Insurance Design and Pharmaceutical Innovation

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If you build it, will we pay?

Technological innovation is a large driver of rising health spending

- Increasing political pressure to limit insurance coverage for high-cost, low-value treatments.
- But coverage restrictions may reduce incentives for medical innovation.

Challenge: How can we balance cost containment and incentives to innovate?

- Policy proposals: federal negotiation of drug prices, reforms to Medicare coverage determination process, etc.
- Limited evidence on how these proposals affect dynamic innovation incentives

This paper: How does the structure of insurance influence the direction of innovation?

New restrictions on prescription drug coverage

In the US, prescription drug plans are typically managed by Pharmacy Benefit Managers (PBMs).

- PBMs design drug formularies, set co-pay tiers, negotiate rebates.
- Historically, PBM formularies covered all approved drugs.

Beginning in 2012, PBMs began excluding coverage for some drugs

- Exclusions target expensive drugs, with covered substitutes.
- Exclusions reduced profits for affected drugs.

How did these new restrictions on Rx coverage affect upstream pharmaceutical R&D?

Payment incentives and the direction of innovation

Public policy influences innovation through:

- Public insurance expansions (Acemoglu et al. 2016, Dranove et al. 2020, Finkelstein 2004, Krieger et al. 2017)
- Patent protection (Kyle and McGahan 2012, Budish et al. 2015)
- Public procurement incentives (Clemens and Rogers 2020)

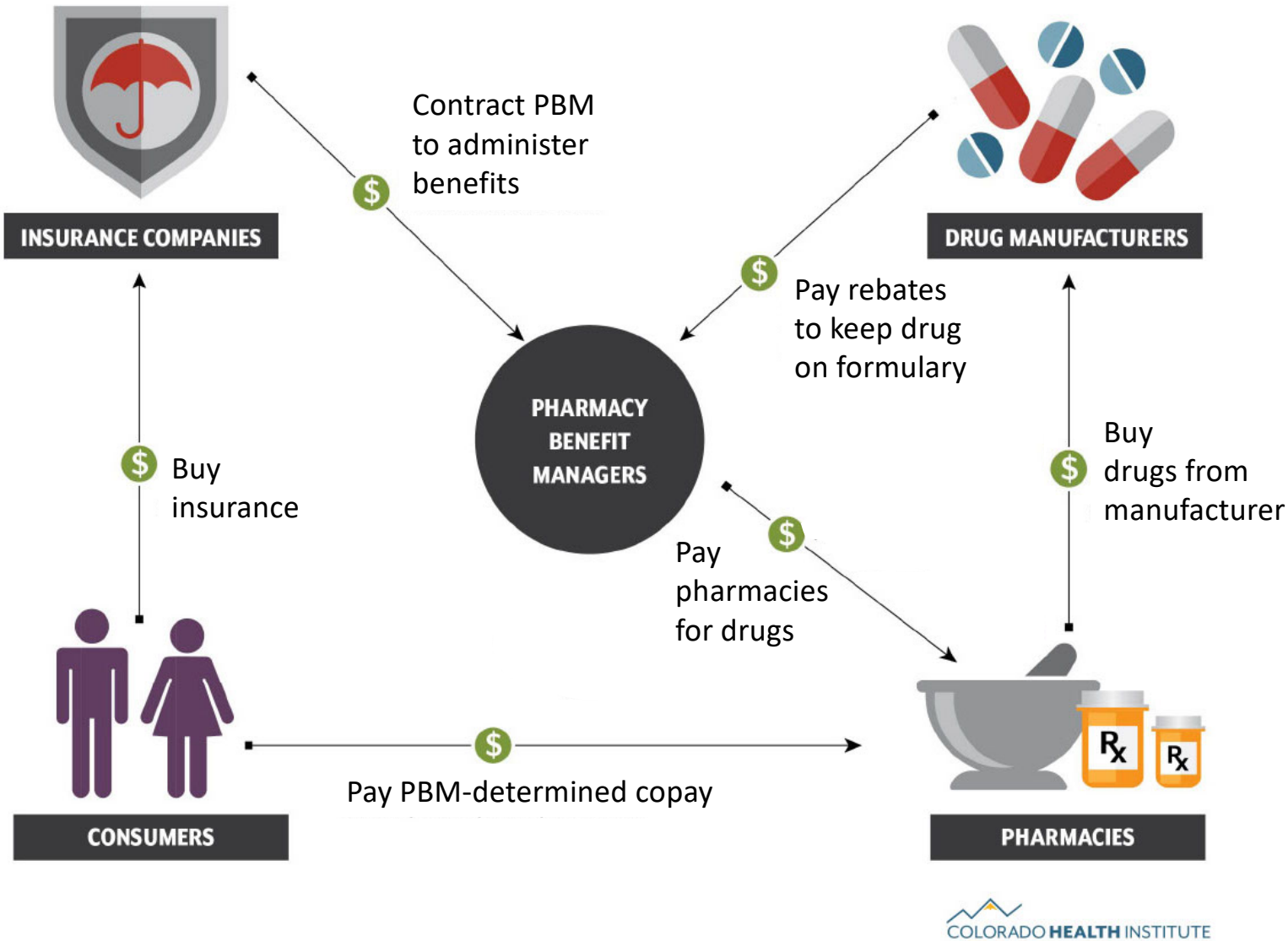
But does insurance design matter? Theory suggests:

- Public insurance may encourage innovation while lowering DWL from monopoly (Lakdawalla and Sood 2009)
- BUT insurance subsidies may spur excess innovation (Garber et al. 2006)

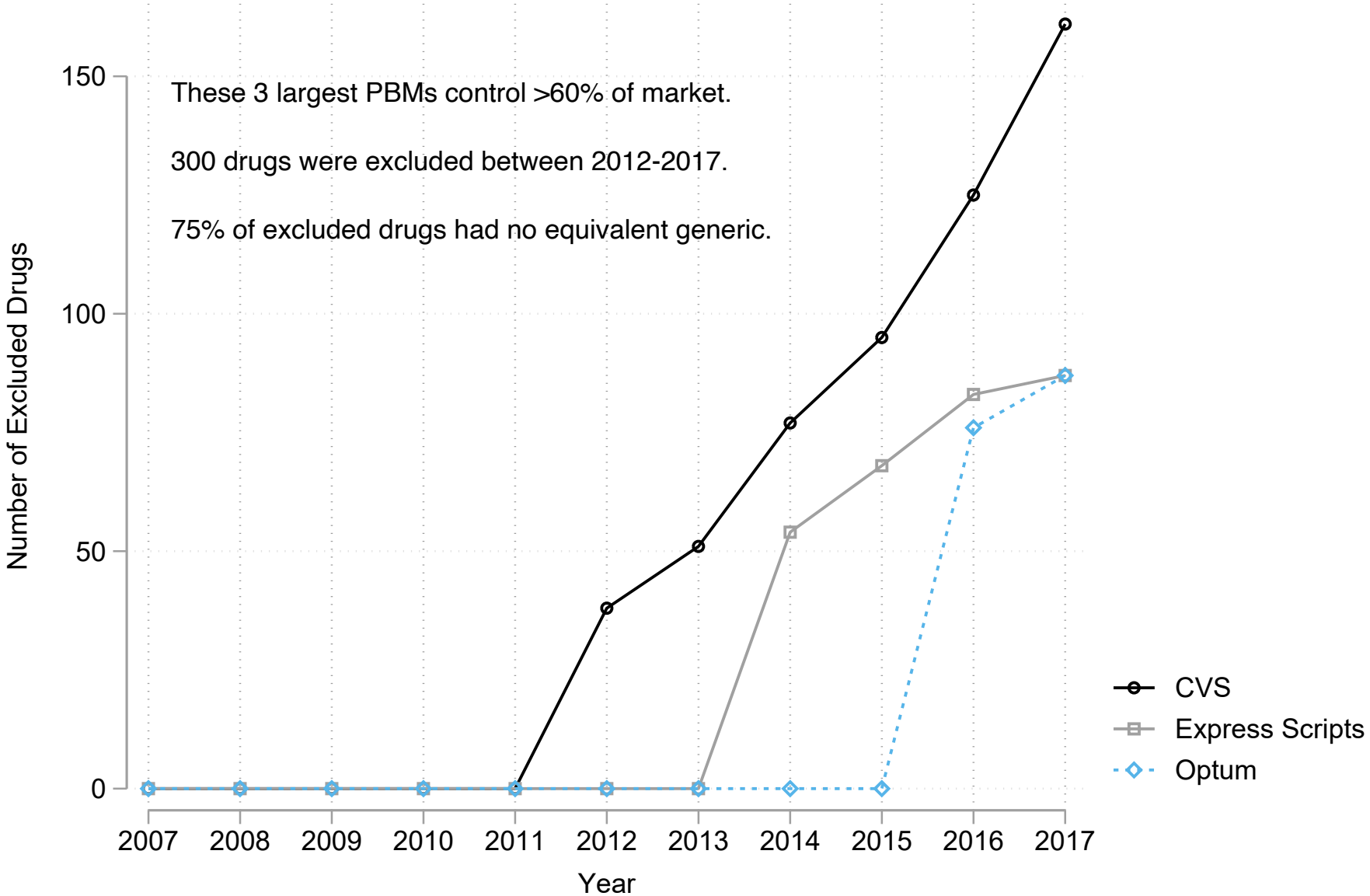
Preview: insurance design and innovation

Question	How does prescription drug coverage shape innovation?
Context	Introduction of closed formularies by major PBMs
Strategy	Compare changes in R&D across drug classes with varying exclusion risk
Data	- PBM formulary lists: document exclusions - Medicare Part D claims: exclusions reduce claims - First Data Bank: predict exclusion risk by drug class - Cortellis Data: track development pipeline
Results	Relative decrease in R&D investment for drug classes with more incremental innovation.

PBMs act as intermediaries in Rx drug markets



Use of formulary exclusions has grown rapidly



Source: Hand-collected data on PBM exclusion lists.

Exclusions strengthen PBMs' bargaining power

- Exclusions gave PBMs stricter control of formularies, and worked in part to circumvent co-pay coupons.

- Exclusions will not only directly affect demand for the excluded drug, but they also likely affect pricing of other products.

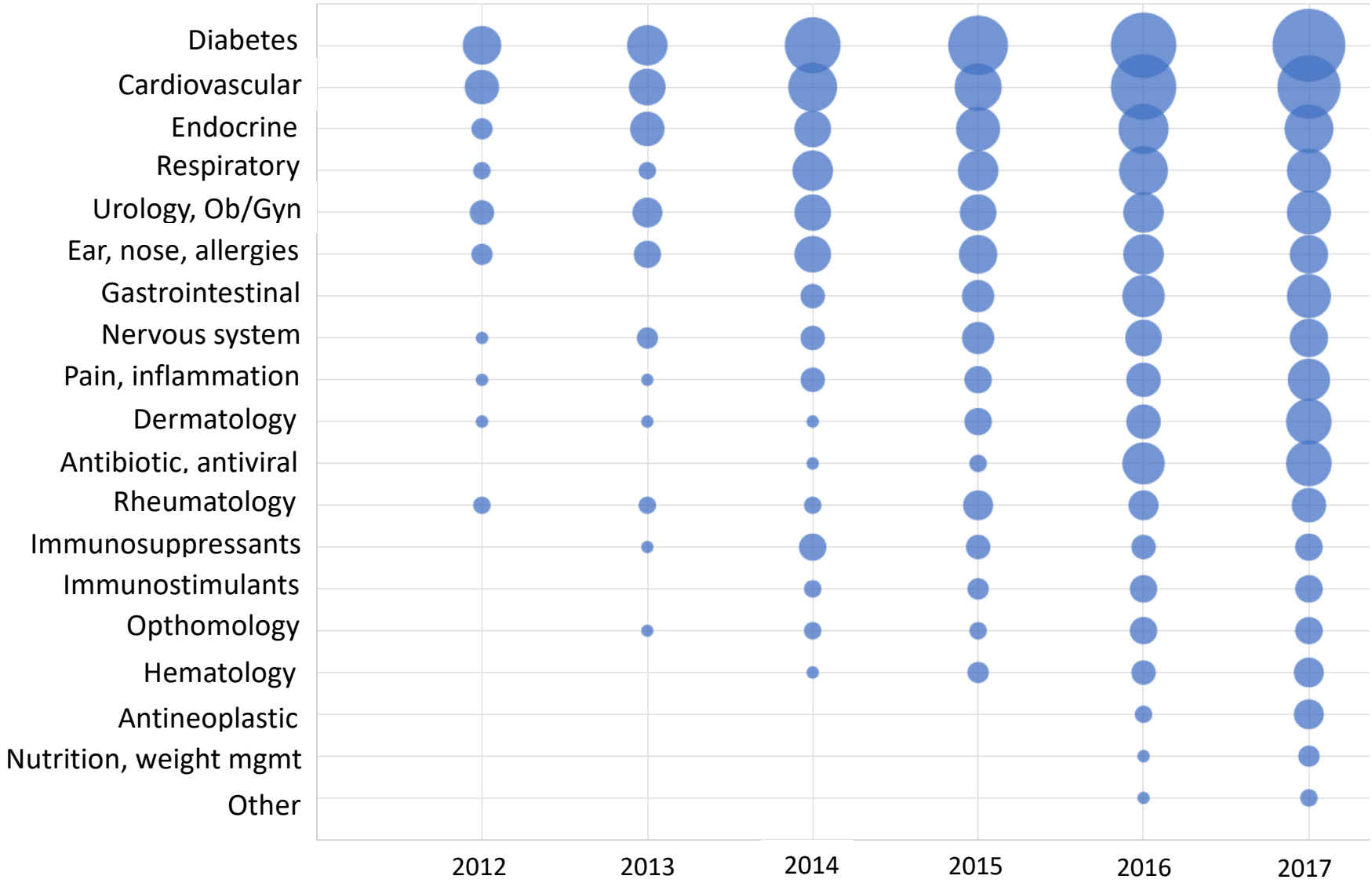
- Industry experts say exclusions target "me-too" drugs with multiple therapeutic substitutes (Reinke 2015).

"We are going to be pitting you all against each other. Who is going to give us the best price? If you give us the best price, we will move the market share to you. We will move it effectively. We'll exclude the other products"

—Steve Miller, CMO of Express Scripts

Exclusions target common, chronic diseases

Number of exclusions by disease category



Exclusions reduce drugmaker's revenues

	(1) Log(Claims)	(2) Log(Claims)	(3) Log(Mkt. Share)	(4) Log(Mkt. Share)
Number of Excluding PBMs	-0.274***	-0.319***	-0.220***	-0.319***
	(0.0638)	(0.0733)	(0.0809)	(0.0733)
Observations	4,626	4,391	4,626	4,391
Drug FE	YES	YES	YES	YES
Cohort X Year FE	YES	YES	YES	YES
Market Controls	NO	YES	NO	YES

Notes: Annual data on Medicare Part D claims per drug 2012-2017. Columns (2) and (4) include controls for ATC4 class $\times$ calendar year FEs. Analyzes exclusions on 161 excluded drugs that are prescribed to Medicare Part D enrollees and are not in a protected class. Standard errors are clustered at the drug level.

Narrow drug class definition: ATC4 code examples

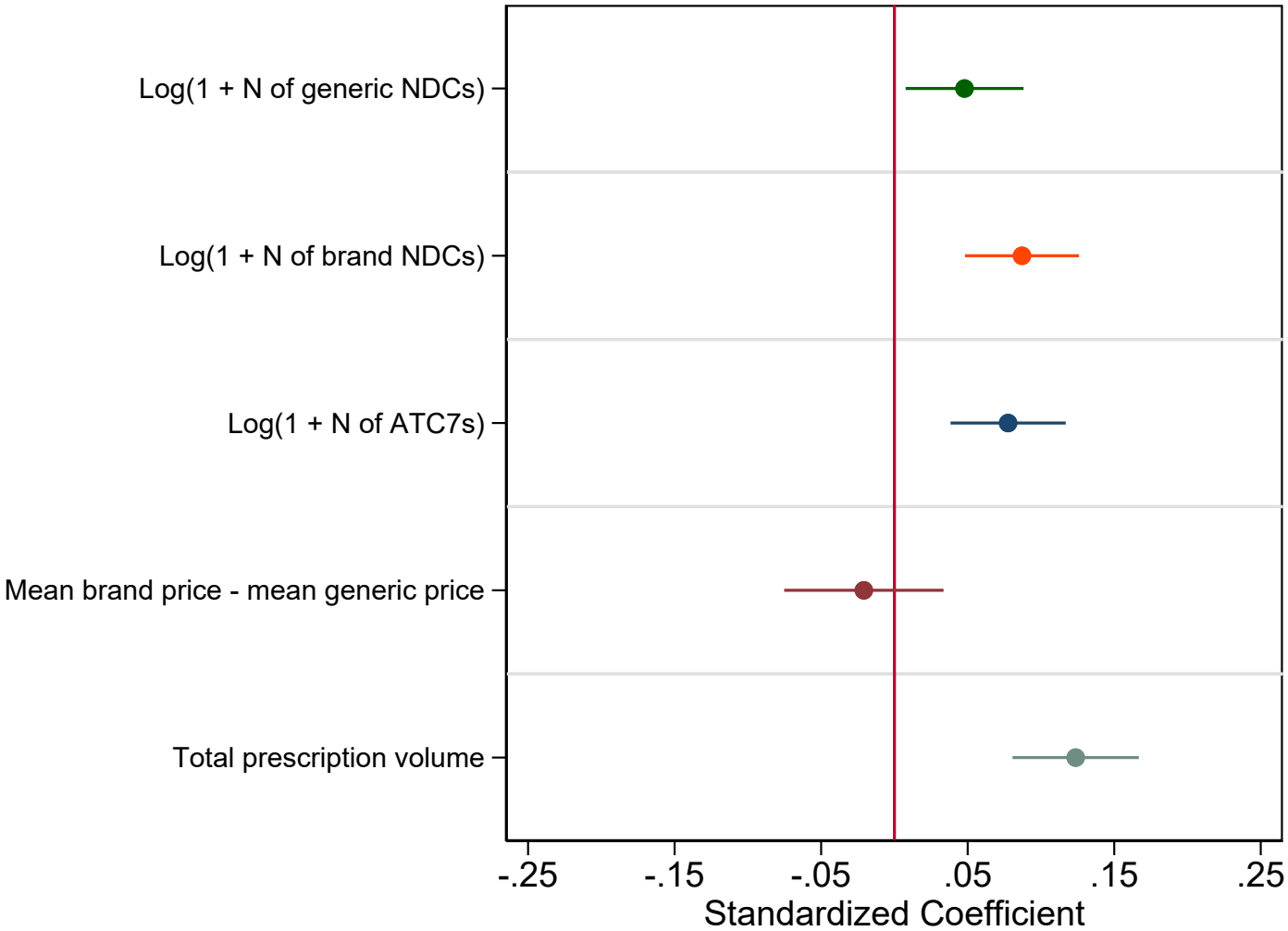
C02 Antihypertensives

C02A Antiadrenergic agents, centrally acting
C02B Antiadrenergic agents, ganglion-blocking
C02C Antiadrenergic agents, peripherally acting
C02D Arteriolar smooth muscle, agents acting on
C02K Other antihypertensives
C02L Antihypertensives and diuretics in combination
C02N Combinations of antihypertensives in ATC-group C02

C07 Beta blocking agents

C07A Beta blocking agents
C07B Beta blocking agents and thiazides
C07C Beta blocking agents and other diuretics
C07D Beta blocking agents, thiazides and other diuretics
C07E Beta blocking agents and vasodilators
C07F Beta blocking agents, other combinations

Predictors of exclusion risk: "Me-too" drugs in large classes



Source: PBM exclusion lists, First Data Bank data on drug markets.

Cortellis data on drug development

- Tracks drug candidates from public records: company documents, press releases, financial filings, clinical trial registries, and FDA submissions.
- Key outcome variable: number of advancing drug candidates at the ATC4 drug class by year level.
- On average, 31 advancing candidates per drug class-year. Standard deviation: 42. ▸ Details

Empirical strategy

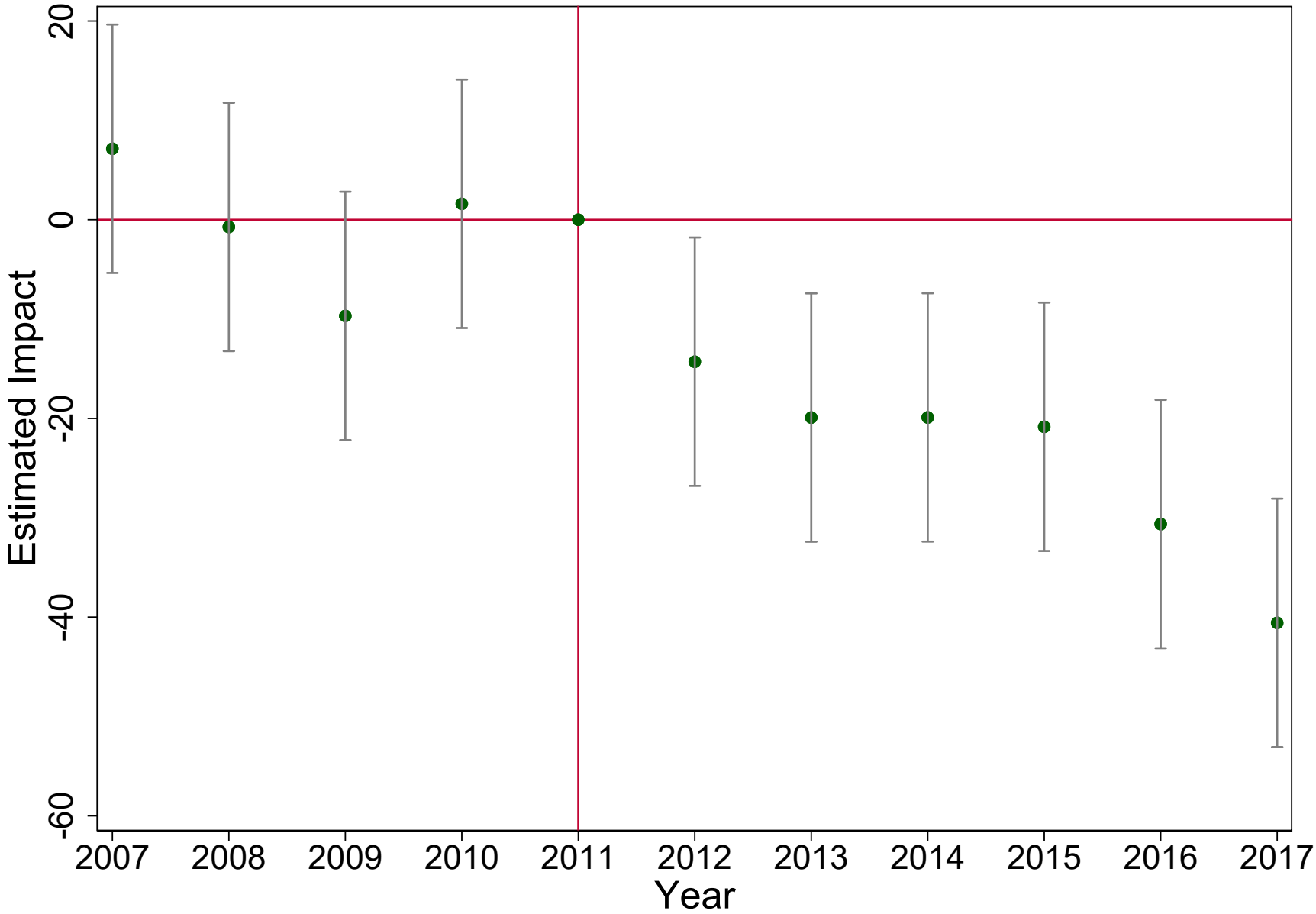
Compare pre/post exclusions for drug classes with varying exclusion risk (predicted with pre-2012 market characteristics).

$$\begin{aligned}\text{Development}_{ct} =& \beta_1 \text{Pr}(\text{Excluded})_c \times \mathbb{I}(\text{Year}_t \geq 2012) \\ &+ \mathbf{X}_{ct}\gamma + \delta_c + \delta_t + \epsilon_{ct}\end{aligned}$$

where c indexes drug class, t years and:

Development_{ct}	-	number of advancing drugs (in class, year)
$\text{Pr}(\text{Excluded})_c$	-	prob. that class has ≥ 1 exclusion in 2012-13
$\mathbf{X}_{ct}$	-	drug class market characteristics
δ_c	-	drug class fixed effects
δ_t	-	year fixed effects

Relative decline in development for high-risk classes



Effect of exclusion risk on new drug development

	(1) New Development	(2) New Development	(3) Log(1+New Dev.)	(4) Log(1+New Dev.)
Post X Pr(Exclusion)	-24.03***	-21.98***	-0.382***	-0.333***
	(5.894)	(6.571)	(0.108)	(0.115)
Observations	1,397	1,397	1,397	1,397
Year FE	YES	YES	YES	YES
ATC FE	YES	YES	YES	YES
Market Controls	NO	YES	NO	YES

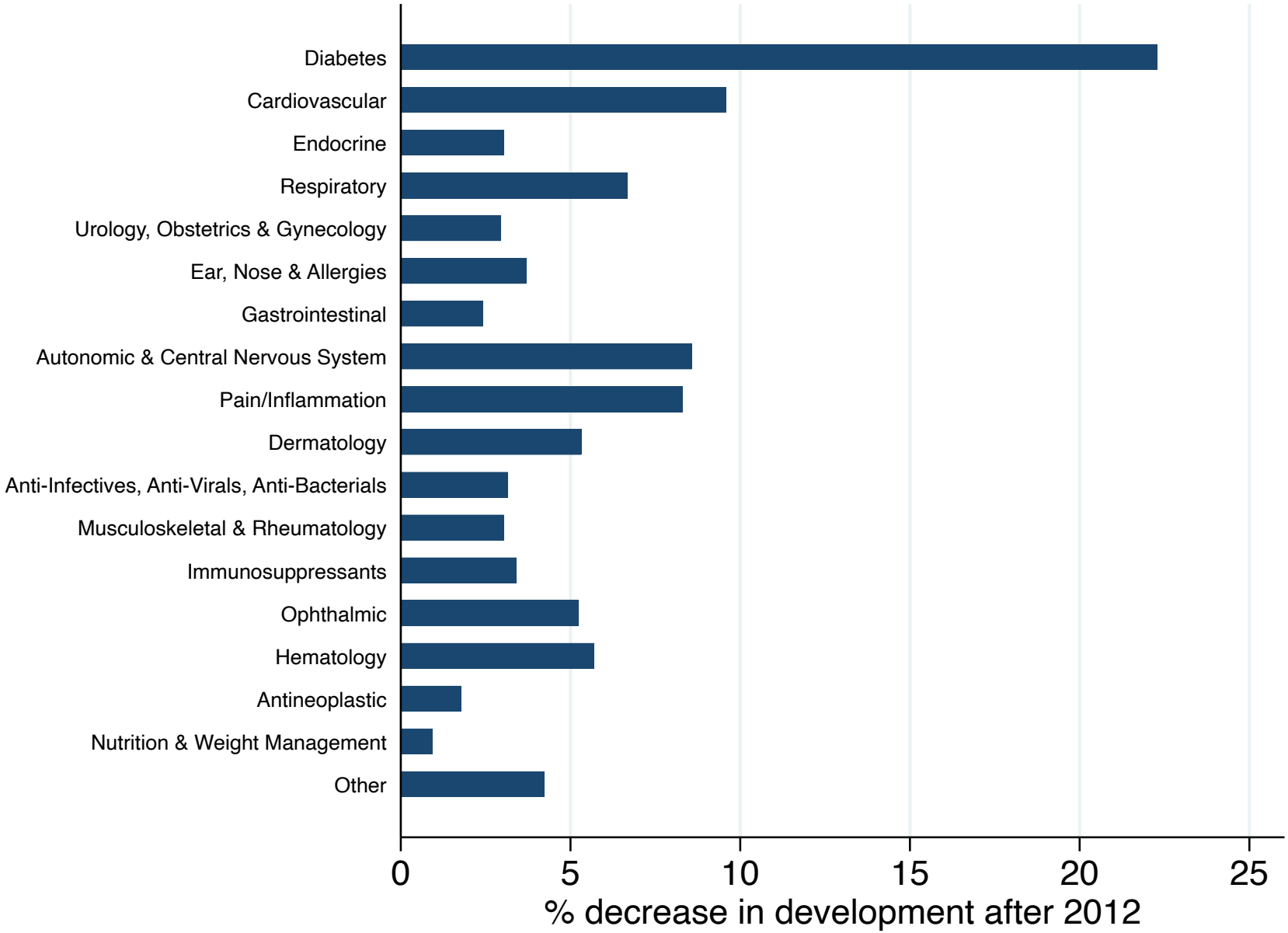
Notes: Standard errors clustered at the drug class level.

5-6% decline in development for every 1 SD increase in exclusion risk.

Similar results with wild cluster bootstrap, IHS outcome ▸ Details

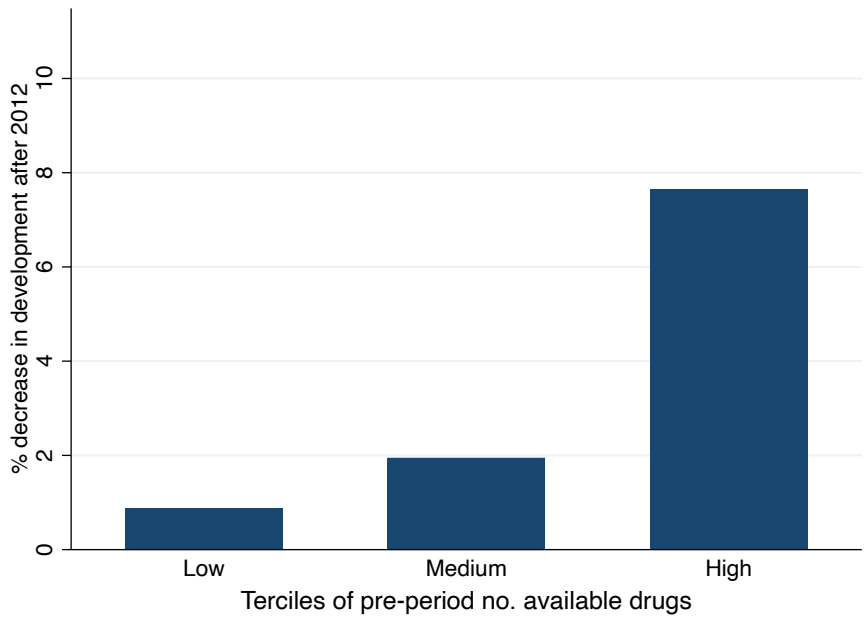
At each development stage, 4% - 7% decline in activity for 1 SD increase in exclusion risk. ▸ Details

Development impact by therapeutic area

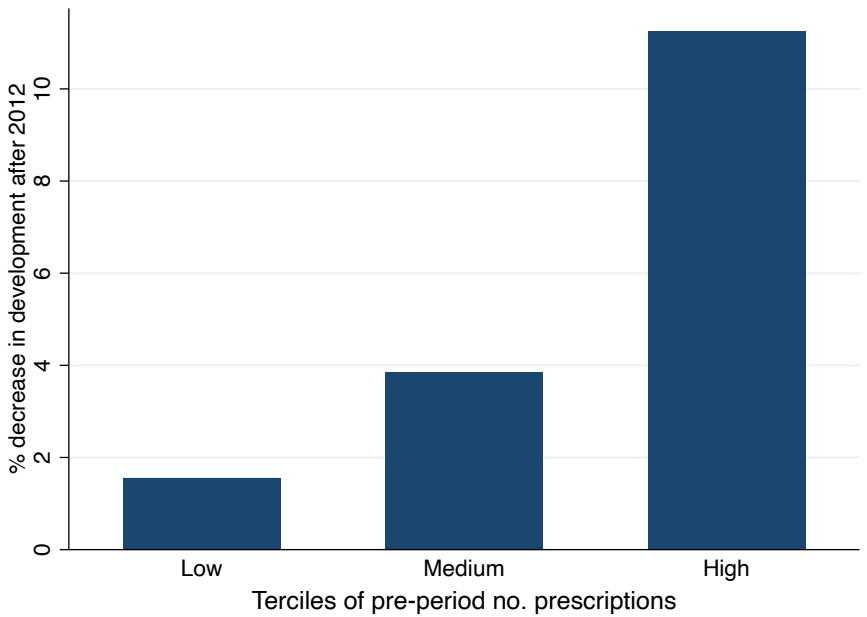


Counterfactuals by pre-period market size

(A) Decrease in development by number of drugs in class



(B) Decrease in development by number of prescriptions in class



Constructing measures of scientific novelty

- We link drug candidates to the scientific articles cited by their underlying patents, using linkages created by Marx and Fuegi (2020).

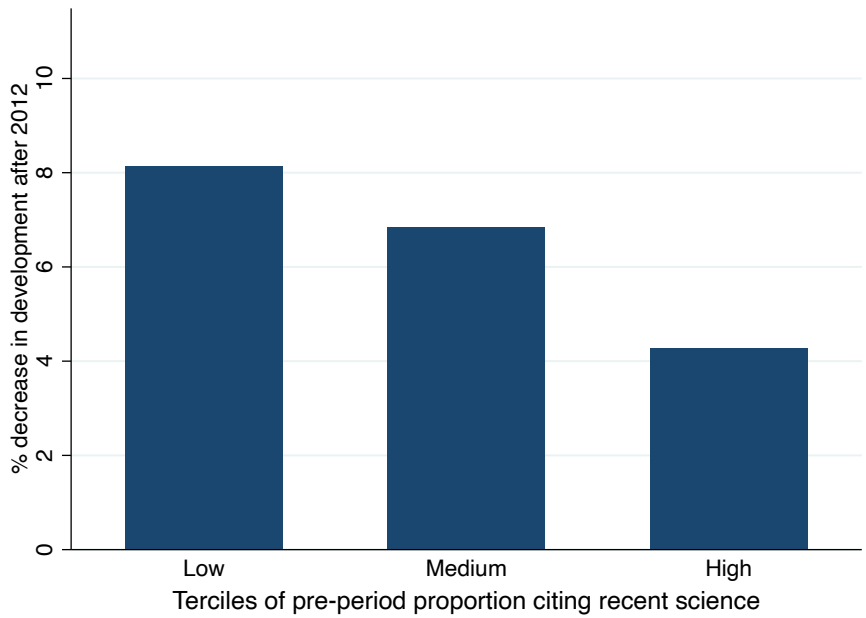
- We then construct two measures of scientific novelty at the drug class level:

    - Proportion of drug candidates citing science that is < 5 years old.

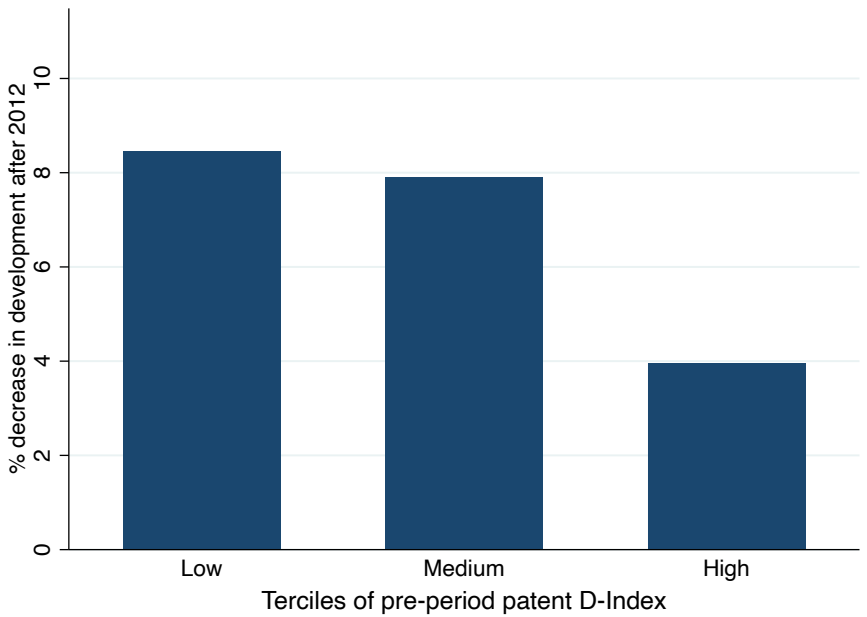
    - Average "disruptiveness" index of the cited science, using measure by Funk and Owen-Smith (2017).

Counterfactuals by scientific novelty of class

(A) Decrease in development by % citing recent science



(B) Decrease in development by average "disruptiveness" index



What does this mean for welfare?

Largest declines were in classes with more incremental innovation

- Incremental drugs may reduce side effects, improve compliance, or generate price competition (Regnier 2013, Hult 2014).
- Even incremental innovation may generate scientific spillovers, leading to further innovation in longer run.

We identify a *relative* decline in R&D in high exclusion risk classes.

- Absent financial frictions, we would expect little change in innovation for classes that are not at risk of exclusion. Exclusions may spur an aggregate decline in drug R&D.
- Finance literature suggests that even large firms behave as if they face financial frictions, particularly in R&D intensive sectors like pharma (Fernandez et al. 2012, Kerr and Nanda 2015, Krieger et al. 2019). Exclusions may spur a reallocation of R&D towards low risk classes.

Conclusions

- Structure of insurance has a substantial influence on the direction of innovation.
- Drug classes facing a 1 SD greater risk of exclusions see a 5% decline in drug development activity.
- Current approach to formulary exclusions tends to reduce R&D investments in drug classes with more incremental innovation.
- Valuing foregone innovation is challenging, and an important direction for future work.

Validating our measure of exclusion risk

Pr(Exclusion) uses 2011 market characteristics to predict exclusions in 2012-2013. To validate it, we test whether it can predict exclusions in 2014-2017.

	(1)	(2)
	Late Exclusion	Late Exclusion
Pr(Exclusion)	0.167***	0.150**
	(0.0413)	(0.0624)
Observations	127	112
Sample	All ATC4s	ATC4s without early exclusions

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Summary statistics on development activity

	Mean	Std. Dev.	Median
All	30.61	42.06	13.05
Preclinical	17.39	26.13	6.64
Phase 1	6.54	8.84	3.07
Phase 2	4.57	6.04	2.17
Phase 3	2.11	3.04	1.04
Launch	1.02	1.63	0.31

Notes: Annual data at ATC4 drug class level, from Cortellis.

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Effect of exclusion risk by stage of development

	(1) Log(1+All)	(2) Log(1+Preclincal)	(3) Log(1+P1)	(4) Log(1+P2)	(5) Log(1+P3)	(6) Log(1+Launch)
Post X Pr(Exclusion)	-0.333***	-0.449***	-0.331***	-0.310***	-0.259**	0.113
	(0.115)	(0.101)	(0.103)	(0.106)	(0.101)	(0.138)
Observations	1,397	1,397	1,397	1,397	1,397	1,397
Year FE	YES	YES	YES	YES	YES	YES
ATC FE	YES	YES	YES	YES	YES	YES
Market Controls	YES	YES	YES	YES	YES	YES
N of Drug Candidates Mean	30.61	17.39	6.54	4.57	2.11	1.02

Notes: Standard errors clustered at the drug class level.

4% - 7% decline in development activity at each stage for 1 SD increase in exclusion risk, with larger declines in earlier stages.

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Bootstrap and inverse hyperbolic sine

	(1) New Development	(2) Log(1+New Dev.)	(3) IHS New Dev
Post X Pr(Exclusion)	-21.98***	-0.333***	-0.316**
	[-37.97, -8.378]	[-.5357, -.03624]	[-.5549, .01335]
Observations	1,397	1,397	1,397
Year FE	YES	YES	YES
ATC FE	YES	YES	YES
Market Controls	YES	YES	YES

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