The Past and Future of Biomedical Research Funding

Bhaven N. Sampat

Johns Hopkins University and NBER

Biomedical Research Funding: An Ideal Testbed for Economics of Science Research

- High-quality, historical grant level data (NIH RePORTER)
  - Links to reported outcomes (publications, patents, clinical trials)
- Patents better measures of innovation in life sciences than other fields
  - Importance of patents
  - Firms take prior art searching seriously
- For small-molecule drugs, patents can be linked to products (and thus private, social value measures) due to FDA regulatory requirements
- Well curated publication data (Pubmed)
- Public and private data on development (clinicaltrials.gov, etc.)
- Periodic interest in using evidence to inform funding by major funders

But much more to be done

- Many perennial policy questions (peer review, indirect costs, patent policy, priority setting, NIH organization) resurface every X years since World War II
- Even where we have made progress (e.g. linking funding to drugs, through patents and citations) much more work needed
- The need for better evidence from economics of science perhaps more important now than ever, as we face a generational need to rethink our biomedical research funding system

The paper

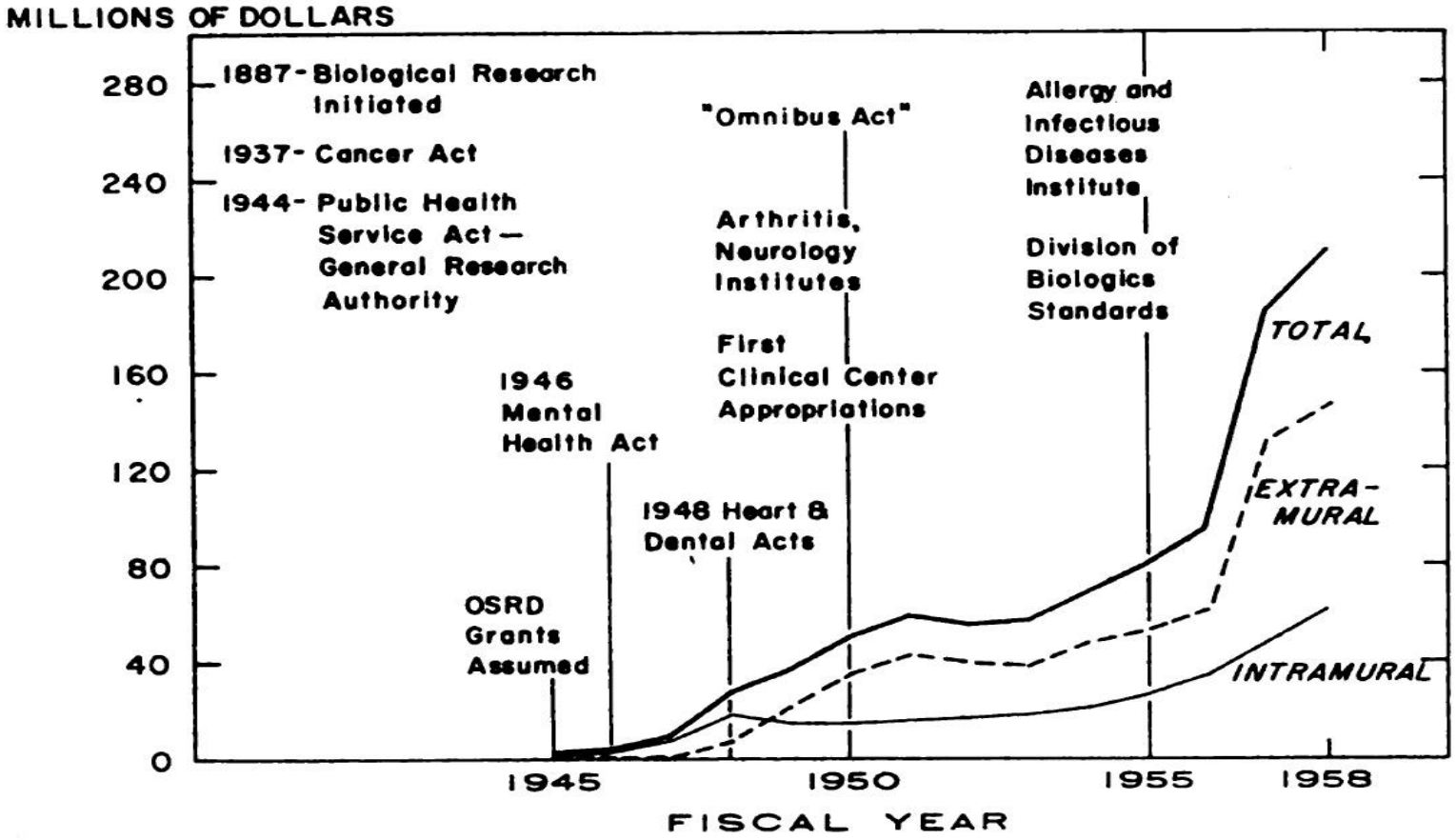
- Looking back: Origins of NIH; the major policy debates historically
- Taking stock: Where have we (economics of science) made progress, what are big questions that have received less attention?
- Looking forward:
  - Does supply of economics of science research match demand?
  - Implications for researchers / funders
  - A plea for more research on the political economy of biomedical research funding

Part I: Relevant NIH History

Origins in World War II

- 1946: NIH takes over 42 contracts from wartime Committee on Medical Research, tripling its budget (Gross and Sampat 2025)
- Hire PHS Venereal Disease head Cassius Van Slyke to administer the program:
  - “an incidental, lower-left-hand-drawer of the desk sort of activity … positively wouldn’t have to work more than two hours a day and probably not more than four or five hours a week”
- Budget windfall as price of penicillin drops
- Letter to medical school deans: “We have limited funds available for research purposes. If you have investigators who need these funds, let us know by return mail.”

The Response is Overwhelming



The Social Contract for Science

SCIENCE

Vol. 104, No. 2711 Friday, 13 December 1946

New Horizons in Medical Research

C. J. Van Slyke

Medical Director, U. S. Public Health Service, and *Chief, Research Grants Division*
National Institute of Health, Bethesda, Maryland

A LARGE-SCALE, NATIONWIDE, peacetime program of support for scientific research in medical and related fields, guided by more than 250 leading scientists in 21 principal areas of medical research, is now a functioning reality. The program, based on U. S. Public Health Service Research Grants financed by public funds, supports research—conducted without governmental control—by independent scientists. The purpose of these grants is to stimulate research in medical and allied fields by ...r such research and by ac- ...fic investigation of specific ...rtists agree that urgently ...cking. Accompanying this ...ance of a basic tenet of the ...he scientific method rests: ...lence of the research worker ...rol, direction, regimentation,

...h Service Research Grants, ... research program of scien- ...y have early and profound ...f medical history and the past a large amount of potentially very important research has not been conducted because funds have not been available to pay for it. Many universities and other nonprofit institutions have extremely limited funds for research, even though their teaching staffs, graduate students, and other personnel have the talent, training, and interest necessary for scientific investigation. Although research conducted by industrial organizations does add considerably to the total fund of medical knowledge, such research quite often must be directed toward specific goals.

The great benefits from all medical research, wherever conducted, are received by the millions of people whose lives are made healthier, happier, and longer through widespread application of knowledge gained in research laboratories. Conversely, research not conducted for want of funds is very costly to the same millions. The essence of these facts, as related to the Research Grants program, has been stated by the National Health Advisory Council: "There are few purposes for which public funds could be used more appropriately than to discover ways to prevent and cure illness and to prolong useful years of life." The

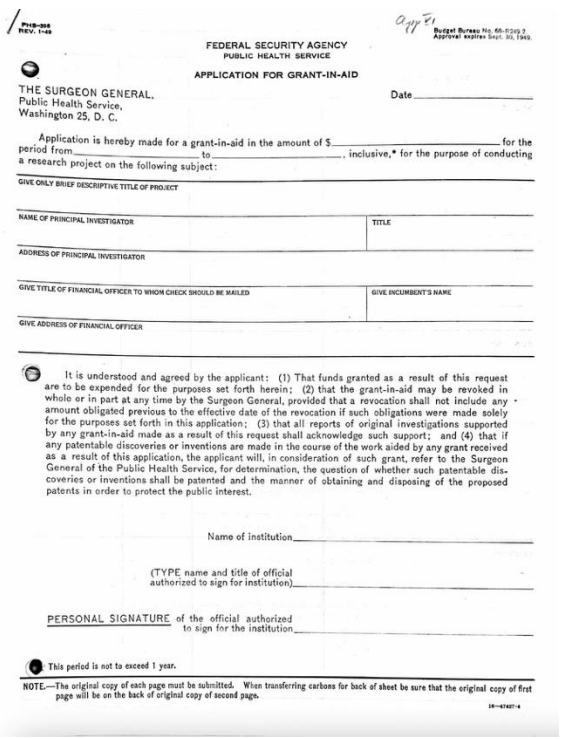
Dr. C. J. Van Slyke
Chief of the Division of Research Grants
1945 to 1948

How Research Is Conducted Under Research Grants

Research under the Research Grants program is conducted with full independence and autonomy of the research investigator. Support of research through the use of Research Grants funds does not imply in any way any degree of Federal control, supervision, or direction of the research project. The autonomy of the individual research worker implied in this philosophy, however, does not exclude self-imposed guidance entailed in the over-all plan of an organized, cooperative research project in which several groups of investigators may collaborate.

In order not to divert the time of the researcher unnecessarily from the actual conduct of the research investigation, only annual scientific progress reports are requested. It is not desired that the preparation of these reports present any long, tedious burden to the investigator, and it is therefore requested that they contain only such data in a brief, clear, and concise manner as will permit the appropriate Study Section and National Advisory Council to be adequately informed as to the conduct of the research investigations since the submission of the previous progress report. In this way the appropriate Study

E.g. the first grant application form



PHS-398
REV. 1-48

Budget Bureau No. 68-R249.2
Approval expires Sept. 30, 1949.

FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

APPLICATION FOR GRANT-IN-AID

THE SURGEON GENERAL,
Public Health Service,
Washington 25, D. C.

Date _____

Application is hereby made for a grant-in-aid in the amount of $_____ for the period from _____ to _____, inclusive,* for the purpose of conducting a research project on the following subject:

GIVE ONLY BRIEF DESCRIPTIVE TITLE OF PROJECT

NAME OF PRINCIPAL INVESTIGATOR | TITLE

ADDRESS OF PRINCIPAL INVESTIGATOR

GIVE TITLE OF FINANCIAL OFFICER TO WHOM CHECK SHOULD BE MAILED | GIVE INCUMBENT'S NAME

GIVE ADDRESS OF FINANCIAL OFFICER

It is understood and agreed by the applicant: (1) That funds granted as a result of this request are to be expended for the purposes set forth herein; (2) that the grant-in-aid may be revoked in whole or in part at any time by the Surgeon General, provided that a revocation shall not include any amount obligated previous to the effective date of the revocation if such obligations were made solely for the purposes set forth in this application; (3) that all reports of original investigations supported by any grant-in-aid made as a result of this request shall acknowledge such support; and (4) that if any patentable discoveries or inventions are made in the course of the work aided by any grant received as a result of this application, the applicant will, in consideration of such grant, refer to the Surgeon General of the Public Health Service, for determination, the question of whether such patentable discoveries or inventions shall be patented and the manner of obtaining and disposing of the proposed patents in order to protect the public interest.

Name of institution _____

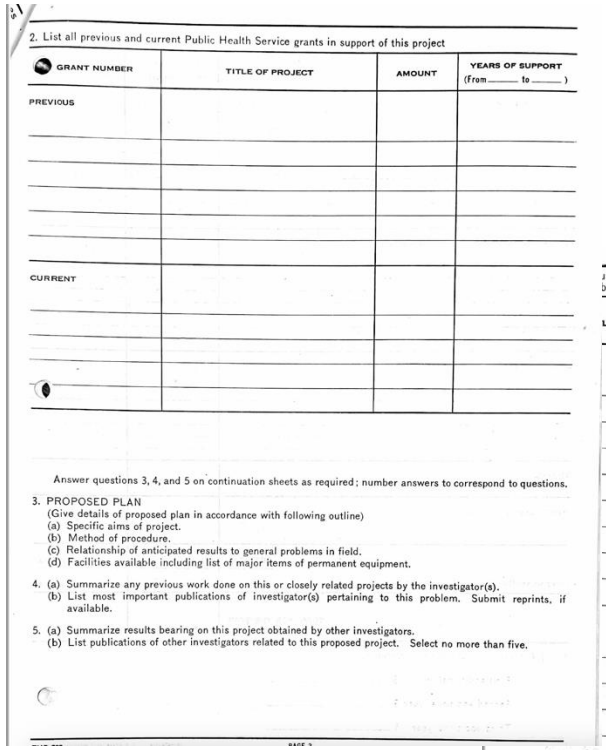
(TYPE name and title of official authorized to sign for institution) _____

PERSONAL SIGNATURE of the official authorized to sign for the institution _____

* This period is not to exceed 1 year.

NOTE.—The original copy of each page must be submitted. When transferring carbons for back of sheet be sure that the original copy of first page will be on the back of original copy of second page.

16—47427-4



2. List all previous and current Public Health Service grants in support of this project

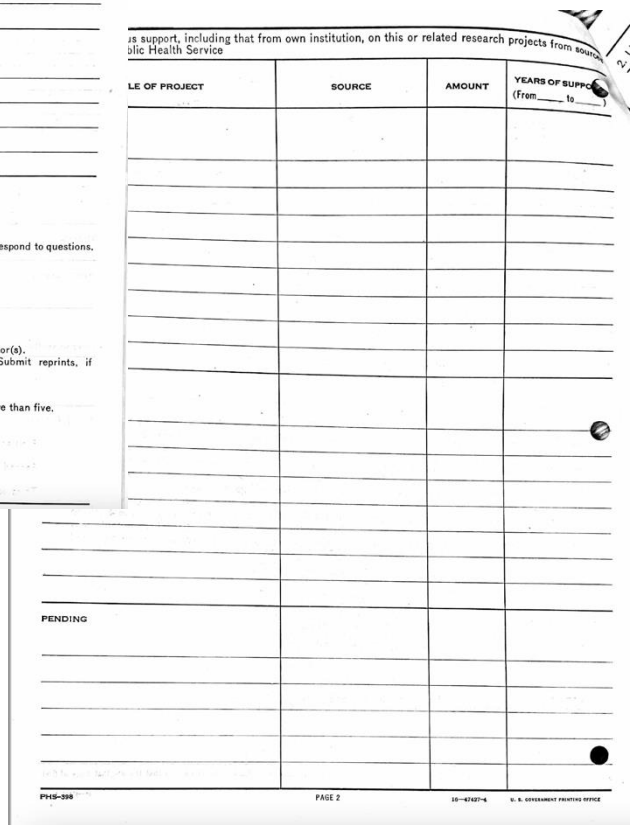
GRANT NUMBER	TITLE OF PROJECT	AMOUNT	YEARS OF SUPPORT (From ____ to ____)
PREVIOUS			
CURRENT			

Answer questions 3, 4, and 5 on continuation sheets as required; number answers to correspond to questions.

3. PROPOSED PLAN
(Give details of proposed plan in accordance with following outline)
(a) Specific aims of project.
(b) Method of procedure.
(c) Relationship of anticipated results to general problems in field.
(d) Facilities available including list of major items of permanent equipment.

4. (a) Summarize any previous work done on this or closely related projects by the investigator(s).
(b) List most important publications of investigator(s) pertaining to this problem. Submit reprints, if available.

5. (a) Summarize results bearing on this project obtained by other investigators.
(b) List publications of other investigators related to this proposed project. Select no more than five.



...s support, including that from own institution, on this or related research projects from sour...
...blic Health Service

...LE OF PROJECT	SOURCE	AMOUNT	YEARS OF SUPP... (From ____ to ____)
PENDING			

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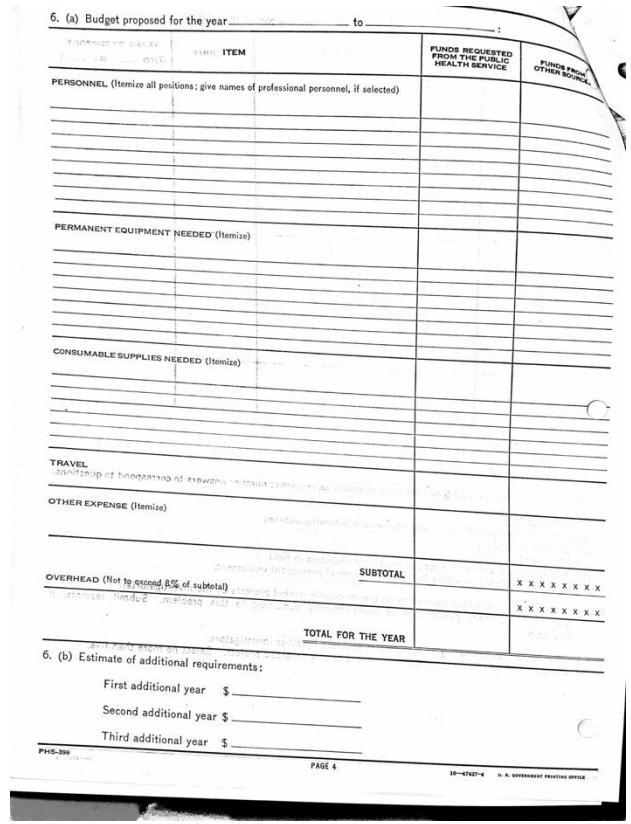

6. (a) Budget proposed for the year _____ to _____:

ITEM	FUNDS REQUESTED FROM THE PUBLIC HEALTH SERVICE	FUNDS FROM OTHER SOURCE
PERSONNEL (Itemize all positions; give names of professional personnel, if selected)		
PERMANENT EQUIPMENT NEEDED (Itemize)		
CONSUMABLE SUPPLIES NEEDED (Itemize)		
TRAVEL		
OTHER EXPENSE (Itemize)		
SUBTOTAL		x x x x x x x x
OVERHEAD (Not to exceed 8% of subtotal)		x x x x x x x x
TOTAL FOR THE YEAR		

6. (b) Estimate of additional requirements:

First additional year $ _____

Second additional year $ _____

Third additional year $ _____

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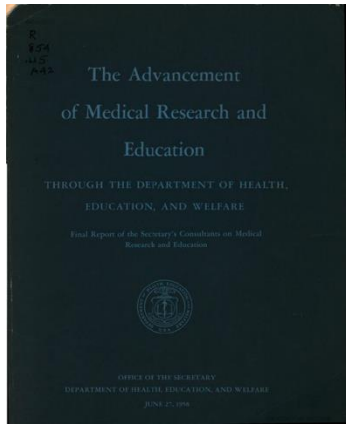
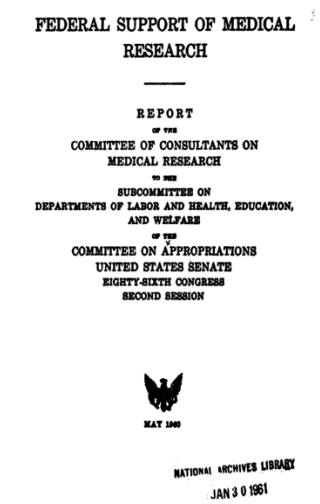
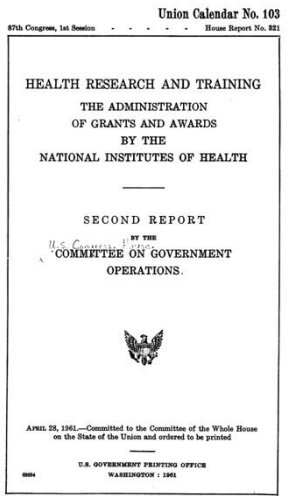
Part II: The Major Policy Questions Since World War II



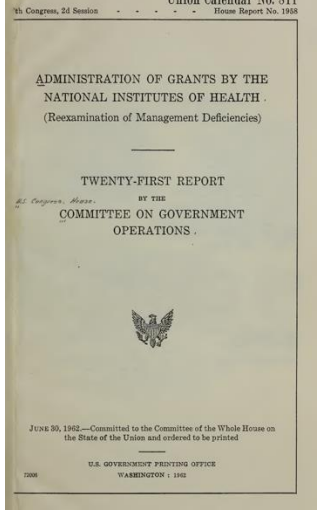
Bayne-Jones Report
1958



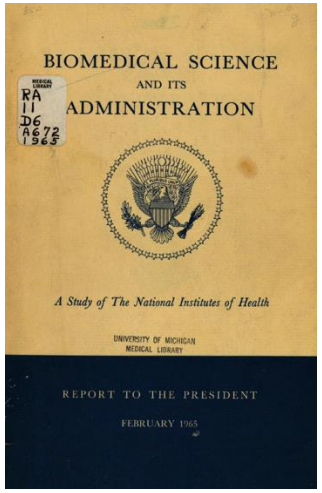
Boisfeuillet "Bo" Jones
Report
1960



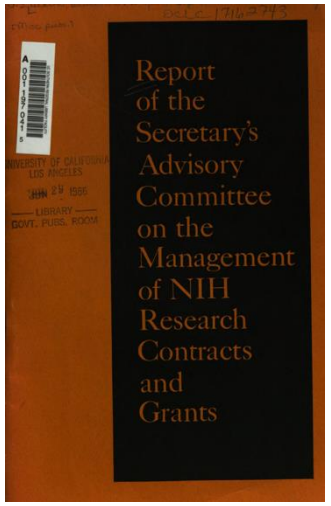
Fountain Committee
Report
1961



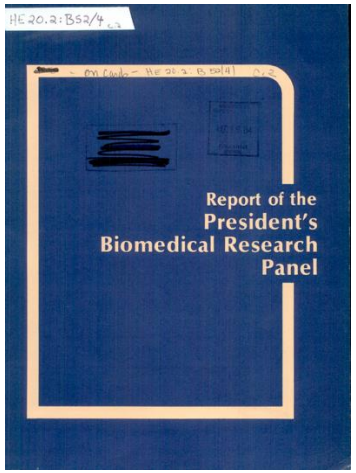
Fountain Committee
Report
1962



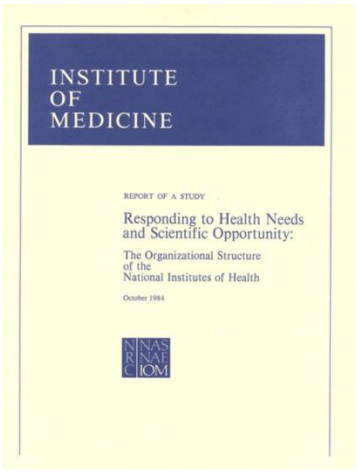
Wooldridge Report
1965



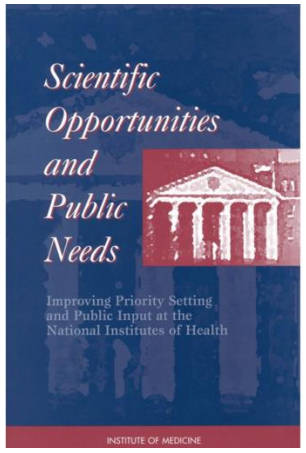
Ruina Report
1965



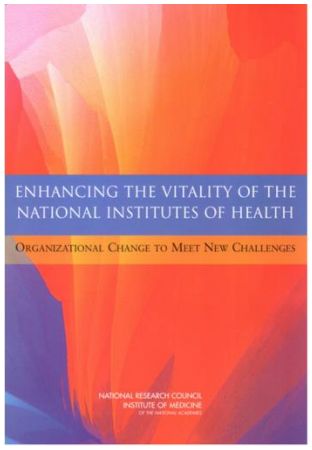
BRP
1976



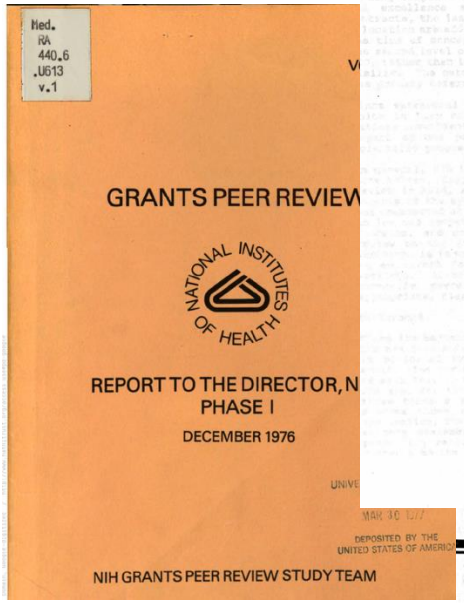
IOM
1984

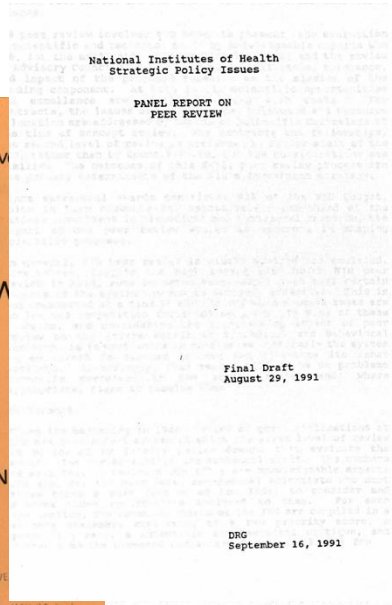


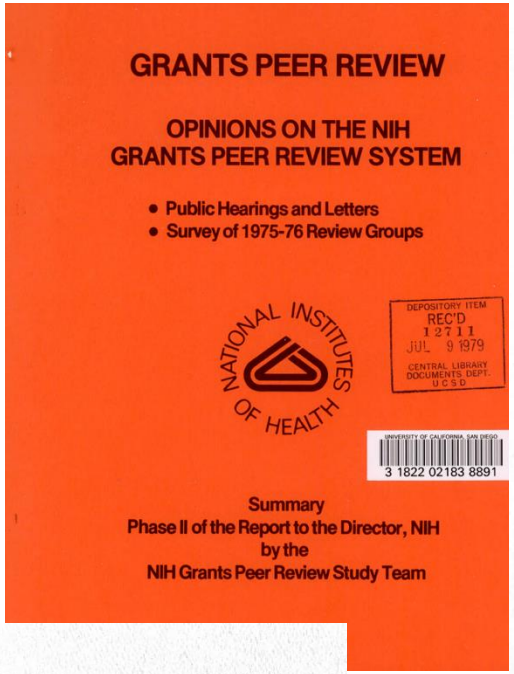
IOM
1998

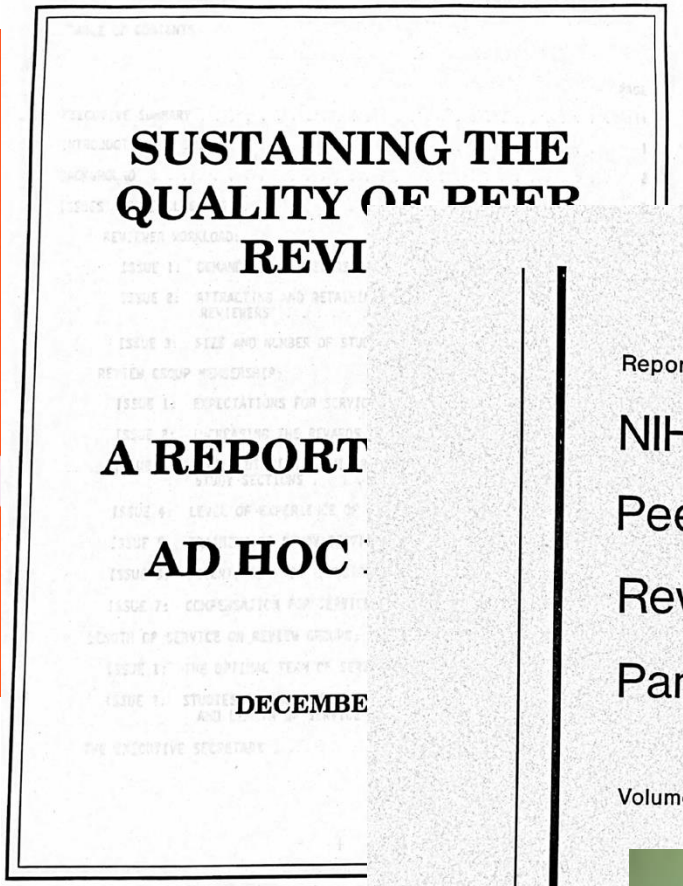


IOM
2003

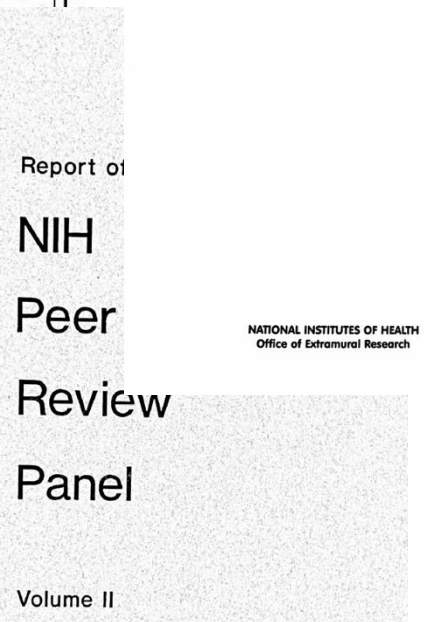




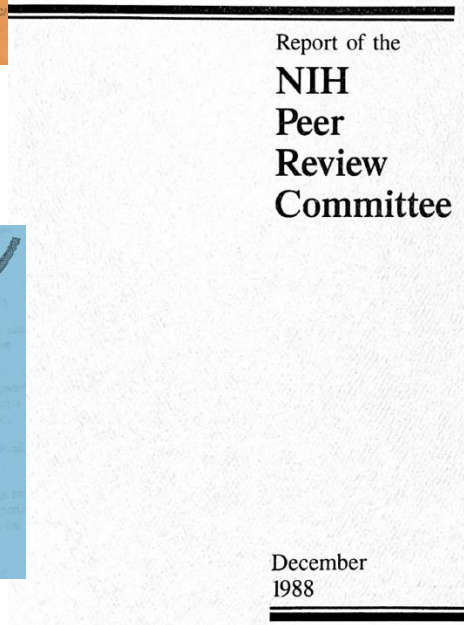


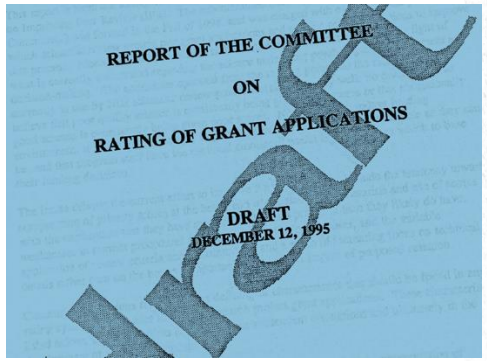


Customer Satisfaction and Research Involvement Among Applicants for NIH R01 and R29 Grants



NATIONAL INSTITUTES OF HEALTH
Office of Extramural Research





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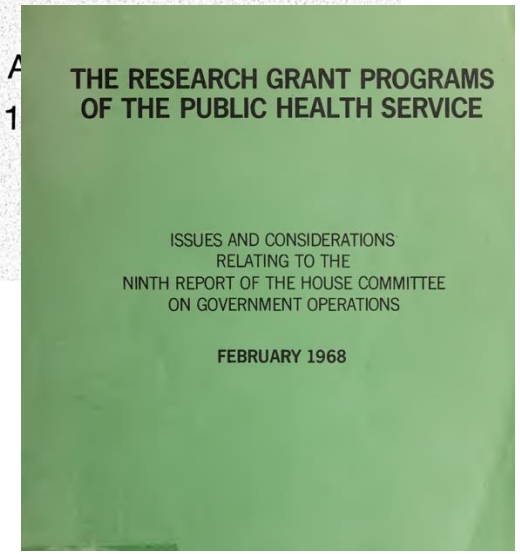
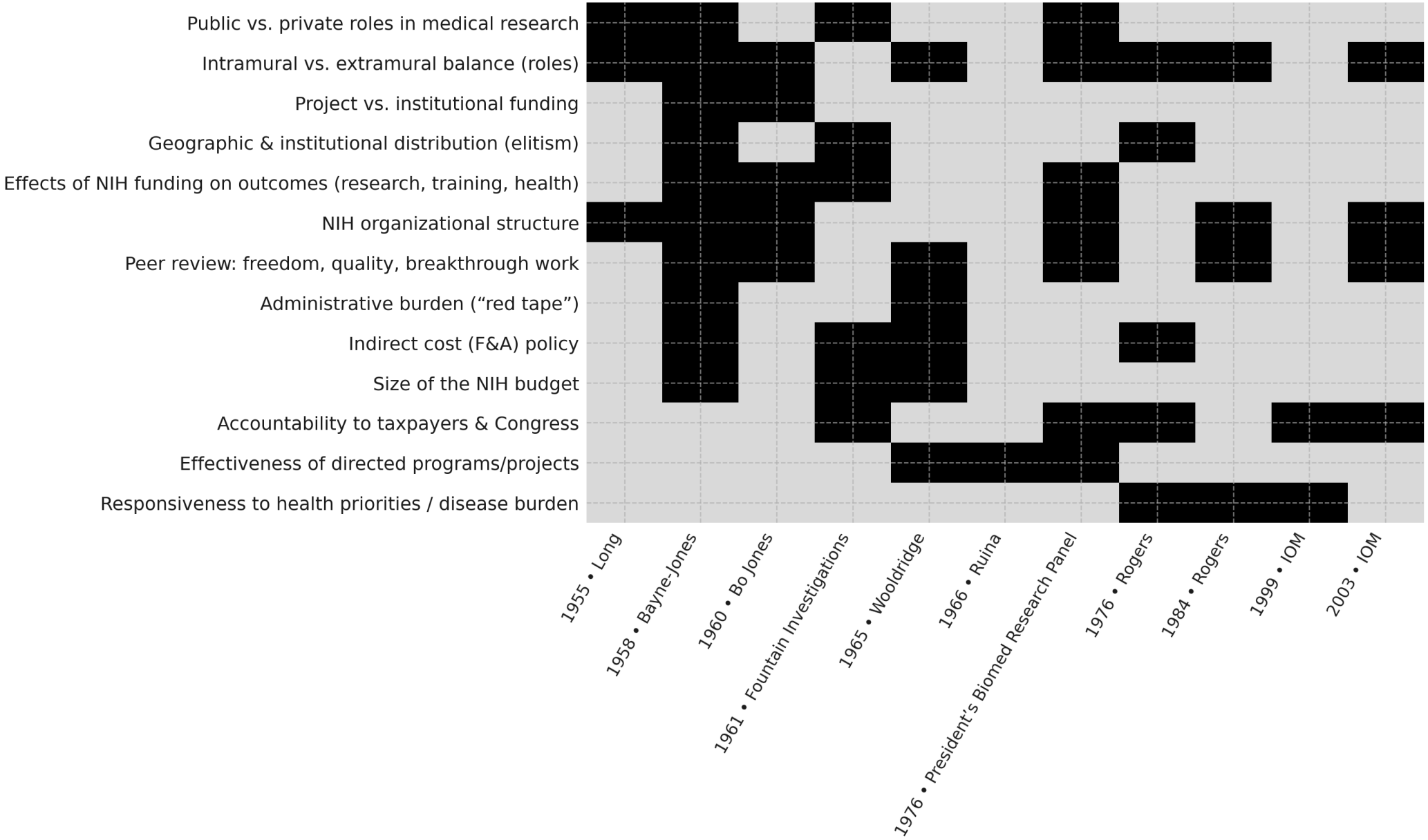
Peer Review Oversight Group (PROG) on the Rating of Grant Applications (RGA): Deliberations and Decisions

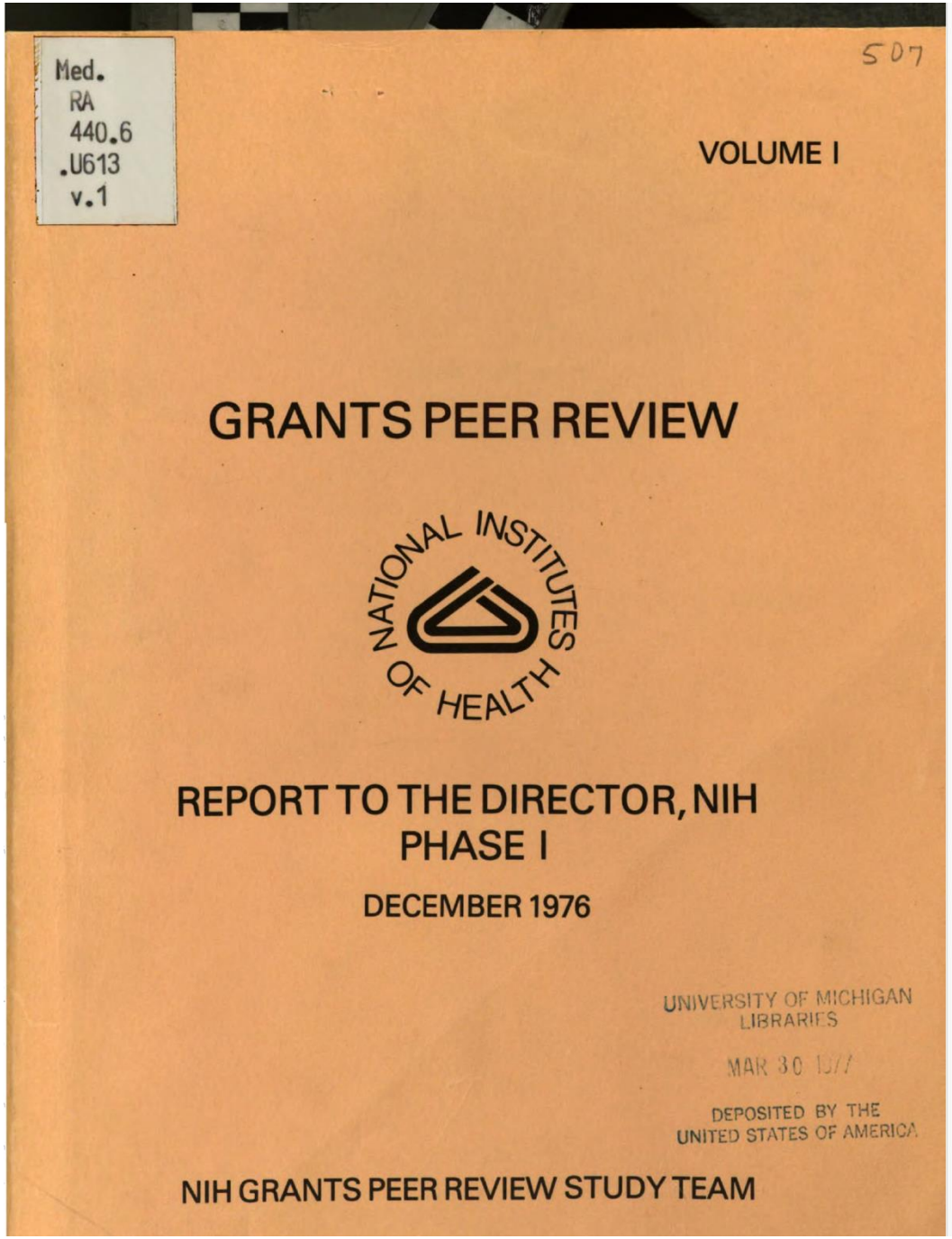
At the November 20-21, 1996, meeting of the Peer Review Oversight Group (PROG), a major topic was the Rating of Grant Applications (RGA). At the previous meeting (July, 1996), PROG members had discussed the recommendations in the RGA report, and considered information which had been obtained from the scientific community through a variety of channels. At that time, the PROG decided to table several of the ten recommendations in the RGA report and to focus primarily on whether to use explicit criteria to structure the review, if so what these criteria should be, whether to score/rate those individual criteria, and whether to retain reviewer assignment of a global score or derive an overall score from criteria subscores. Pilot experiments were recommended, and the preliminary results of pilots by both the Division of Research Grants and the National Institute of Allergy and Infectious Diseases were presented to the members at the November meeting.

Based on the information available, the following decision was made after the November meeting: **There will be no changes in the basic numerical scoring system at this time.** There was enthusiasm for having reviewers continue to assign a global score to each application and that practice will continue. There was generally low enthusiasm for the idea of assigning scores, whether numeric or alphabetic, to the individual criteria or deriving an overall score using such subscores, and those practices will not be adopted, but will be discussed further at the Feburary PROG meeting. The issue of the rating scale itself has been tabled for future discussion; for the present time, the 1.0-5.0 rating scale, with 1 as the best possible score, will be retained.



Major Questions in External Evaluations





- How to select peer reviewers?
- How to support innovative and unorthodox research?
- The effects of IC discretion (in second stage of peer review)
- Information vs bias
- Do scores reliability measure "quality"?
- The mechanics of scoring (single score? Normalization? Intervals)
- How to aggregate peer review scores from multiple reviewers?

(4) consider the feasibility of developing an experiment involving limited support for certain speculative, high-risk, unorthodox or innovative research proposals. Such a study might be part of a larger, much-needed effort to examine the processes of decision-making in allocating research support..... 171

In 1986 Jerome G. Green becomes head of DRG, with a focus on “well-designed experiments to improve peer review”

- Green: “It is regrettable that many who go from conducting research to administering research lose their fondness for careful experimentation and tend to accept their intuitions about the process of review”
- 1986 Florida Demonstration Project: 2 year test with streamlined award instrument (five agencies, FSU and University of Miami) *to reduce administrative burden, reduce costs of monitoring*
- 1989: Paul Meier study of using .5 intervals rather than .1 intervals; tested on a subset of randomly selected study sections
- 199x: Selected study sections asked to give proposals separate scores for innovation (“a dismal failure”)
- 1993: Evaluation of triage for review of RFA applications *to relieve pressure on peer-review*
  - 1994: Broader tests of triage (selected study sections asked to flag half of applications as non-competitive, score the rest) *to relieve pressure on peer-review*
- 1994: Expedited production of summary statements (52 study sections) *to promote applicant satisfaction, lower workload*
- 2006: Cut 1.5 months from review process for new investigators (forty SS participate)
- Most of these look at about process, don’t follow long-term outcomes.

Where have we (economics of science, science of science) made the most progress?

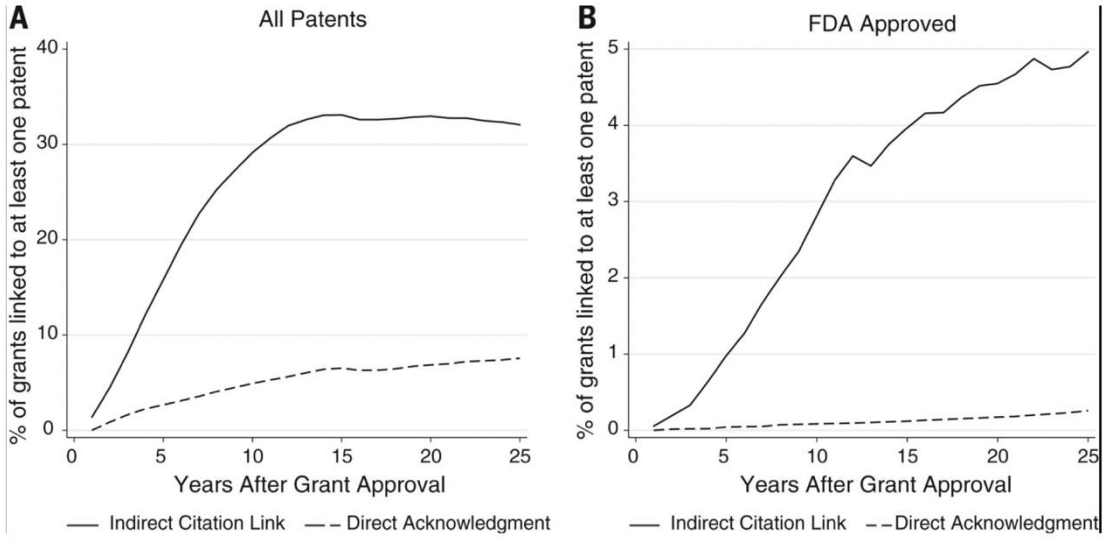
- Measuring and assessing the effects of NIH research (on science, scientists) and the value of NIH research (mainly in terms of patents, drugs)
- Understanding peer review process, how well it works, and its pathologies, potential reform
- Responsiveness to health priorities / disease burden
- Labor markets for science, scientists

Topics that have received less attention in the economics of science/science of science literature

- **Public vs. private roles in medical research**: substitutes/complements?
- Intramural program
- Project vs. institutional funding
- **Geographic & institutional distribution**: efficiency, equity, political economy
- **NIH organizational structure**
- **Administrative burden ("red tape"):** Causal effects?
- **Indirect cost (F&A) policy**
- Size of the NIH budget: Effects of the doubling?
- Effects/effectiveness of second-stage discretion
- Effectiveness of directed programs/projects: Artificial heart program? Framingham heart study? Cancer chemotherapy program? War on Cancer? Congressionally directed biomedical research program? Relative value of basic vs. applied funding mechanisms?

Part IV: Looking Forward

Even where we have made progress on the data front, much more to be done



Li, Azoulay, and Sampat (2017)

- What do citations mean? How to mix and stir? In-text vs. front-page better? Are some more informative than others?
- How to link patents to products beyond small-molecule drugs? (Biologics; devices)
- Which patents on a product should count? (Primary vs secondary)
- What about stuff that isn't patented but still improves health?
- Welfare benefits of different products (beyond sales, priority review markers)
- More attention to validation of existing measures, development of better ones needed. Do our proxies for innovation/health outcomes measure what we want?

Note: This may end up being an Appendix, inset text box, or omitted, but keeping for discussion purposes

Does the supply of economics of science research match (policy and agency) demand?

- Many big (previously neglected) questions seem ripe for exploration, especially given advances in data and measurement
- Even where we have seen progress, more effort needed to validate measures, from outputs to outcomes; validate surrogate endpoints
- What funding agencies might do to promote (more) useful economics research?
  - Priority topic announcements
  - Bringing in researchers behind the curtain, both to access sensitive data but also to understand the process
  - Processes for providing broader data on unfunded applications, scores
  - Institutionalizing RCTs/experimentation (useful for some of the big questions, not all)
  - Historical information on big changes to process: learning from natural experiments
  - And more …

Open questions on political economy of biomedical research funding (1)

- Interest Group Influence: How do the main interest groups (universities, scientific interest groups, disease lobbies) shape the funding agenda, and for better or worse?

- Allocation Mechanisms: Assessing value of congressional mandates/earmarks vs. peer-reviewed funding

Open questions on political economy of biomedical funding (2)

- Benefit Distribution & Support: How broadly are benefits from biomedical research funding distributed? Does broader benefit translate to broader support? (Gruber and Johnson)

- Efficiency vs. Equity: What are the tradeoffs between efficiency and equity in funding?

- Economic Value vs. Public Salience: Is the "value" of biomedical research funding (based on our measures) salient to taxpayers? Are we getting close to the outcomes people care about? (Validate surrogate measures)

- Public Trust: What factors shape public trust in biomedical science?

Suggestions?