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

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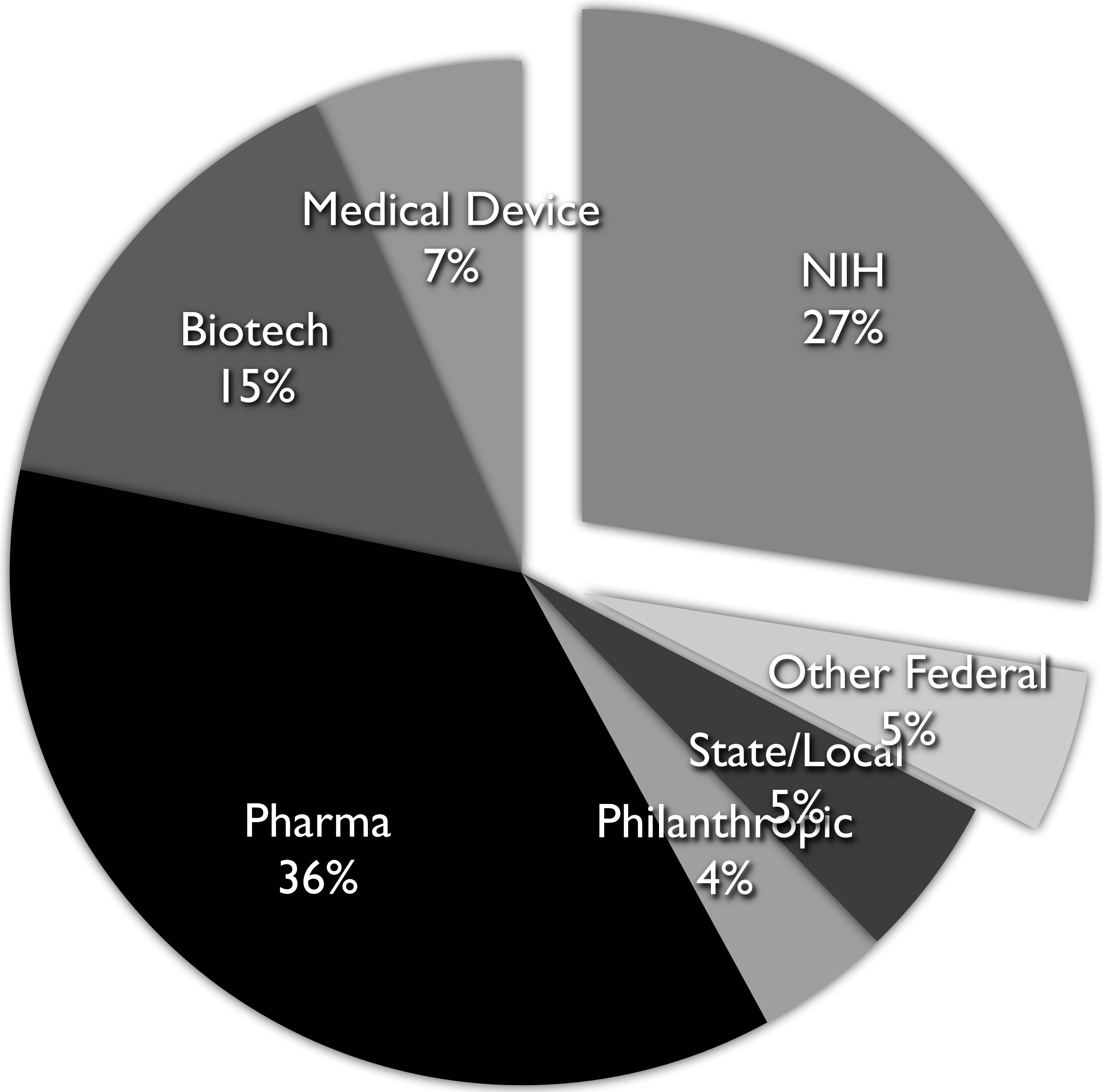
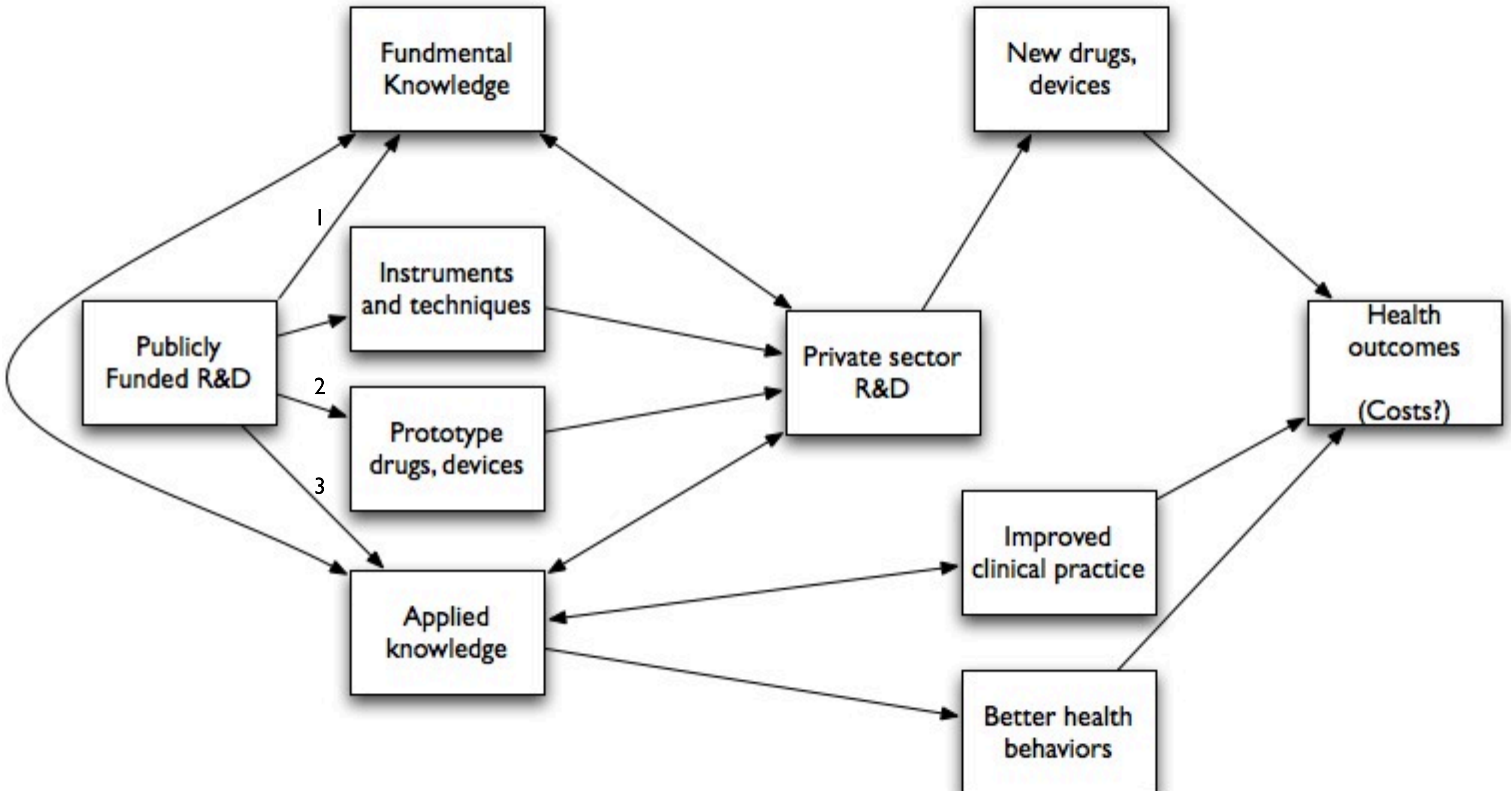
Funding for biomedical research in 2007 (total = $101 billion)



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, clincaltrials.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

Public Funding and Health Outcomes

Authors	***Question***	***Empirical Approach***	***Measures/Data***	***Results***
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

Authors	***Question***	***Empirical Approach***	***Measures/Data***	***Results***
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

Public Funding and Health Outcomes

Authors	***Question***	***Empirical Approach***	***Measures/Data***	***Results***
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

Public Research and Private R&D, Patenting

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
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

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
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

Public Research and Private R&D, Patenting

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
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 form 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

Public Research and Private R&D, Patenting

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
Cohen, Nelson, Walsh (2002)	What are the roles of public sector research on industrial R&D? What are the channels through which public research affect industrial R&D?	Survey	• 1994 Carnegie Mellon Survey of Industrial R&D managers • Merged with publicly available data on respondents	• Pharmaceutical industry an outlier: reports public research the most important source of new project ideas *and* contributing to project completion • Medical instruments industry R&D projects less frequently use any of three outputs of public research than other industries • Drug industry makes use of public research much more frequently • Top three fields contributing to R&D in pharmaceuticals: Medicine, Biology, Chemistry • Top three fields contributing to R&D in medical instruments industry: Medicine, Materials Science, Biology

Public Funding and New Drugs, Devices

Authors	*Question*	*Empirical Approach*	*Measures*	*Results*
Cockburn and Henderson (1996)	How does public sector research affect pharmaceutical innovation?	Case studies of 15 clinically important drugs	• Qualitative determinations of roles of public sector in drug development	• Of 15 drugs, public sector research made key enabling discovery for 11 • Public sector involved in synthesis of major compound in 2 cases
Ward and Dranove (1995)	How do MEDLINE "drug" articles respond to NIH funding?	Panel regressions articles in a disease area to NIH R&D by relevant institute	• NIH data on R&D by institute • MEDLINE data on publications by disease area	• Strong relationship between NIH funding and later MEDLINE articles • Indirect effect (from research outside disease area) stronger than direct effect
Sampat and Lichtenberg (2011)	What are the roles of the public and private sectors in drug development?	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)	• 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	• 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%)

Public Funding and New Drugs, Devices

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
Sampat (2007)	On how many drugs do academic institutions own patents?	Examine share of drug approvals where academic and public sector institutions own key patents	• FDA approved NDAs 1988-2005 • Orange Book patents on these drugs • USPTO data on patent ownership • Azoulay-Sampat concordance of academic assignees	• 72 of 1546 NDAs have an academic patent • 10.3 percent of NMEs • 5.9 percent of non-NMEs • 19.2 percent of priority NMEs have an academic patent
Keyhani et al (2005)	Do drug prices reflect development time and government investment?	Regression analyses relating drug prices to measures of government support	• 180 drugs listed in the Federal Register between 1992 and 2002 • Federal Register data on their patents • Information on government assignees and government interest statements for these patents • Data from NIH clinical trials database and FDA on whether NIH trials supported FDA approval	• Government supported clinical trials for 6.6 percent of the drugs • Government owned or supported patents for 7.2 percent of the drugs

Public Funding and New Drugs, Devices

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
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

Public Funding and New Drugs, Devices

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
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

Public Funding and New Drugs, Devices

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
Dorsey et al (2009)	Are new drug approvals by therapeutic area associated with NIH funding in those areas?	Correlations of NIH funding data with future drug approvals	• 1995-2000 FDA drug and approvals, mapped to nine disease areas • NIH funding by Institute; allocated to disease areas based on Congressional justifications • Note: Also estimate R&D by biotechnology firms, medical device firms, pharmaceutical companies, non-profits	• Despite a rise in NIH (and other funding), drug approvals flat overall • Within class analyses of drug approvals also show little correlation with research inputs
Blume-Kohut (2009)	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?	Panel regression	• CRISP and RePORTER data on NIH grants/funds 1975-2004 • Grants associated with disease areas using parsing of abstracts, keywords, concordance with MeSH thesaurus • PharmaProjects data on drugs in development, by phase and category	• Some evidence of responsiveness of Phase I trials: elasticity .25-.31 • No evidence of responsiveness of Phase III trials

Public Funding and New Drugs, Devices

Authors	***Question***	***Empirical Approach***	***Measures***	***Results***
Mansfield (1998)	How important is academic work for industrial innovation?	Survey	• Survey results from 77 firms	• 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) • 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)

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

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