Marketing Authorization and Strategic Patenting: Evidence from Pharmaceuticals

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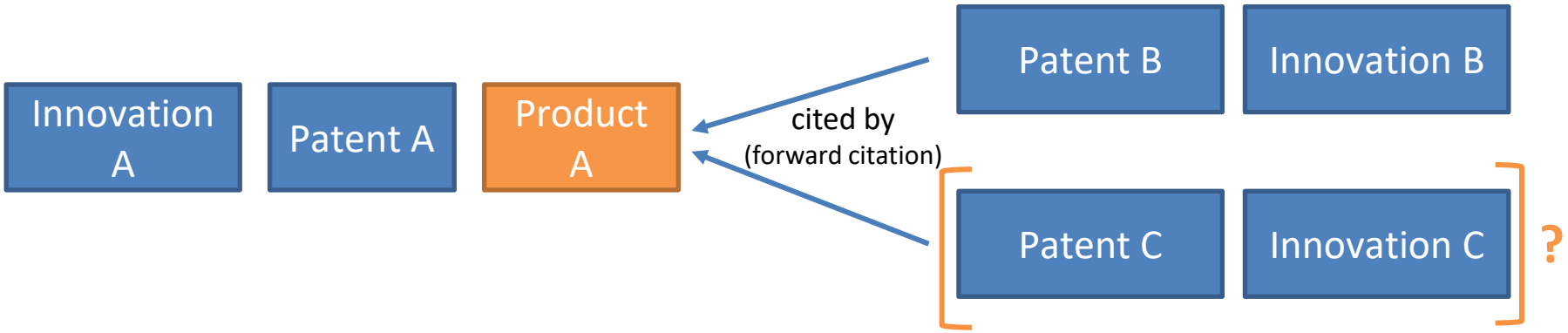
AEA “tech. and innovation” lightening round session, 2025.1.5

Drugs save lives, but too costly with many patents!

- Patent systems are designed to promote innovation (Mansfield 1986; Lakdawalla 2018), but strategic patenting limits drug access (EC 2009)
  - E.g., evergreening (extends length) and fencing (extends breadth)
- Trade-off: static efficiency vs. R&D incentives -> debates on patentability
  - US Supreme Court cases: Mayo 2012, Myriad Genetics 2013
- This paper: how info disclosure in market authorization (MA) affect follow-on patenting (Trial docs disclosed can function as new "prior arts")



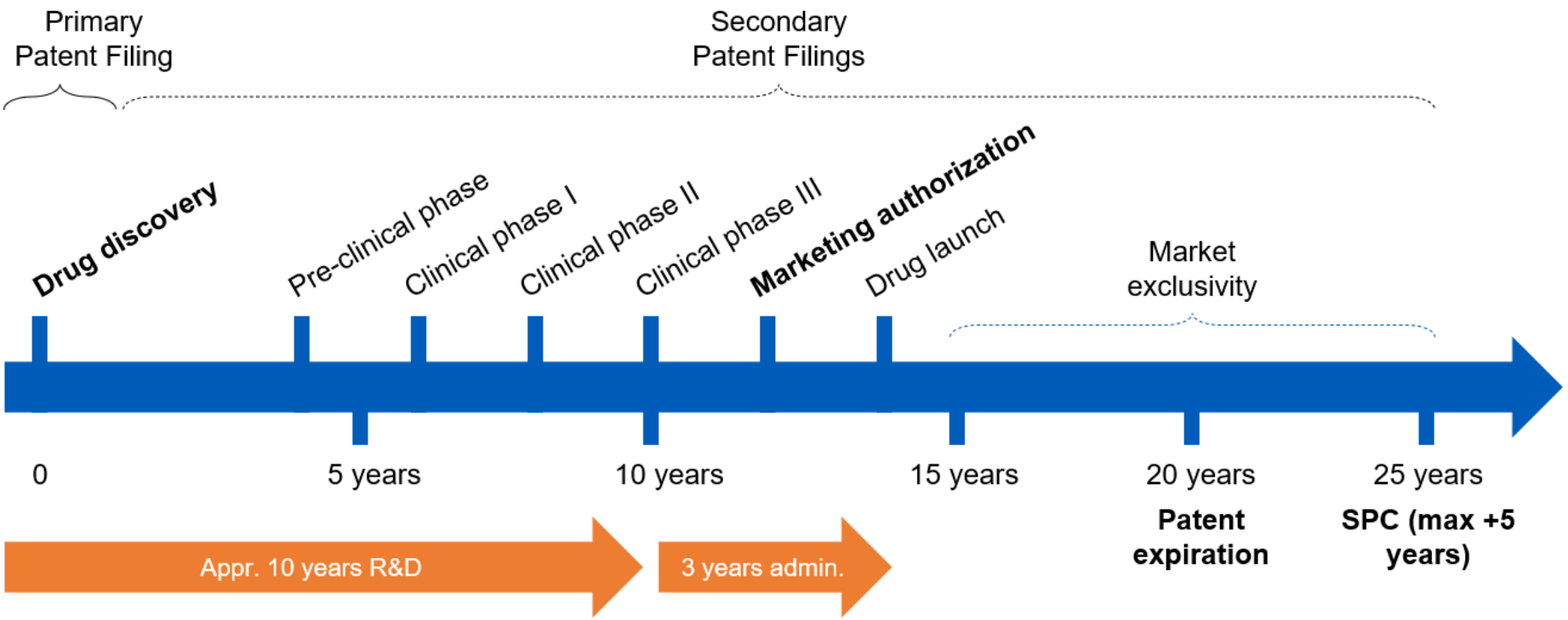
EPO "gold standard" examination quality (Chien 2018), patent citation: follow-on patenting

Research Question:

Q: How does marketing authorization of a new drug (new NME) affect follow-on innovation building upon focal drug?

- Intuitively, follow-on patenting can go either way (an empirical Q):
  - More: “Time to explore other new indications and expand the market!”
  - Less: “Time to lay flat and relax, as profit is coming in our way!”
  - Same: “I cannot decide, so maybe just good to patent as usual?”
- Exploit the authorization of new drugs to the (EU/EEA) market, utilize the variation in approval lags (that do not differ by ex-ante patent char.)
- Examine how a drug’s marketing authorization affects the rate & direction on follow-on patenting by firms (selves, related parties, others)

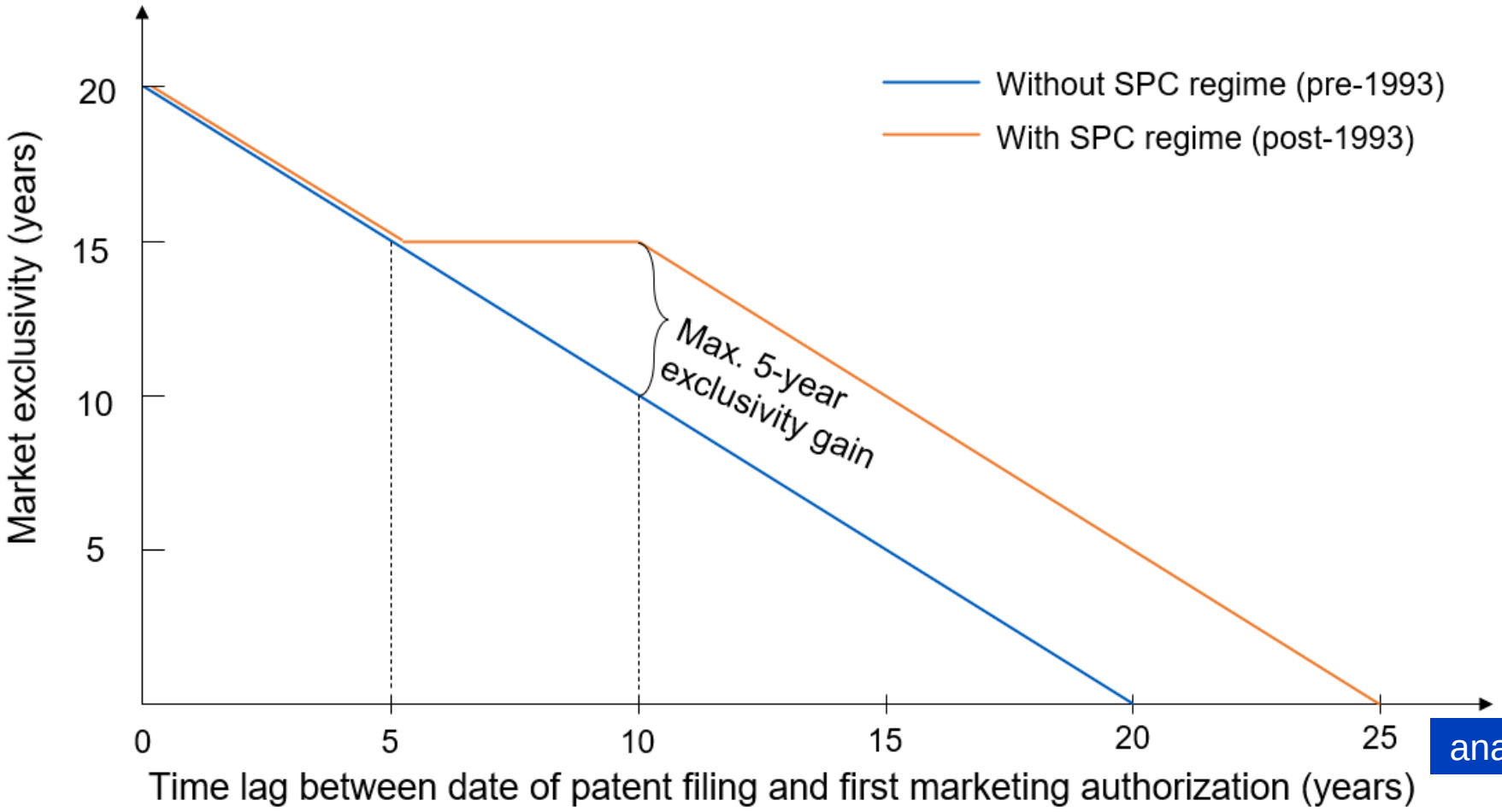
The Drug Development Process in EU (EEA)



- In European Economic Area (EU+Iceland, Liechtenstein, Norway), originators submit applications for market authorization to European Medicines Agency (/national)
  - verifies safety, efficacy, quality; drugs can then be sold for approved indications
- Market exclusivity: firms hold exclusive right to market/sell a patented drug

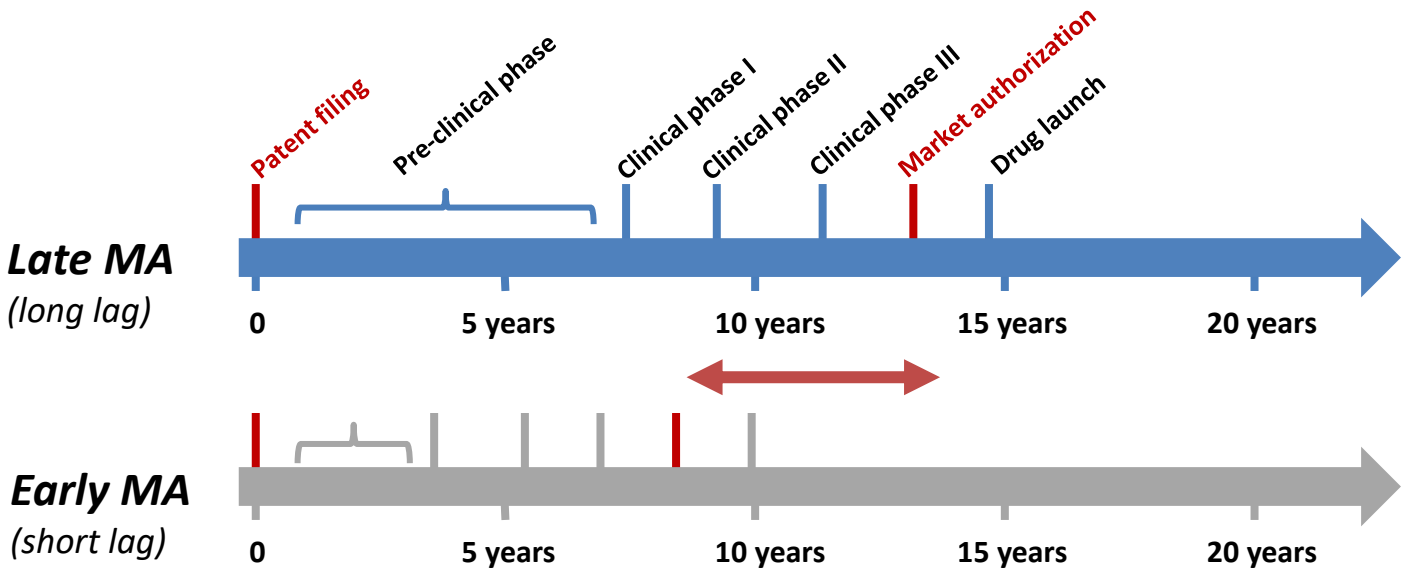
EU Patent Term Extension (SPC Regime)

- Supplementary Protection Certificates (SPC) regime, 1993- : extension capped at 5 years; market exclusivity constant for patents w/ 5-10 years' approval lag
- SPC term (≤5 years)= date of 1st MA in EEA – filing date of basic patent – 5



analysis

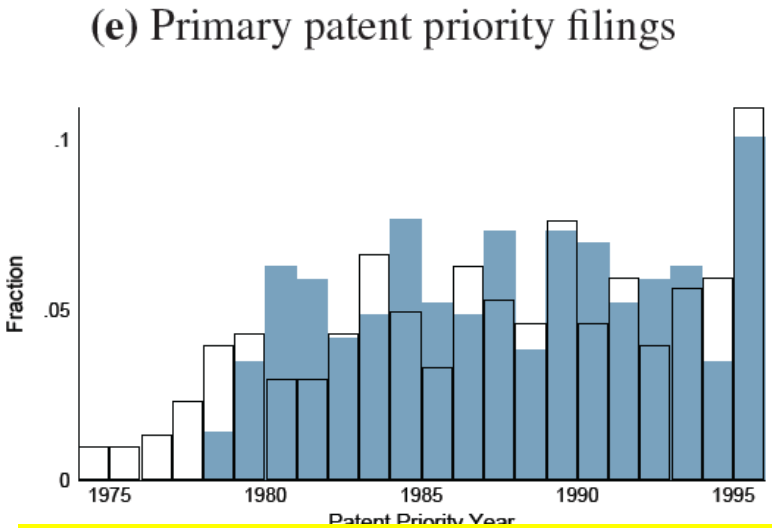
It takes a long & uncertain time to develop a drug…

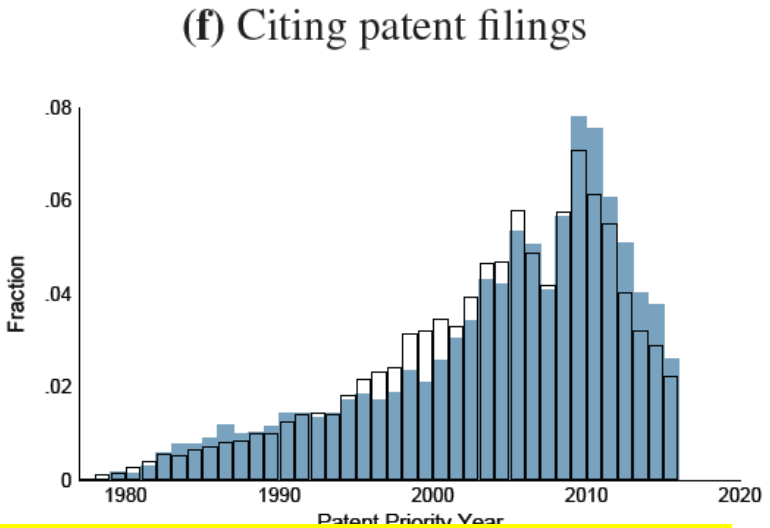


- Approval lag *cannot* be predicted perfectly at the time of the patent filing: whether/when the drug will be on the market (à la Gilchrist 2016)
  - Scientific uncertainty & organizational factors: finance, M&A, $, licensing, …

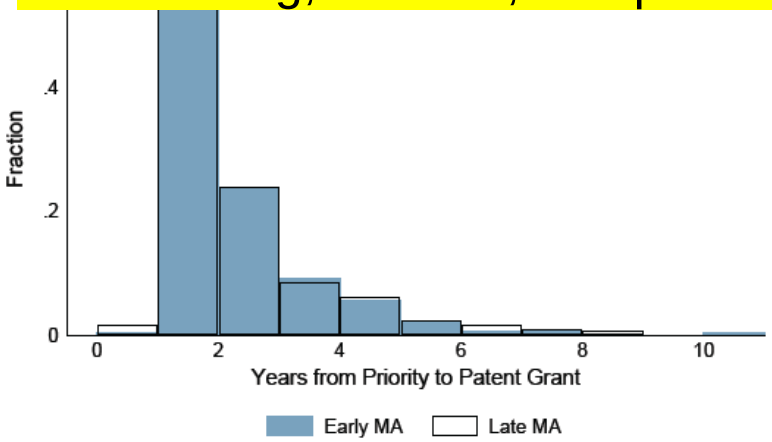
- **Data**: 1) patent-drug linkage: SPC data from DPMA; 2) patent data on primary patents from EPO PATSTAT, family level patent info; 3) drug data: Cortellis, link by family id; 4) crosswalk diseases w WHO ICD-9.

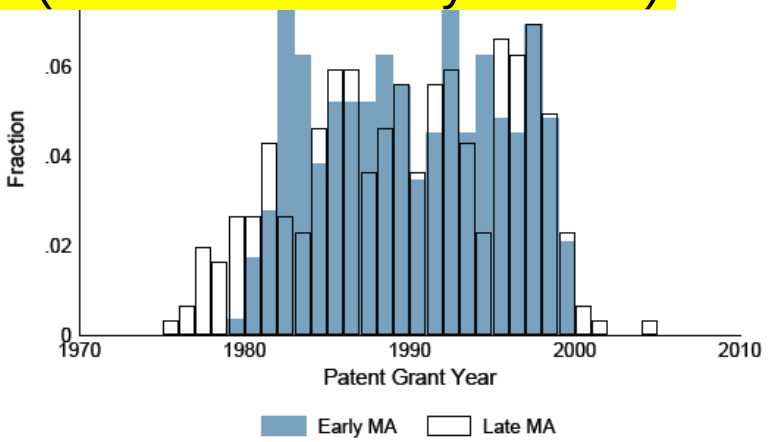
Distribution of characteristics (split by median MA)





Patents with early vs. late MA (split approval lag at median: 10 years) are similar regarding priority time, time span at the patent offices (time to patent grant), similar technological nature (e.g., ICD-9, complexity, resubmissions), and similar ex-ante drug, disease, and patent characteristics (t-test across many metrics).





Empirical Strategy: Event Studies (à la S&S 2023)

- Drugs that never been approved should not be valid counterfactuals; rather, drugs approved but with early/later MAs (within drug comparison)
- Staggered event study exploits the variation in approval lags & end-binning (Schmidheiny & Siegloch, 2023)
  - Robust to: count data models e.g., PPML; other DiD estimators, e.g., stacked

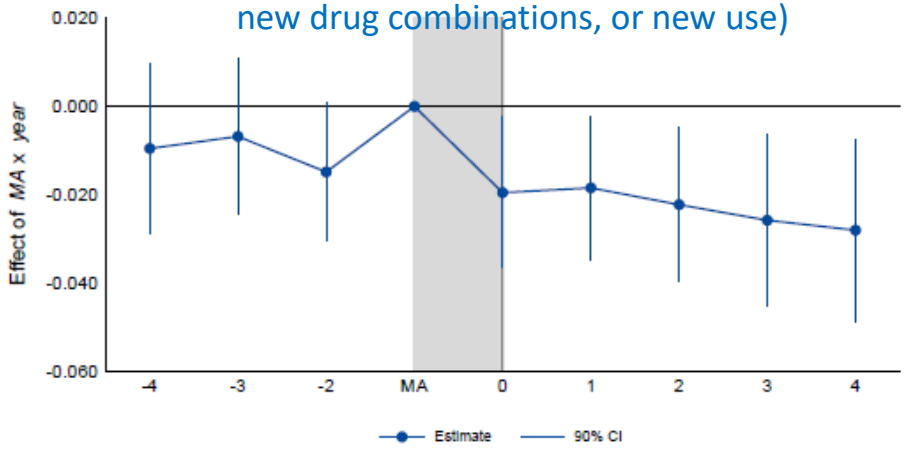
$$\mathbf{E}[y_{it}|\, X_{it}] = \exp[\alpha + \sum_{j=\underline{j}}^{\bar{j}} \beta_j\, MA_{it}^{j} + \sum_{j=\underline{j}}^{\bar{j}} \gamma_j\, patent_{it}^{j} + \sum_{j=\underline{j}}^{\bar{j}} \eta_j\, SPC_{it}^{j} + \delta_t + \theta_i]$$

- y_{it} : # of forward citations (other DVs: examiner citations, self, other, etc)
- MA_{it}^{j}: drug approval happening j periods away from t
- δ_t & θ_i: citation year and patent fixed effects (drug-patent 1-1 level)
- Baseline: no patent and SPC controls; preferred: with demanding patent grant and SPC grant controls; estimates w a “partial effects” interpretation

Market Authorization & self-citations: by type of patent

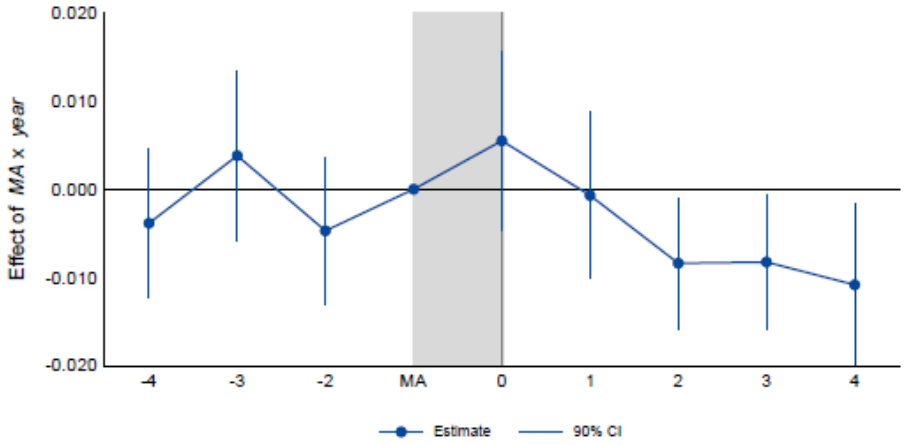
(a) Self-citations - secondary patents

(e.g., new formulations, new dosage forms, new drug combinations, or new use)



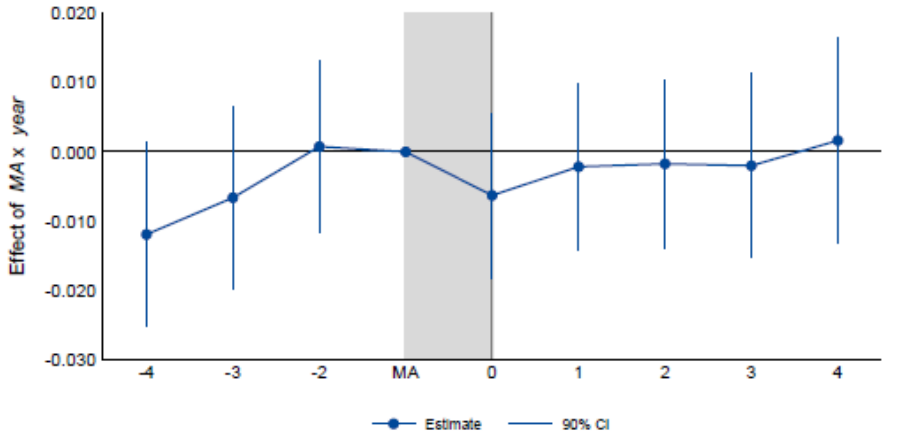
(b) Self-citations - process patents

(e.g., new manufacturing process)



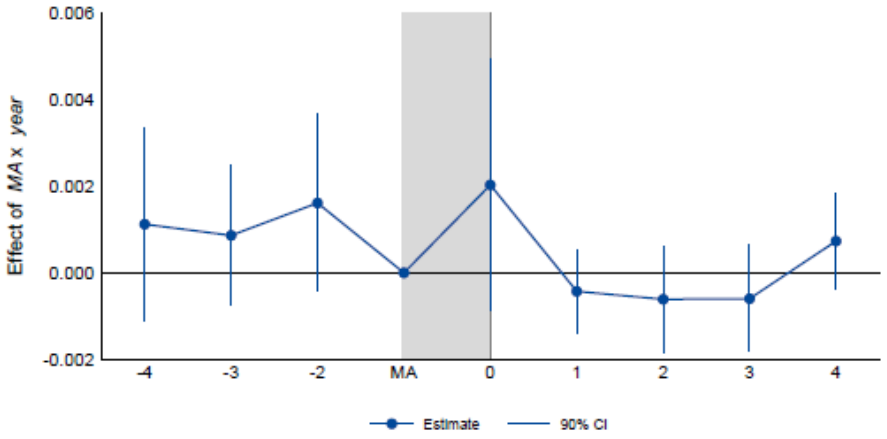
(c) Self-citations - product patents

(e.g., new products (derivatives), new macromolecule)



(d) Self-citations - biotech patents

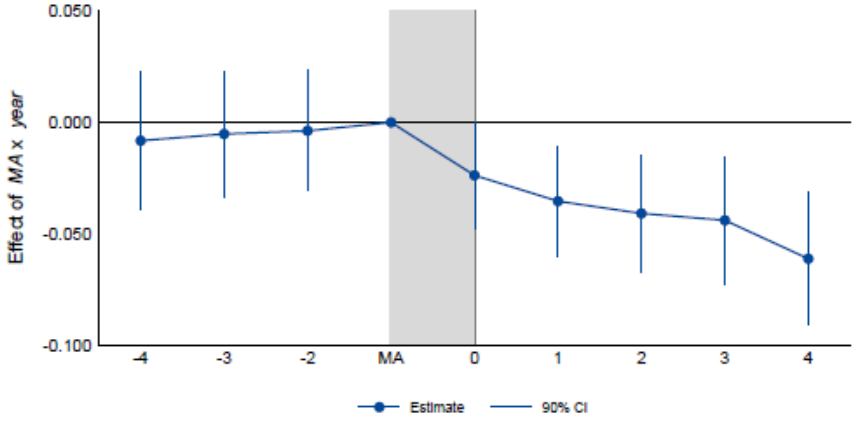
(e.g., biological product/process patents)



Marketing authorization & self-citations: by source/type

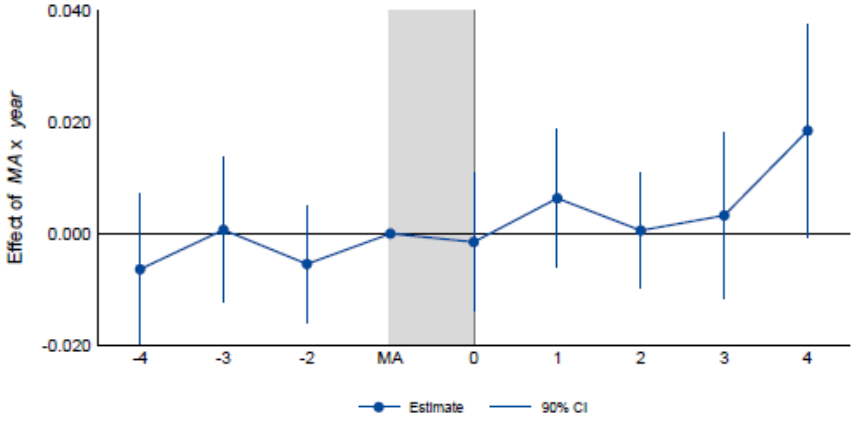
(c) Examiner citations

Self-citations added by examiners (high quality)



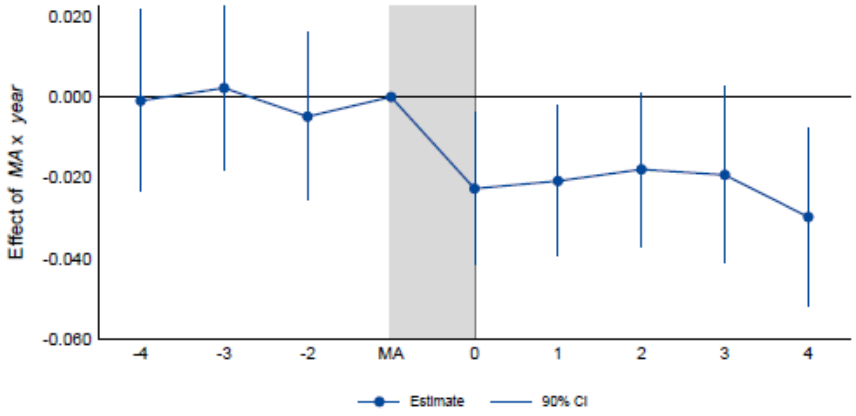
(d) Applicant citations

Self-citations added by applicants

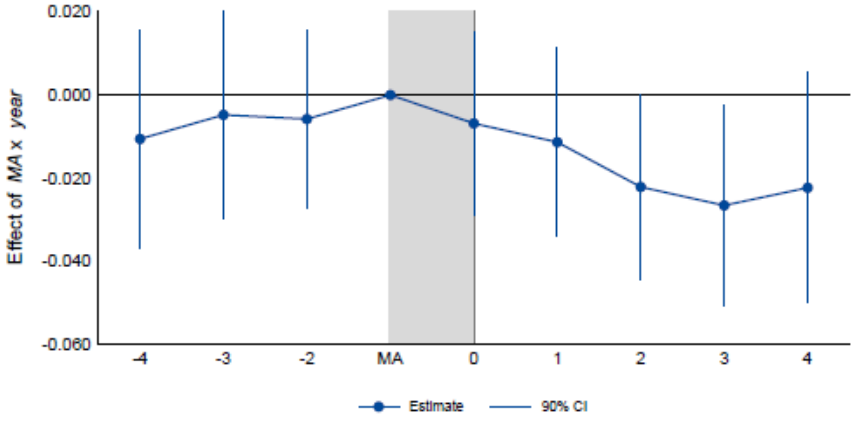


(e) XY-citations

X/Y-ref.: suggest legally "weak" patents as they increase the likelihood of a post-grant validity challenge (Wagner & Wakeman, 2016)



(f) No XY-citations

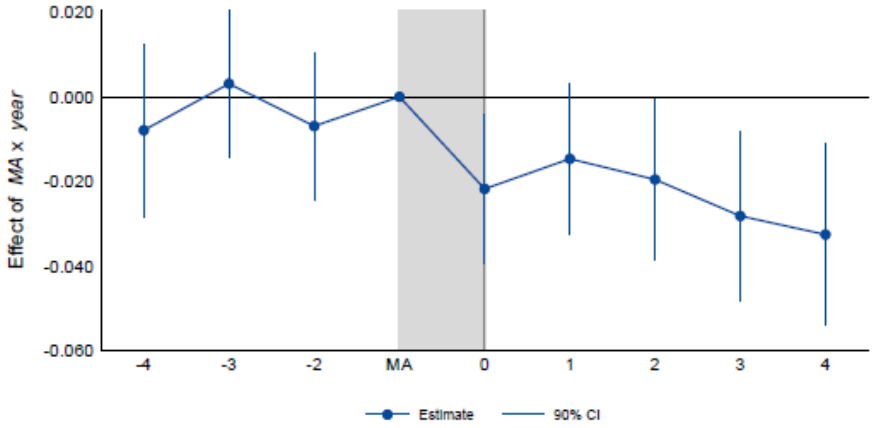


(X: a single prior patent doc can undermine the novelty/inventiveness of claimed invention; Y: do so in combination w/ other docs)

MA & self-citations: by disease; & placebo events

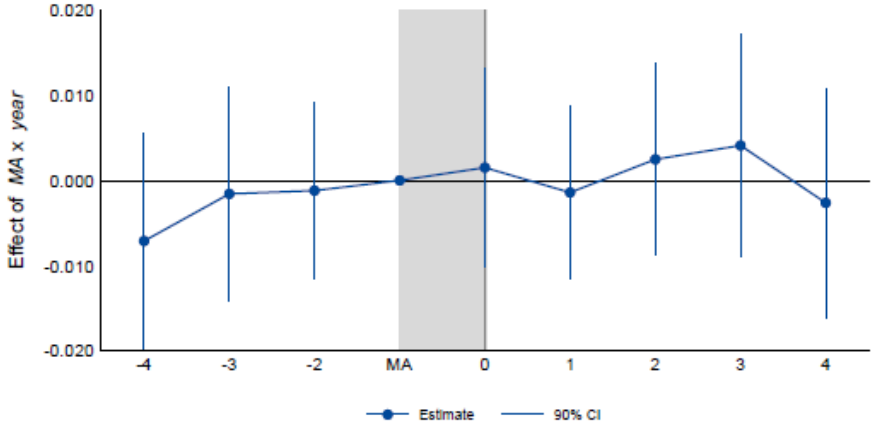
(e) Self-citations - same ICD-9

Same disease area/indication as approved drug



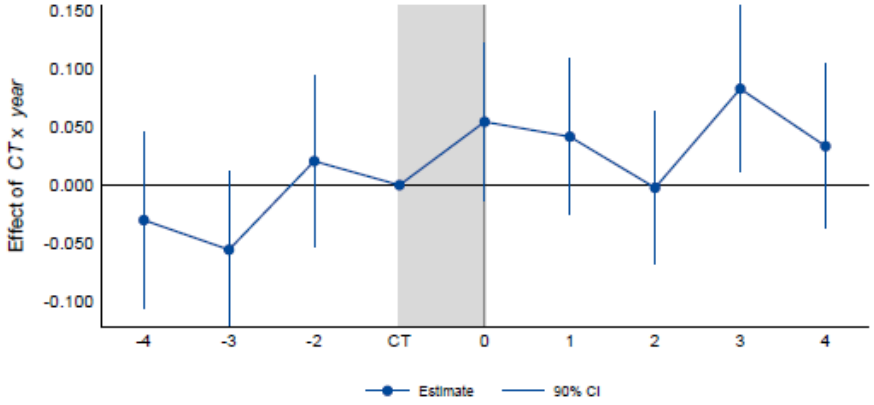
(f) Self-citations - different ICD-9

Explore new treatment options for a focal drug

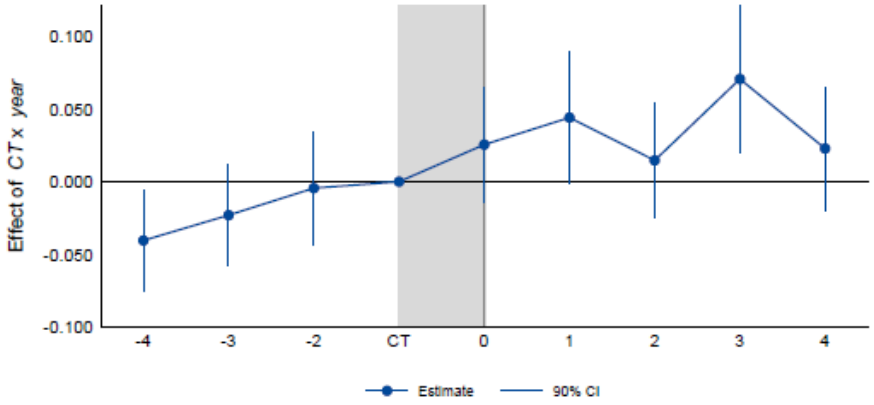


(g) Phase II/III: self-citations - all patents

Use end of phase II/start of phase III as a major milestone event to test the mechanism (disclosure/enforceability)



(h) Phase II/III: self-citations - secondary patents



Others' citations broadly follow a similar pattern, but with about 2 years lags

Robustness Checks, Conclusion, & Discussion

- **Market exclusivity & incentives for competitive entry**:
  - earlier MA -> longer market exclusivity -> + competitive entry -> under-est.
  - Strategy: Zoom in a subset with constant ME due to a kink in SPC regime
- **Unobserved quality**: if + unobserved value w/ – approval lag -> upward bias
  - Strategy: instrumental variable approach (IV: time-to-phase I)
- **Field of application**: whether results are driven by a few disease areas
  - Strategy: leave-one-out ICD-9 disease area specific analyses

- We find that strategic follow-on patenting **decreases** after a drug's market authorization, when follow-on drug patents are harder to obtain
  - More drop for less novel patents; No change in meaningful patents
  - Empirical test indicates it's harder to obtain enforceable patents post-MA
- *Policy implications*: leveraging existing regulatory disclosure requirements may provide a practical approach to improving patent examination without changing formal patentability standards

Megaprojects, Digital Platforms, & Productivity: Evidence from the Human Brain Project

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AEA “tech. and innovation” lightening round session, 2025.1.5

Background and Research Question

- Declining productivity in biomedical science (Bloom et al. 2020); AI showed potential in life sciences (e.g., drug development).
  - But integrating AI with lab science is not always easy
- This paper: how does a ten-year megaproject affect AI-brain sciences?
  - Launched in 2013, the HBP aims to advance brain science in 10 years
  - with €1B grants & AI-powered research infrastructure
- Research Q: How does the HBP affect the rate and direction of R&D?
  - How does accessing to the HBP network matter across research types & career stages? More collaboration/interdisciplinary/novel output?

Human Brain Project

European Commission

Conceptual Considerations

Q: How does the HBP affect the rate and direction of research publications? (in neurosciences/AI/joint)

- Ideas are harder to get. Large teams w complementary skills can help (Jones 2009). But large teams can be inefficient & non-creative
  - Moral hazard with credit sharing (Che & Yoo 2001)
- Intuitively, productivity can go different ways (an empirical Q):
  - More: “Time to explore new areas and expand the network!”
  - Less: “Time to take more risks and invest in new yet slower areas!”
  - Similar: “Time to change $ source, but I still only have 24 hours/day!”
- Q: quantity, quality; network expansion; career/gender; topic areas

Data & Measures

- Data: HBP audited reports, official sites, online forum, CORDIS, Scopus
  - Details on 639 individual researchers actively participated in the HBP (2013-2020) from about 180 institutions in 20+ countries
  - Full publication record of these HBP individuals and control group
  - Matching-based control pool and corresponding research profiles
  - Aggregate to individual-year panel for main analyses
- Measures: publications, citations, text-based research topic areas
  - # of publications, # pubs as the first or last authors
  - # of pubs in top CS outlets, # of pubs top neuroscience journals
  - # of coauthors, # of citations
  - # of pubs by topic groups, and # pubs by topics and journal quality
- Topic classification: use neural, prompt-based, LLMs (GPT3.5turbo/4)
  - Neurobiology, neurotechnology, AI-robotics, clinical focus, others
  - In-progress: annotation & fine-tuning using GPT4o-mini, cross-validation

Methods: TWFE, staggered & matching-based DiD

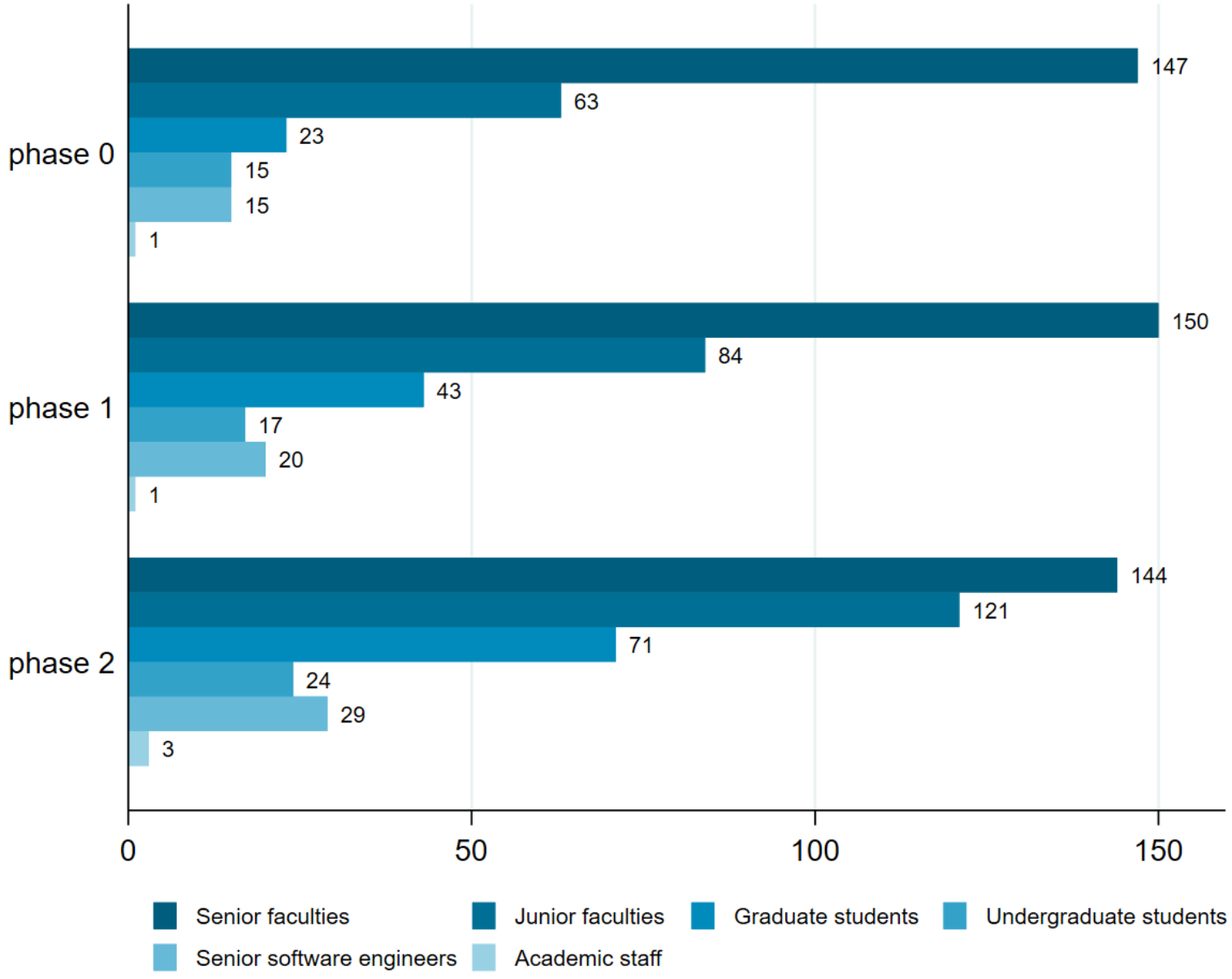
- Start with TWFE DiD for ever-HBP sample: exploit the staggered access
- Individuals fixed effects: comparison within the same person over time

$$y_{it} = \beta HBP_{it} + \delta_i + \delta_t + \varepsilon_{it}$$

  - y_{it} : outcome variables at the author-year-level (log +1, numbers)
  - HBP_{it}: indicates if individual i has actively participated in HBP by t
  - δ_t & δ_i: individual and year fixed effects; s.e. clustered at individual level
  - Apply current methods (e.g., Callaway & Sant'Anna 2021; stacked DID,…)

- Ongoing: matching-based DiD w doppelgängers (Sosia, Rose & Baruffaldi 2020)
  - Identify HBP "doppelgänger" (academic twins) based on first year publishing, #co-authors, #pubs, #citations (pre-treatment, +/- margins)
    - Implementation using socia and pybliometrics over entire Scopus
    - … then refine the control pool by training, institutions, and topics
    - Control group: propensity score matching or coarsen exact matching

Descriptive: participants by phase & seniority level



Results: author-year panel, log DV

- Do researchers actively engaged in the HBP produce more work?

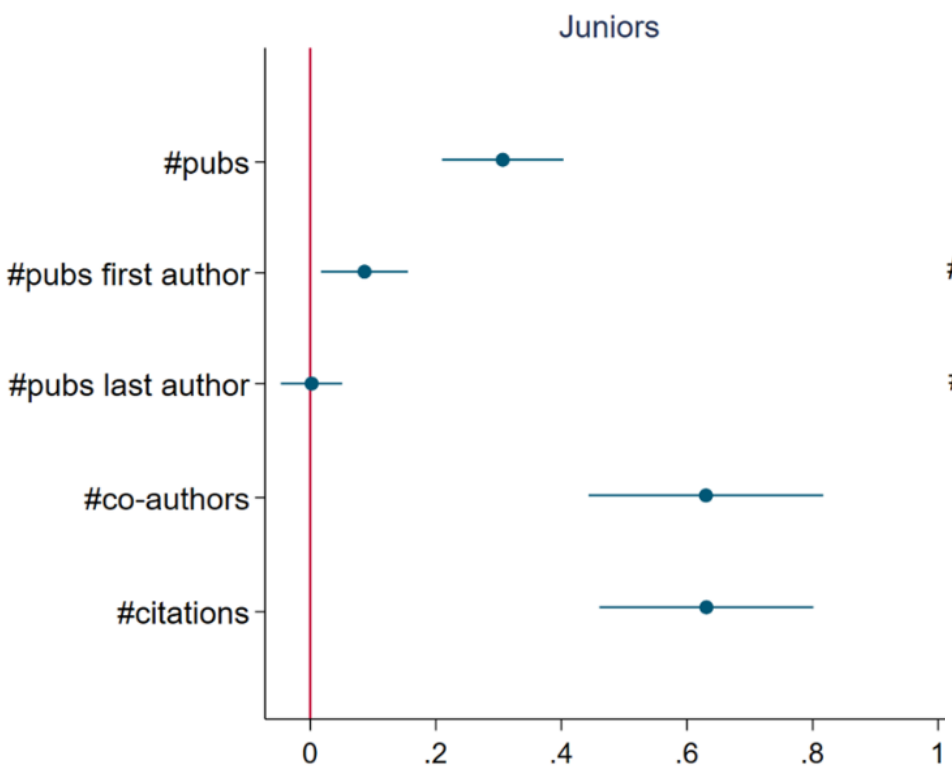
	(1) #pubs	(2) 1st author	(3) last author	(4) #co-authors	(5) #citations
HBP	0.140***	0.0322**	0.0430**	0.294***	0.281***
	(0.0255)	(0.0162)	(0.0178)	(0.0483)	(0.040)
LHS mean	4.1235	0.3528	1.3752	24.5028	271.553
Observations	9,585	9,585	9,585	9,585	9,585
#authors	639	639	639	639	639

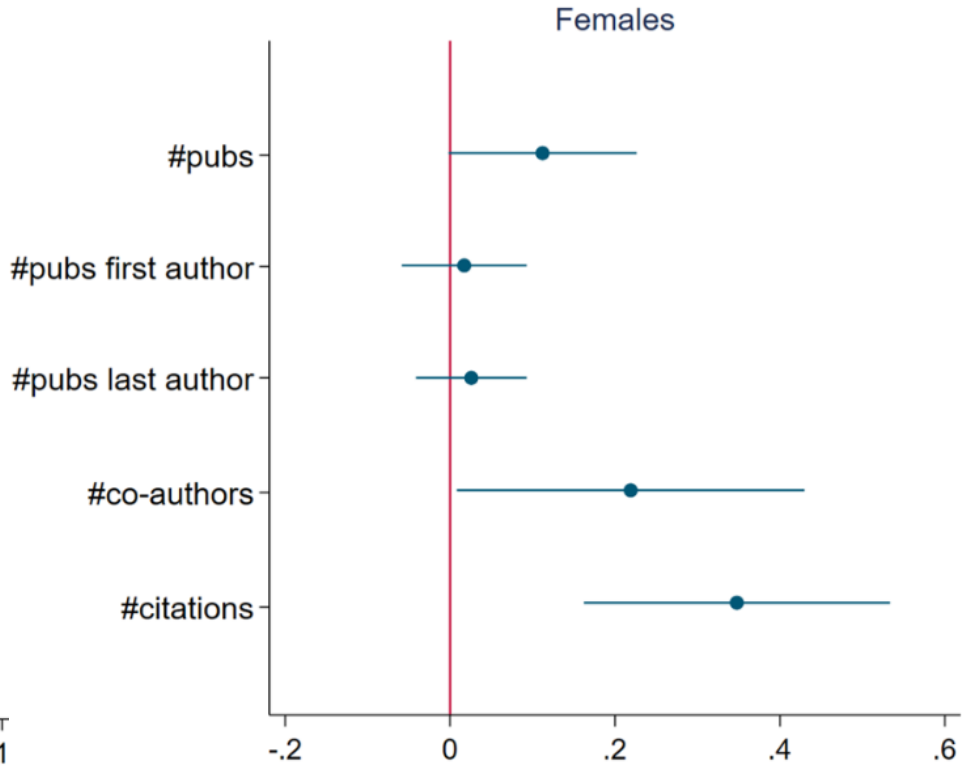
Note: Robust standard errors in parentheses: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

- Researchers show a higher productivity and receive more citations after HBP participation (note: w/ individual fixed effects)
- Participation in the HBP expands researchers' networks (# of distinct co-authors per author-year in revealed publications)

Junior/female subsample: author-year, 2008-2022

- Does the HBP's impact differ by researchers' career stage and gender





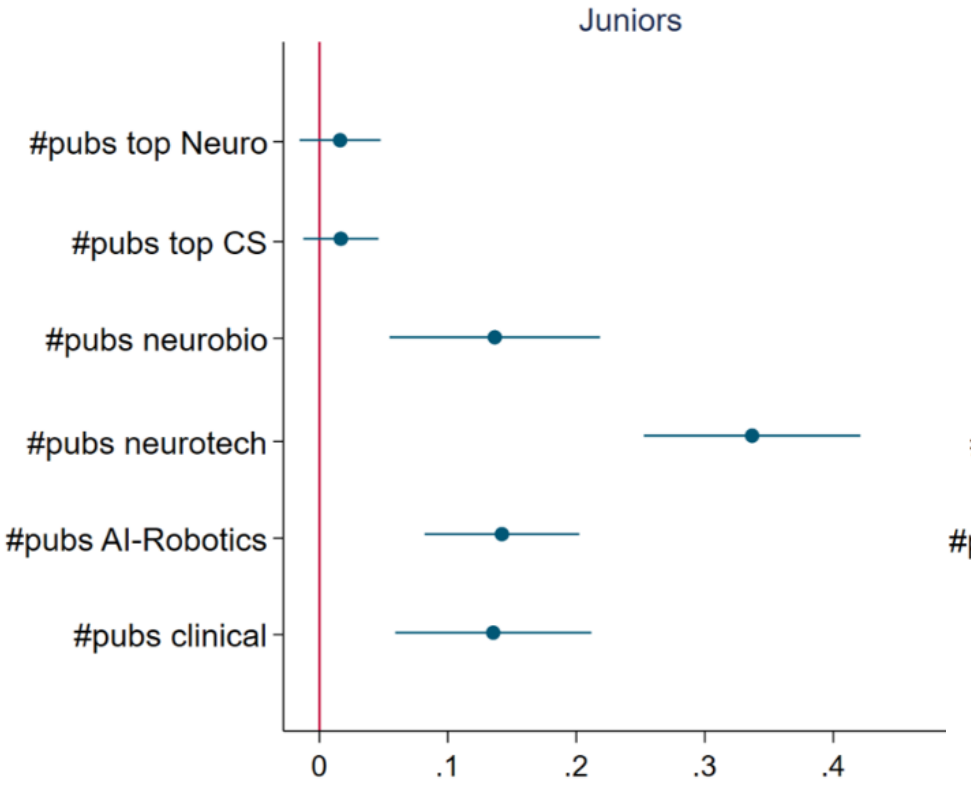
- Juniors (junior faculties and graduate students) benefit the most from the HBP research infrastructure and collaboration
- Female researchers experience a significant productivity increase

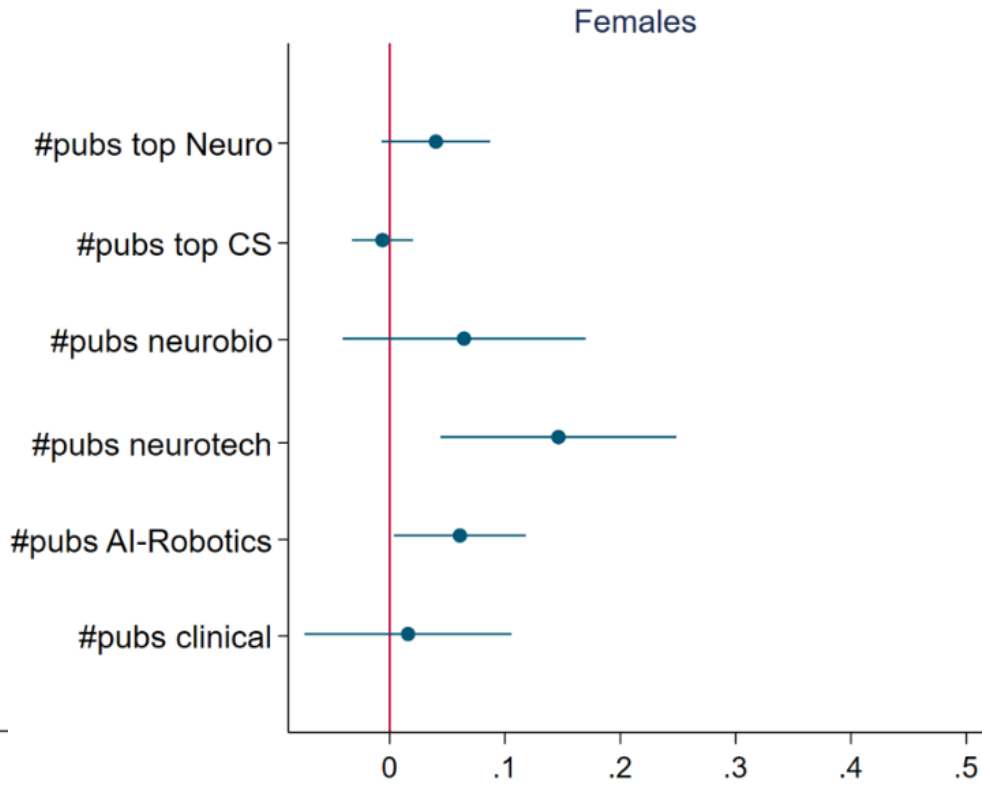
Results by journal quality and topic areas

	(1)	(2)	(3)	(4)
Panel A: Journal Quality (Top neuroscience/CS outlets)				
	Top Neuro	Top CS	CS A*	CS A
HBP	0.0266**	0.00746	-0.00279	0.0125*
	(0.0108)	(0.00820)	(0.00334)	(0.00686)
LHS mean	0.2678	0.1129	0.0371	0.0757
Panel B: Topic Classification				
	Neurobio	Neurotech	AI-Robotics	Clinical
HBP	0.0648***	0.140***	0.0784***	0.0522***
	(0.0220)	(0.0234)	(0.0158)	(0.0196)
LHS mean	2.6266	2.2341	0.8288	1.3723
Observations	9,585	9,585	9,585	9,585
#authors	639	639	639	639

- Higher probability of publishing in top neuroscience journals.
- Increased probability of publishing esp. in topics of neurotechnology.

Junior/female quality: author-year, 2008-2022





- Juniors increases research across topics, especially neurotech areas
- Female yield more top neuro research, & more in neurotech/AI areas

Conclusion & Discussion

The HBP appear to yield positive synergy among AI-neuroscience scholars, and pushed more high-quality interdisciplinary research

- Active involvement in the HBP appears to increase productivity and citations, esp. for juniors and (to a lesser extent) female researchers.
- Researchers have a higher likelihood of publishing in top neuro journals, esp. within the area of AI-neuro intersection: neurotechnology
- Scholars benefit regardless of their *affiliated country* at the beginning of HBP participation, more for German, Italian, & Belgian-based scholars
- Some evidence that a *combination* of training and expanded network at the beginning of one's career is most crucial for productivity gains
- *Lots of work-in-progress, aim to release a draft by summer 2025!*

Thank you! Contact: xiaoluwang@umass.edu; ann-christin.kreyer@ip.mpg.de