What inventions are we missing?

Heidi L. Williams
(joint work with Eric Budish and Ben Roin)

March 2019
What inventions are we missing?

Example: Why don’t we yet have a cure for Alzheimer’s disease?

- Common characterization: Basic science is challenging
- Economic perspective:
  - Available scientific opportunities may reflect past research investments
  - Potential role for gov’t policies – e.g. patents – to impact innovation
Motivation

- Over last five years, eight new drugs approved to treat lung cancer
- All eight were approved based on evidence of incremental survival improvements in patients with most advanced form of the disease
  - Well-known example: Genentech’s Avastin (10.3 vs. 12.3 months)
- In contrast, no drug has ever been approved to prevent lung cancer, and only six drugs have ever been approved to prevent any cancer
While this pattern could solely reflect market demand or scientific challenges, in this paper we investigate an alternative hypothesis: private firms may (differentially) underinvest in long-term research.

- Late-stage cancer drugs can be brought to market comparatively quickly, relative to early-stage treatments or preventatives.
  - Key: Time required to show a statistically significant treatment effect
  - Excess impatience or patents may under-incentivize long-term research

We document that such underinvestment is quantitatively significant in markets for cancer drugs, and analyze potential policy responses.
Cancer markets as an empirical setting

Key empirical challenge: We do not observe the (counterfactual) commercialization lags of projects that are never developed

Two useful features of cancer markets:

1. Cancer treatment is organized around organ and stage, providing a natural categorization of both observed and potential R&D

2. For each group of cancer patients, we observe a good predictor of how long it would take to develop drugs for those patients: survival time
   - Key: observed even if no drugs have ever been developed
Two examples: Prostate cancer drugs

1. de Bono et al.: Metastatic patients (5-yr survival ≈ 20%)
   - Median follow-up time for measuring patient survival: 12.8 months
   - Trial length: 3 years

2. Jones et al.: Localized patients (5-yr survival ≈ 80%)
   - Median follow-up time for measuring patient survival: 9.1 years
   - Trial length: 18 years

Consistent with commercialization lags distorting private R&D incentives:
- Metastatic clinical trial funded by Cougar Biotechnology
- Localized clinical trial funded by US National Cancer Institute
Survival time and R&D investments: Stage-level data

Notes: See Figure 1(a) in paper.
How to interpret this fact?

By itself, this fact is difficult to interpret for two reasons:

1. Correlation need not reflect a causal relationship between commercialization lags and R&D investments

2. Even if this correlation did reflect a causal relationship, it need not be evidence of a distortion because the social planner is also more likely to pursue research projects that can be completed more quickly
Surrogate endpoints and R&D investments

This suggests that there is a causal relationship: if commercialization lags were shortened, there are scientific opportunities available that would be pursued.

Notes: See Figure 4 in paper.
Share of clinical trials that are privately financed

Taken together, this - together with the surrogate endpoints evidence - provides support for the idea that commercialization lags distort private R&D investments.

Notes: See Figure 5(b) in paper.

Notes: See Figure 6(a) in paper.

Notes: See Figure 6(b) in paper.
Rough back-of-the-envelope: Value of lost life

Value of life lost among US cancer patients diagnosed in 2003:

1. Using the cancer registry data, we translate the gap between the hematologic and non-hematologic survival curves into an estimate of life-years lost per cancer patient: 1.07 life-years per patient

2. For each cancer-stage, multiply by the number of US patients $c_{s}$ diagnosed in 2003: 890,000 life-years lost for that cohort

3. Multiplying by a standard value of a statistical life-year (Cutler 2004: $100,000) monetizes this lost life at a value of $89 billion
Our evidence is directly relevant to two policy levers:
1. Allowing firms to rely on valid surrogate endpoints
2. R&D subsidies targeting long commercialization lag projects

Estimates cannot speak directly to patents
Anecdote: Surrogate endpoints and heart disease

- Heart disease is the leading cause of death in the US, but the age-adjusted rate of death has dropped by 50% since 1968
- Decline largely attributed to beta-blockers, ACE-inhibitors, statins
- These drugs were approved based on blood pressure, LDL cholesterol
  - Surrogates first identified by decades-long Framingham Heart Study
  - Some have argued that w/o surrogate endpoints, these drugs may not have reached the market [Lathia et al. (2009); Meyskens et al. (2011)]

Both our empirical evidence for cancer and this historical case study for heart disease suggest that research investments aimed at establishing and validating surrogate endpoints may have a large social return