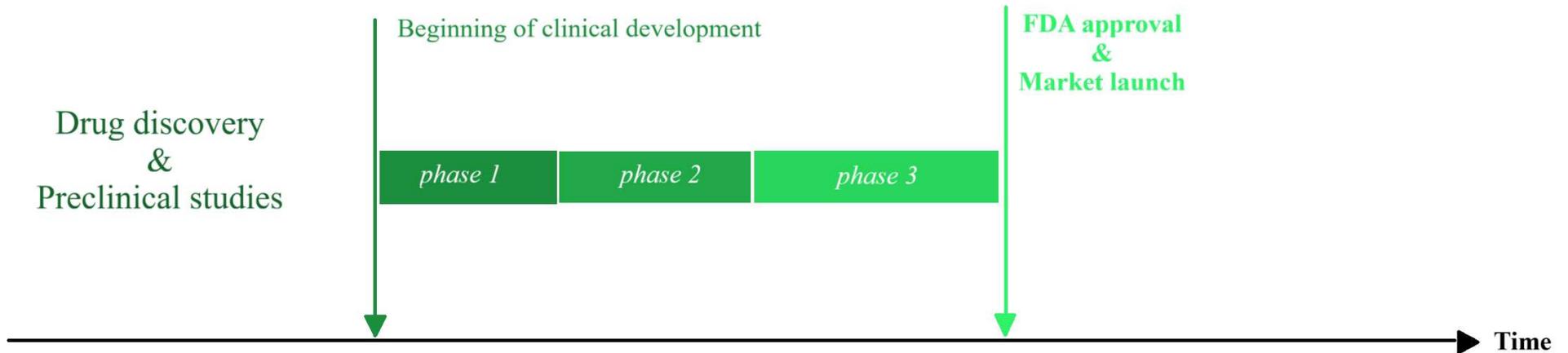
Related literature

- **On the market size elasticity of drug innovation**
Adams 2021 CBO WP; Acemoglu & Linn, 2004; Blume-Kohout & Sood, 2013; Dubois et al, 2015; Finkelstein, 2004
- **On market exclusivity**
Yin (2008) on the Orphan Drug Act of 1983
- **On antibiotics or the GAIN Act**
Adda, 2020; Alsan et al., 2021; Darrow and Kesselheim, 2020; Majewska, 2022 working paper
- **Other innovation policies (patents, AMCs, direct grants)**
Budish et al, 2015; Gaessler & Wagner, 2022; Kyle & McGahan, 2012; Kremer et al, 2020; Howell, 2017

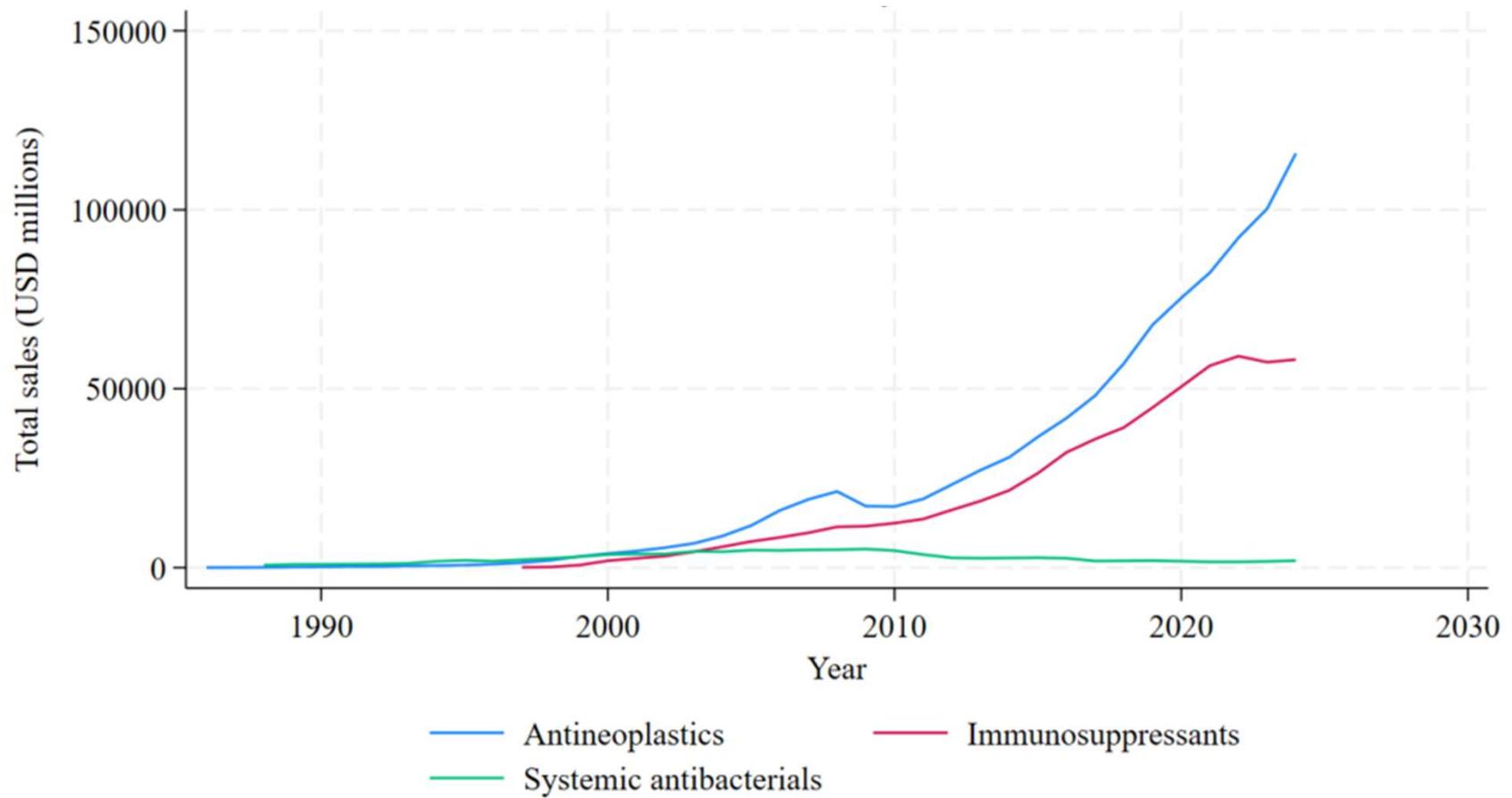
Antibiotics Innovation and the GAIN Act

- Background on drug development and antibiotics
- Empirical approach, data, and sample construction
- Results
 - Aggregate
 - Heterogeneity by patent characteristics

Overview of drug development and exclusivities



Antibiotics are a particularly small market



Antibiotic developers face unique challenges

New antibiotics generally believed to have limited market size

- Short-course treatments
- Weaker correlation between quality/efficacy and demand due to stewardship
- Risk of obsolescence due to developing resistance

The New York Times

Crisis Looms in Antibiotics as Drug Makers Go Bankrupt

First Big Pharma fled the field, and now start-ups are going belly up, threatening to stifle the development of new drugs.

New antibiotics are key to combatting resistance

Drug-resistant pathogens are a significant public health issue

- 2.8m antibiotic-resistant infections in the US each year
- 35,000 annual deaths

Widely held that there is too little innovation in antibiotics

- Only 17 new systemic antibiotics and 1 biologic approved 2010-2021

Different policies implemented:

- **US GAIN Act (proposed 2011): +5 years of market exclusivity for antibiotics**
- UK subscription model (2022): contracts of \$10m per year, set based on other countries paying equivalent GDP-scaled amounts
- CARB-X (2016): global nonprofit partnership that directly funds projects

Identification using the GAIN Act

“Generating Antibiotic Incentives Now” (GAIN) Act

- Introduced in Congress in 2010, enacted in 2012 (consider 2011 as first treatment year)
- Provided +5 years of non-patent market exclusivity for drug candidates deemed “qualified infectious disease products” (QIDPs)
 - Specific list of qualifying bacteria/fungi released in 2014
 - Also granted priority review and fast-track status

Antivirals + vaccines form a good control group

- Likely share similar demand-side shocks (e.g., common co-infections with virus and bacteria)
- Different development processes, hence spillovers between treatment & control are unlikely
 - Among all drugs with phase 2 or higher trials, 93% of firms only in treatment or control
 - Weighting by number of drugs, 79% have >90% in one of either treatment or control

Data

We need to observe when **various innovation outcomes** occur, where observations can be **categorized into treatment versus control indications.**

- Clarivate *Cortellis Competitive Intelligence* database
 - Patents by indication (and some drug linkage)
 - Milestones (preclinical, phase 1/2/3 clinical trial, market launch) by drug, indication, and country
- All treated or control outcomes applicable to the United States, 2005-2019
- ~1,500 treated drugs and ~3,500 control drugs

Sample descriptives

Table 1. Descriptive Statistics, 2005-2019

	Treatment	Control	Total
Total patent applications	26,589	27,157	53,746
Total unique drug candidates	1,473	3,485	4,958
Drugs with QIDP status	110	1	111
Oral dosage form	20%	16%	17%
Has matched patent	43%	41%	42%
Has product patent	18%	18%	18%
Private firm originator	81%	81%	81%
Orphan drug	9%	7%	7%

Empirical approach

Create annual time series data of logged counts of outcome variables, separately by treatment and control.

- Log-transformation helps with differences in scale, especially for patent and preclinical outcomes
- Outcomes only counted once for drugs with multiple indications

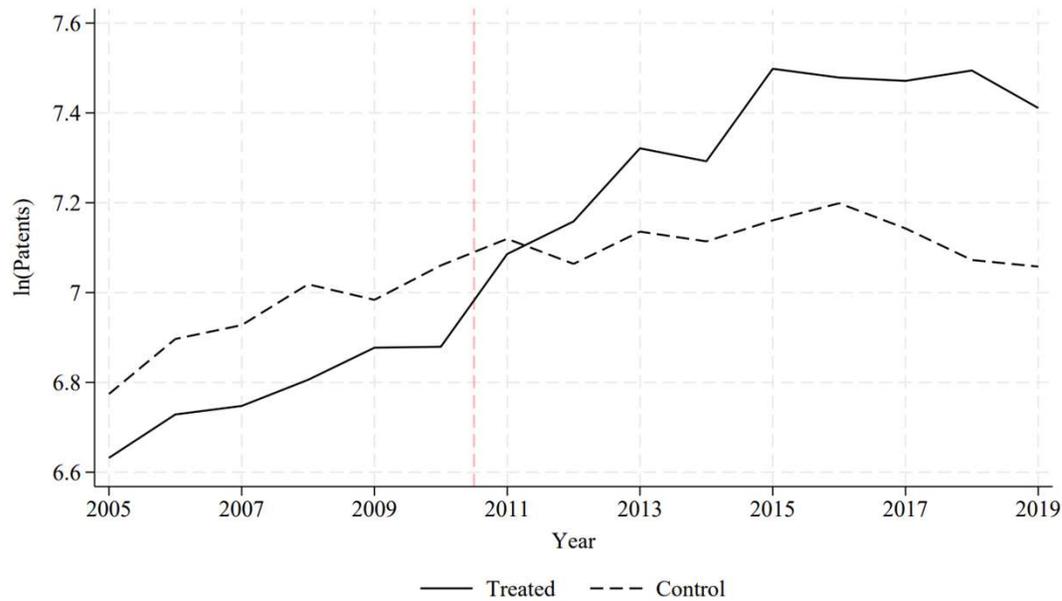
Event study (GAIN Act = 2011)

$$Y_{gt} = \sum_t \beta_t \times 1\{treat\}_g + \alpha_t + 1\{treat\}_g + \epsilon_{gt}$$

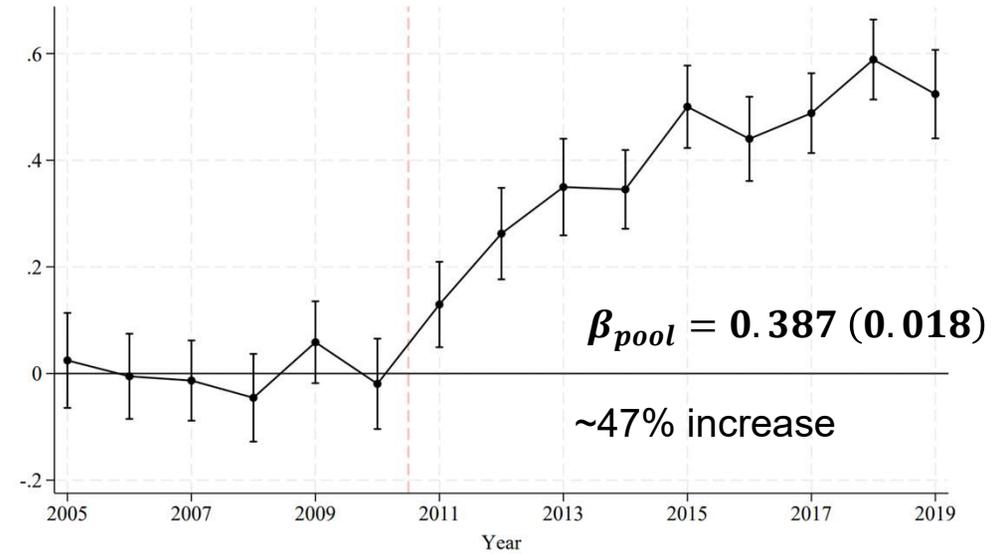
- β_t captures normalized difference in logged means between g (treatment and control)
- Standard errors obtained via bootstrapping procedure

Results: Patenting

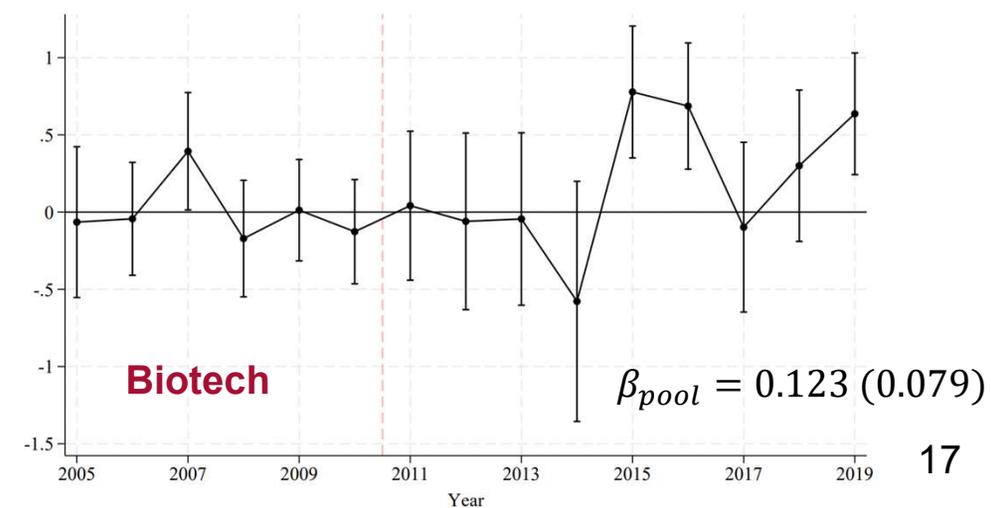
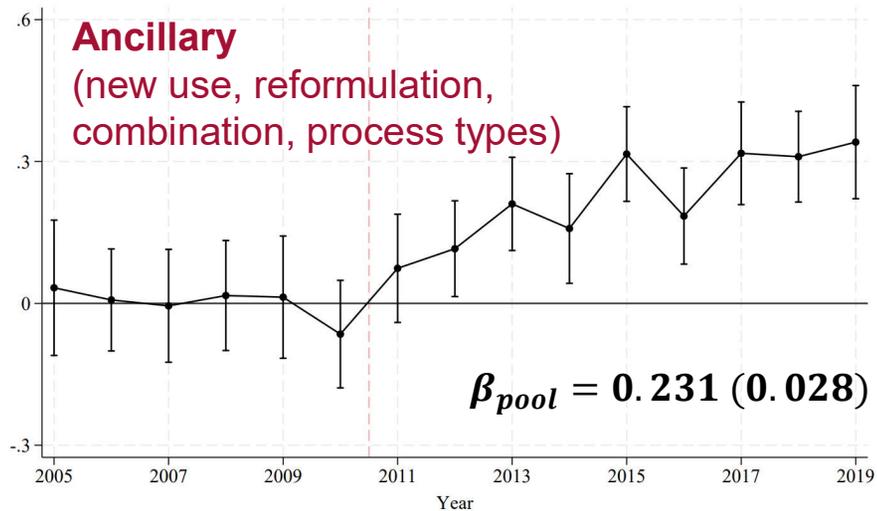
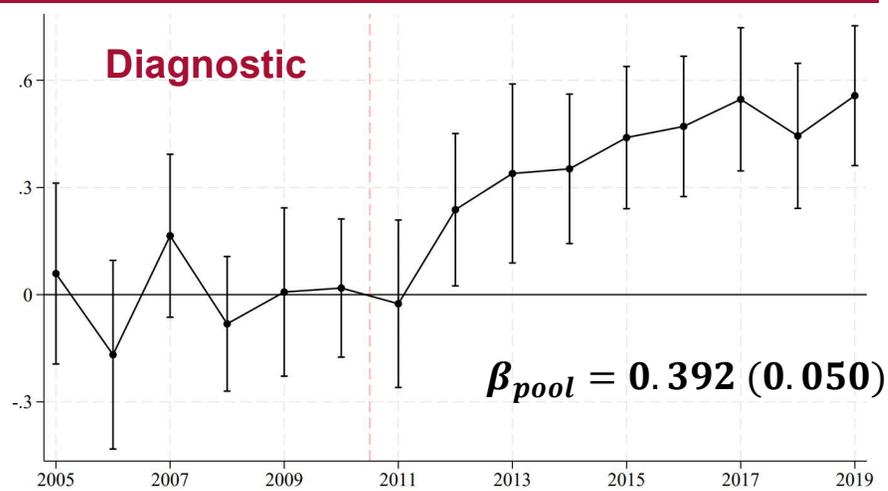
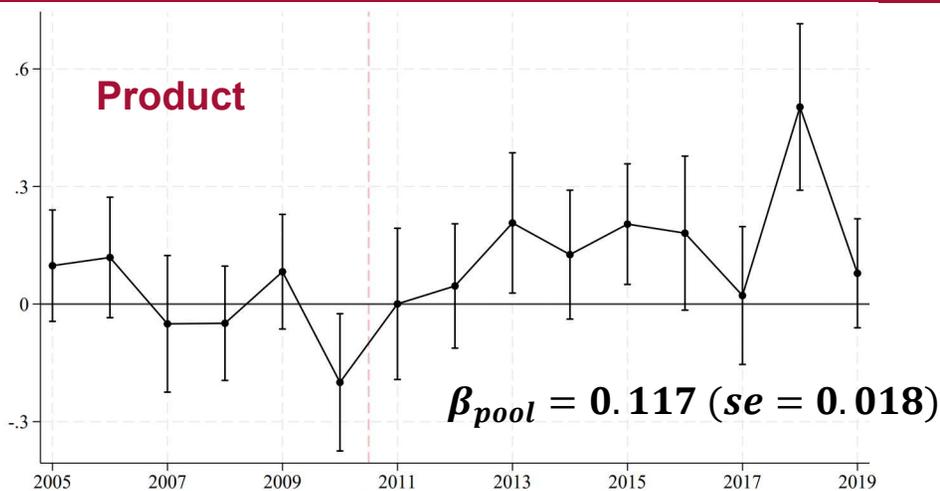
A. Raw Trends in In(Patent Filings)



B. Event Study Estimates

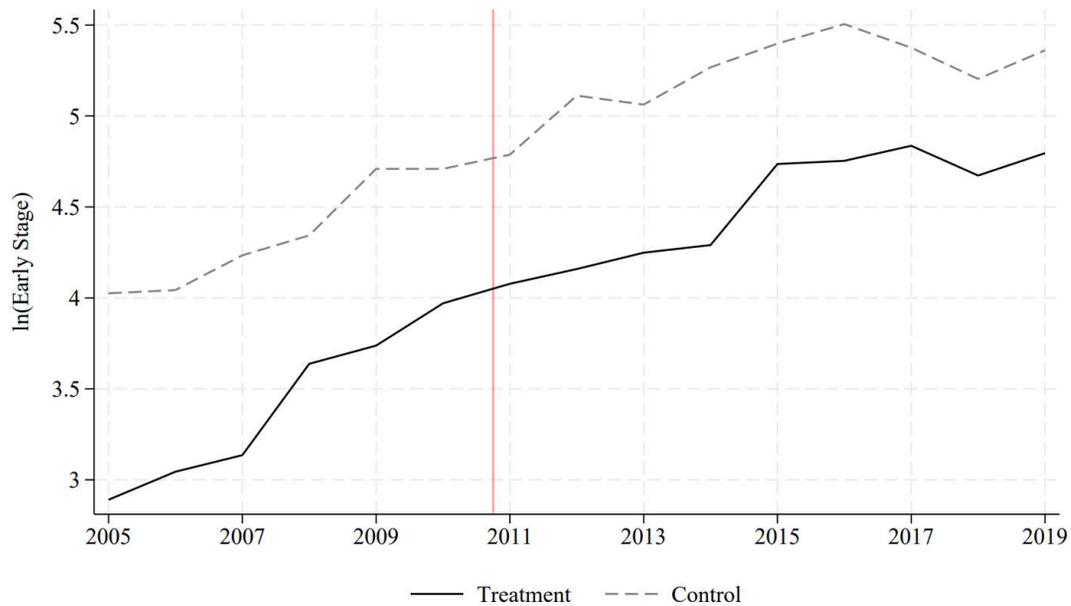


Patenting results *by type of patent*

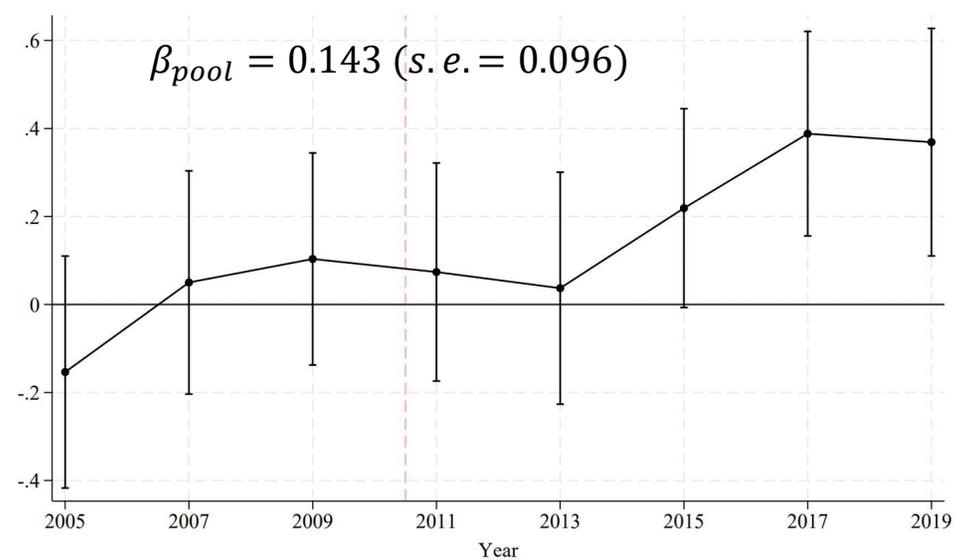


Results: Preclinical studies

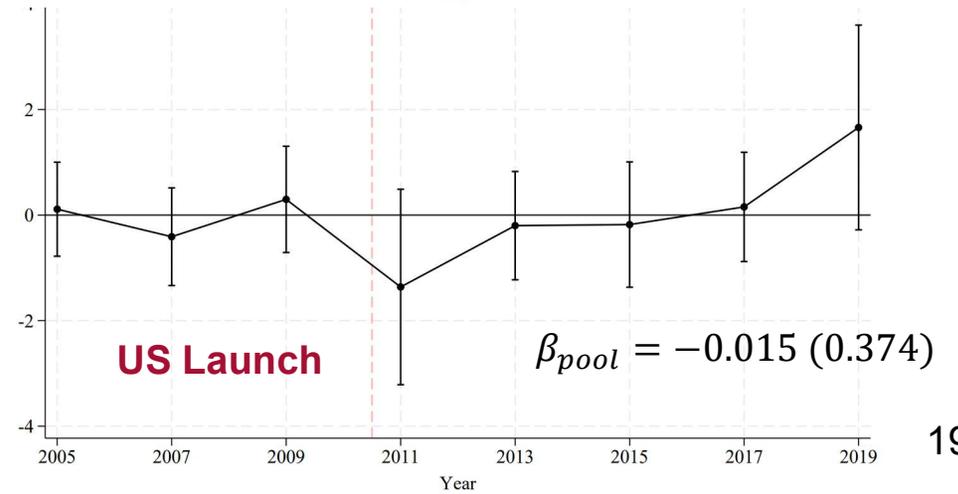
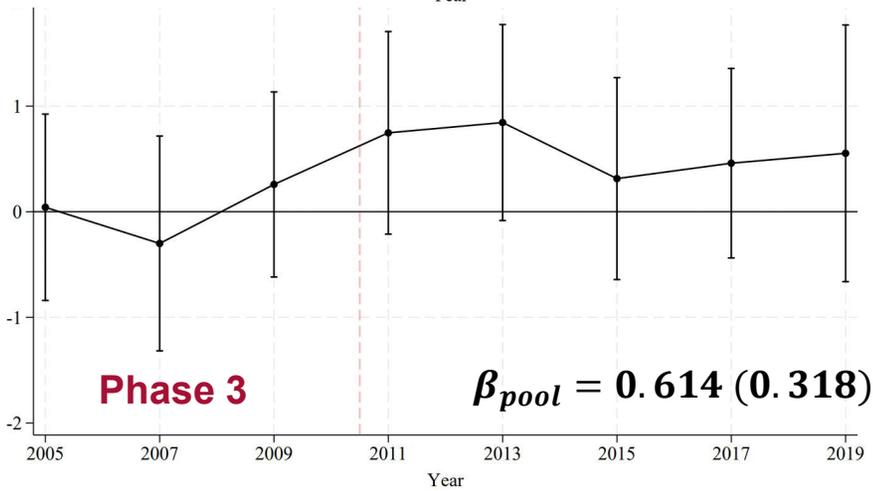
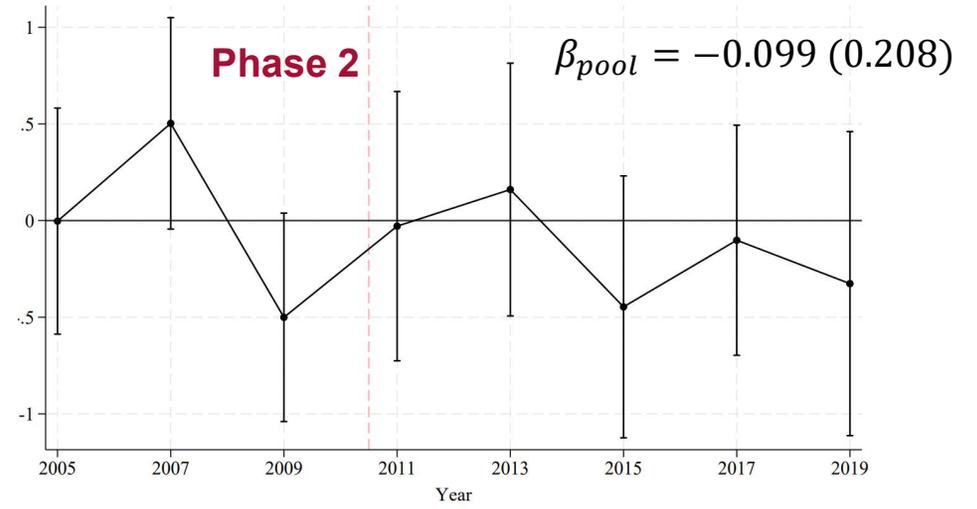
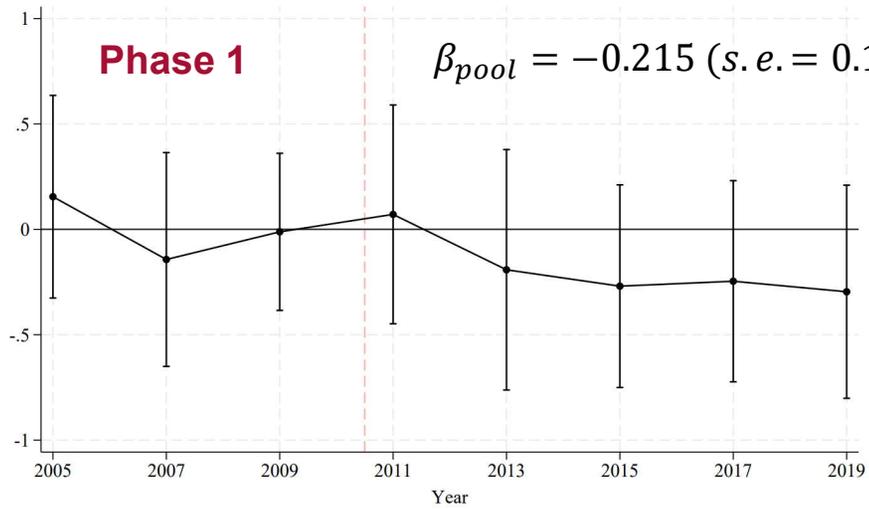
A. Raw Trends in ln(Preclinical studies)



B. Event Study Estimates



Results: Clinical trials



Alternative specification: phase transition approach

Can also take a drug-level approach and look at the probability that drug i in phase k transitions to phase k' in any given year

- Helps with statistical power
- Allows us to control for drug-level characteristics and conduct heterogeneity analyses by drug characteristics

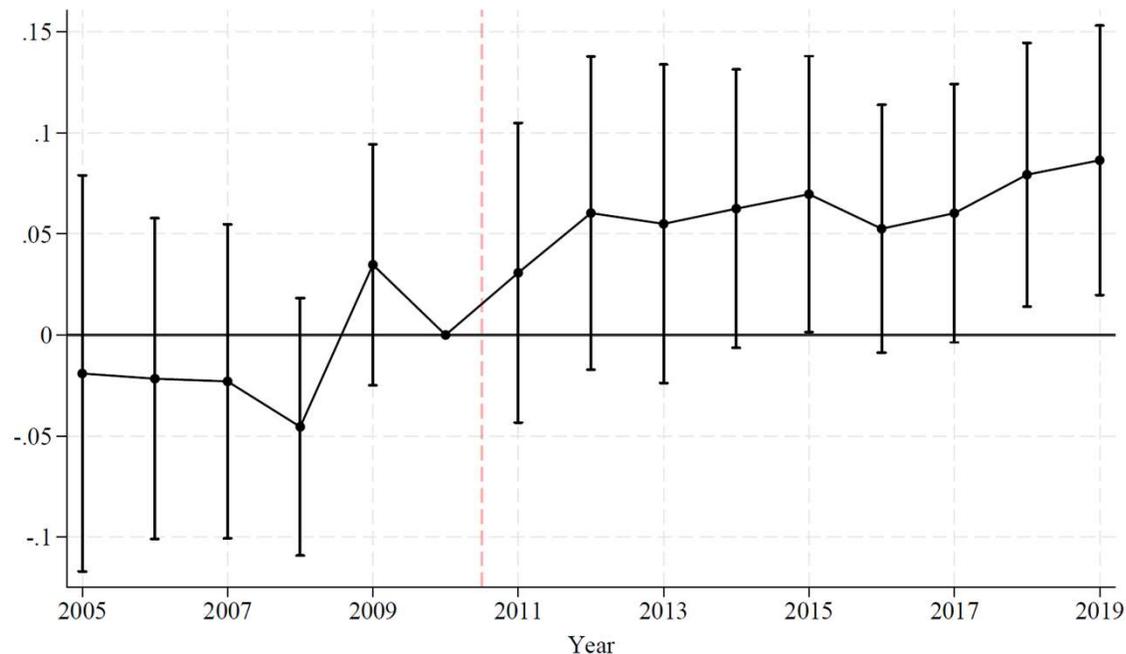
$$Y_{ict}^{k,k'} = \sum_{t \neq 2010} \gamma_t \times 1\{treat\}_i + \pi_c + \pi_c \times 1\{treat\}_i + \delta_i + \alpha_t + \alpha_g + \epsilon_{it}$$

- Including cohort (c) by group FE and group FE
- Interpret Y as the annual transition probability

Results: phase transition success, heterogeneity by drug characteristics

Phase transition approach confirms approach using $\ln(\text{trial initiations})$

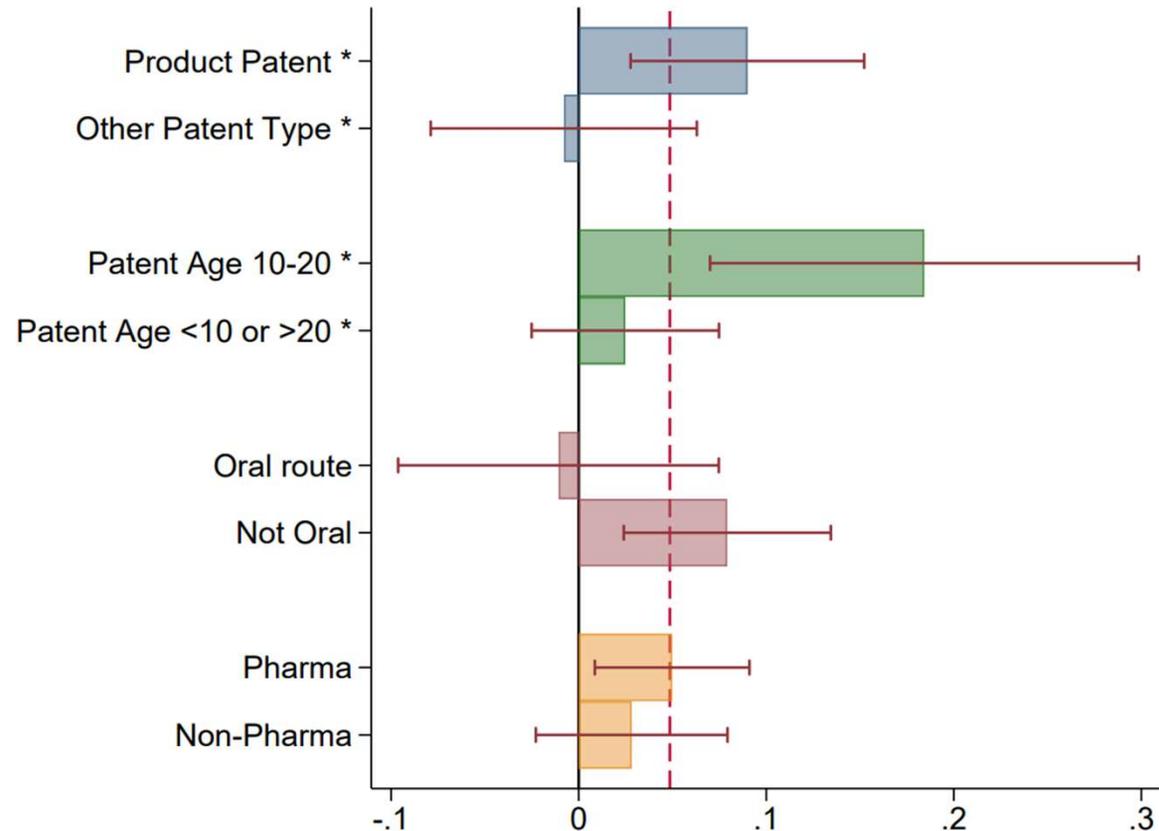
- Effect on advancing to phase 3 trial is **4.9pp (s.e. = 0.019)**, 94% increase over pre-period mean
- Suggests that existing/pre-GAIN phase 1 and 2 trials are advancing more quickly



Results: phase transition success, heterogeneity by drug characteristics

Heterogeneity analyses reveal the importance of drug's patent characteristics

- Restricts to drugs with matched patent(s)
- Larger effects on phase 3 transition for drugs with product patents, **+0.098 (0.048)**
- Larger effects on phase 3 transition for drugs with older (but not yet expired) patents, **+0.184 (0.058)**

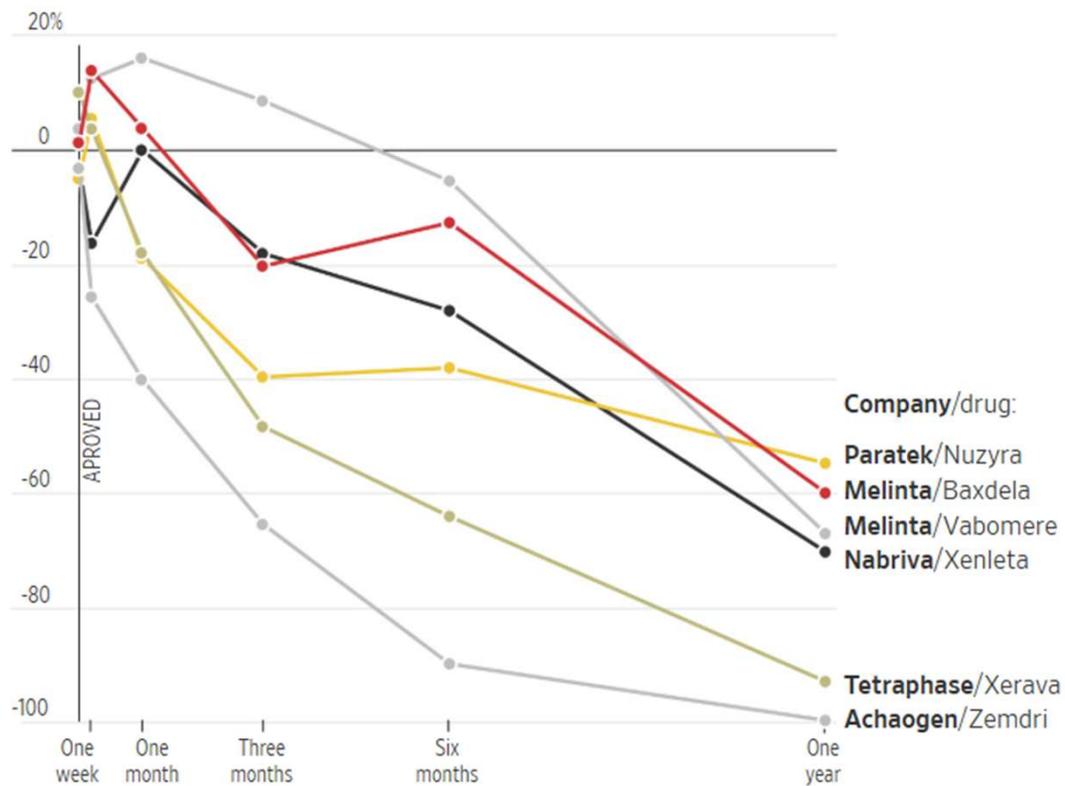


Takeaways

1. Antibiotic innovation responds to incentives, but still unclear whether policy has a “meaningful” impact on treatment of antibiotic resistant infections.
2. Effects visible across range of outcomes: patenting, pre-clinical, and phase 3 clinical stages
 - Limitations in ending analysis window before COVID-19 pandemic
3. Meaningful increases in patenting activity AND stronger responses for drugs with older patents
 - Support for identification strategy; patent exclusivity remains relevant
 - Echoes of Budish, Roin, and Williams (2015) or Gaessler and Wagner (2022)
4. Stronger responses for drugs with product patents
 - Also see effects on the number of *new* product patents (but more modest in size)

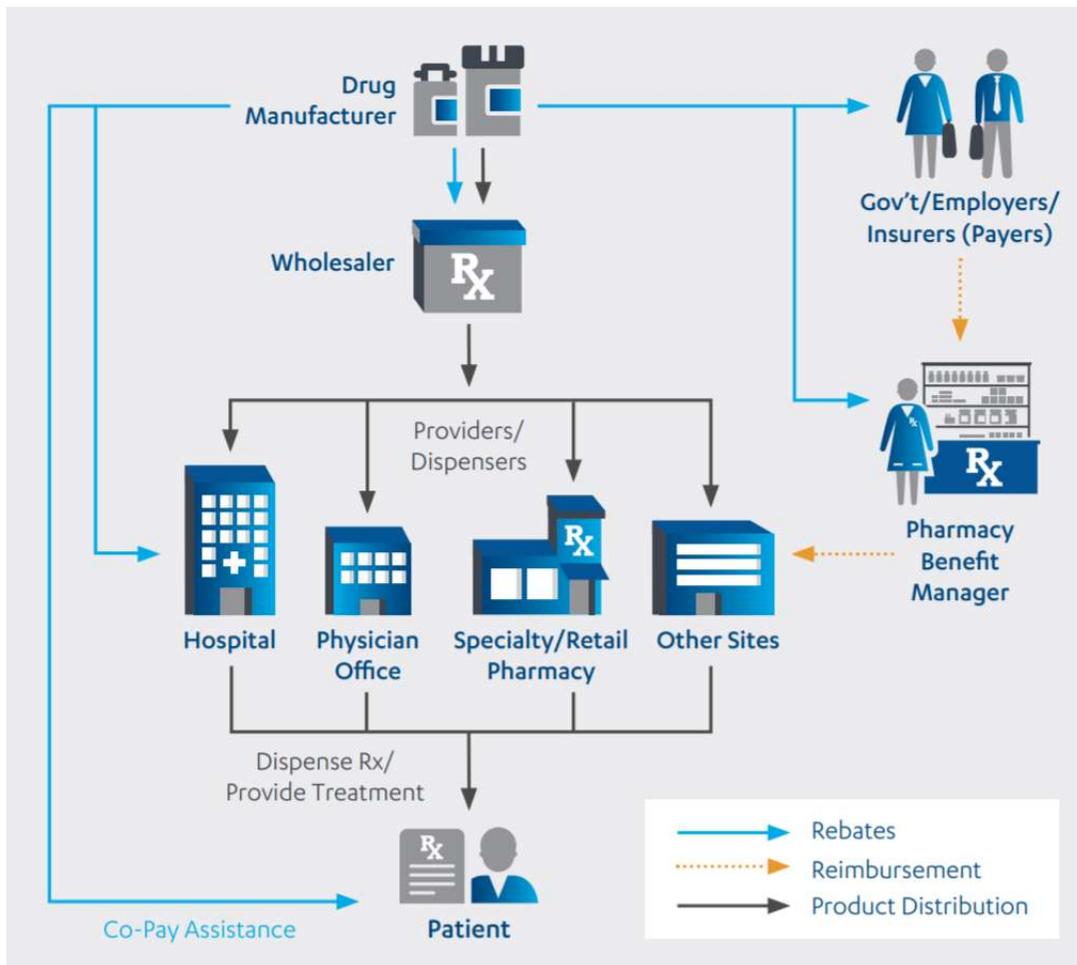
Where are we now?

Change in companies' stock prices after FDA approval

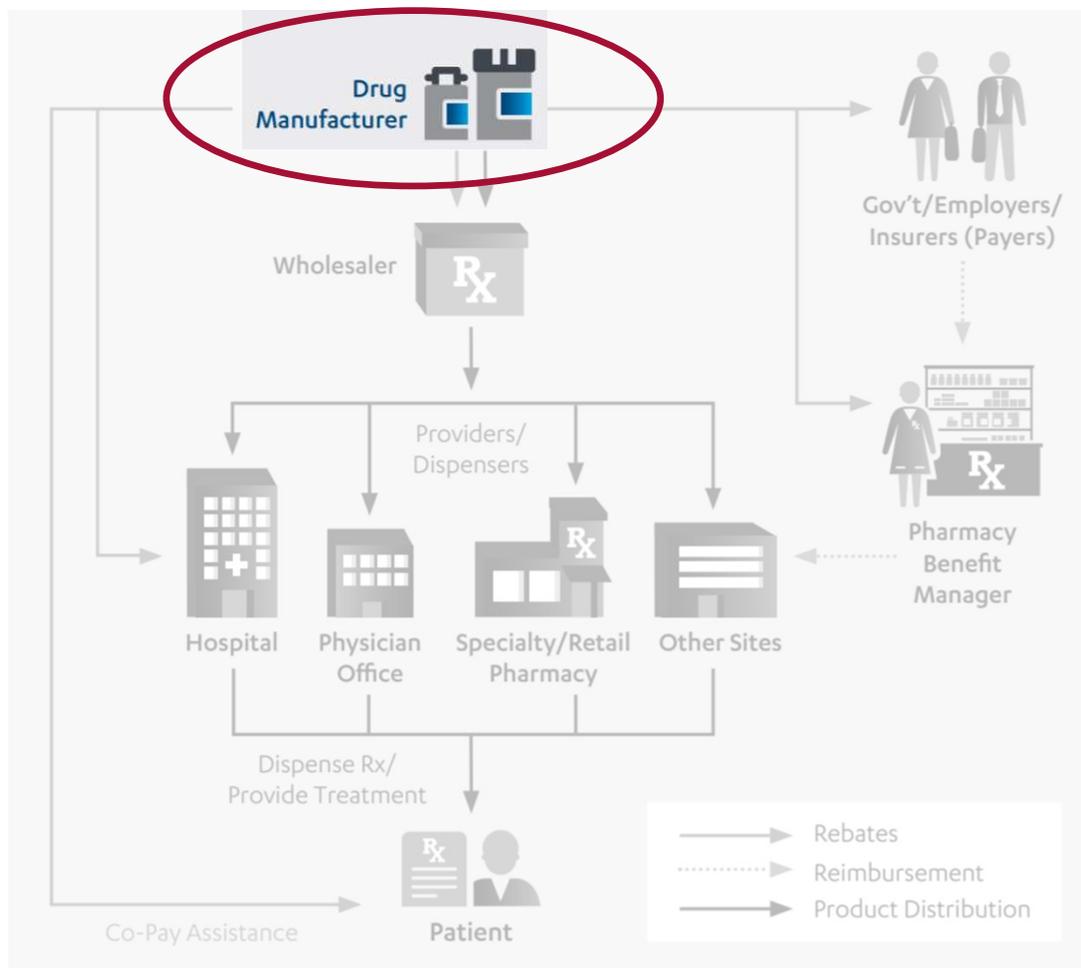


Note: Performance on day of FDA approval based on change from the previous day. Performance for other dates based on change since approval date.
Source: Dow Jones Market Data; FactSet
Josh Ulick/THE WALL STREET JOURNAL

My research portfolio



My research portfolio



Pharmaceutical Innovation

Market Incentives and the Drug Development Pipeline: Evidence from Antibiotics
(WP with Edward Kong, PhD, MD)

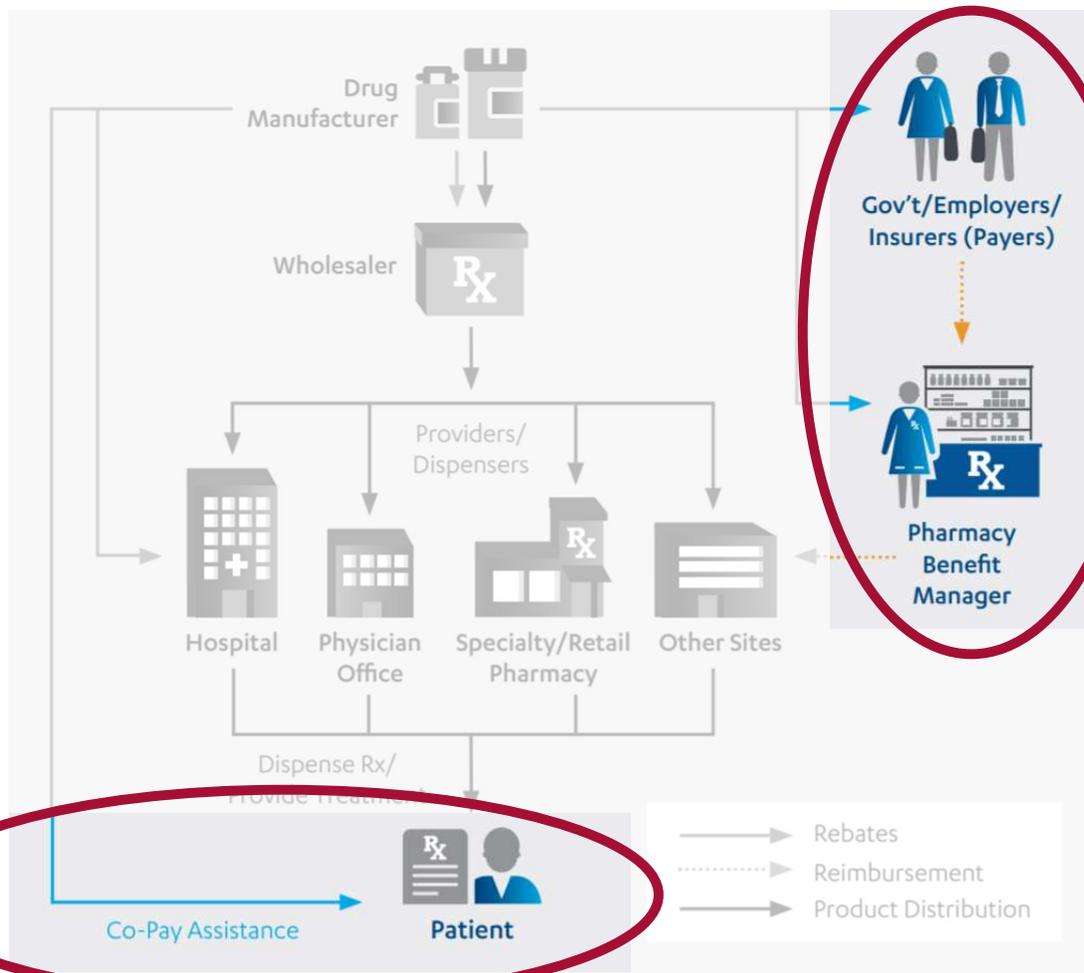
Effects of Expanding Medicaid Coverage for Clinical Trial Participants
(with Grace Park)

future ideas

Effects of the IRA on firm development decisions

Clinical evidence “production function”

My research portfolio

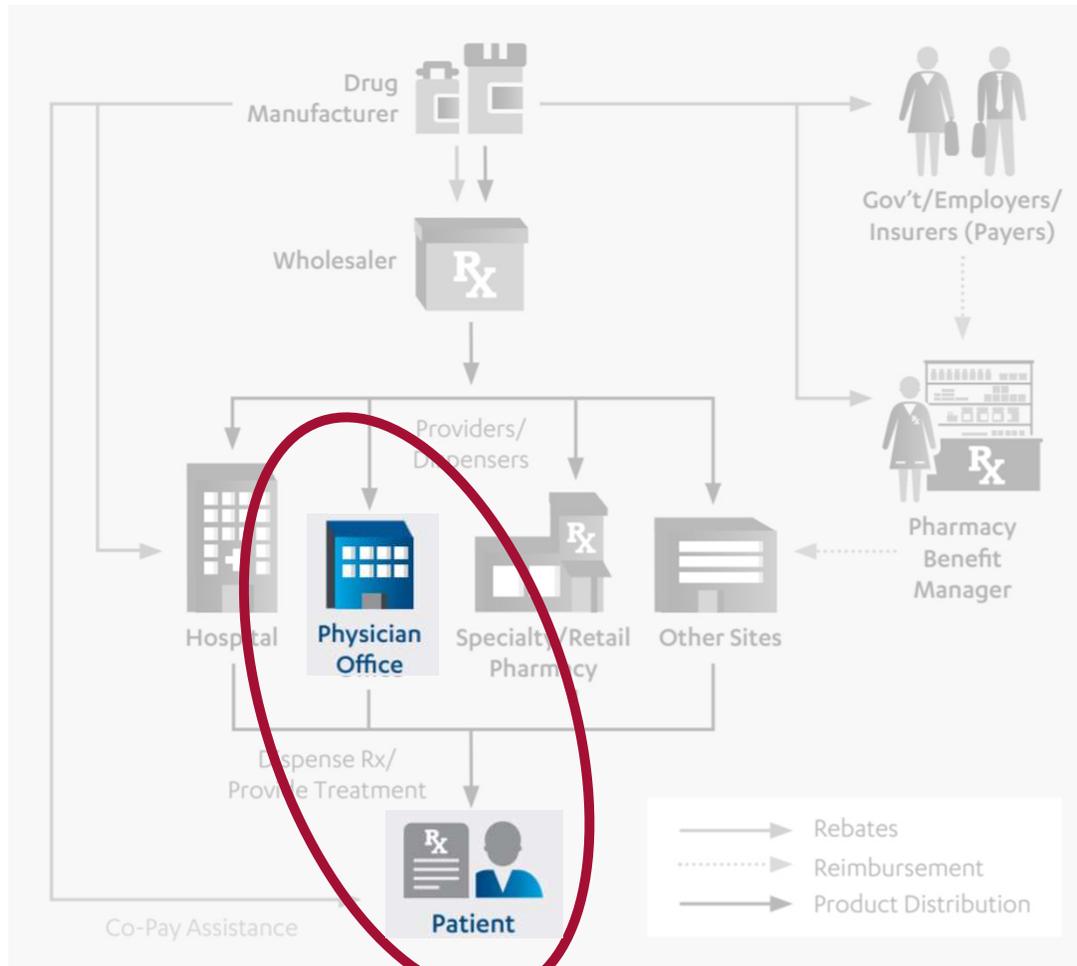


Payers

Cost of Exempting Sole Orphan Drugs From Medicare Negotiation
(*JAMA IM*, with Matthew Vogel and co-authors)

How Patient Assistance Programs Can Benefit Pharmaceutical Manufacturers and Employers: The Case of Copay Maximizers
(WP with Leemore Dafny)

My research portfolio



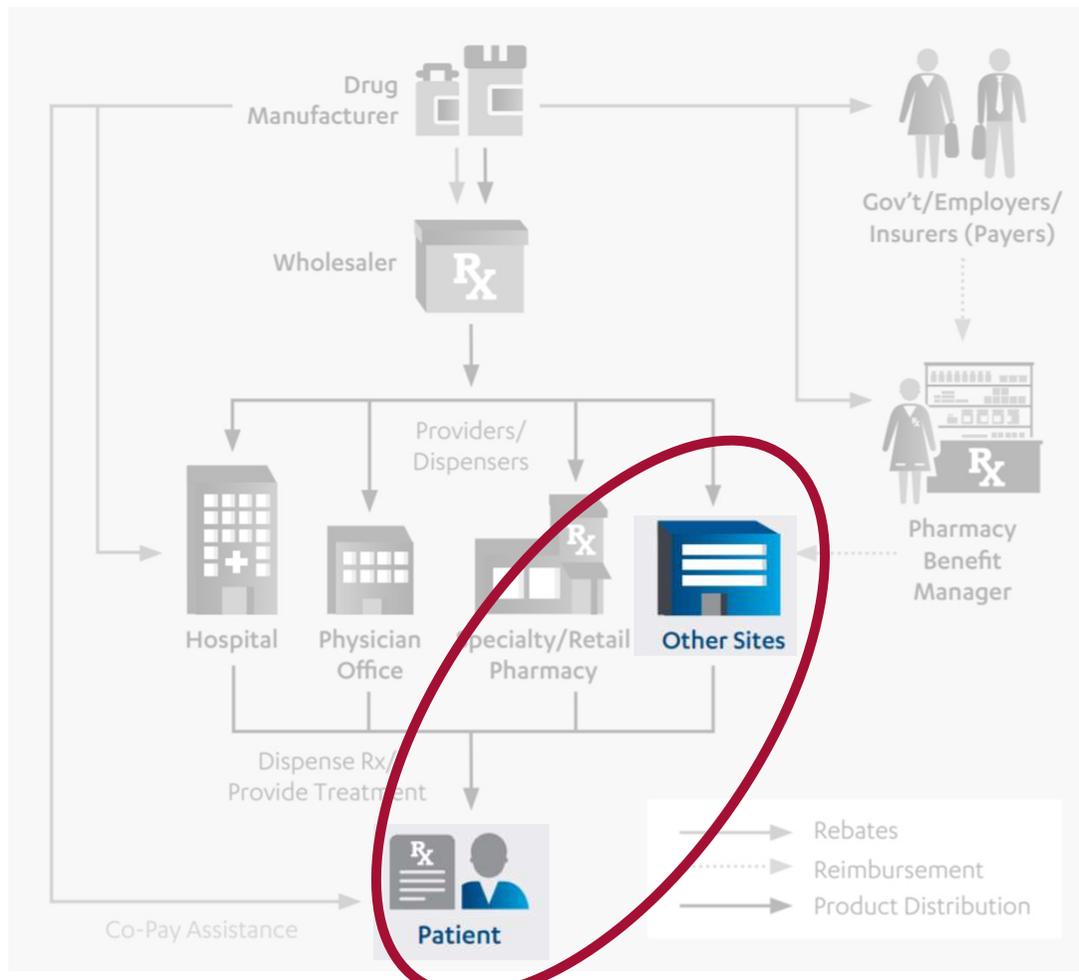
Prescribing and Patient Access

Clinician Response to Patient Medication Prices Displayed in the Electronic Health Record
(*JAMA IM*, Anna Sinaiko and co-authors)

Effects of a Real-Time Information-Based Intervention on Physician Prescribing Behavior
(*Academy of Management Proceedings*, with Anna Sinaiko)

The Doctor Will See Your Cost-Sharing Now: Price Transparency for Prescription Drugs
(WP with Anna Sinaiko)

My research portfolio



Physician Labor Supply and Patient Access

Telehealth Expansion, Physician Licensing Decisions, and Patient Access (with Mitchell Tang)

Thank You!

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