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)
- Some precedent for sharing peer review data (scores, unfunded applications) with researchers
- 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
- 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
- The NIH budget has increased 1000x since World War II, but our knowledge on how to effectively spend the funds less so (Sampat 2023)
- 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

This paper: my current plan

- 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?
- Science of science at NIH*
- Looking forward:
  - Questions for economists
  - Where agencies/funders can help
  - A need for more research on the political economy of biomedical research funding

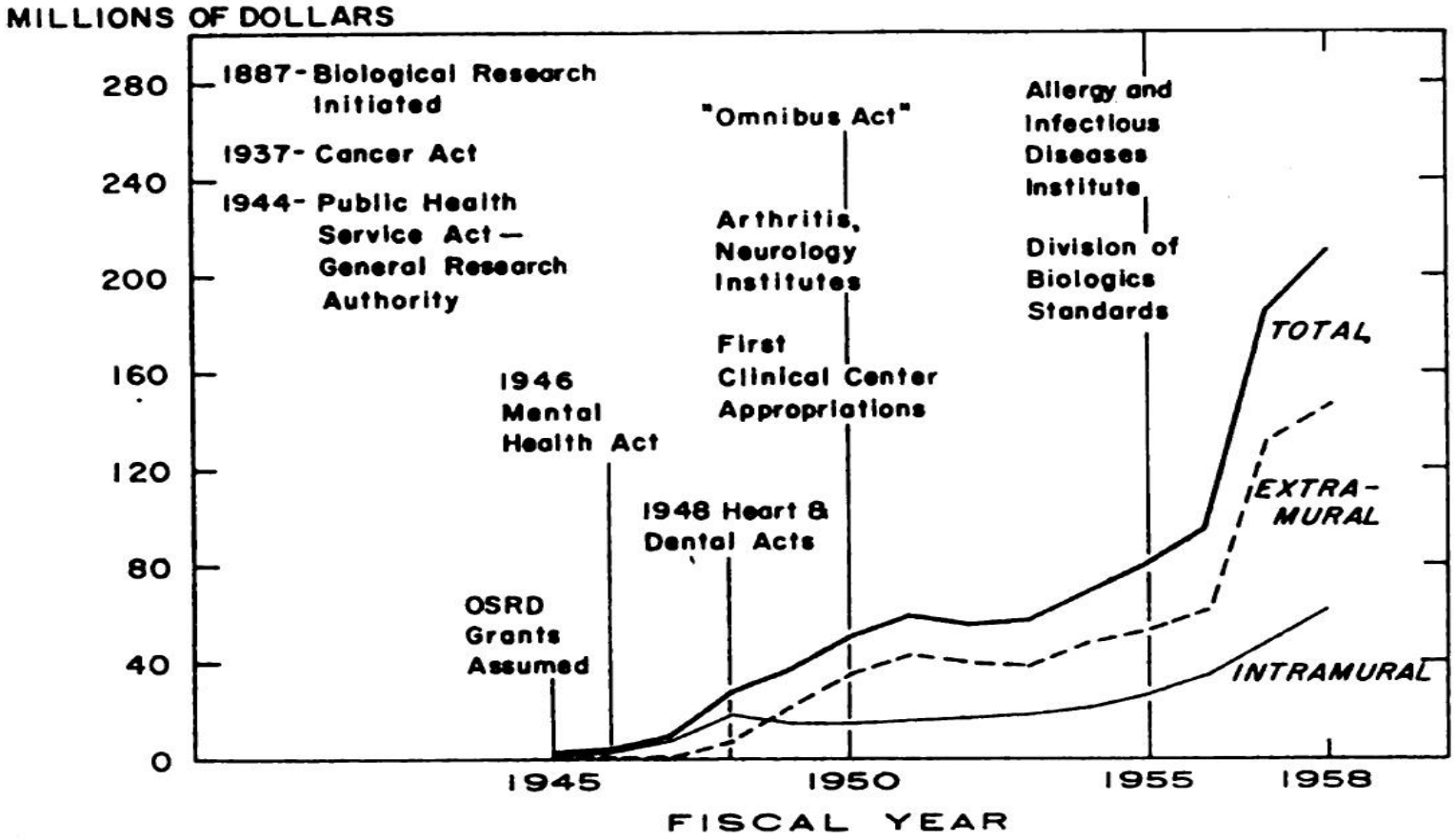
* This may not make it into the paper, beyond a footnote

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



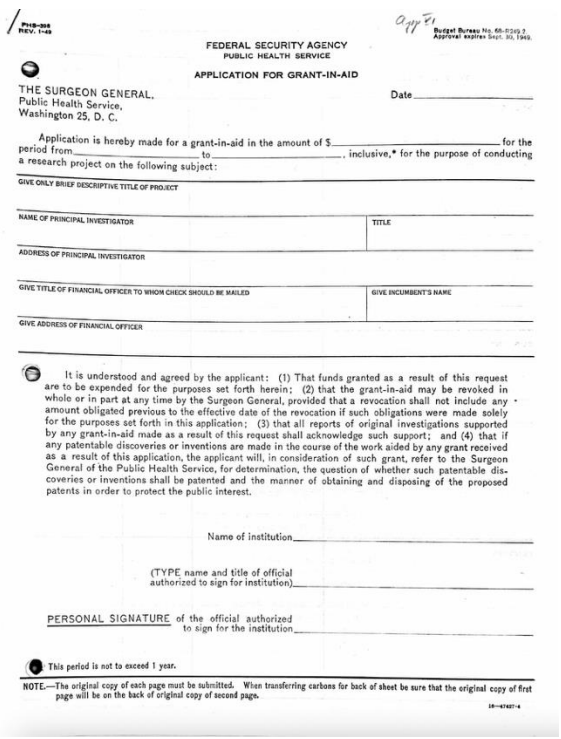
Dr. C. J. Van Slyke
Chief of the Division of Research Grants
1945 to 1948

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-R349.2
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 _____

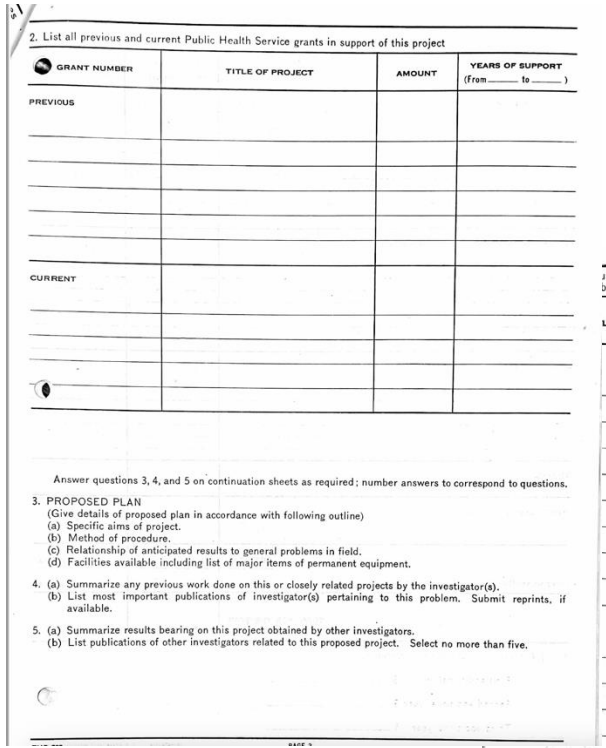
(TYPE name and title of official authorized to sign for institution) _____

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

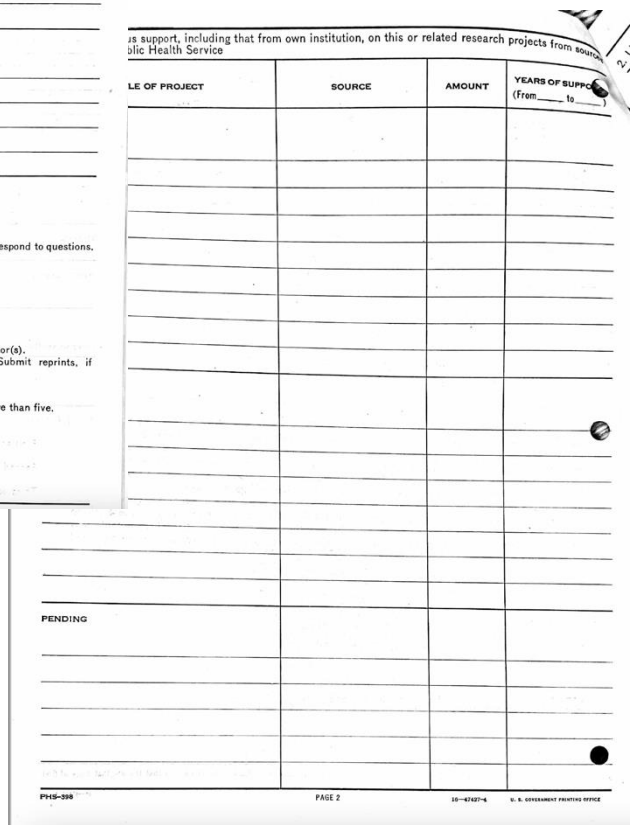
GRANT NUMBER	TITLE OF PROJECT	AMOUNT	YEARS OF SUPPORT (From ____ to ____)
PREVIOUS			
CURRENT			

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.

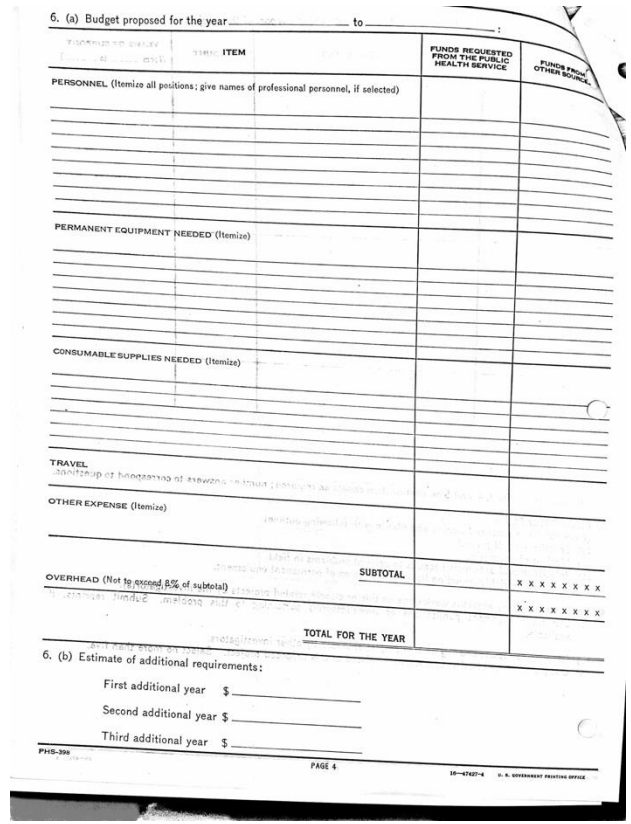
5. (a) Summarize results bearing on this project obtained by other investigators.
(b) List publications of other investigators related to this proposed project. Select no more than five.



...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:

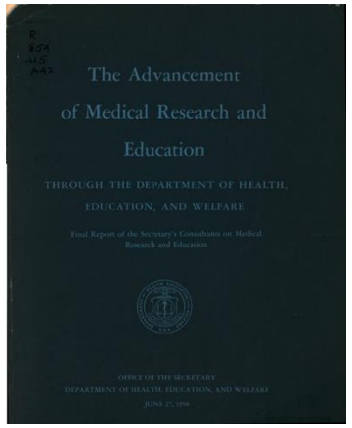
First additional year $ _____

Second additional year $ _____

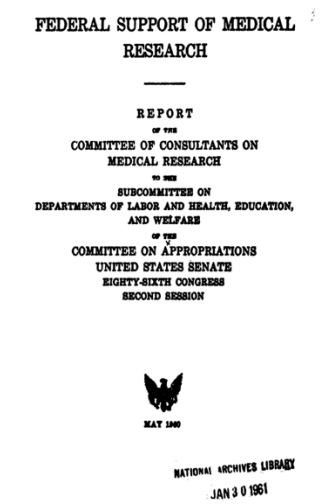
Third additional year $ _____

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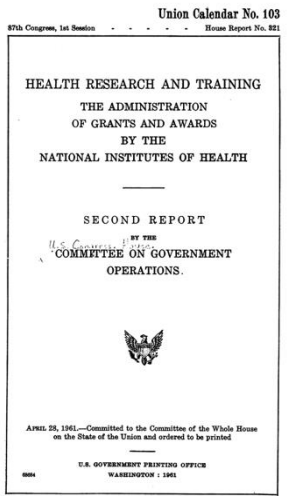
Part II: The Major Policy Questions Since World War II



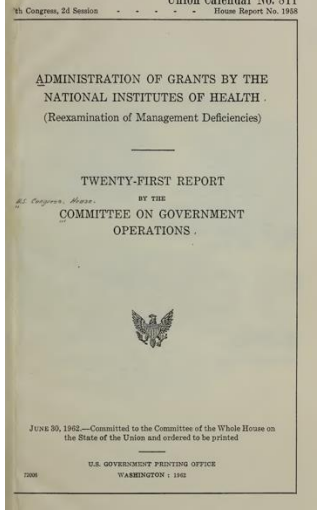
Bayne-Jones Report
1958



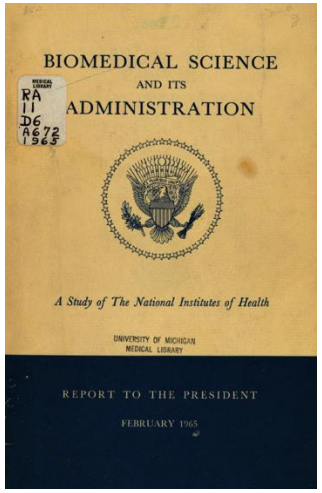
Boisfeuillet "Bo" Jones
Report
1960



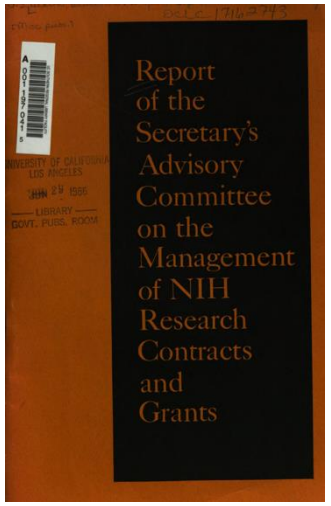
Fountain Committee
Report
1961



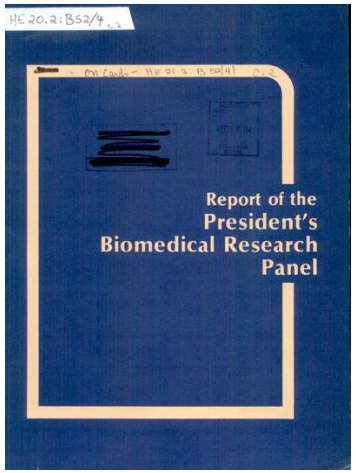
Fountain Committee
Report
1962



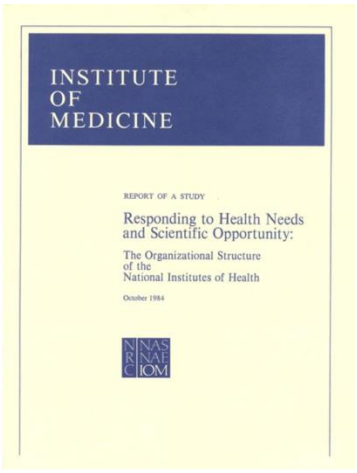
Wooldridge Report
1965



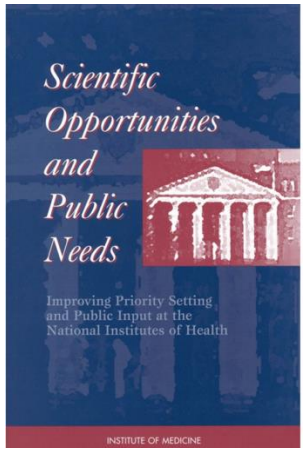
Ruina Report
1965



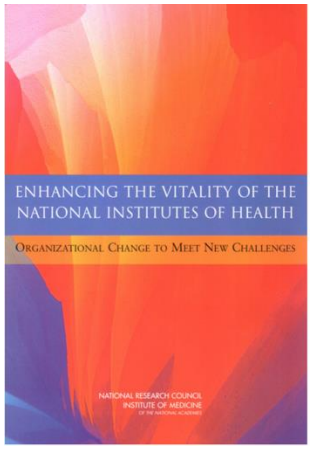
BRP
1976



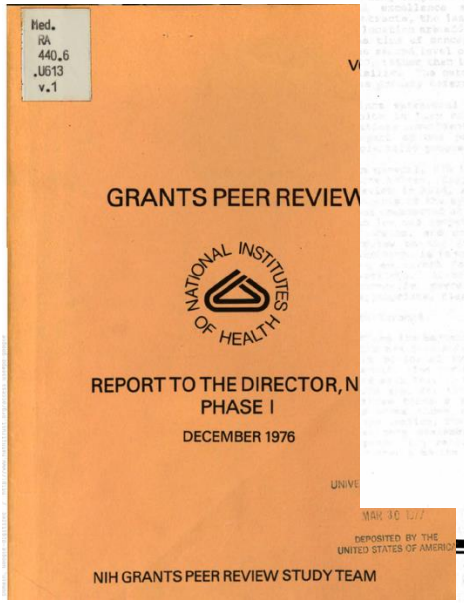
IOM
1984

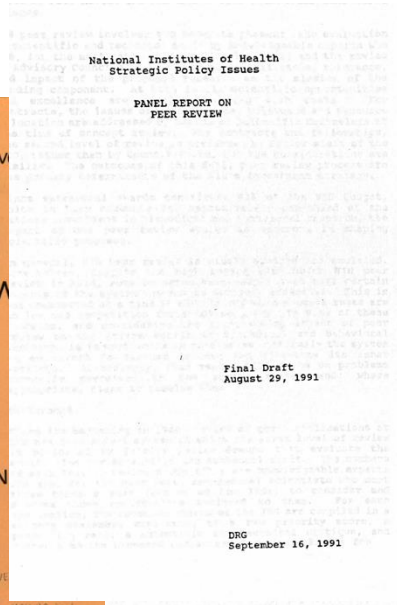


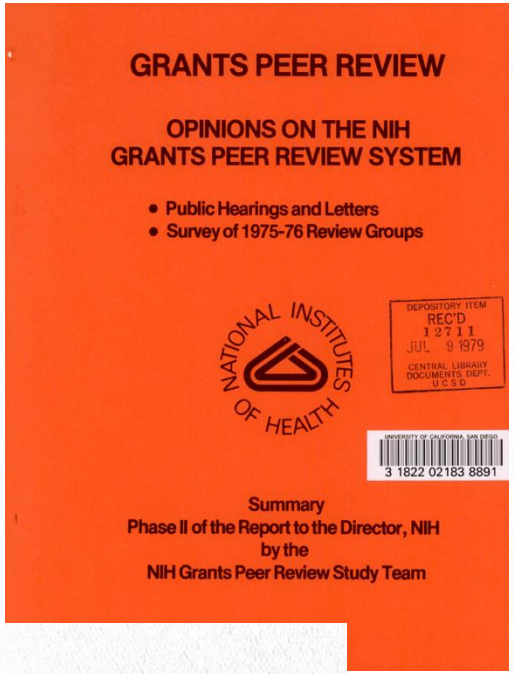
IOM
1998

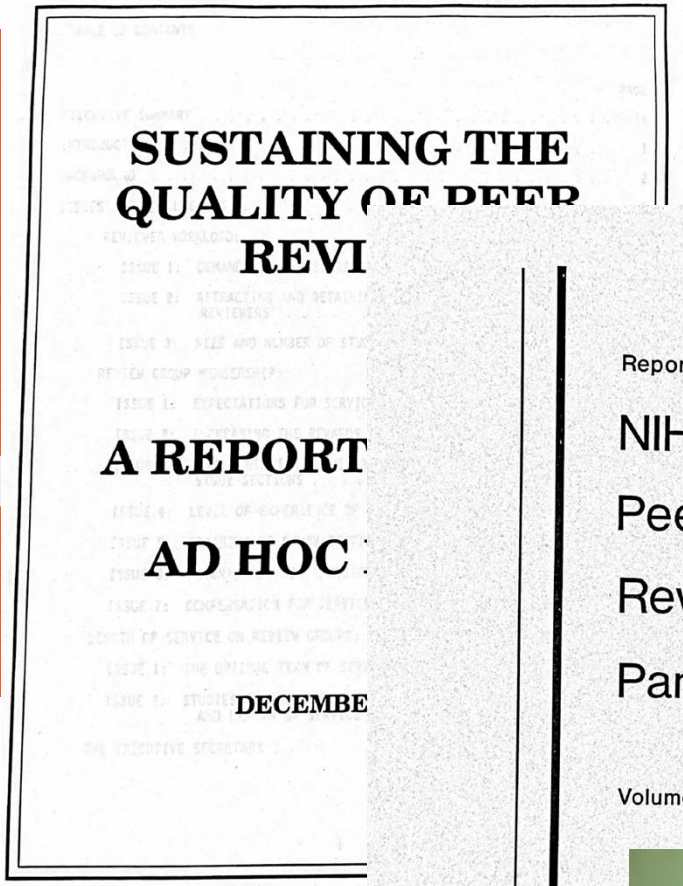


IOM
2003

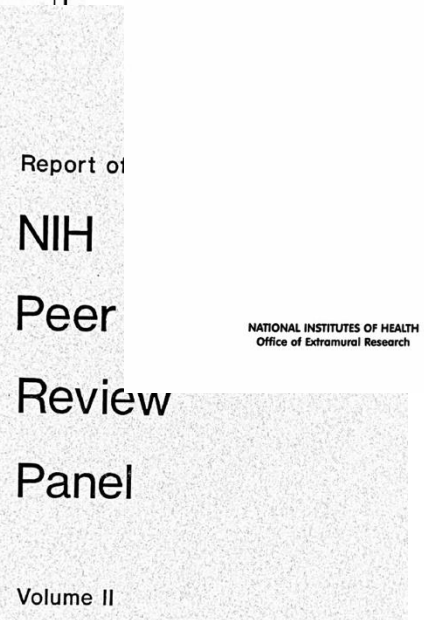




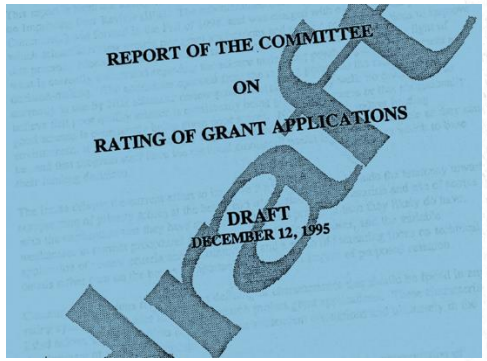


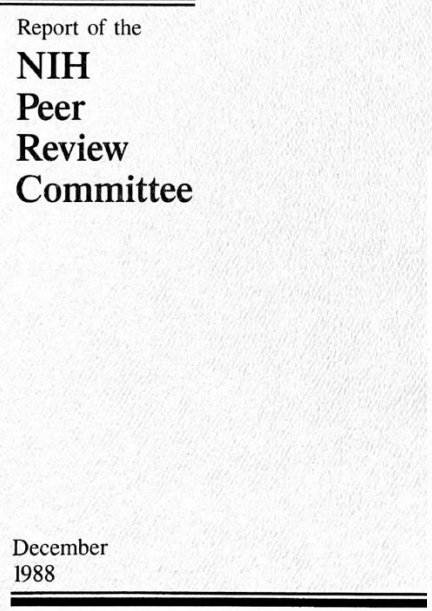


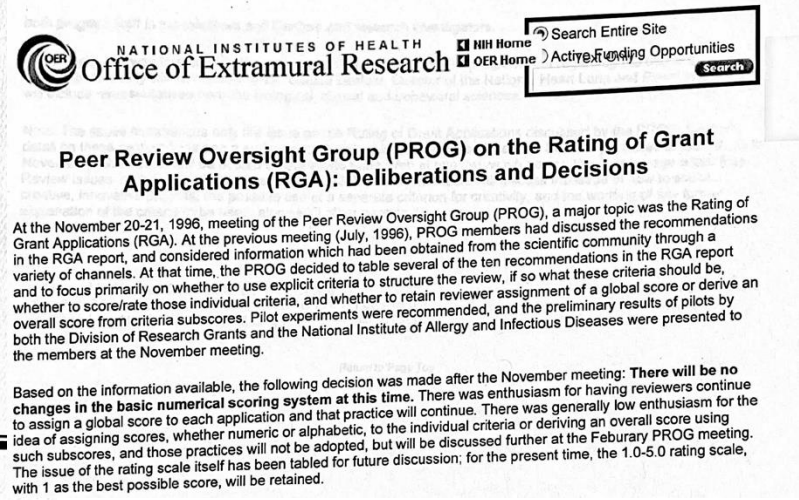
Customer Satisfaction and Research Involvement Among Applicants for NIH R01 and R29 Grants

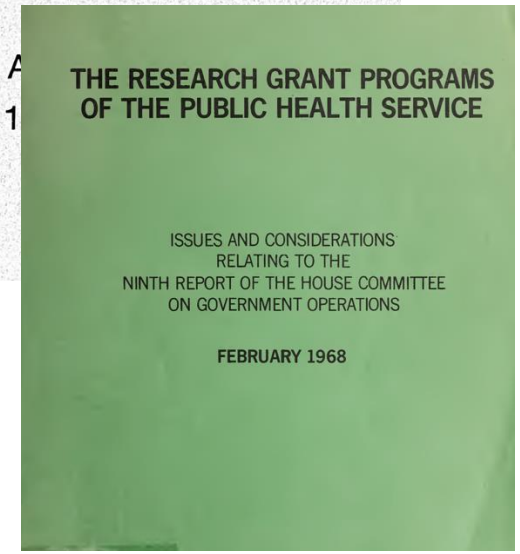


NATIONAL INSTITUTES OF HEALTH
Office of Extramural Research

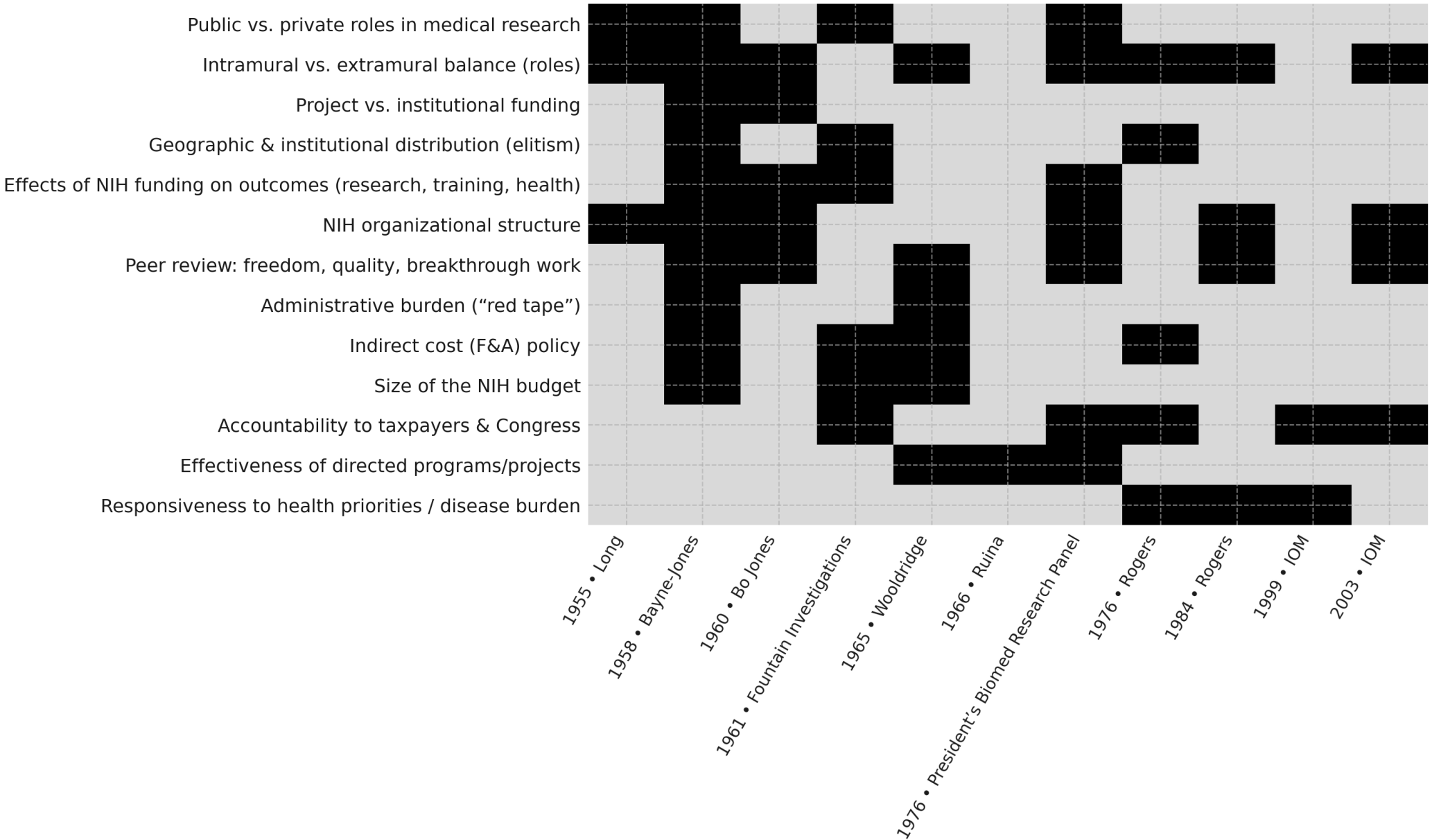


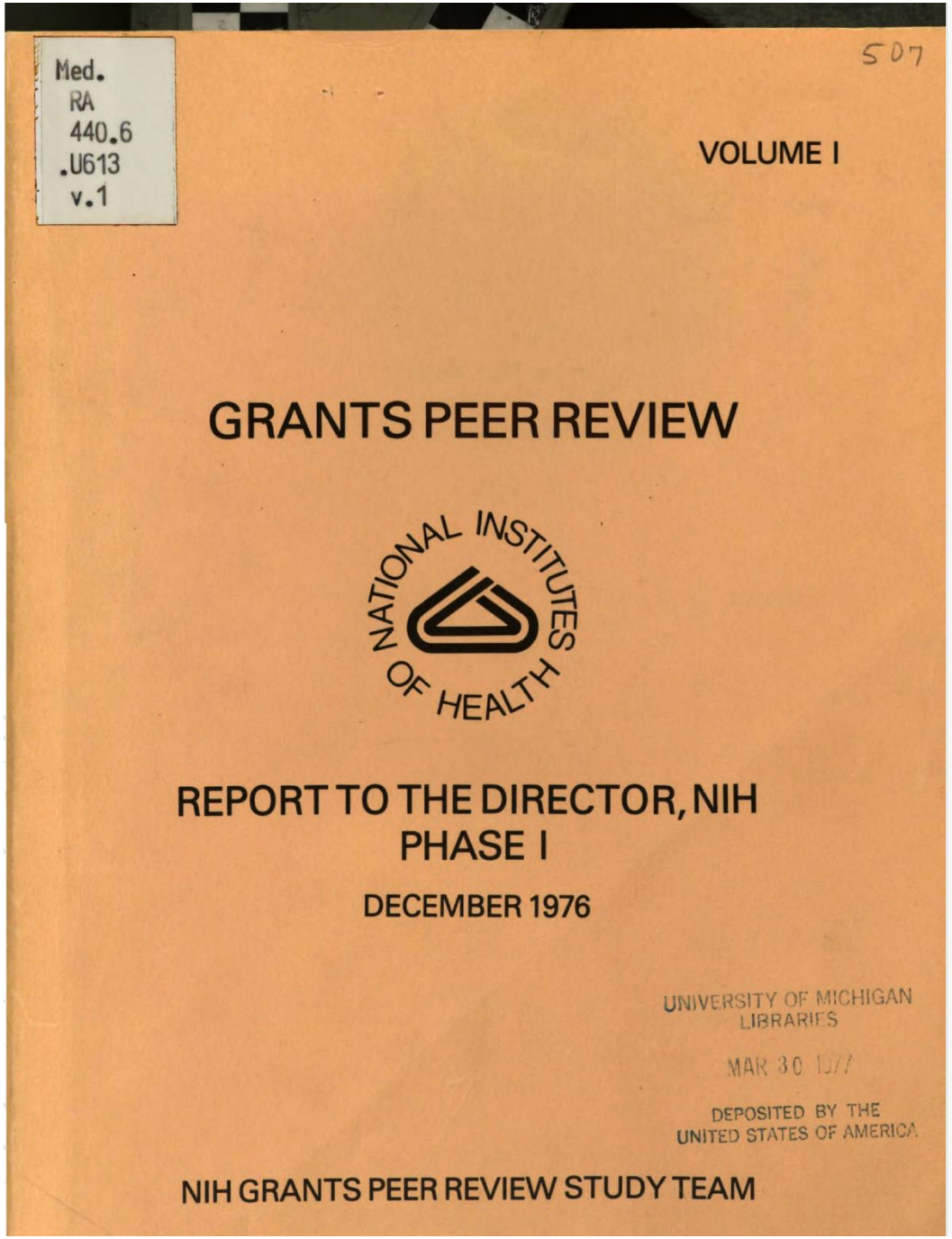






Major Questions in External Evaluations





- 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?

Part III: Taking Stock

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

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?

Historically there has been some interest in things like a “science of science” at NIH to make progress on these issues

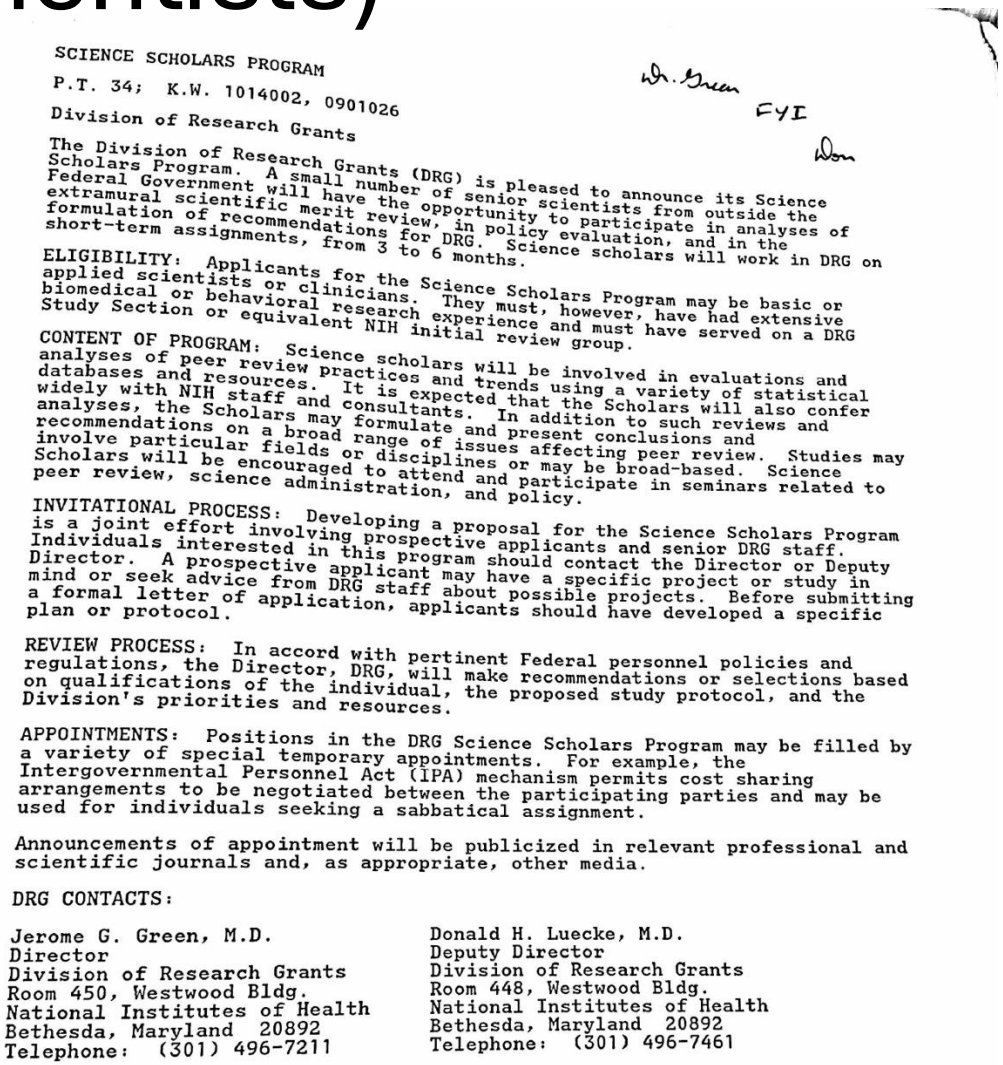
NIH Director James Shannon (1974)

- In funding policy debates “there has been a tendency … for the informational channels to be jammed by a combination of press interviews and public presentations … In all this the scientists have been surprisingly silent”
- “The situation which appears to have developed now results in discussions largely limited to an after-the-decision exchange of biases rather than a search for sound solutions to difficult national problems with a conviction that each is amenable to open and dispassionate examination.”
- Calls for funding of a “selected group of thoughtful professionals within the university community” to assemble and analyze data on major medical funding issues and assess changes in policy
- “Such an effort will require an institutional base, a willingness of a number of professionals to devote substantial time to the undertaking, and moderate support for about a two year period”

In 1986 Jerome G. Green becomes head of the division of research grants, 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. (See Sampat 2023)

Green also wanted to bring in outsiders (but not social scientists)



SCIENCE SCHOLARS PROGRAM

P.T. 34; K.W. 1014002, 0901026

Division of Research Grants

Dr. Green
FYI
Don

The Division of Research Grants (DRG) is pleased to announce its Science Scholars Program. A small number of senior scientists from outside the Federal Government will have the opportunity to participate in analyses of extramural scientific merit review, in policy evaluation, and in the formulation of recommendations for DRG. Science scholars will work in DRG on short-term assignments, from 3 to 6 months.

ELIGIBILITY: Applicants for the Science Scholars Program may be basic or applied scientists or clinicians. They must, however, have had extensive biomedical or behavioral research experience and must have served on a DRG Study Section or equivalent NIH initial review group.

CONTENT OF PROGRAM: Science scholars will be involved in evaluations and analyses of peer review practices and trends using a variety of statistical databases and resources. It is expected that the Scholars will also confer widely with NIH staff and consultants. In addition to such reviews and analyses, the Scholars may formulate and present conclusions and recommendations on a broad range of issues affecting peer review. Studies may involve particular fields or disciplines or may be broad-based. Science Scholars will be encouraged to attend and participate in seminars related to peer review, science administration, and policy.

INVITATIONAL PROCESS: Developing a proposal for the Science Scholars Program is a joint effort involving prospective applicants and senior DRG staff. Individuals interested in this program should contact the Director or Deputy Director. A prospective applicant may have a specific project or study in mind or seek advice from DRG staff about possible projects. Before submitting a formal letter of application, applicants should have developed a specific plan or protocol.

REVIEW PROCESS: In accord with pertinent Federal personnel policies and regulations, the Director, DRG, will make recommendations or selections based on qualifications of the individual, the proposed study protocol, and the Division's priorities and resources.

APPOINTMENTS: Positions in the DRG Science Scholars Program may be filled by a variety of special temporary appointments. For example, the Intergovernmental Personnel Act (IPA) mechanism permits cost sharing arrangements to be negotiated between the participating parties and may be used for individuals seeking a sabbatical assignment.

Announcements of appointment will be publicized in relevant professional and scientific journals and, as appropriate, other media.

DRG CONTACTS:

Jerome G. Green, M.D.
Director
Division of Research Grants
Room 450, Westwood Bldg.
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-7211

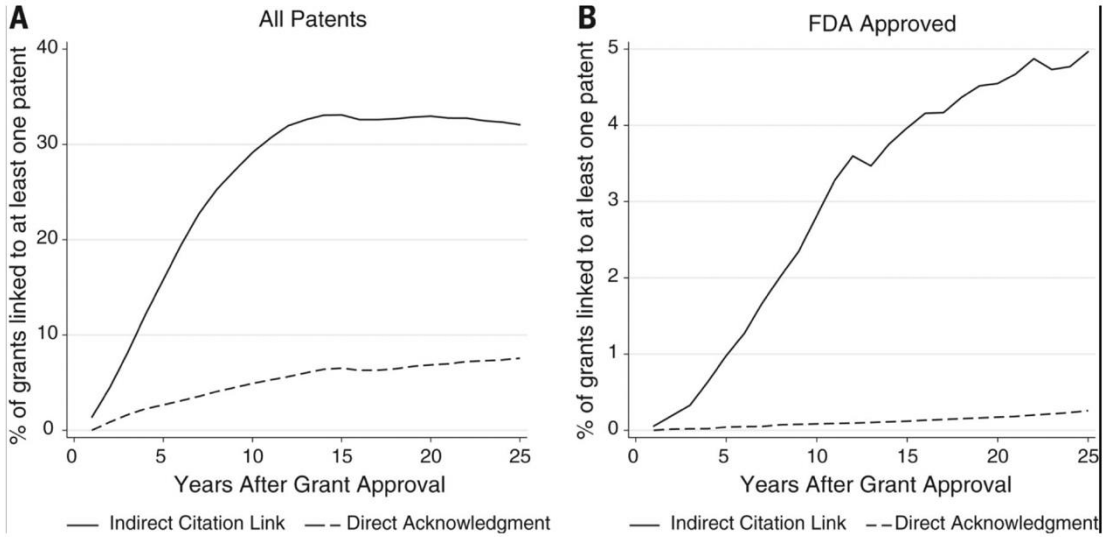
Donald H. Luecke, M.D.
Deputy Director
Division of Research Grants
Room 448, Westwood Bldg.
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-7461

NIH has historically been reluctant to share data on process (unfunded applications, scores)

- Washington Research Project, Inc. v. Department of Health, Education and Welfare (1973)
- 1980: George Kurzon prevails on FOIA requests at NCI to get data on unfunded applications to evaluate if NIH is biased against innovative applications
- In general, NIH reluctant to share unfunded applications and scores, citing privacy concerns
- In practice, there may be other considerations as well

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?
- Beyond measurement, unfunded applications and scores can help with counterfactuals

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 (policymaker) demand?

- Many big (previously neglected) questions seem ripe for exploration, especially given advances in data and measurement
- More effort needed to validate measures, develop/validate surrogate endpoints for health outcomes
- 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 funding (1)

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

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

- 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?

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

Open questions on political economy of biomedical research funding (2)

- 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: Congressional mandates/earmarks vs. peer-reviewed funding

- The Social Contract for Science: What level of scientific freedom, self-governance, and autonomy is compatible with large-scale government funding of health-related science?
  - The Vannevar Bush/Cassius Van Slyke/James Shannon question, seen in debates around new categorical institutes, paperwork and red tape, "people not projects," Congressional earmarking, …

Suggestions?