The Impact of Publicly Funded Biomedical and Health Research: A Review

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Funding for biomedical research in 2007 (total = $101 billion)

- NIH: 27%
- Pharma: 36%
- Biotech: 15%
- Medical Device: 7%
- Philanthropic: 4%
- Other Federal: 5%
- State/Local: 5%

Notes: Adapted from Dorsey et al. 2008
Logic model*

*Yes, it's too stylized, simple, and linear
Literature review

- Focus on impact of public sector research on short run outcomes (e.g. patents, private R&D) and long-run impact (health, drugs, devices, costs)
- Based on Pubmed, EconLit, ISI, Google Scholar searches
- Snowball method for identifying additional references
- Limit to empirical articles (including qualitative, quantitative, historical, case studies)
- Exclude NIH publications (e.g. Cost Savings Resulting from NIH Research Support)
- Representative, not exhaustive
Frequently used measures

- **Public sector inputs:**
  - NIH: Funding by Institute; CRISP data on funding by disease area
  - Medline: NIH-funded publications
  - Medline, FDA, clinicaltrials.gov: NIH-funded trials
  - Medline: Publications by funding source

- **Private sector R&D:**
  - Pharma: R&D by therapy area
    - Biotech, device R&D figures imputed
    - Pharmaprojects data on drugs in development

- **Drug approvals, innovation:**
  - FDA: drugs, therapy class, therapeutic benefit
  - Medline: "Drug therapy" articles
  - USPTO data on patenting in biomedical classes (including inventors, institutional affiliation, and location)
  - Orange book data on patents associated with marketed drugs

- **Health outcomes: mortality, age-adjusted mortality**
  - Dollar value of these improvements

- **“Spillovers” or Knowledge Flows**
  - USPTO Patent-Patent Citations; Patent-Paper Citations
  - Survey data on inputs into industrial R&D
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| Cutler and Kadiyala (2007) | What is the role of biomedical research in reduction in CVD mortality? What is rate of return on biomedical research funding? | • Detailed case study of the roles of high tech invasive treatments, medications, behavioral changes in overall improvement  
• Residual based approach to decompose roles of each in improvement  
• Analyses of the roles of medical research in advancements above  
• Estimate costs of total research  
• Relate benefits to costs to calculate rates of return; rely on historical record for causality claims; robustness checks using alternative assumption | • Economic value of clinical benefits of medical treatments, changes in behavior  
• Data on NIH funding for cardiovascular disease 1953-1997 | • Returns to basic research 30-1  
• Much of the benefit is through effects on behavioral change (smoking etc.) which they attribute to NIH via historical record |
| Weisbrod (1983)   | What was rate of return on public investments in polio research?            | • Detailed case study  
• Counterfactual: what would clinical and economic costs be in absence of vaccine? | • Economic value of clinical outcomes  
• Relate to data on public expenditures on “polio” | • Rate of return 11-12% |
# Public Funding and Health Outcomes

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| Heidenreich and McClellan (2007) | How important has biomedical research been in care of heart attacks?     | • Focus on applied research “not because we view basic research as unimportant, but because it is much easier to identify connections between these applied studies in medical care and health”  
  • Decompose sources of improved outcomes for heart attack treatment over 1975-1995  
  • Use information on timing of key trials to infer causality  
  • Qualitative analyses relating trials to outcomes | • Medline data on relevant trial, timing of major RCTs  
  • Trends in use of interventions  
  • 30 day mortality post-AMI  
  • Funding sources for the trials | • Mini-case studies show RCTs have some effect on clinical practice (thrombolytic drugs), but small  
  • Most other trials had a limited effect  
  • Negative trials had lagged but real effects  
  • Clinical practice leads doesn’t lag  
  • Formal applied studies alone don’t explain much of the decline; a lot of learning is informal |
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| Manton et al (2009) | How do U.S. health dynamics relate to NIH funding patterns from 1950 to 2004? | • Correlate 10 year lagged NIH funding to outcomes for four major chronic diseases: CVD, stroke, cancer, diabetes | • NIH funding overall (lagged 10 years)  
• NIH funding for four relevant institutes (NHLBI, NINDS, NCI, NIDDK)  
• Outcome measures: cause specific mortality (deaths/100,000); age adjusted death rates | • Temporal correlation between funding from relevant institute and deaths for 3 of the 4 diseases  
• Lagged NIH funding negatively correlated with age adjusted death rates for 2 of 4 diseases (heart disease, stroke)  
• Using counterfactuals based on historical trends, project significant deaths averted due to NIH funding (mostly CVD) |
| Comroe and Dripps (1976) | What types of research (clinical vs. basic) are important in the advance of clinical practice, health? | • Interviews, expert opinions used to determine of top 10 clinical advances in cardiovascular and pulmonary arena  
• Content analyses of key articles | • Top 10 clinical advances  
• "Key articles" associated with these advances  
• Coding of whether the key articles are clinical or non-clinical | • 41 percent of all work judged to be essential or crucial for later clinical advances was not clinically oriented at the time of research |
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| Ward and Dranove (1995) | How does industry funded R&D respond to NIH R&D?                          | Panel regressions relating private R&D in a disease area to NIH R&D by relevant institute | • PhRMA data on R&D by field  
• NIH data on R&D by institute  
• Controls for disease burden, drug development, time | • A 1 percent increase in NIH research associated with .76 percent increase by private sector over next seven years (direct)  
• A 1 percent increase in NIH research associated with 1.7 percent increase by private sector over next seven years (indirect)  
• Contemporaneous correlations highest |
| Cockburn and Henderson (1996) | How does interaction with public sector science (collaboration, hiring of “star” scientists) affect firm-level R&D productivity | Panel regression models relating productivity to within firm variation in interaction with public sector, with firm fixed effects | • MEDLINE data from 35,000 articles on firms’ co-authorship, publication by “star” scientists for 10 firms, 1980-1988  
• Data on “important” patents/R&D for these firms | • Statistically significant association between propensity to co-author with academics and important patents/dollar  
• Statistically significant association between share of publications from “star” scientists and important patents/R&D dollar |
## Public Research and Private R&D, Patenting

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| Toole (2007)          | Does public scientific research complement private R&D investment?       | Panel regression models relating pharmaceutical R&D by to NIH funding across disease areas, over time | • CRISP data on NIH basic and clinical research mapped to 7 therapeutic classes, 1972-1996  
• PhRMA data on private sector R&D in these classes, 1980-1999 | • Public and private sector research complements  
• A 1 percent increase in basic research funding associated with a 1.7 percent increase in private sector R&D  
• A 1 percent increase in clinical research funding associated with a .40 percent increase in private sector R&D |
| Azoulay, Graff Zivin, Sampat (2011) | Do elite life scientists benefit local firms? | Panel regression models examining geography of citations to scientists' work before and after they move | • Data on 10,450 elite life science researchers (most publicly funded)  
• Historical information on productivity, employment locations of each scientist  
• MEDLINE data on their publications  
• ISI data on citations to their publications  
• USPTO data on their patents  
• USPTO data citations to their patents and publications | • Professional transitions lead to a decrease in citations (in patents and articles) to movers' pre-move patents at original location  
• Weaker evidence of increase in citations from firms at destination location |
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| Zucker, Darby and Brewer (1998) | How important was academic science in the creation of new biotech firms? | Panel regression models relating location of new biotechnology firms to number of “star” scientists in area | • 337 “star” scientists (based on articles, genetic discoveries in Genbank)  
• Data on their collaborators  
• Location and affiliation of stars (from journal articles)  
• Data on biotechnology firms and firm formation from North Carolina Biotechnology Center and Bioscan | • Presence of stars and their collaborators – “intellectual capital” – in an area has a statistically significant and positive relationship with the number of new biotechnology enterprises later formed in that area |
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<td>Cohen, Nelson, Walsh (2002)</td>
<td>What are the roles of public sector research on industrial R&amp;D? What are the channels through which public research affect industrial R&amp;D?</td>
<td>Survey</td>
<td>• 1994 Carnegie Mellon Survey of Industrial R&amp;D managers&lt;br&gt;• Merged with publicly available data on respondents</td>
<td>• Pharmaceutical industry an outlier: reports public research the most important source of new project ideas and contributing to project completion&lt;br&gt;• Medical instruments industry R&amp;D projects less frequently use any of three outputs of public research than other industries&lt;br&gt;• Drug industry makes use of public research much more frequently&lt;br&gt;• Top three fields contributing to R&amp;D in pharmaceuticals: Medicine, Biology, Chemistry&lt;br&gt;• Top three fields contributing to R&amp;D in medical instruments industry: Medicine, Materials Science, Biology</td>
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# Public Funding and New Drugs, Devices

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<td>Cockburn and Henderson (1996)</td>
<td>How does public sector research affect pharmaceutical innovation?</td>
<td>Case studies of 15 clinically important drugs</td>
<td>Qualitative determinations of roles of public sector in drug development</td>
<td>Of 15 drugs, public sector research made key enabling discovery for 11</td>
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<td>Public sector involved in synthesis of major compound in 2 cases</td>
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<td>Ward and Dranove (1995)</td>
<td>How do MEDLINE “drug” articles respond to NIH funding?</td>
<td>Panel regressions articles in a disease area to NIH R&amp;D by relevant institute</td>
<td>NIH data on R&amp;D by institute, MEDLINE data on publications by disease area</td>
<td>Strong relationship between NIH funding and later MEDLINE articles, Indirect effect (from research outside disease area) stronger than direct effect</td>
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<td>Sampat and Lichtenberg (2011)</td>
<td>What are the roles of the public and private sectors in drug development?</td>
<td>Examine share of new molecular entities where public sector developed patent (direct effect) and where private sector patents cite public sector patents/publications (indirect effect)</td>
<td>FDA approved NMEs 1988-2005, Orange Book patents on these drugs, Government interest statements/assignment in patents, Backward citations in patents to public sector patents, MEDLINE articles acknowledging public sector funding</td>
<td>Direct effect: public sector owns key patent for 9% of drugs, Indirect effect: Public sector patents or publications cited by 48% of drugs, Both direct and indirect effects more pronounced for most clinically important drugs (17%, 65%)</td>
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<td>Sampat (2007)</td>
<td>On how many drugs do academic institutions own patents?</td>
<td>Examine share of drug approvals where academic and public sector institutions own key patents</td>
<td>• FDA approved NDAs 1988-2005&lt;br&gt;• Orange Book patents on these drugs&lt;br&gt;• USPTO data on patent ownership&lt;br&gt;• Azoulay-Sampat concordance of academic assignees</td>
<td>• 72 of 1546 NDAs have an academic patent&lt;br&gt;• 10.3 percent of NMEs&lt;br&gt;• 5.9 percent of non-NMEs&lt;br&gt;• 19.2 percent of priority NMEs have an academic patent</td>
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<td>Keyhani et al (2005)</td>
<td>Do drug prices reflect development time and government investment?</td>
<td>Regression analyses relating drug prices to measures of government support</td>
<td>• 180 drugs listed in the Federal Register between 1992 and 2002&lt;br&gt;• Federal Register data on their patents&lt;br&gt;• Information on government assignees and government interest statements for these patents&lt;br&gt;• Data from NIH clinical trials database and FDA on whether NIH trials supported FDA approval</td>
<td>• Government supported clinical trials for 6.6 percent of the drugs&lt;br&gt;• Government owned or supported patents for 7.2 percent of the drugs</td>
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| Stevens et al (2011) | On how many drugs and vaccines emanate from public sector research institutions? | Examine number of drug approvals in-licensed from PSRIs (excluding licenses to platform technologies) | • FDA data on drug and biologic approvals  
• Orange Book data on FDA approved drugs  
• AUTM data on academic patents and licenses  
• rDNA data on licensing transactions | • 153 FDA-approved drugs discovered by public sector institutions over past 40 years (102 NMEs, 36 biologics, 15 vaccines)  
• 13 percent of NMEs (21 percent of priority NMEs) licensed from public sector research  
• Virtually all important vaccines introduced over past 25 years come from public sector  
• Broad correlation between NIH Institute budgets and therapy classes with public sector drugs |
| Kneller (2010) | How important are new companies/universities (and other actors) in drug discovery? | Examine place of employment of inventors on key patents for drugs | • 252 FDA approved drugs 1998-2007  
• Data on patents from Orange Book, Merck Index, other sources  
• Data from concurrent publications and from interviews on inventors’ places of employment | • Overall 24% of drugs from universities  
• By novelty: 31% of most scientifically novel drugs  
• By priority: 30% of priority-review drugs |
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| Morlacchi and Nelson (2011) | What were the sources of innovation behind development of the left-ventricular assist device (LVAD)? How important was the NIH? | Longitudinal case study of the development of the LVAD      | • Interview data  
• Information from key patents and publications on LVAD | • NHLBI contracts important in spurring firm formation and evolution in 1960s/1970s  
• NHLBI important in sponsoring conferences, centers to promote diffusion of best practice among academics and industry  
• Public funding of key trials and development of component technologies also important  
• Application led scientific understanding; basic understanding of heart failure remains weak |
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<td>Dorsey et al (2009)</td>
<td>Are new drug approvals by therapeutic area associated with NIH funding in those areas?</td>
<td>Correlations of NIH funding data with future drug approvals</td>
<td>• 1995-2000 FDA drug and approvals, mapped to nine disease areas</td>
<td>• Despite a rise in NIH (and other funding), drug approvals flat overall</td>
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<td>• NIH funding by Institute; allocated to disease areas based on Congressional justifications</td>
<td>• Within class analyses of drug approvals also show little correlation with research inputs</td>
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<td>• Note: Also estimate R&amp;D by biotechnology firms, medical device firms, pharmaceutical companies, non-profits</td>
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<td>Blume-Kohut (2009)</td>
<td>How does NIH funding in a disease area relate to the number of drugs subsequently in Phase I and Phase III trials in that area?</td>
<td>Panel regression</td>
<td>• CRISP and RePORTER data on NIH grants/funds 1975-2004</td>
<td>• Some evidence of responsiveness of Phase I trials: elasticity .25-.31</td>
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<td>• Grants associated with disease areas using parsing of abstracts, keywords, concordance with MeSH thesaurus</td>
<td>• No evidence of responsiveness of Phase III trials</td>
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<td>• PharmaProjects data on drugs in development, by phase and category</td>
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<tr>
<td>Mansfield (1998)</td>
<td>How important is academic work for industrial innovation?</td>
<td>Survey</td>
<td>• Survey results from 77 firms</td>
<td>• Percent of new products that could not have been developed (without substantial delay) in absence of recent academic research, 1986-1994: 31 in drugs/medical products (15 across all industries)</td>
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<td>• Percent of new processes that could not have been developed (without substantial delay) in absence of recent academic research, 1986-1994: 11 in drugs/medical products (11 across all industries)</td>
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Overview of representative studies
Public funding and health

- Cutler and Kadiyala (2007) [case study, statistical analyses]
  - Relate improvements in CVD mortality to high-tech treatments, drugs, behavioral changes
  - Relate economic value of mortality reduction to a) costs of the treatments and b) NIH expenditures on CVD to calculate rates of return

- Heidenreich and McClellan (2007) [case study]
  - Relate improvements in heart attack care to results from clinical trials

- Manton et al. (2009) [case study, statistical analyses]
  - Relate health improvements in 4 disease areas to lagged NIH funding by relevant institutes
Public funding and private R&D

- Ward and Dranove (1995); Toole (2007) [statistical]
  - Relate private R&D to public R&D by disease area
- Cockburn and Henderson (1996); Zucker, Brewer, Darby (1998); Azoulay, Graff-Zivin, Sampat (2011) [statistical]
  - Relate firm patenting, productivity to interaction with/proximity to elite public sector scientists
- Cohen, Nelson, Walsh (2002); Mansfield (1998) [survey]
  - Surveys on role of public science in private R&D; drugs and devices included
  - Examine extent and channels of public sector influence on private research efforts
Public funding and drug/device innovation

- Stevens et al. (2011); Kneller (2010); Sampat and Lichtenberg (2011); Keyhani et al. (2005) [accounting]
  - Use patent, publication data to assess roles of public sector in development of FDA approved drugs

- Dorsey et al (2009); Blume-Kohut (2009) [statistical]
  - Relate drug innovation to lagged NIH funding across disease areas, over time

- Morlacchi and Nelson (2011) [case study]
  - Roles of public sector and other sources of innovation in development of left-ventricular assist device
Taking stock

• Consistent evidence of effects of public funding on private sector innovative effort

• Less so on innovative output in econometric analyses

• Though accounting exercises suggest public sector itself generates ~20% of “important” drugs

• Surprisingly little research on health benefits: most of the evidence from CVD

• Case studies suggest critical importance of clinical research, applied, and diffusion-oriented activities: understudied in large-sample work

• Device industry relatively understudied: available evidence suggests very different relationships with public sector than drugs

• Not enough research on effects of public research on health costs
Common evaluation difficulties

• Measurement and traceability
• Inputs and outputs
• Footprints
• Lags
• Counterfactuals and causality
• Case studies tend to focus on “successes”
The road forward?

- More case studies: successes and failures
- Better data needed
  - Survey data to complement citation-based indicators of public sector influence
  - Device-side product-patent linkages to facilitate bibliometrics
  - Funding data: NIH and private sector
- Important neglected questions:
  - Publicly funded research and health costs
  - Large-sample work on the effects of clinical and applied research
- Quasi-experimental approaches?
Current work

• We can map comprehensively and systematically the entire vertical chain of knowledge

• NIH Grants → Pubs → Patents → Drugs

• Through patent-publication citations, can construct measures of firm reliance on different NIH study sections

• Peculiar aspects of NIH funding can enable us to partially solve the endogeneity problem

• Scientific evaluation (in study sections) more focused on science rather than diseases

• Exogenous variation in institute-specific funding may also be useful in generating shocks to funding for grants from particular study sections, even at other Institutes
References
References


References


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