Updates from Building 1: Next Generation Researchers Initiative and Clinical Trials Reforms

Michael S Lauer, MD
Deputy Director for Extramural Research
National Institutes of Health

82nd Meeting of the National Advisory Council for Human Genome Research
Monday, February 12, 2018
Fishers Lane Terrace-Level Conference Center, Rockville, MD

Disclosures: None

Signs of Stress

NEWS FEATURE

YOUNG, TALENTED AND FED-UP

BY KENDALL POWELL

Martin Tingley was coming undone. It was late autumn 2014, just over a year into his assistant-professor job at Pennsylvania State University in State College, and he was on an eight-hour drive home after visiting his wife in Boston. He was stressed, exhausted and close to tears. As the traffic zipped past in the dark hours of the early morning, the headlights gave him the surreal feeling that he was inside a video game.

Usually, Tingley thought of himself as a "pretty stoic guy" — and on paper, his career was going well. He'd completed a master's degree in statistics and a PhD in Earth science, both at Harvard University. With these, and four years of postdoctoral experience, he had landed a rare tenure-track faculty position. He thought he would soon be successfully combining statistics and climate science to produce the type of interdisciplinary research that funding agencies say they want.

In fact, scientific life was proving tough. He found himself working 60–80 hours per week doing teaching and research. His start-up funding had run out, he had yet to secure a major grant and, according to a practice com-

Scientists starting labs say that they are under historically high pressure to publish, secure funding and earn permanent positions — leaving precious little time for actual research.

an opportunity to direct their own creative,

Young scientists and senior scientists alike feel an acute pressure to publish and are weighed down by a growing bureaucratic burden, with little administrative support. They are largely judged on their record of publishing and of winning grants — but without clear targets, they find themselves endlessly churning out paper after paper. The crucial question is whether this is harming science and scientists. Bruce Alberts, a prominent biochemist at the University of California, San Francisco, and former president of the US National Academy of Sciences, says that it is. The current hyper-competitive atmosphere is stifling creativity and pushing scientists "to do mediocre science", he says — work that is safe and uninteresting. "We've got to reward people who do something differently."

Our informal survey suggests that the situation is already making research an unwelcoming career. "Frankly, the job of being a principal investigator and running a lab just looks horrible," wrote one neuroscientist from the United States. Tingley wouldn't disagree.

FUNDING FIGHT

Tingley has always had broad interests. At

Nature 2016;538:446-9

"The funding cycle is brutal."

MARTIN TINGLEY

Media

The Upshot

FOLLOW US:
GET THE UPSHOT IN YOUR INBOX

LOST IN ACADEMIA

So Many Research Scientists, So Few Openings as Professors

Gina Kolata @ginakolata JULY 14, 2016

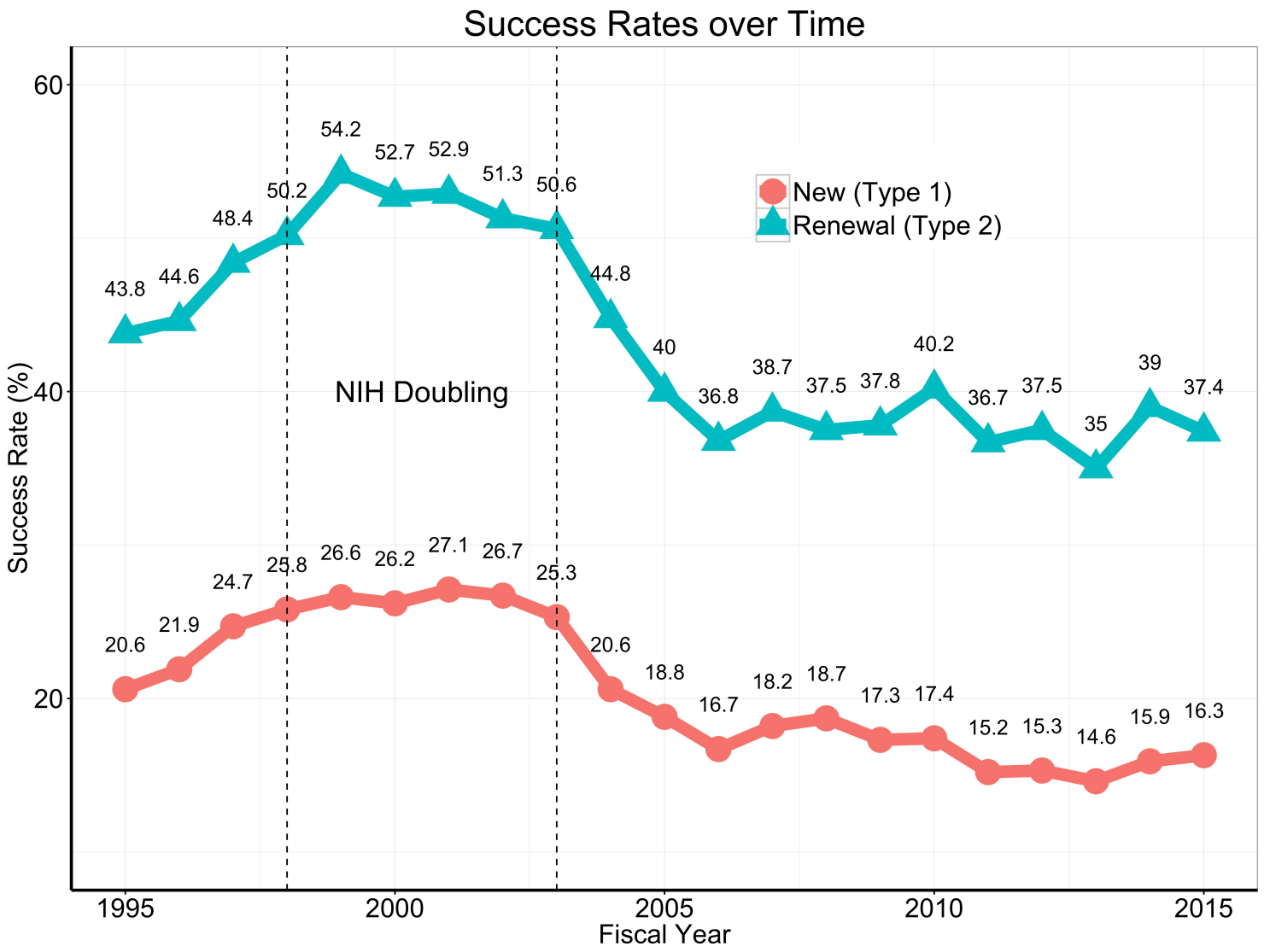
352

"The average age at which the lucky few actually get a grant has steadily increased — it is now 42, up from 35 in 1980, which means biomedical scientists in academia are essentially apprentices until middle age. And the tendency is for the grants to go to scientists who already have them, making it harder and harder to break into the system."

Emmanuelle Charpentier, who became leader of the Max Planck Institute for Infection Biology last year, spent the previous 25 years moving through nine institutions in five countries. Karsten Moran for The New York Times

https://www.nytimes.com/2016/07/14/upshot/so-many-research-scientists-so-few-openings-as-professors.html?_r=0

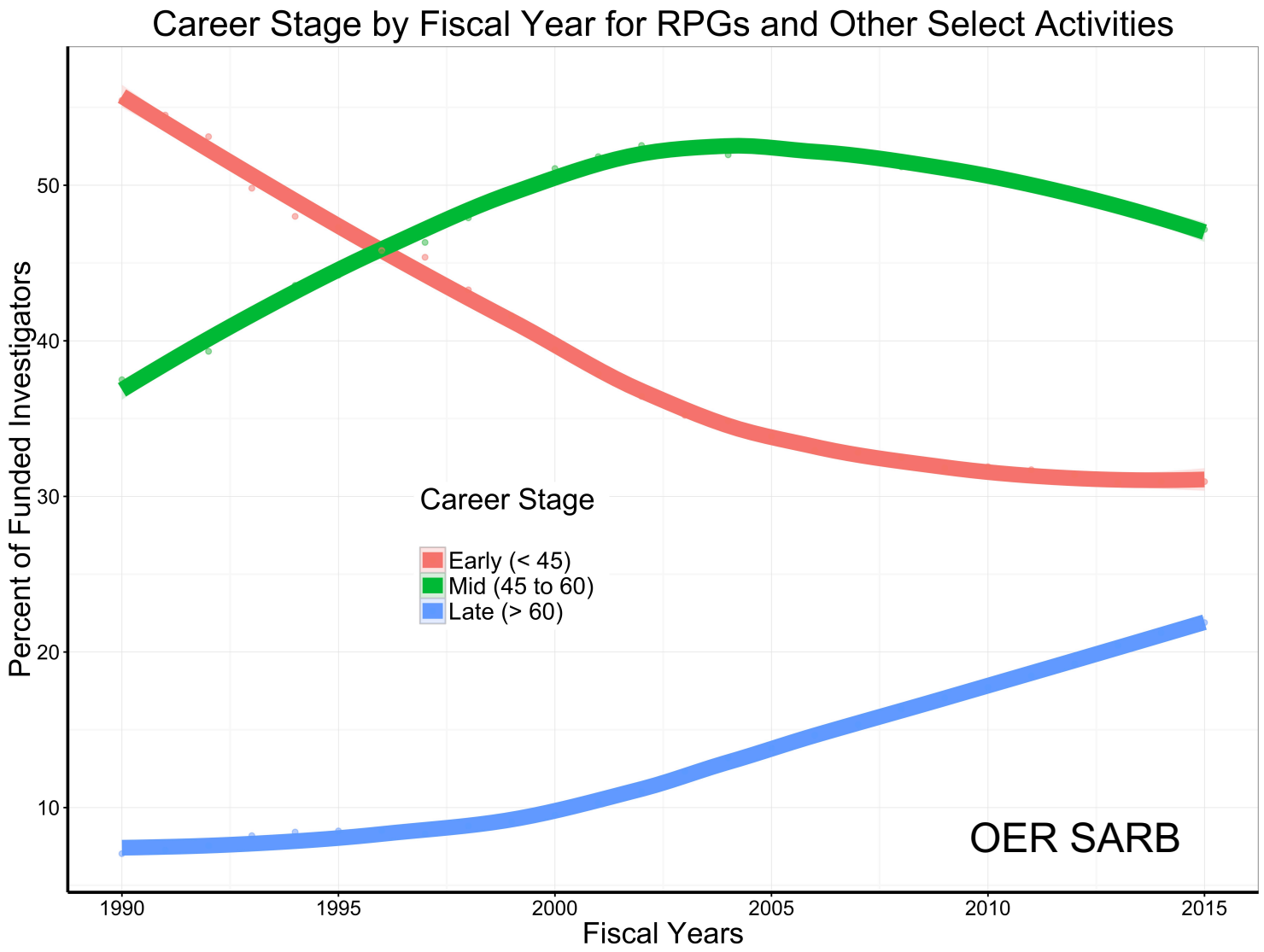
Is This True (Part 1)?



Much easier to get a grant renewed than to get it funded in the first place

OER SARB

Is This True (Part 2)?



Future of fundamental discovery in US biomedical research

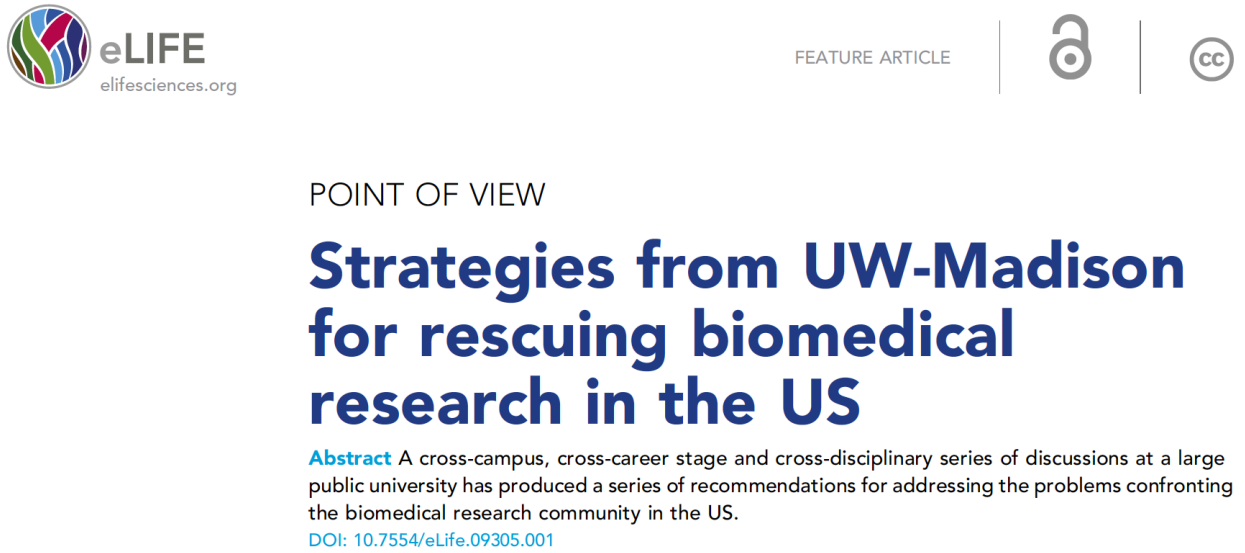
Michael Levitt[a,1] and Jonathan M. Levitt[b]

PNAS

"What caused the drop in number of young scientists? Older grantees are getting money at the expense of younger grantees … Study sections are biased against those whose ages are ..."

www.pnas.org/cgi/doi/10.1073/pnas.1609996114

Root Causes …



eLIFE elifesciences.org

FEATURE ARTICLE

POINT OF VIEW

Strategies from UW-Madison for rescuing biomedical research in the US

Abstract A cross-campus, cross-career stage and cross-disciplinary series of discussions at a large public university has produced a series of recommendations for addressing the problems confronting the biomedical research community in the US.

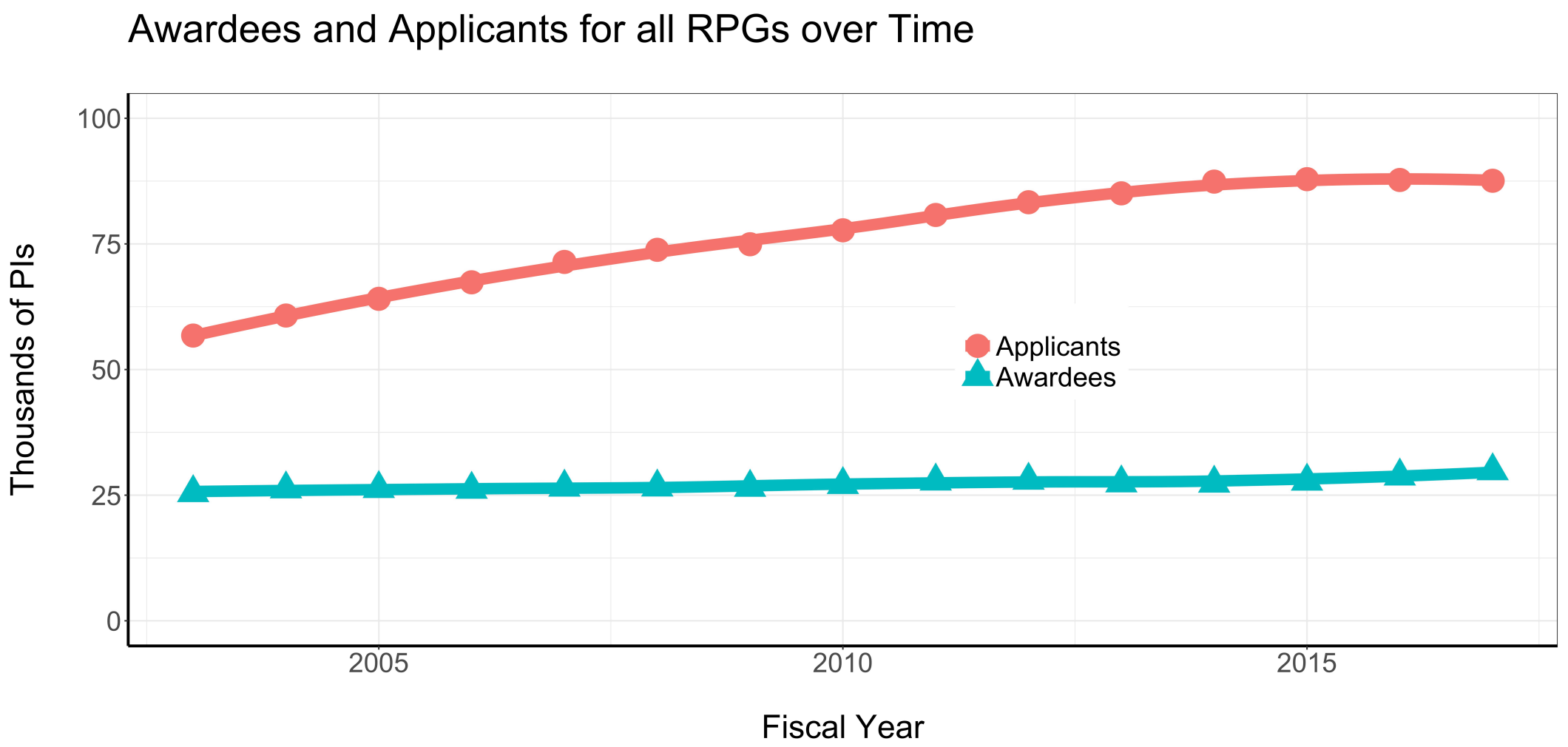
DOI: 10.7554/eLife.09305.001

"We identified two **core problems**:

- Too many researchers vying for too few dollars.
- Too many postdocs competing for too few positions.

Most other issues can be viewed as symptoms."

“Too Many Researchers…”



Who is Most Affected by Hypercompetition?

"In the United States, for example, **funding success rates for all age brackets are less than half what they were in 1980**, so researchers have to spend more time seeking funds. That **burden falls most heavily on new faculty members … makes them conservative rather than ambitious**."

Nature 2016;538:427

CONGRESS.GOV | Legislation

H.R.34 - 21st Century Cures Act

114th Congress (2015-2016) | Get alerts

Subtitle C—Supporting Young Emerging Scientists

SEC. 2021. INVESTING IN THE NEXT GENERATION OF RESEARCHERS.

(a) IN GENERAL.—Part A of title IV of the Public Health Service Act (42 U.S.C. 281 et seq.) is amended by adding at the end the following:

"SEC. 404M. NEXT GENERATION OF RESEARCHERS.

What the Law Calls For

"The Director of the National Institutes of Health shall … develop, modify, or prioritize policies, as needed … to promote opportunities for new researchers and **earlier research independence**, such as policies **to increase opportunities for new researchers to receive funding** … , and **enhance workforce diversity**."

NIH Intentions

OPINION

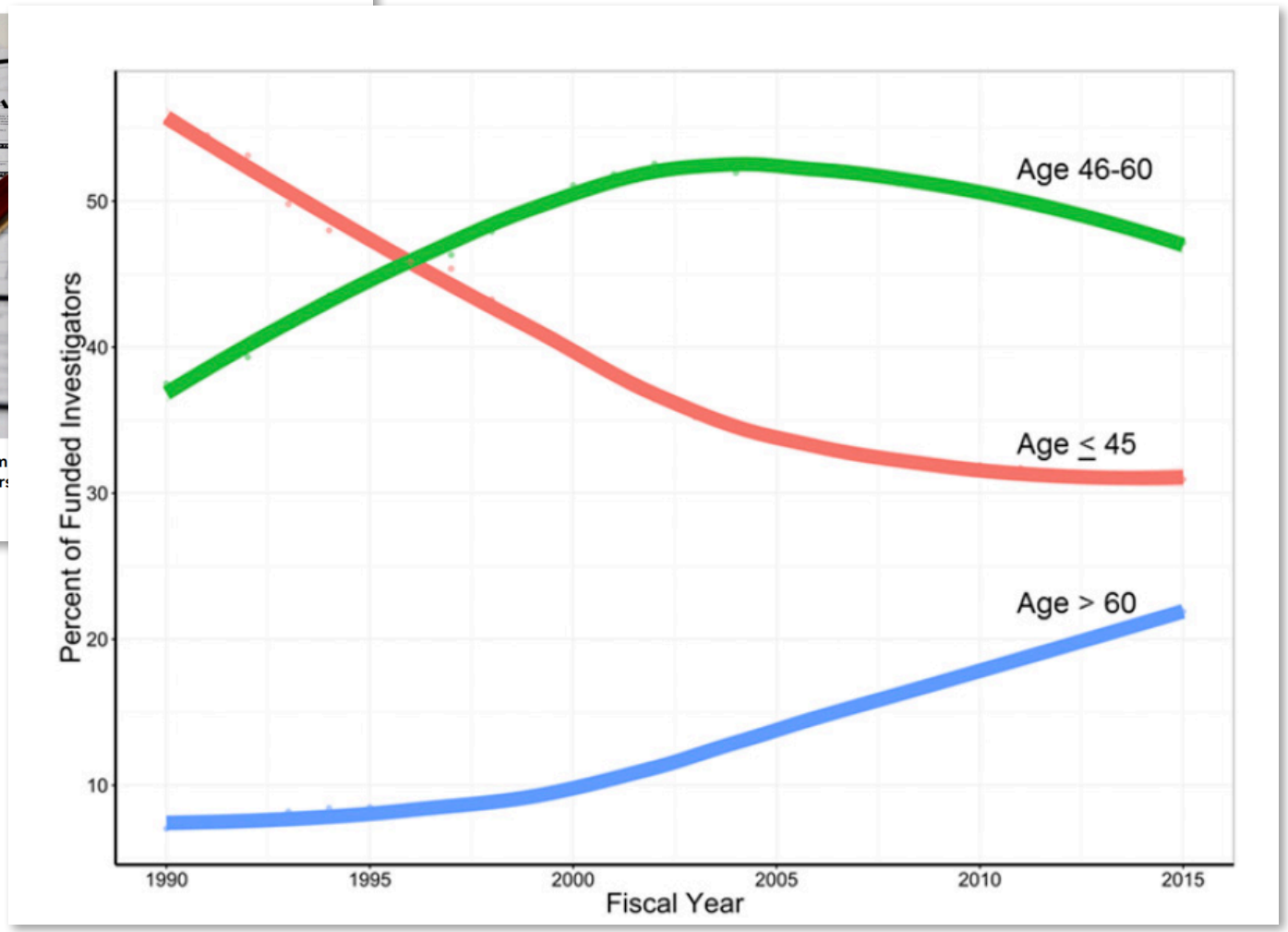
The Next Generation Researchers Initiative at NIH

Michael Lauer[a,1], Lawrence Tabak[a], and Francis Collins[a]

Growing concerns about the wellbeing and stability of the biomedical research workforce are well documented. Over the last 15 years (since the end of the doubling of the NIH budget), we have observed worsening "hypercompetition" as more scientists vie for fewer available dollars (1, 2). Within this hypercompetitive environment, the research workforce is growing older at a rate that is disproportionate to the general American labor force (3). Late-career investigators have been awarded a greater proportion of available research funding, raising concerns that early-career investigators risk being crowded out of the workforce before they have a chance to launch independent scientific careers (3). Other analysts have suggested that adverse effects are also being felt by midcareer investigators (4); large numbers of meritorious investigators may achieve research independence only to lose it because they are unable to renew their one grant or obtain a second new grant.

In our latest effort to tackle this problem, the NIH is launching the "Next Generation Researchers Initiative,"

Fig. 1. The NIH hopes its latest initiative will im
prospects for early- and midcareer investigators
Shutterstock/Stephen_Payne.



Lauer M, Tabak L, Collins F. *PNAS* 2017;45:11801-11803

NGRI Considerations

- Where will the money come from?
  - IC Priorities
  - Leverage budget increases
  - Other: R56, R35, NIAMS STAR
- Monitoring
  - Workforce size and diversity
  - Scientific excellence and outcome

And Now … For Something a Bit … Different

https://i.pinimg.com/originals/12/e2/59/12e259ef9f5d201309b0b451acd49c6f.jpg

Problems!

BMJ

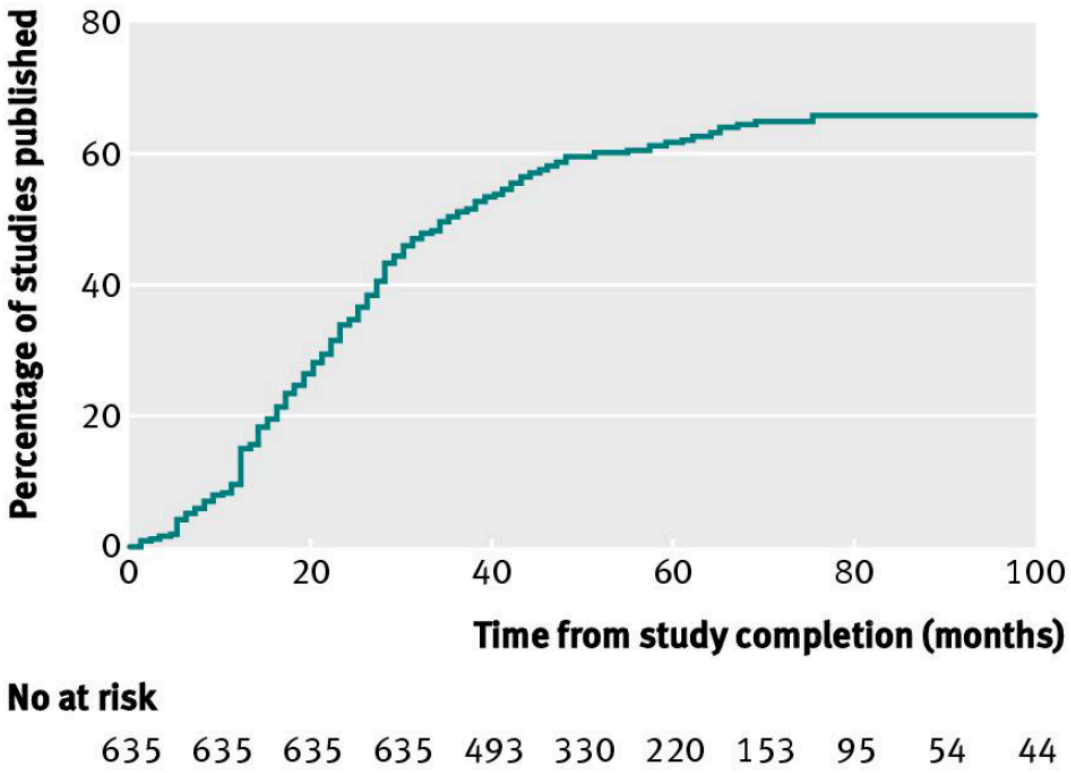
BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

RESEARCH

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

OPEN ACCESS

Joseph S Ross *assistant professor of medicine*[1 2], Tony Tse *program analyst at ClinicalTrials.gov*[3], Deborah A Zarin *director of ClinicalTrials.gov*[3], Hui Xu *postgraduate house staff trainee*[4], Lei Zhou *postgraduate house staff trainee*[4], Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*[2 5 6]



”There are many [NIH-funded] trials not covered by [FDAAA], such as trials of behavioral interventions and surgical procedures. **No policies exist** to make sure that the public has access to results from NIH funded research that is not published ”

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

We Did Not Believe It

The NEW ENGLAND JOURNAL of MEDICINE

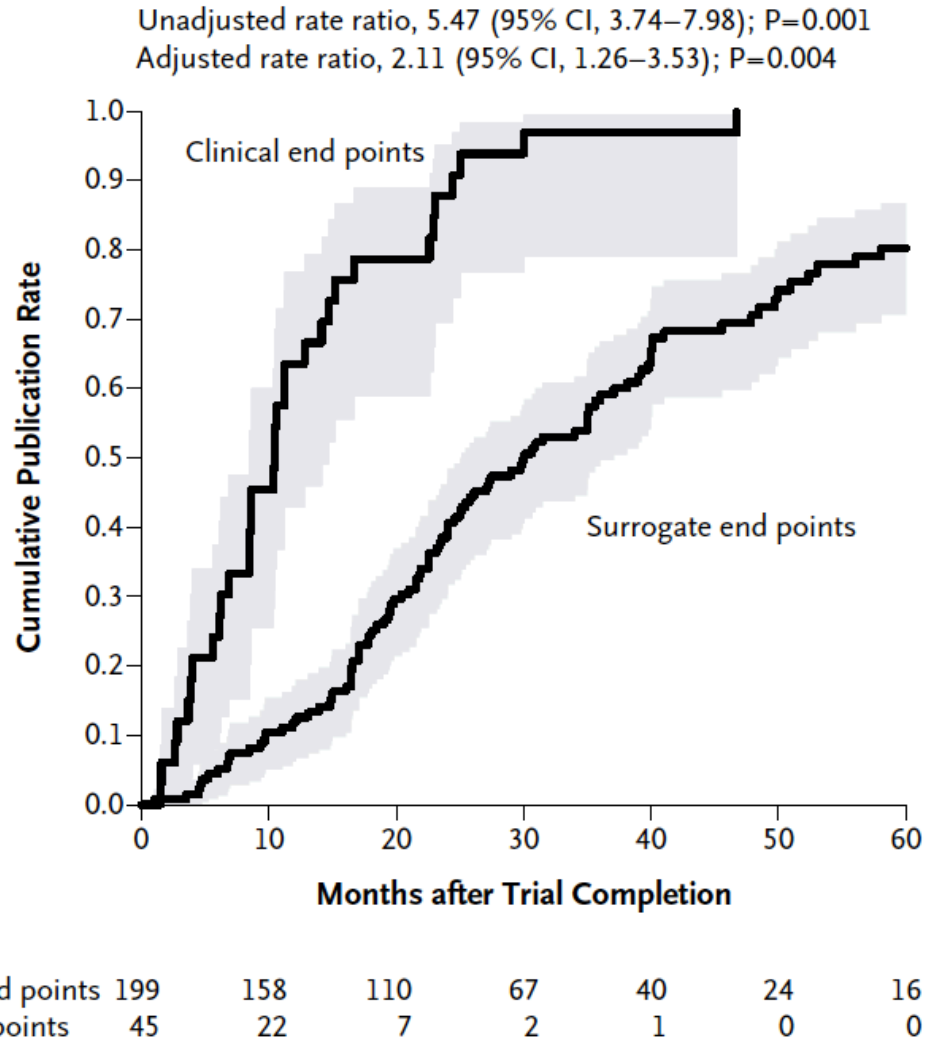
SPECIAL ARTICLE

Publication of Trials Funded by the National Heart, Lung, and Blood Institute

David Gordon, M.D., Ph.D., Wendy Taddei-Peters, Ph.D., Alice Mascette, M.D., Melissa Antman, Ph.D., Peter G. Kaufmann, Ph.D., and Michael S. Lauer, M.D.

ABSTRACT

"A number of parties share responsibility, **including funders**, investigators, academic medical centers, [universities], clinical research organizations, and ... journals."



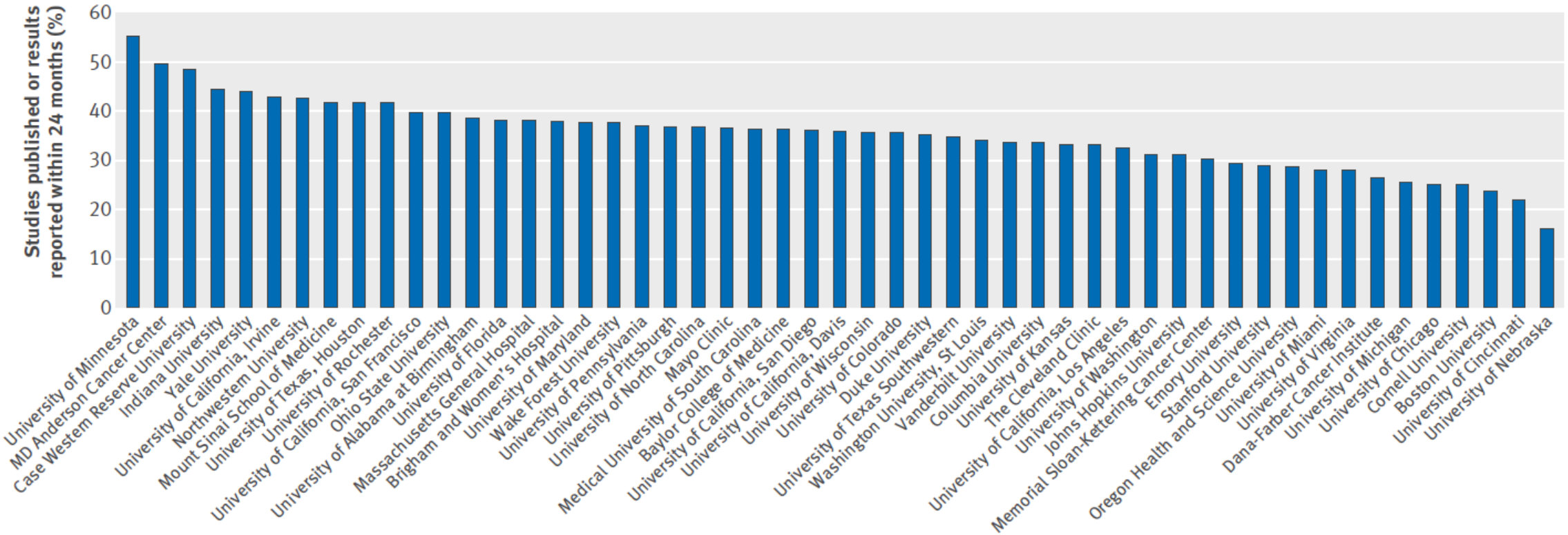
N Engl J Med 2013;369:1926-34

At *Your* Institution

OPEN ACCESS

Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers

Ruijun Chen,[1] Nihar R Desai,[2,3] Joseph S Ross,[3,4,5,6] Weiwei Zhang,[3] Katherine H Chau,[1] Brian Wayda,[7] Karthik Murugiah,[8] Daniel Y Lu,[9] Amit Mittal,[8] Harlan M Krumholz[2,3,5,6]



"Despite the **ethical mandate** and expressed values of academic institutions, there is poor performance and noticeable variation in the dissemination of clinical trial results across leading academic medical centers."

BMJ 2016;352:i637

Just How Serious This Is…

OPINION POLICY-ISH

Academic Medical Centers Get An F In Sharing Research Results

February 23, 2016 · 1:59 PM ET

HARLAN KRUMHOLZ

Who will check the study results if they aren't made public?

Simone Golob/Corbis

"We have a bottleneck at our nation's bastions of research excellence. Too many times, study results are neither reported on the government website, clinicaltrials.gov, nor published in a journal.

The failure to share results is so pervasive that it seems inappropriate to blame individuals. Instead, it is a systemic problem."

http://www.npr.org/sections/health-shots/2016/02/23/467712481/academic-medical-centers-get-an-f-in-sharing-research-results

Continued… “Sharing Results Should Not Be Optional”

OPINION POLICY-ISH

Academic Medical Centers Get An F In Sharing Research Results

February 23, 2016 · 1:59 PM ET

HARLAN KRUMHOLZ

Who will check the study results if they aren't made public?

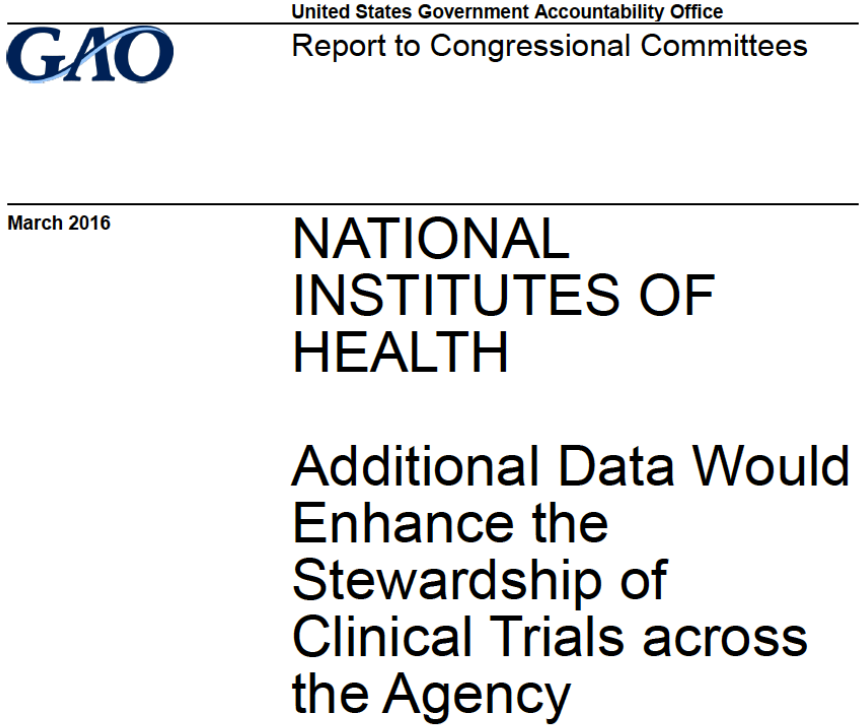
Simone Golob/Corbis

“Not reporting results violates the basic principle of the scientific method. It hurts patients, society and science. It dishonors the people who gave their consent and bore the risk of participating...

The holding back of the results impedes progress toward scientific breakthroughs, corrupts the medical literature and wastes research funding.”

http://www.npr.org/sections/health-shots/2016/02/23/467712481/academic-medical-centers-get-an-f-in-sharing-research-results

More Problems


United States Government Accountability Office

GAO

Report to Congressional Committees

March 2016

NATIONAL INSTITUTES OF HEALTH

Additional Data Would Enhance the Stewardship of Clinical Trials across the Agency

"NIH's OD reviews some data on clinical trial activity across NIH but has not finalized what additional data it needs or established a process for using these data to enhance its stewardship.

NIH is limited in its ability to make data-driven decisions regarding the use of its roughly $3 billion annual investment in clinical trials."

GAO-16-304

Notice of Revised NIH Definition of "Clinical Trial"

A Long Road

Notice Number:

NOT-OD-15-015

Key Dates

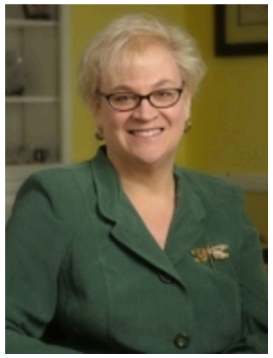
Release Date: October 23, 2014

Rock Talk

Helping connect you with the NIH perspective

Posted on **November 19, 2014** by **Sally Rockey**

A Proposed HHS Regulation and NIH Policy to Further the Impact of Clinical Trials Research



Dr. Sally Rockey

VIEWPOINT

Sharing and Reporting the Results of Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

The principle of data sharing dates to the dawn of scientific discovery—it is how researchers from different disciplines and countries form collaborations, learn from others, identify new scientific opportunities, and work to turn newly discovered information into shared knowledge and practical advances. When research involves human volunteers who agree to participate i
to test new drugs, devices, or other inter
principle of data sharing properly assumes
ethical mandate. These participants

be blamed entirely. A recent analysis of 400 clinical studies revealed that 30% had not shared results through publication or through results reporting in ClinicalTrials.gov within 4 years of completion.[4] This is a serious issue and the proposed rule underscores the intent of NIH to take strong action to promote timely

Compendium of Public Comments on the
Draft NIH Policy on Dissemination of NIH-Funded Clinical Trial Information
November 19, 2014 – March 29, 2015

Now the Policy Exists…

42 CFR Part 11

[Docket Number NIH-2011-0003]

RIN: 0925-AA55

Clinical Trials Registration and Results Information Submission

Effective Date

This policy is effective January 18, 201

Date: September 12, 2016

Francis S. Collins, M.D., Ph.D.

Director

National Institutes of Health

"A fundamental premise of all NIH-funded research is that the results must be disseminated …

In research involving human beings, scientists have **an ethical obligation** to ensure that the burden and risk that volunteers assume comes to something, at the very least by ensuring that others are aware of the study and that its findings contribute…"

https://www.federalregister.gov/documents/2016/09/21/2016-22379/nih-policy-on-the-dissemination-of-nih-funded-clinical-trial-information

Publicity

JAMA Published online September 16, 2016

Opinion

VIEWPOINT

Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

Supplemental content

Clinical trials are the most publicly visible component of the biomedical research enterprise, from the potential human application of novel laboratory findings to the generation of robust evidence about treatments or preventive interventions in routine clinical care. These trials are also the point at which biomedical research most directly engages human participants—dedicated volunteers who trust investigators to uphold the highest standards of scientific rigor and ethical oversight. While clinical trials have evolved and improved over time—producing impressive advances in diagnosis, treatment, and prevention—there are still major challenges. Therefore, fundamental changes are needed to reflect science and society's movement to increase efficiency, accountability, and transparency in clinical research.

As the largest public funder of clinical trials in the United States, currently investing more than $3 billion

The aim is to help ensure that all involved in the clinical trial enterprise have the appropriate knowledge about the design, conduct, monitoring, recording, analysis, and reporting of clinical trials. While GCP training on its own may not be sufficient, it provides a consistent and high-quality standard.

Another important change at the beginning of the clinical trial lifecycle is a new NIH policy that will require all applications for clinical trials to be submitted in response to clinical trial–specific Funding Opportunity Announcements (FOAs). This will mean that applications including one or more clinical trials will no longer be accepted in response to parent funding announcements, which are broad FOAs that allow researchers to submit investigator-initiated applications without specific elements appropriate to describe and evaluate a trial. Under this policy, NIH trial applications will need to con-

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Open Mike

Helping connect you with the NIH perspective, and helping connect us with yours

Posted on **September 16, 2016** by **Mike Lauer and Carrie Wolinetz**

Building Better Clinical Trials through Stewardship and Transparency

— *Dr. Carrie Wolinetz is NIH's Associate Director for Science Policy, and writes*

NIH is the largest public funder of clinical trials in the United States. As stewards of this research enterprise, we have been actively listening and discussing how to overcome hurdles and shortcomings that we, and others in the research community, have identified. If you've been following the conversation, you'll know that NIH already has implemented some key reforms to enhance clinical trial stewardship. Today, in a Viewpoint Essay published in the Journal of the American Medical Association (JAMA), we provide an overview of how these reforms, and new initiatives, fit in to the broader picture of building a better clinical trial enterprise through better stewardship, accountability, and transparency.

Dr. Michael Lauer is NIH's Deputy Director for Extramural Research, serving as the principal scientific leader and advisor to the NIH Director on the NIH extramural research program.

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NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information

Notice Number: NOT-OD-16-149

NIH National Institutes of Health
Office of Extramural Research

Policy & Compliance

NIH Grants Policy Statement

Notices of Policy Changes

Compliance & Oversight

Select Policy Topics

Animal Welfare

Application Submission Policies

Clinical Trial Requirements

- Clinical Trial Definition
- Why the Changes
- Good Clinical Practice
- Specific Funding Opportunities
- New Form
- Single IRB Policy
- Protocol Template
- Registration and Reporting

Clinical Trial Requirements for Grants and Contracts

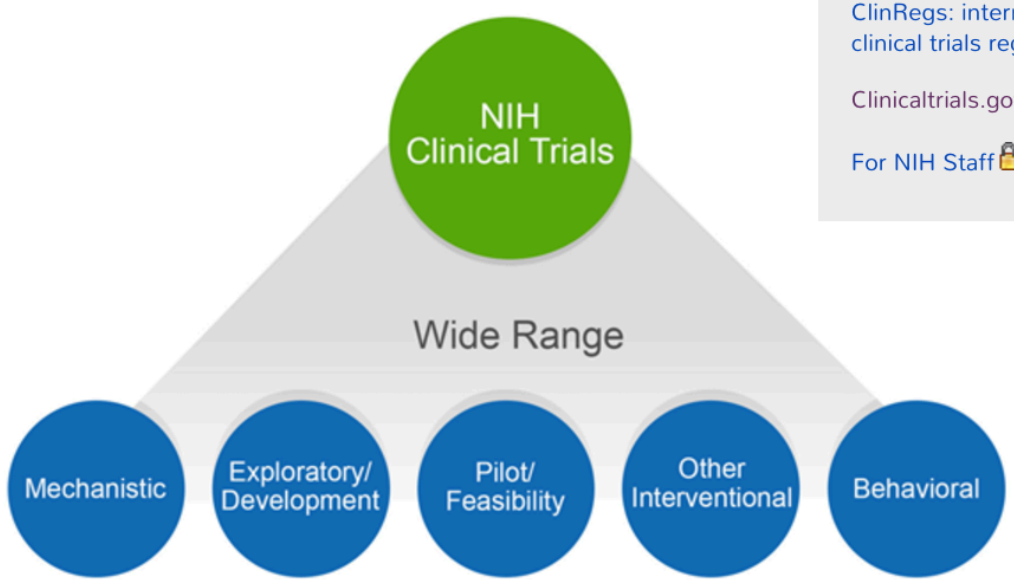
NIH is launching a series of initiatives that are rolling out in 2017-2018 to enhance the accountability and transparency of clinical research. These initiatives target key points along the whole clinical trial lifecycle from concept to results reporting. Learn more about these changes and how they will affect your research.

NIH Definition of a Clinical Trial

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Learn more

Your human subjects study may meet the NIH definition of a clinical trial.

FIND OUT HERE



Related Resources

FAQs

Training Resources

Research Involving Human Subjects

ClinRegs: international clinical trials regulations

Clinicaltrials.gov

For NIH Staff

https://grants.nih.gov/policy/clinical-trials.htm

Accountability, Ethical Mandate, Transparency

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30 FOR 30 Stories you need to hear to believe. Listen on Apple Podcasts

A surprising amount of medical research isn't made public. That's dangerous.

Updated by Stephanie Wykstra | Aug 1, 2017, 8:40am EDT

TWEET SHARE

Dan Kitwood / Staff

30 FOR 30
Stories you need to hear to believe.
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THE BIG IDEA

Outside contributors' opinions and analysis of the most important issues in politics, science, and culture.

When the results of clinical trials aren't made public, the consequences can be dangerous — and potentially deadly.

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NEWS RELEASES

Wednesday, November 19, 2014

HHS and NIH take steps to enhance transparency of clinical trial results

UPDATE: The deadline for comments on the Notice of Proposed Rule Making (NPRM) and the NIH policy for clinical trials reporting has been extended to 5:00 p.m. ET on Monday, March. 23. For more information, please see the latest Federal Register Notices for the NPRM and for the proposed NIH Policy, which posted on February 13, 2015.

Institute/Center

NIH Office of the Director (OD)

Contact

NIH News Media Branch
301-496-5787

Related Links

NPRM Federal Register Notice pdf

NIH Guide to Proposed NIH Policy

Summary of Proposed Changes

https://www.vox.com/the-big-idea/2017/8/1/16012946/clinical-trial-research-public-transparency
https://www.nih.gov/news-events/news-releases/hhs-nih-take-steps-enhance-transparency-clinical-trial-results