

# Do fixed patent terms distort innovation? Evidence from cancer clinical trials

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- 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)
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- 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 cancer treatments or preventatives
- We document that such underinvestment is quantitatively significant in markets for cancer drugs, and analyze potential policy responses

# Why might private firms underinvest in long-term research?

Simple model: Two reasons why firms may (differentially) underinvest

- ① Short-termism: widely discussed, little empirical evidence (Stein 2003)
- ② R&D markets, add'l potential mechanism: Structure of patent system
  - ▶ Patents award innovators a fixed (20-year) period of market exclusivity
  - ▶ Yet, many firms file patents at discovery (“invention”) rather than first sale (“commercialization”)  $\Rightarrow$  inventions with long commercialization lags receive reduced - in extreme cases, zero - effective patent terms
  - ▶ Implies that in some markets, the patent system provides very little incentive for private firms to engage in long-term research

# Testing for “missing” R&D

This idea - while intuitive - is difficult to test empirically

- Key prediction: “missing” private R&D on long-term projects
- In practice, testing this prediction encounters two challenges:
  - ① Measurement: don't observe commercialization lags for missing projects
  - ② Inference: “missing” R&D hard to distinguish from alternative explanations, e.g. lack of market demand or scientific opportunities

Three features of cancer markets allow us to make progress:

- ① The treatment of cancer patients is organized around the organ (e.g. lung) and stage (e.g. metastatic) of disease, which provides a natural categorization of observed and potential R&D activity
- ② For each such group of cancer patients we observe a good predictor of how long it would take to commercialize a new drug: survival time
- ③ There exist sources of variation that can provide levers for inference

## Two examples: Prostate cancer drugs

Two prostate cancer trials in *New England Journal of Medicine* in 2011:

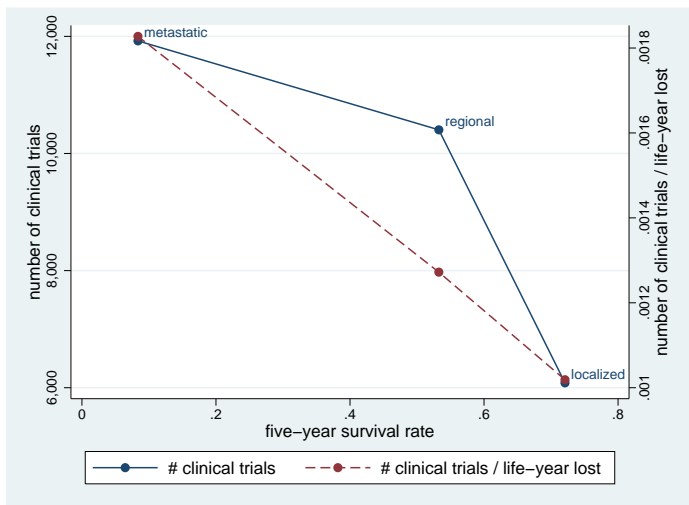
- 1 de Bono *et al.*: Metastatic patients (5-yr survival  $\approx$  20%)
  - ▶ Median follow-up time for measuring patient survival: 12.8 months
  - ▶ Trial length: 3 years
- 2 Jones *et al.*: Localized patients (5-yr survival  $\approx$  80%)
  - ▶ Median follow-up time for measuring patient survival: 9.1 years
  - ▶ Trial length: 18 years

Consistent with commercialization lags reducing private R&D incentives:

- Metastatic clinical trial funded by Cougar Biotechnology
- Localized clinical trial funded by US National Cancer Institute

We construct data on all such clinical trials over the last three decades, which we match to data on patient survival over the same period

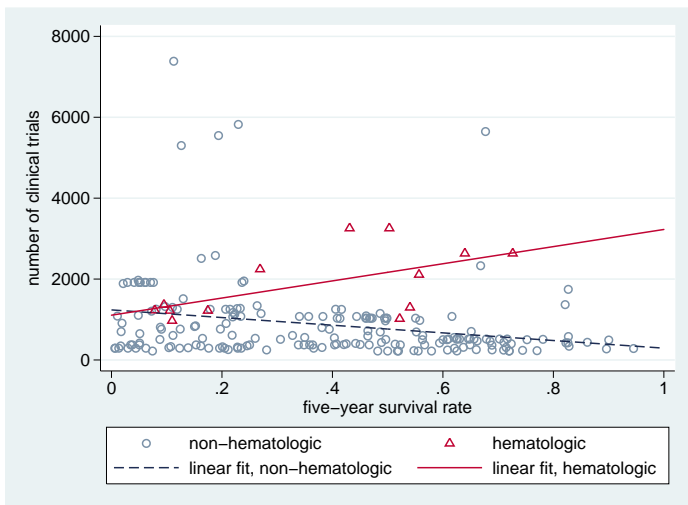
# Survival time and R&D investments: Stage-level data



Notes: See Figure 1(a) in paper.

This pattern is consistent with our model, but by itself is not evidence of a distortion: heterogeneity in demand or R&D costs could also generate this negative correlation.

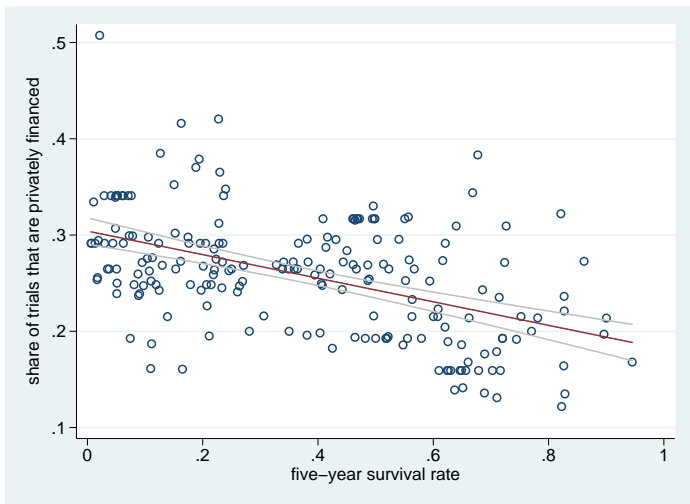
# Surrogate endpoints and R&D investments



Notes: See Figure 4 in paper.

This test leaves open the possibility that the social planner and private firms symmetrically value commercialization lags, and thus does not provide direct evidence of a distortion.

# Share of clinical trials that are privately financed



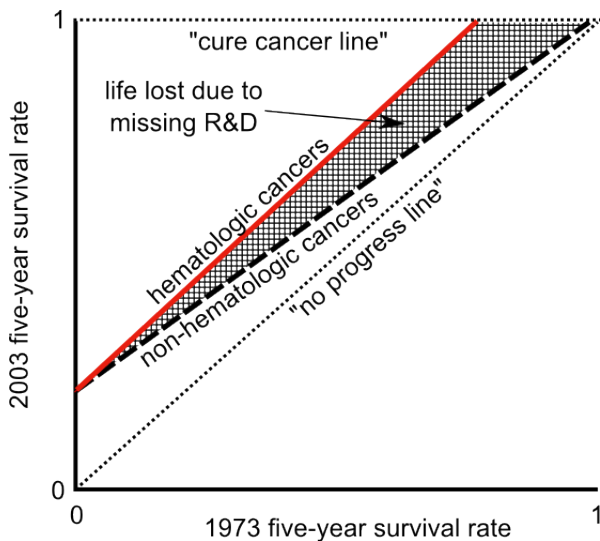
Notes: See Figure 5(b) in paper.

This test shows that the commercialization lag-R&D correlation is economically and statistically significantly more negative for privately financed trials than for publicly financed trials.

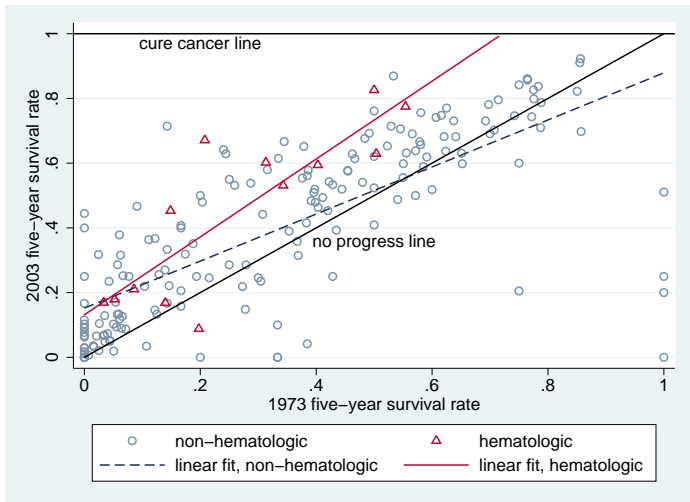
# Analyzing FDA-approved chemoprevention drugs

- Meyskens *et al.* (2011): six FDA approved chemoprevention drugs
- All six approvals either relied on the use of surrogate endpoints, or were approved on the basis of publicly financed clinical trials
  - ▶ Tamoxifen: prevention trials publicly financed
  - ▶ Cervical cancer vaccine: HPV incidence as endpoint

## Counterfactual: Survival gains, 1973-2003



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## 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<sub>CS</sub> 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

⇒ Net present value over future cohorts of  $\frac{\$89 \text{ billion}}{0.05-0.01} \sim \$2.2 \text{ trillion}$

# Policy analysis

Analyze innovation, social welfare consequences of three policy levers:

- 1 Policy design: Surrogate endpoints
  - ▶ Valid surrogate endpoints likely to be very valuable (shorten commercialization lag)
- 2 Policy design: Targeted R&D subsidies
  - ▶ Direct public funds to R&D the private sector is unlikely to undertake
- 3 Patent design: Start patent (or FDA exclusivity) at commercialization
  - ▶ Currently provide patent protection that decreases in commercialization lag; our analysis suggests that if anything this should be increasing
  - ▶ Importantly: addresses patent distortion, but not short-termism bias

## Anecdotal evidence from industry interviews

- *...Quite often we've declined to take advantage of an opportunity because we thought there wouldn't be enough time under the patent term to earn a return on the investment.*
- *The shorter the remaining patent term, the more certainty you need that the drug will work, and the more it needs to have a large market. Also, the ramp is important. You want at least a couple years of peak sales. It happens all the time that we pass on a drug, one we think would probably work, because there wouldn't be enough life left on its patent by the time it reached the market.*

# Conclusions

- Simple conceptual point: commercialization lags may distort R&D away from inventions that take a long time to bring to market
- In the context of cancer R&D, this implies there may be too little R&D on cancer prevention and treatment of early-stage cancers
- Several sources of evidence are consistent with this distortion
- Analyze potential policy responses:  
surrogate endpoints, R&D subsidies, patent design

## Closing example: 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))