Combining Complements:

Theory and Evidence from Cancer Treatment Innovation

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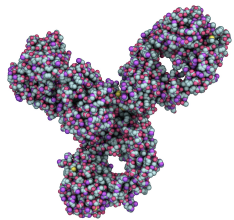


Combination Innovation: Promise and Limits

- Innovations often combine existing ideas/products
  - drug combinations for COVID-19, ADHD, HIV/AIDS, cancer, ...
  - combinations important for long-run technological progress: many potential innovations
- Combination innovation subject to externalities:
  1. Standard externalities: business stealing ($-$); consumer surplus, knowledge spillovers ($+$)
  2. Additional positive externality on firms: market expansion ($+$) raises demand for complementary components, free-riding

How important is the market expansion externality? Policy responses?

Setting: cancer drug combination therapies, clinical trials

Overview

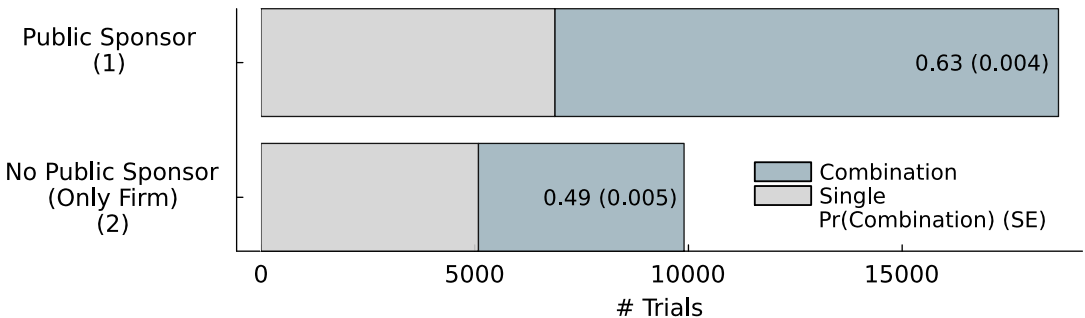
1. **Model** stylized combination innovation decision
   - market expansion and other externalities
2. **Describe** evidence consistent with market expansion externalities
   - direction of innovation: combos with own drugs or generics
3. **Quantify** externalities from new combinations
   - patient cancer drug demand, drug price setting
   - market expansion $>$ business stealing
4. **Evaluate** policies to support combination innovation
   - dynamic discrete choice combination innovation game: free riding, public crowd-out
   - increase welfare with budget neutral policies changing public direction

Cancer Treatment, Innovation, and IP

- Cancer drug combinations: common treatment, mostly via IV
- Clinical trial before wide use: sponsored by firm or publicly-funded
- Missing property right: patents difficult to enforce, collaboration (contracting) frictions
  - not packaged together (staggered delivery in clinic) $\Rightarrow$ no price discrimination
  - contrast from fixed dose combinations (e.g., HIV)
- Market expansion: increase in profits from drug use new combination
- Data: innovation decision via clinical trials, treatment usage/prices from insurance claims

Who Funds Combination Innovation?

Firms less likely to trial combinations than are public researchers



What is the Direction of Combination Innovation?

Firm combination trials biased towards own patented drugs

trial regimen r, year t — event study alternative

$$\text{Trial}_{rt} \,/\, \beta^{\text{unif}}(L_t) = \gamma_1 \text{2-Patented Same}_{rt} + \gamma_2 \text{2-Patented Diff}_{rt} + \gamma_3 \text{Has Generic}_{rt} + \varepsilon_{rt}$$

relative to uniform

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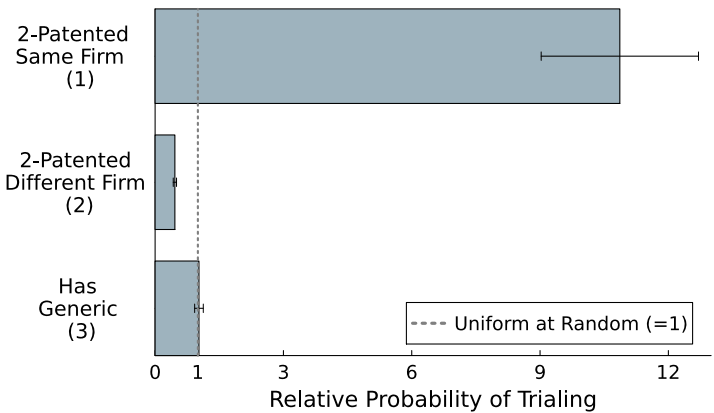


What is the Direction of Combination Innovation?

Result not driven by:

- intra-firm complementarity: lab tests of efficacy similar for combos with 2 same-firm drugs versus different-firm drugs
  - NCI ALMANAC: "A Large Matrix of Anti-Neoplastic Agent Combinations" (2017)
    measure growth rates of tumors from all 2-drug combos from 100 approved cancer drugs

- intra-firm familiarity: firms trial combos of on-patent + generic, whether initially patented by same firm or not, with similar relative probabilities

- crowd-out: low relative probability of public trials of 2-patented different-firm drugs
  - most likely to trial generics

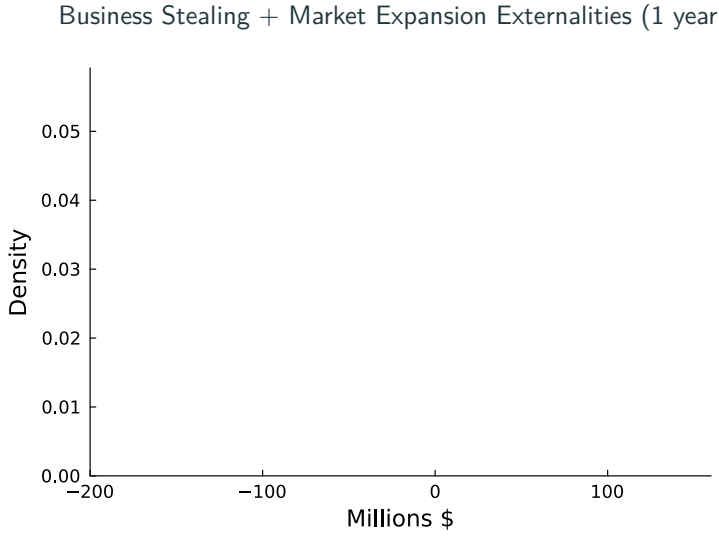
Measuring Combination Innovation Externalities

1. **Drug demand:** value to patients $CS(p)$, substitution patterns $s_r(p)$
   - demand system over bundles (complementarity), micro-moments
   - products: medical guidelines to determine successful treatment regimens (single + combo)
   - market shares, prices: public (Medicare) and private (Marketscan) claims, 1998-2019

2. **Drug price setting:** marginal costs, pricing conduct
   - Nash bargaining between firms and private insurer (Medicare prices function of ASP)

3. **New regimens:** calculate ΔW, ΔCS, externalities after introducing r^+
   - simulate model 1 year after introduction
   - successful innovations in sample: 131 combinations, 92 single-drugs

Market Expansion > Business Stealing



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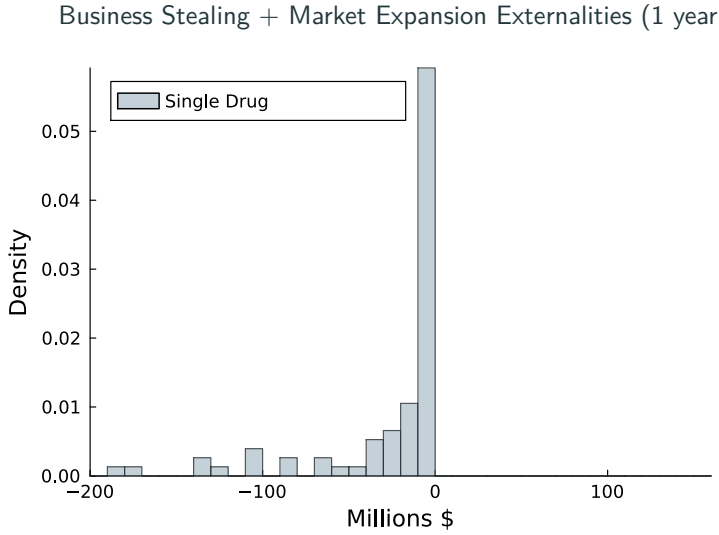

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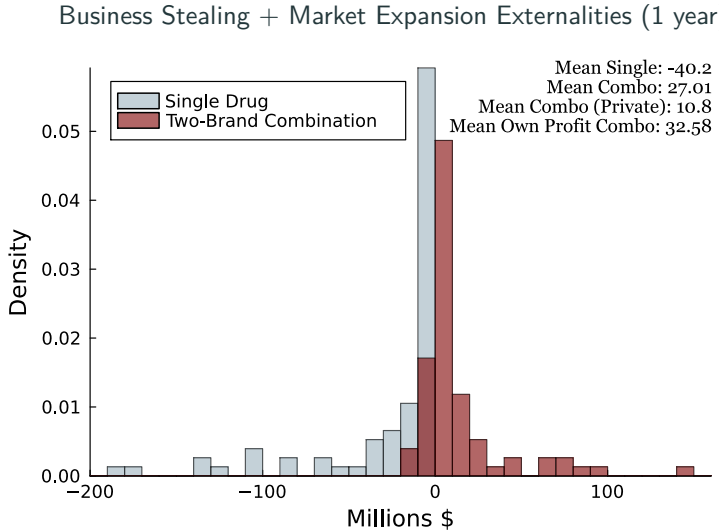


profit externalities $200M over life-cycle of combination

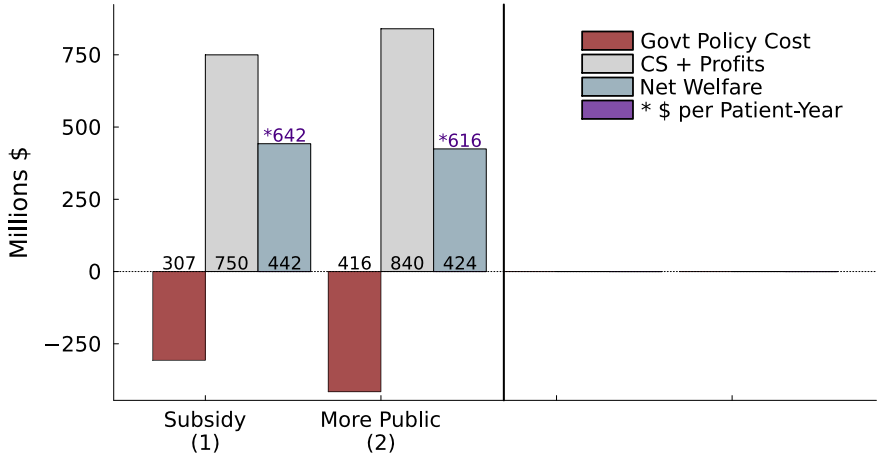
Externalities and the Path of Innovation

- Dynamic discrete choice game for each combination *regimen r*, trial to learn quality
- Players: drug owners (π), public innovator ($CS + \lambda\Pi$)
- Actions: trial, don't trial; State: trialing status of regimens
  - incentive to free ride (market expansion externality), public crowd out
- Simplications: seperability across regimens, reduce state, estimate for trialed regimens
- Estimation: full-solution MLE recovering cost of innovation, objective of public innovator
  - focus on colon cancer

Counterfactual Combination Innovation Funding

Cost-effective policies to increase arrival rate of combination innovation?

- policies requiring less information than dynamic Pigouvian subsidy



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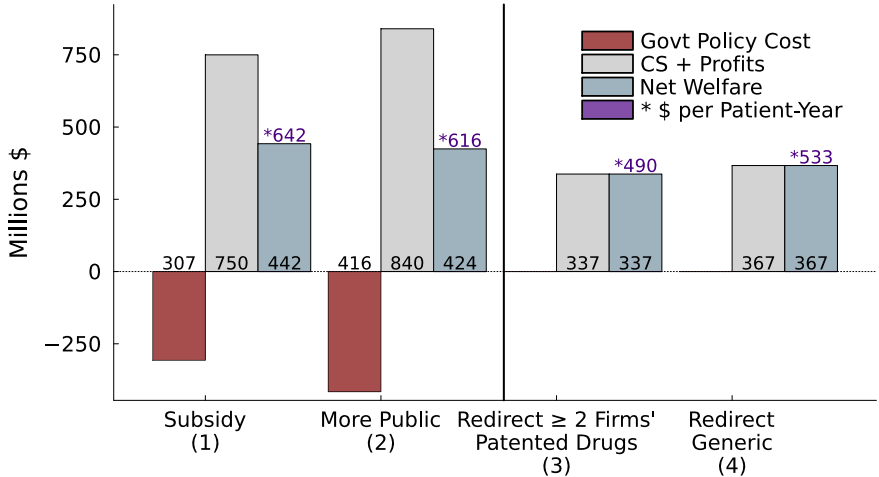

Conclusion

- Combination innovation introduces forces that may lead to underinvestment
  - market expansion, missing property rights, free-riding
- Empirical case study of cancer drug combination therapies
  - estimate externalities: market expansion often dominates business stealing
  - design budget neutral policies to advance combination innovation
- Implications: innovation of individual drugs, tools for screening combinations
- Similar economics with other property rights institutions, complements more generally
  - ex: hybrid seeds, hardware and software

Thank you!

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