Supporting More Investigators Sustainably and Efficiently

Prepared by the Office of Extramural Research (OER) and the Efficiency and Sustainability of Funding Policies Working Group of the EAWG (Jon Lorsch, Chair)

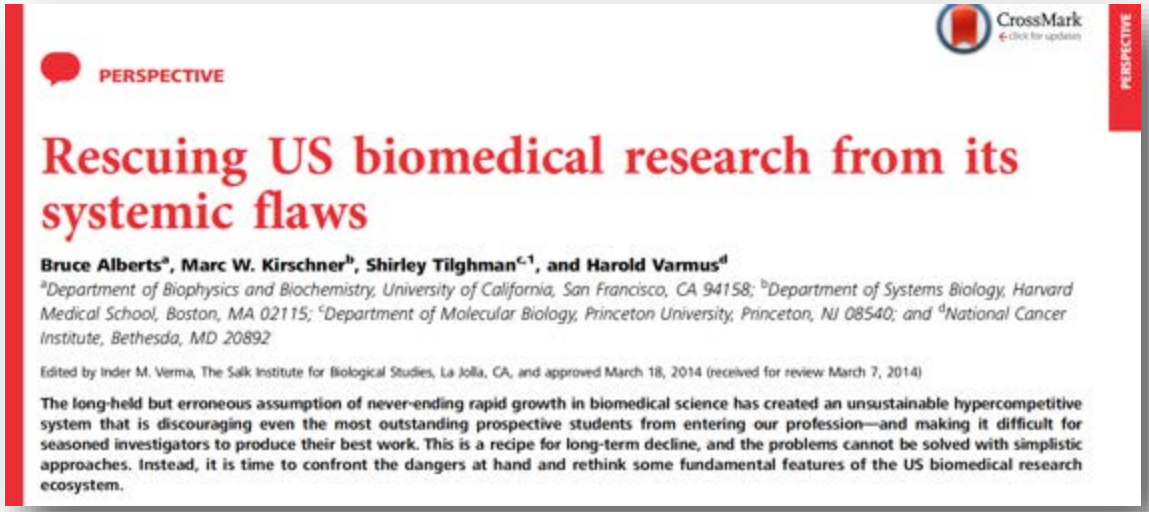
Presented by Michael Lauer and Jon Lorsch (EAWG Co-Chairs) with many thanks to OD/OER/OPAC/DPEA/Statistical Analysis and Reporting Branch, Luci Roberts, Katrina Pearson, Katie Patel, Deepshikha RoyChowdhury, and Rachael Walsh

113th Meeting of the NIH Advisory Committee to the Director

Thursday, December 8, 2016

Building 31C6, Room 6, NIH Main Campus, Bethesda, MD

Instability: Era of Hypercompetition



PERSPECTIVE

Rescuing US biomedical research from its systemic flaws

Bruce Alberts[a], Marc W. Kirschner[b], Shirley Tilghman[c,1], and Harold Varmus[d]

[a]Department of Biophysics and Biochemistry, University of California, San Francisco, CA 94158; [b]Department of Systems Biology, Harvard Medical School, Boston, MA 02115; [c]Department of Molecular Biology, Princeton University, Princeton, NJ 08540; and [d]National Cancer Institute, Bethesda, MD 20892

Edited by Inder M. Verma, The Salk Institute for Biological Studies, La Jolla, CA, and approved March 18, 2014 (received for review March 7, 2014)

The long-held but erroneous assumption of never-ending rapid growth in biomedical science has created an unsustainable hypercompetitive system that is discouraging even the most outstanding prospective students from entering our profession—and making it difficult for seasoned investigators to produce their best work. This is a recipe for long-term decline, and the problems cannot be solved with simplistic approaches. Instead, it is time to confront the dangers at hand and rethink some fundamental features of the US biomedical research ecosystem.

"The erroneous assumption of never-ending rapid growth has created an **unsustainable hypercompetitive system** that is discouraging even the most outstanding prospective students from entering our profession—and making it difficult for seasoned investigators to produce their best work. This is a recipe for long-term decline."

Alberts B, Kirschner MW, Tilghman S, Varmus H. PNAS 2014;111:5773-7

Core Problems Underlying an Unstable System

eLIFE
elifesciences.org

FEATURE ARTICLE

POINT OF VIEW

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

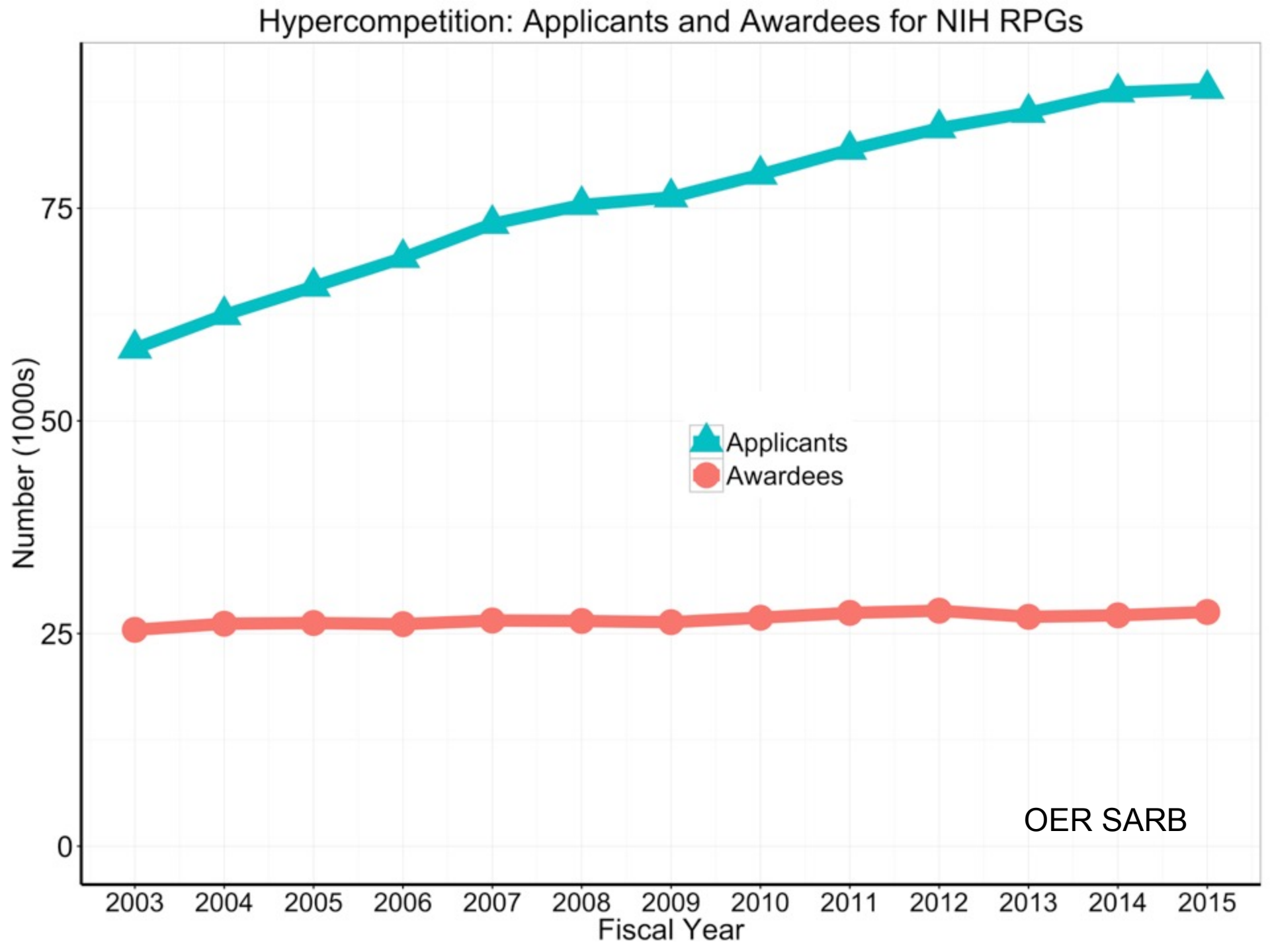
Abstract A cross-campus, cross-career stage and cross-disciplinary series of discussions at a large public university has produced a series of recommendations for addressing the problems confronting the biomedical research community in the US.

DOI: 10.7554/eLife.09305.001

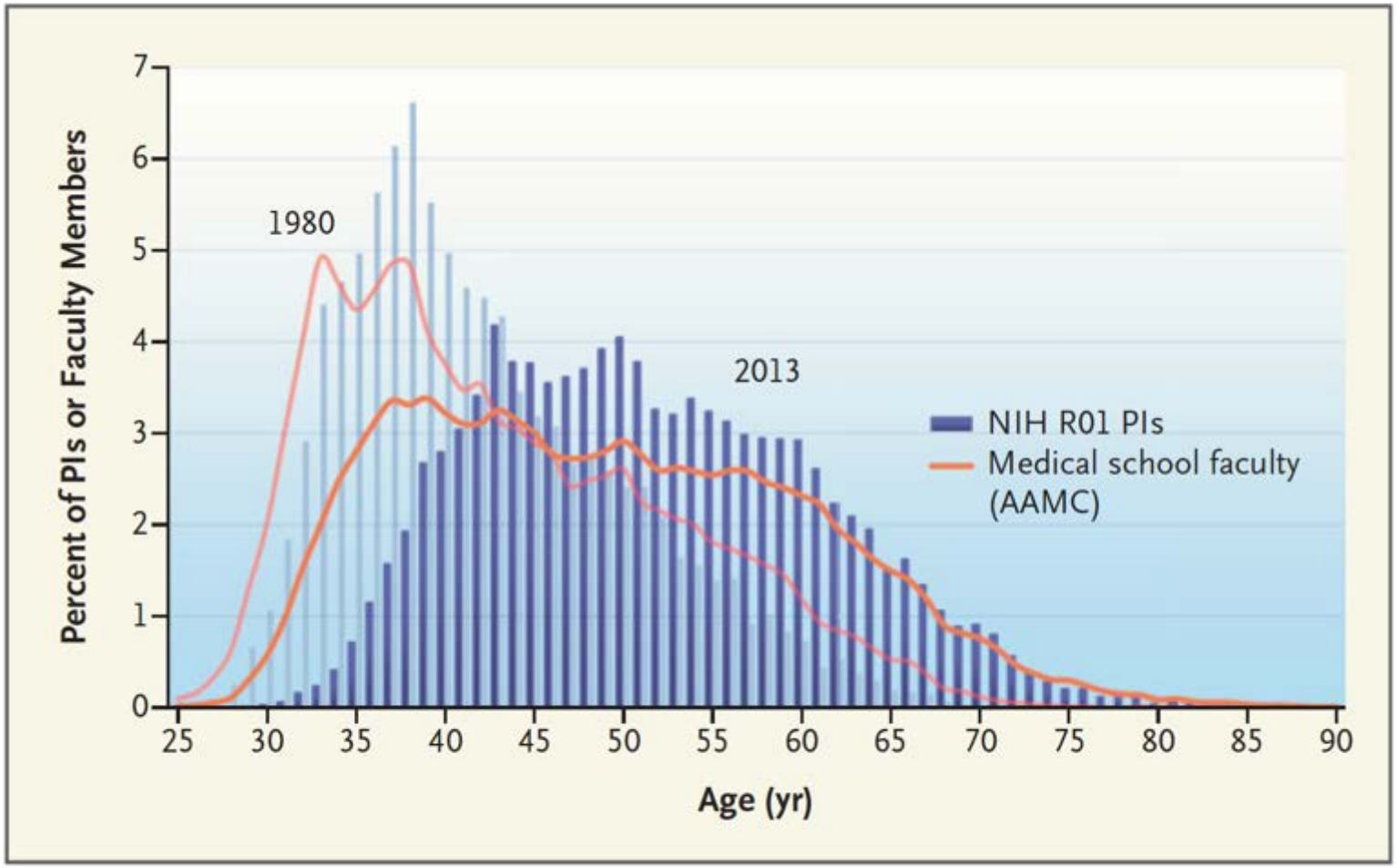
"We identified two **core problems**:

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

Most other issues can be viewed as symptoms."

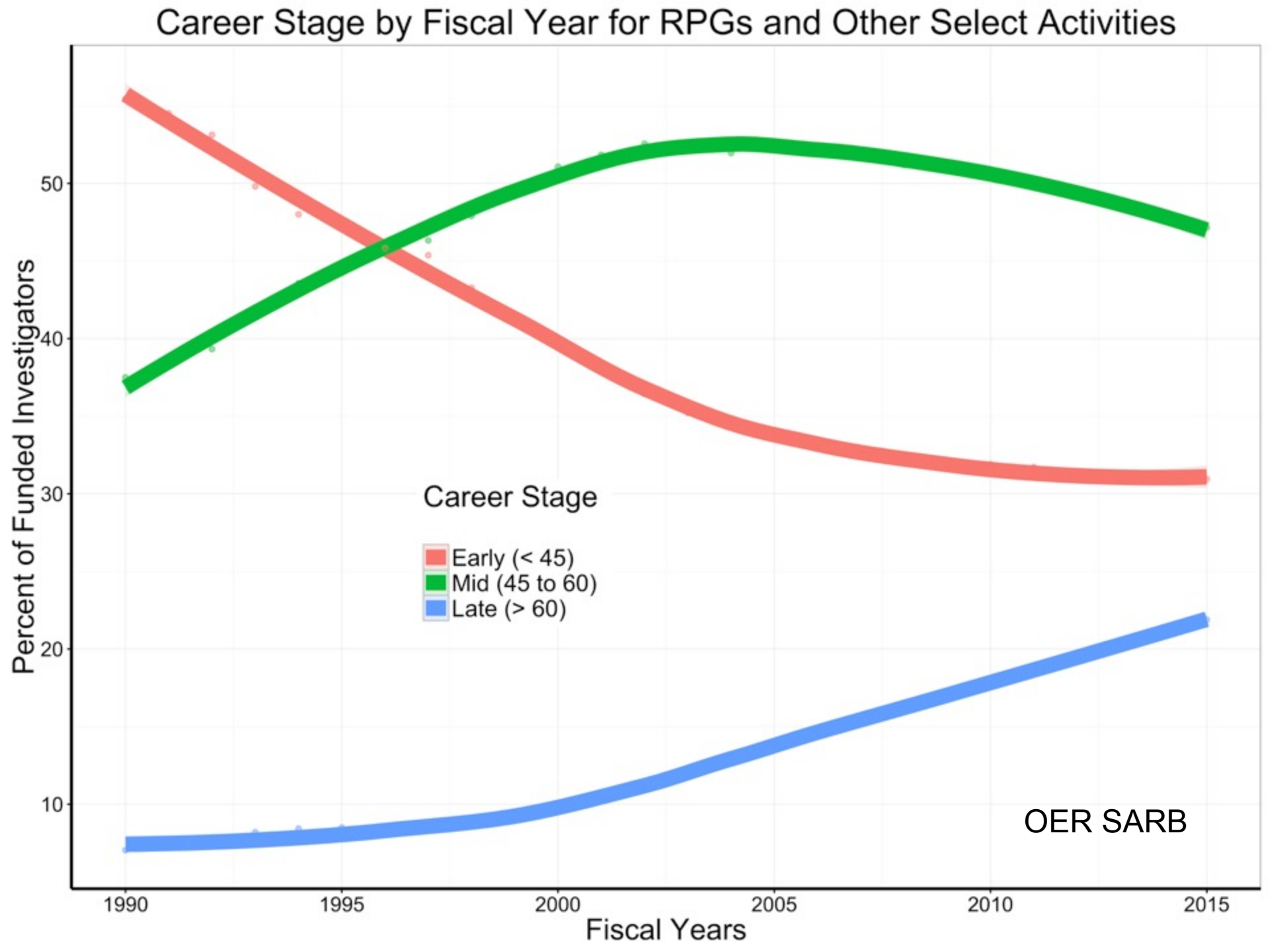

Hypercompetition: Applicants and Awardees for NIH RPGs
Number (1000s)
75
50
25
0
Applicants
Awardees
OER SARB
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Fiscal Year

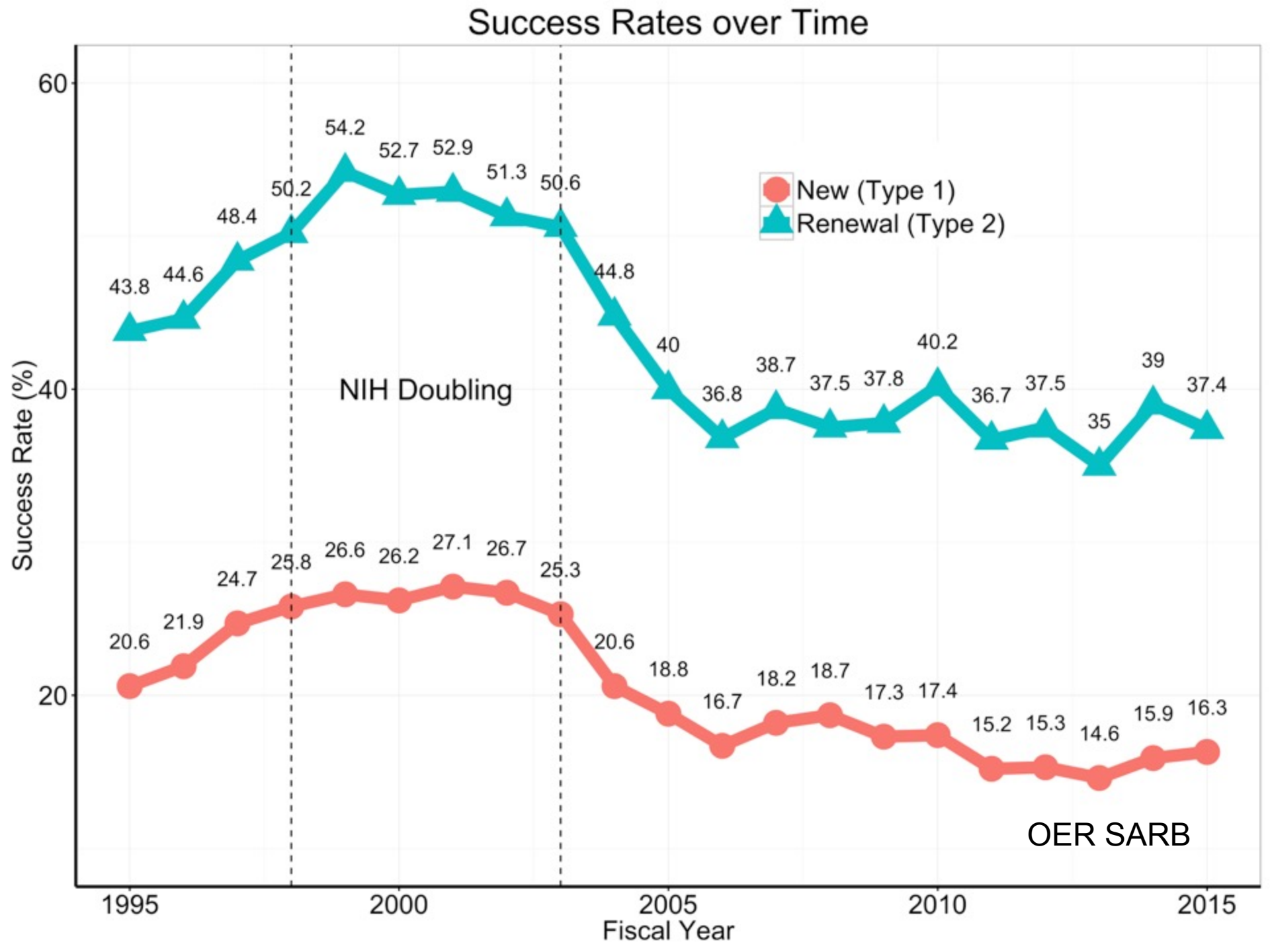
We Also Know That …



Age Distribution of NIH Principal Investigators (PIs) and Medical School Faculty, 1980–2010.

Orwoll E. N Engl J Med 2016;374:2514-7


Career Stage by Fiscal Year for RPGs and Other Select Activities
Percent of Funded Investigators
50
40
30
20
10
1990
1995
2000
2005
2010
2015
Fiscal Years
Career Stage
Early (< 45)
Mid (45 to 60)
Late (> 60)
OER SARB


Success Rates over Time
Success Rate (%)
60
40
20
New (Type 1)
Renewal (Type 2)
NIH Doubling
43.8
44.6
48.4
50.2
54.2
52.7
52.9
51.3
50.6
44.8
40
36.8
38.7
37.5
37.8
40.2
36.7
37.5
35
39
37.4
20.6
21.9
24.7
25.8
26.6
26.2
27.1
26.7
25.3
20.6
18.8
16.7
18.2
18.7
17.3
17.4
15.2
15.3
14.6
15.9
16.3
OER SARB
1995
2000
2005
2010
2015
Fiscal Year

Growing Recognition of the Problem

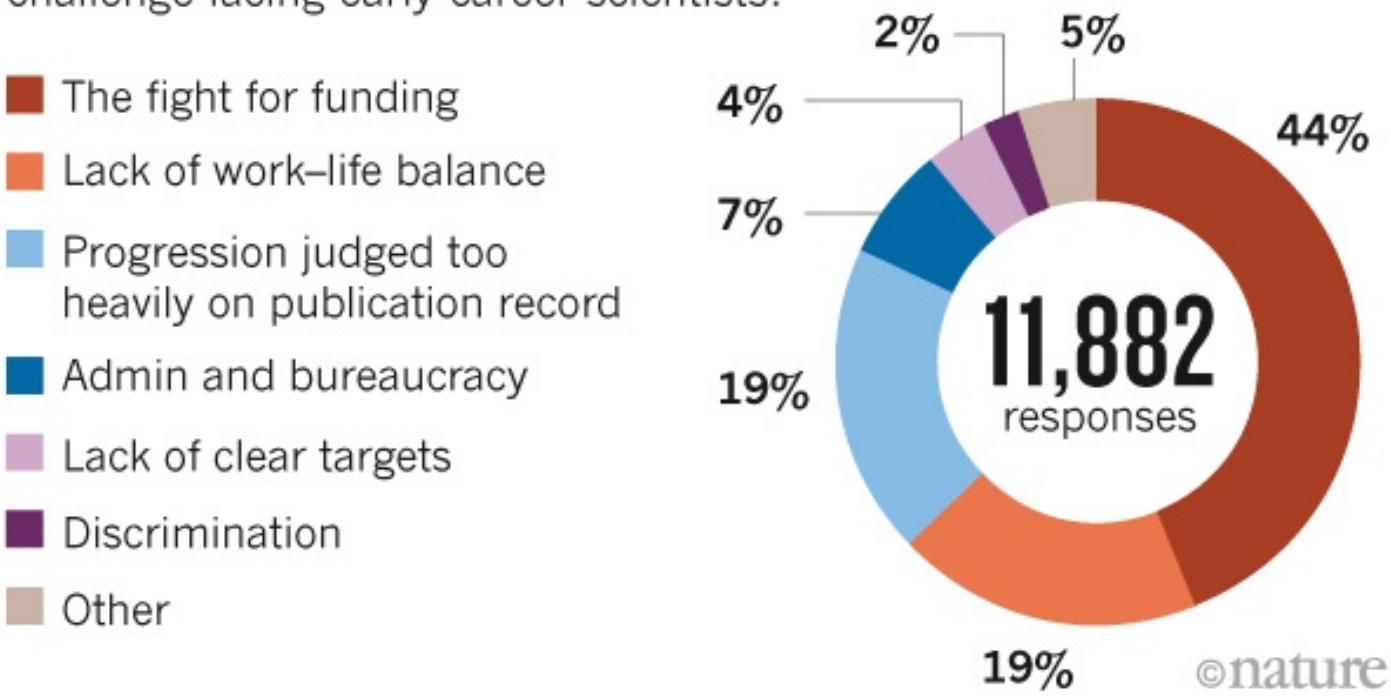
"In the United States, for example, **funding success rates for all age brackets are less than half what they were in 1980**, so researchers have to spend more time seeking funds. That **burden falls most heavily on new faculty members**. Extreme competition means that researchers have little time for anything not directly tied to getting ahead. That **makes them conservative rather than ambitious**."

The “Fight for Funding” Is The Biggest Concern

FIGHT FOR FUNDING

The biggest challenge facing early-career scientists is the struggle to get grants, *Nature*’s readers say.

Poll question:
What do you think is the biggest challenge facing early-career scientists?



Not Just Unstable, but Also Inefficient …

PERSPECTIVE

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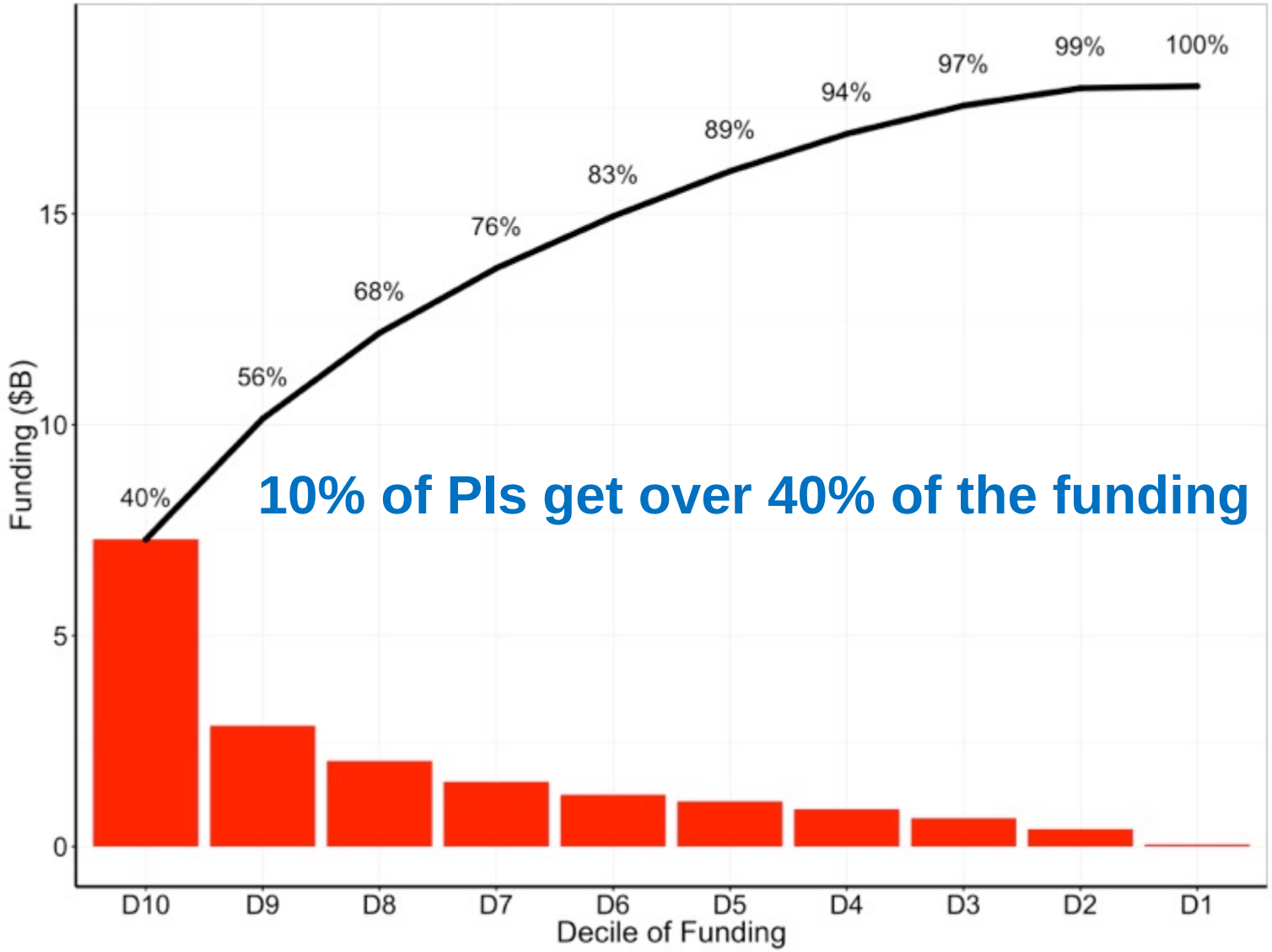
"Agencies **should be sensitive to the total numbers of dollars** granted to individual laboratories…—although **different research activities have different costs**—at some point, **returns per dollar diminish**. We applaud the recent decision by the NIH to examine grant portfolios carefully before increasing direct research support for a laboratory beyond $1M per year."

Alberts B et al. PNAS. 2014;111:5773-7

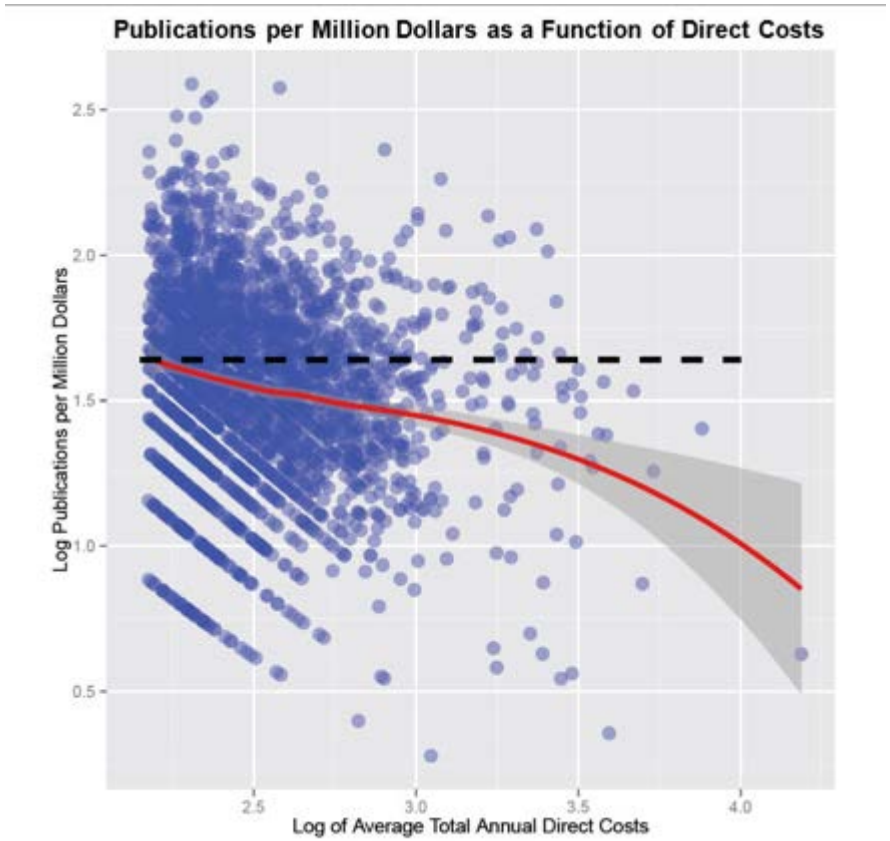
Sensitive to Dollars: Skewed Distribution



10% of PIs get over 40% of the funding

OER SARB

Signs of Inefficiency: Diminishing Returns



NIMH: Mol Psychiatry. 2015 Sep;20(9):1030-6

NHLBI: Circ Res. 2015 Jul 17;117(3):239-43.

Canada: PLoS One. 2013 Jun 19;8(6):e65263.

UK: PeerJ. 2015 Jun 9;3:e989

New drugs: Nat Rev Drug Disc. 2012;11:191-200

Alberts: Cell. 1985;41:337-8

Physics: Comp Sys. 2012;21:183-192

https://loop.nigms.nih.gov/wp-content/uploads/2016/07/fig4_bg.jpg

Tools to Measure Input and Output

- Input
  - **Dollars, effort & grant count – problematic**
  - New tool: “Research Commitment Index”
- Output
  - Relative Citation Ratio
  - Others: mentorship, patents, guidelines
  - “Cure Networks”

Input: What About Number of Grants?

- Couldn't we simply count grants?
- Problems:
  - R01 ≠ R03 ≠ R21
  - R01 ≠ P01
  - R01 ≠ U10
  - Etc…

Tools to Measure Input and Output

- Input
  - Dollars, effort & grant count – problematic
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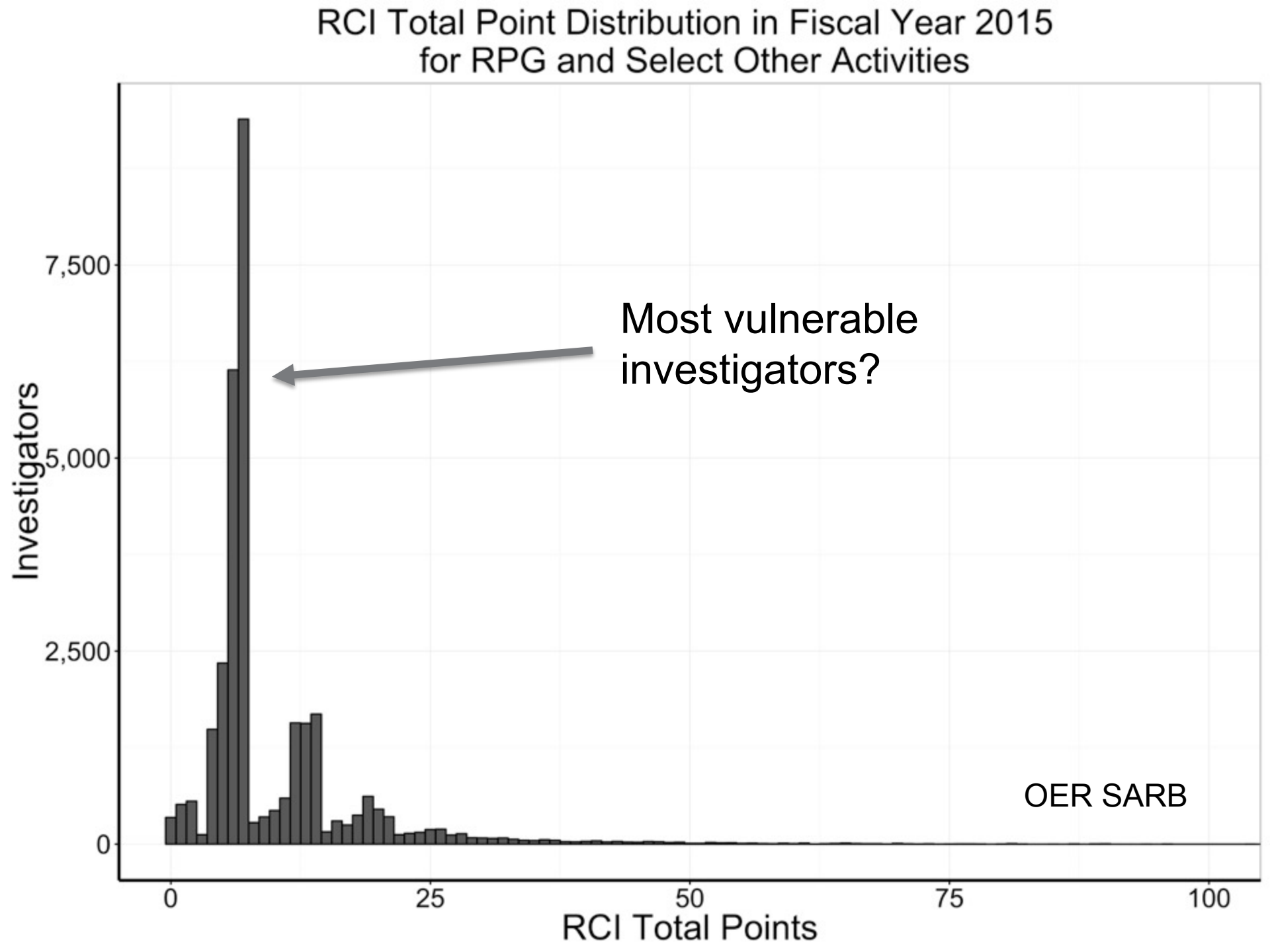
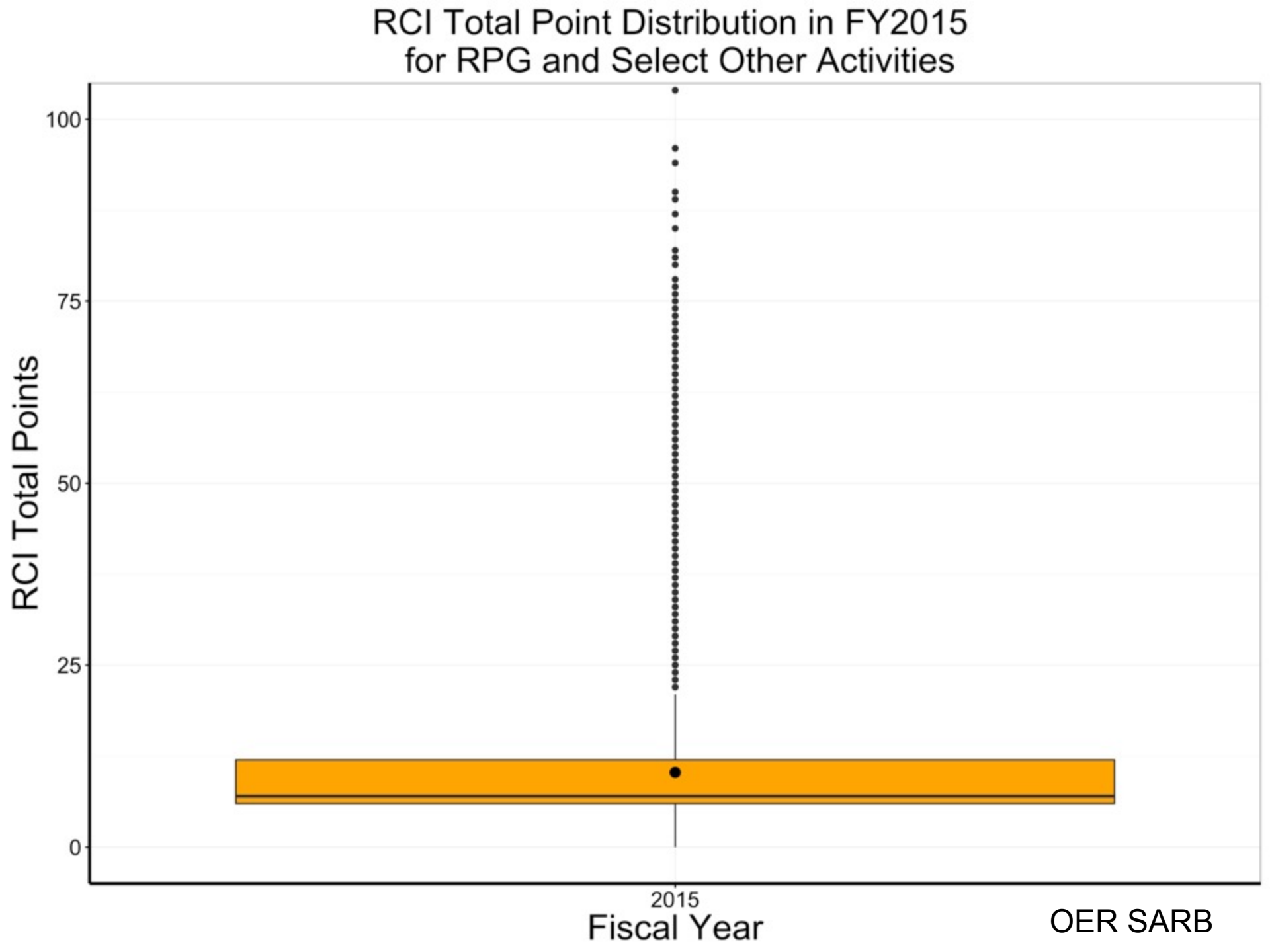
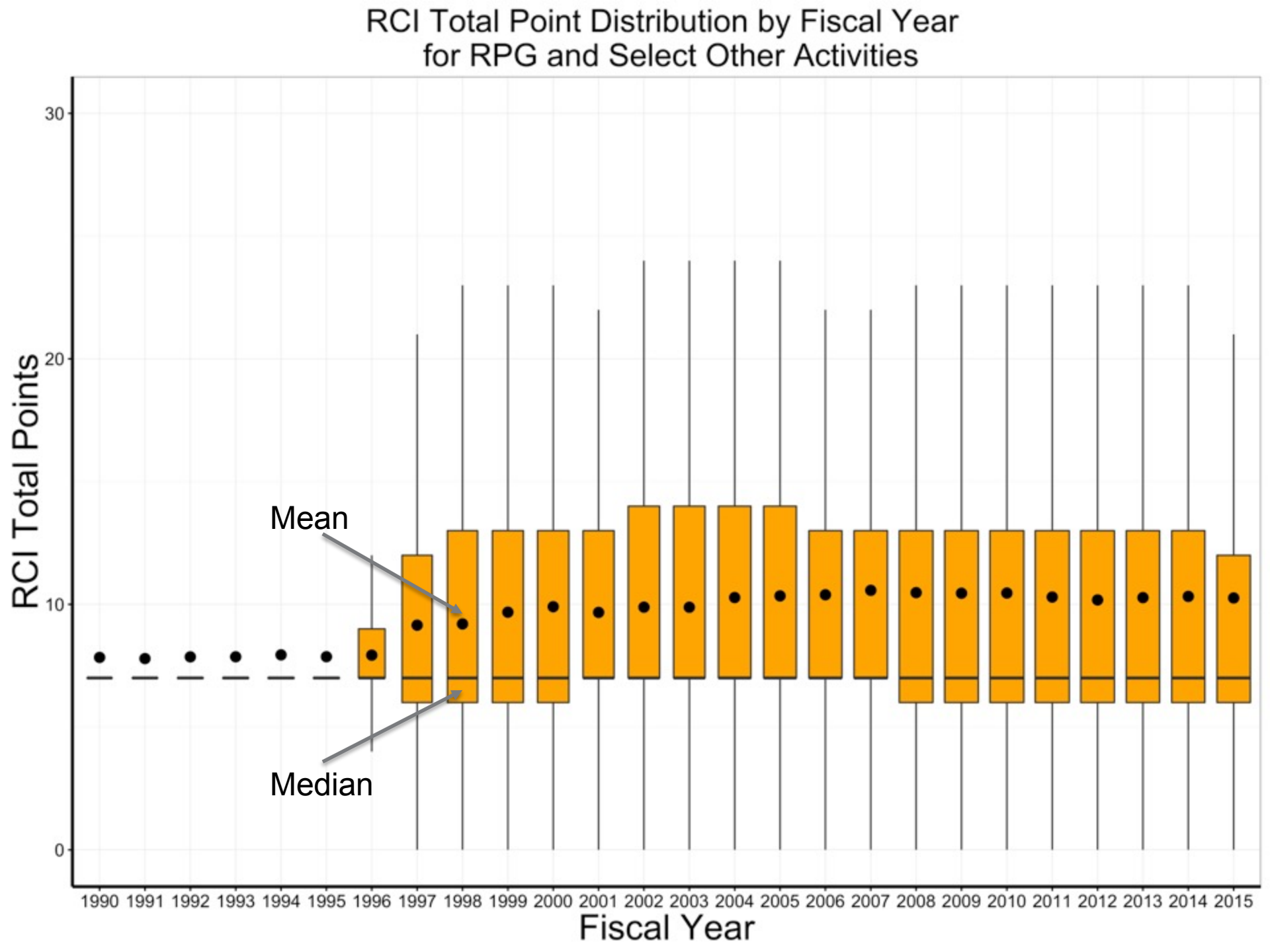
- Output
  - Relative Citation Ratio
  - Others: mentorship, patents, guidelines
  - "Cure Networks"

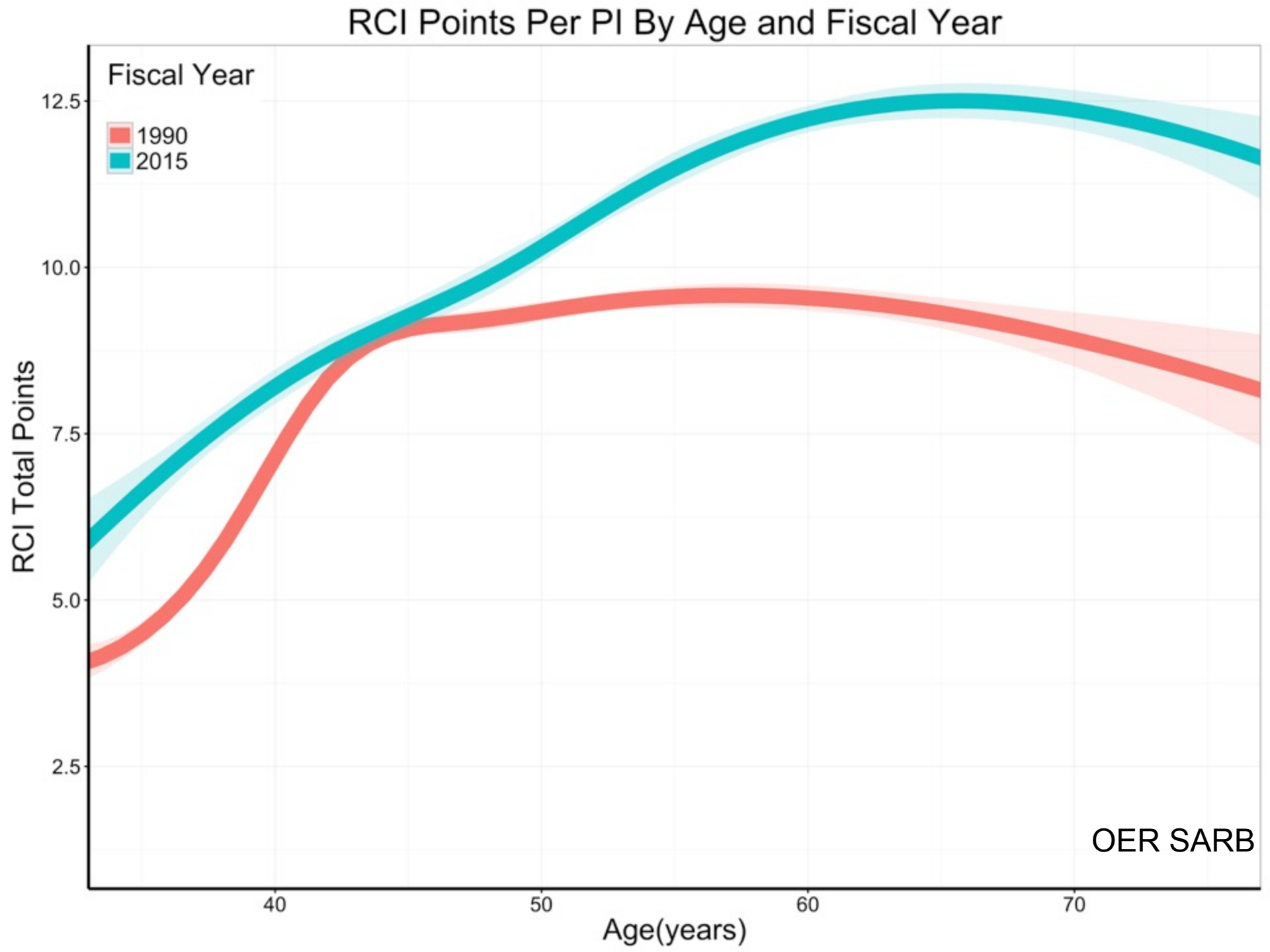
Research Commitment Index (RCI)

- Measure of PI's committed bandwidth
- Not simply measure of dollars
- Benchmarked to R01 (7 points)
  - R03, R21 less
  - P50, U54 (PI) more
- Effectively, a modified grant count


RCI Total Point Distribution in Fiscal Year 2015
for RPG and Select Other Activities
Investigators
7,500
5,000
2,500
0
0
25
50
75
100
RCI Total Points
Most vulnerable investigators?
OER SARB


RCI Total Point Distribution in FY2015
for RPG and Select Other Activities
RCI Total Points
100
75
50
25
0
2015
Fiscal Year
OER SARB


RCI Total Point Distribution by Fiscal Year
for RPG and Select Other Activities
RCI Total Points
30
20
10
0
Mean
Median
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Fiscal Year


RCI Points Per PI By Age and Fiscal Year
Fiscal Year
1990
2015
12.5
10.0
7.5
5.0
2.5
RCI Total Points
40
50
60
70
Age(years)
OER SARB

Tools to Measure Input and Output

- Input
  - Dollars, effort & grant count – problematic
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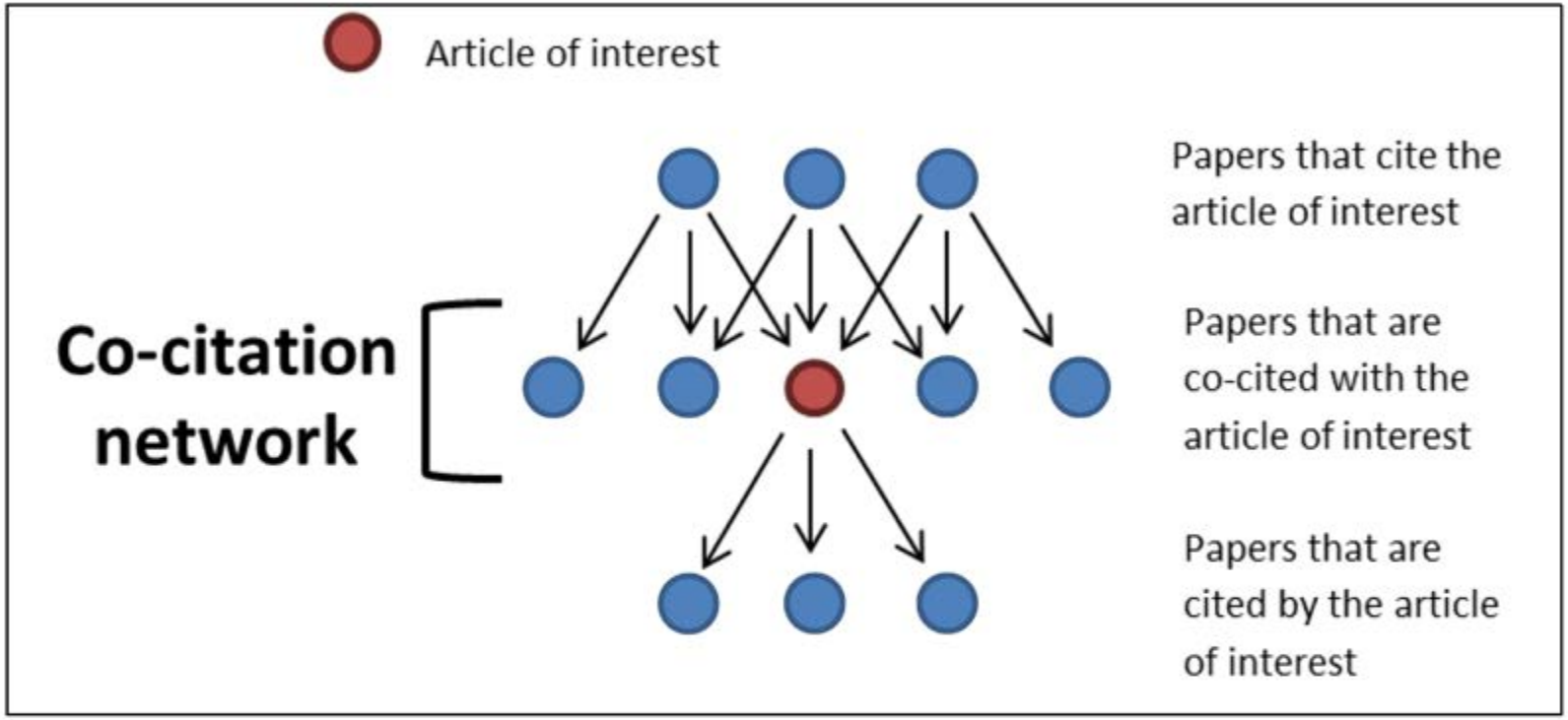
  - **Relative Citation Ratio**
  - Others: mentorship, patents, guidelines
  - “Cure Networks”

Relative Citation Ratio

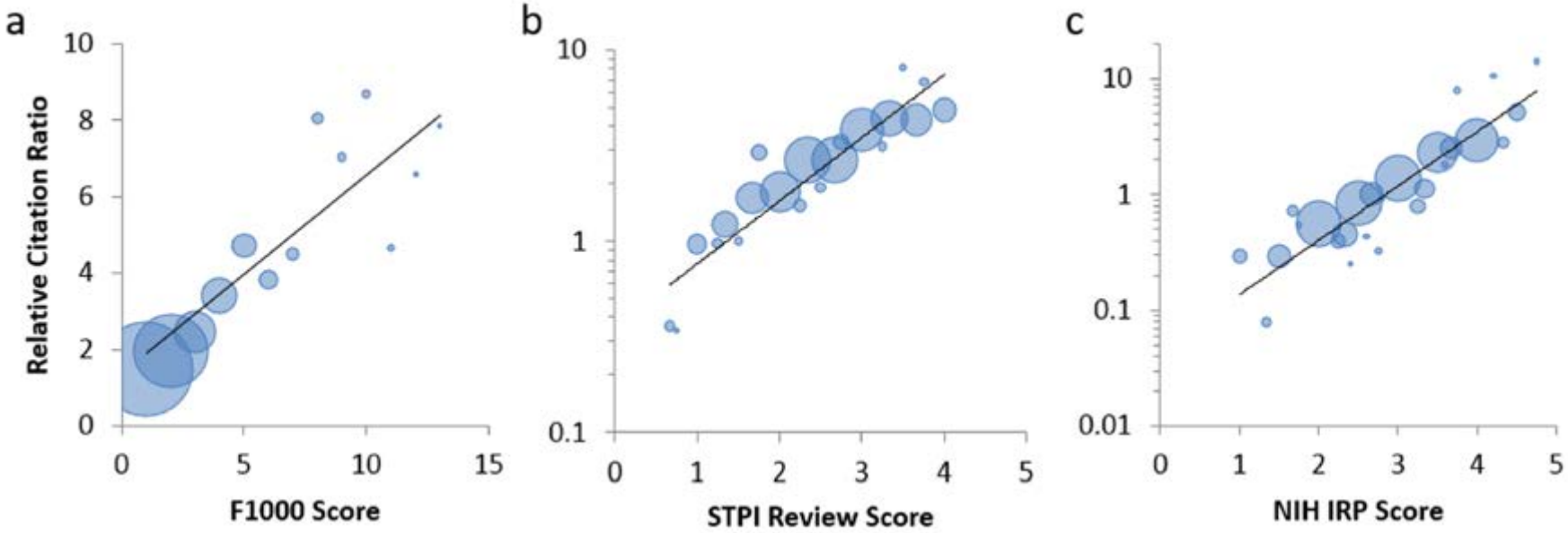


0 = never cited
1 = average
2 = twice the average
>20 = exceptionally highly cited

NIH Office of Portfolio Analysis
PLoS Biology (September 6, 2016)

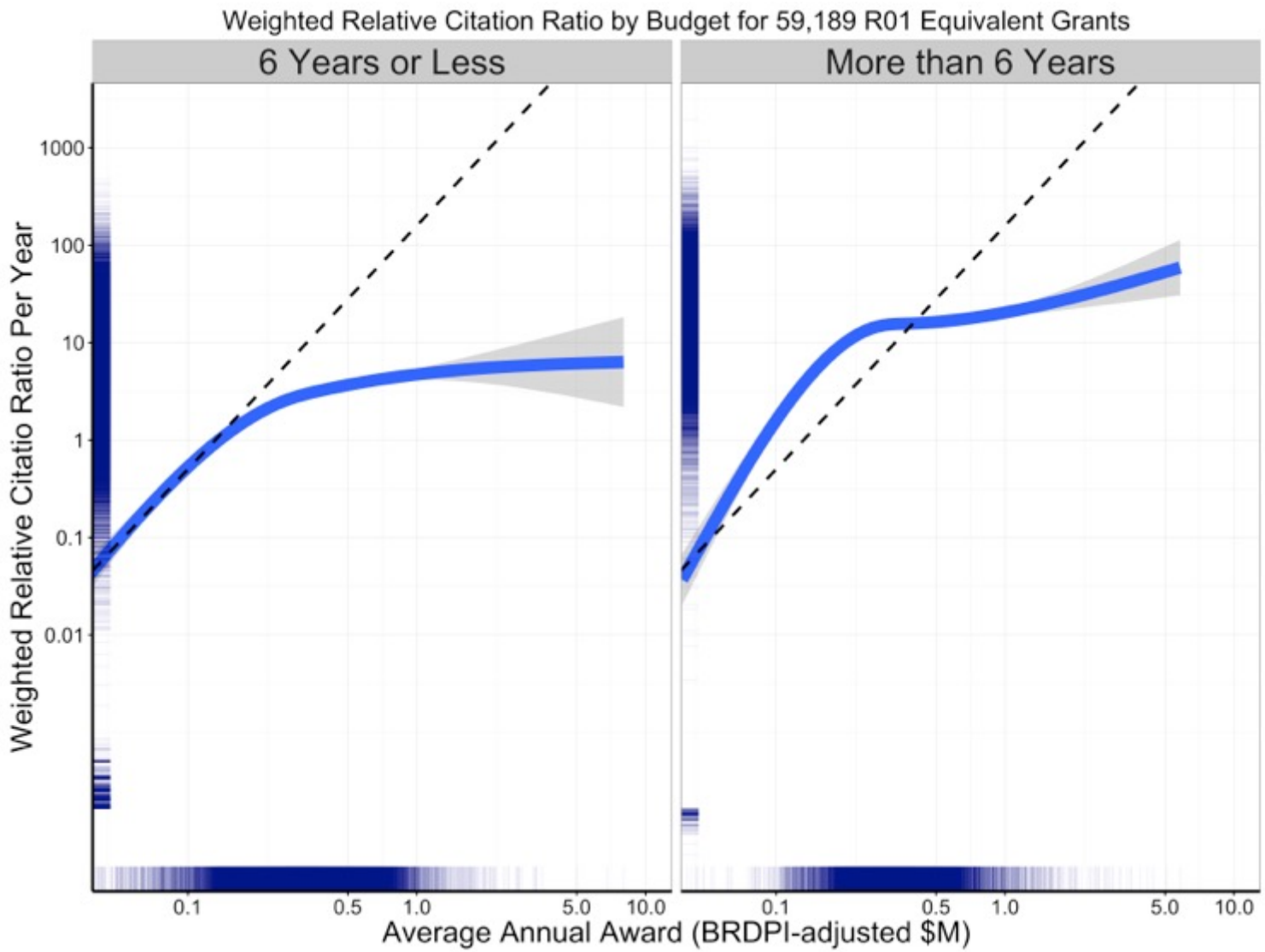
How Do We Know Whether It Means Anything?

2193 R01 papers | 430 HHMI/NIH papers | 290 R01 papers

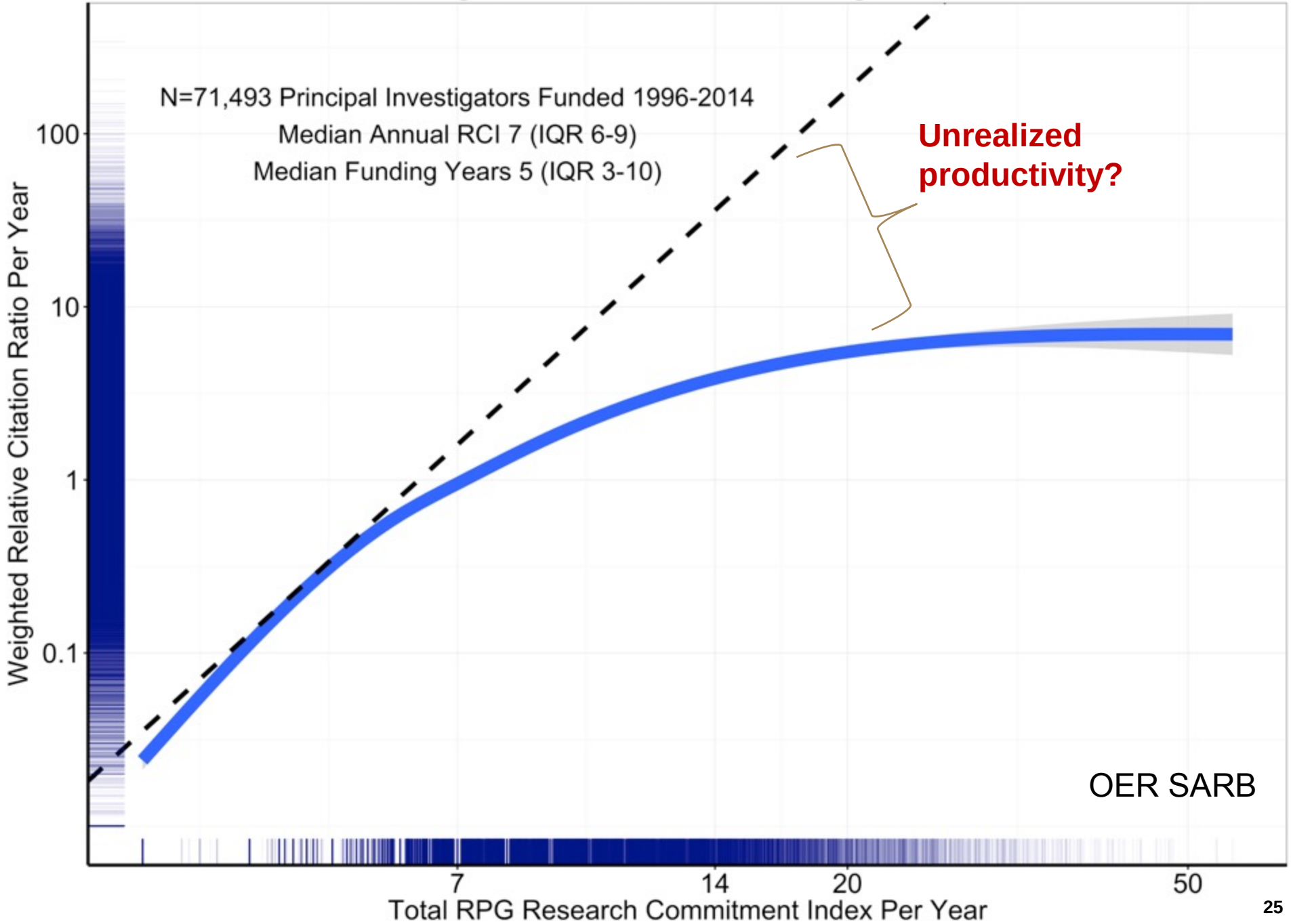


NIH Office of Portfolio Analysis
PLoS Biology (September 6, 2016)

Diminishing Returns Across NIH



Strong Evidence of Diminishing Returns



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- Output
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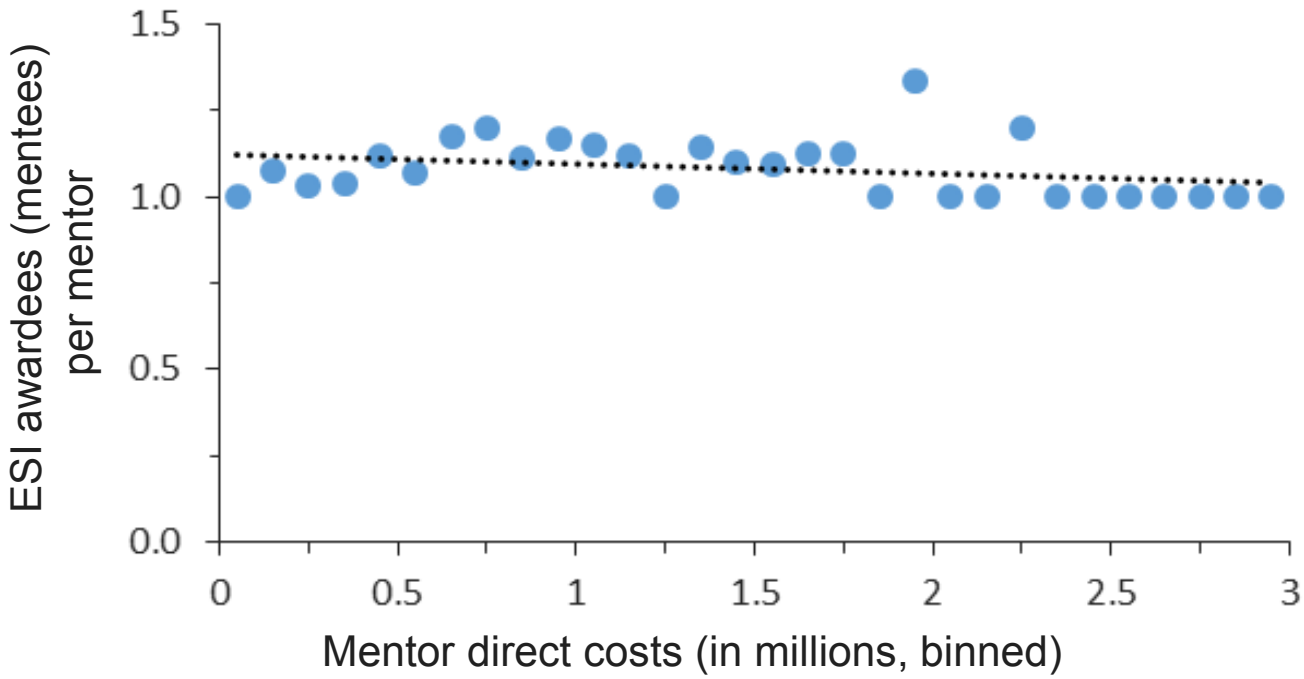
Funding Not Correlated with Mentorship

No relationship between funding level of mentors and the number of ESI awardees that they train

ESI RPG awardees per mentor versus
the FY16 direct costs of their RPG-funded mentors



Thanks to George Santangelo and OPA

Tools to Measure Input and Output

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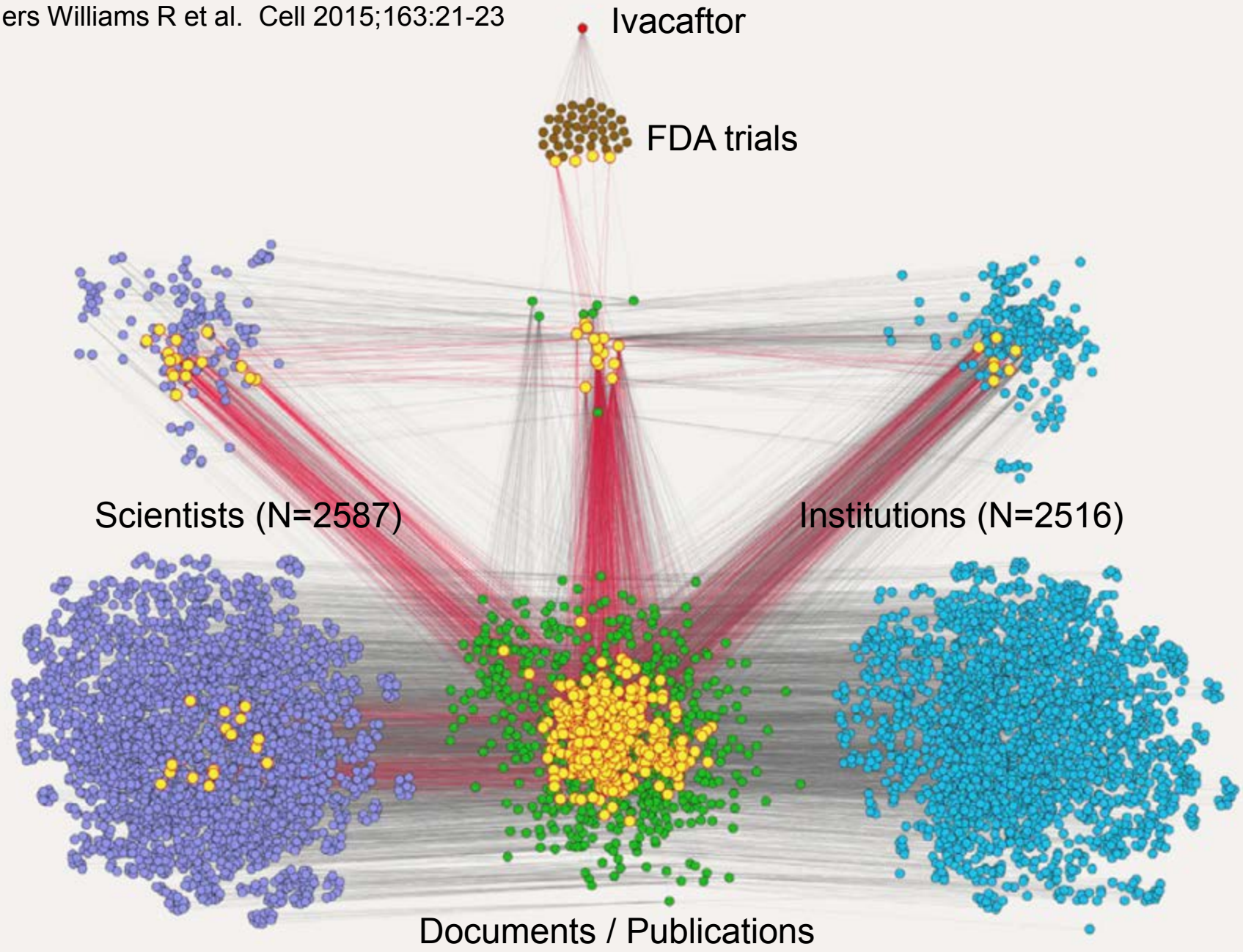
B

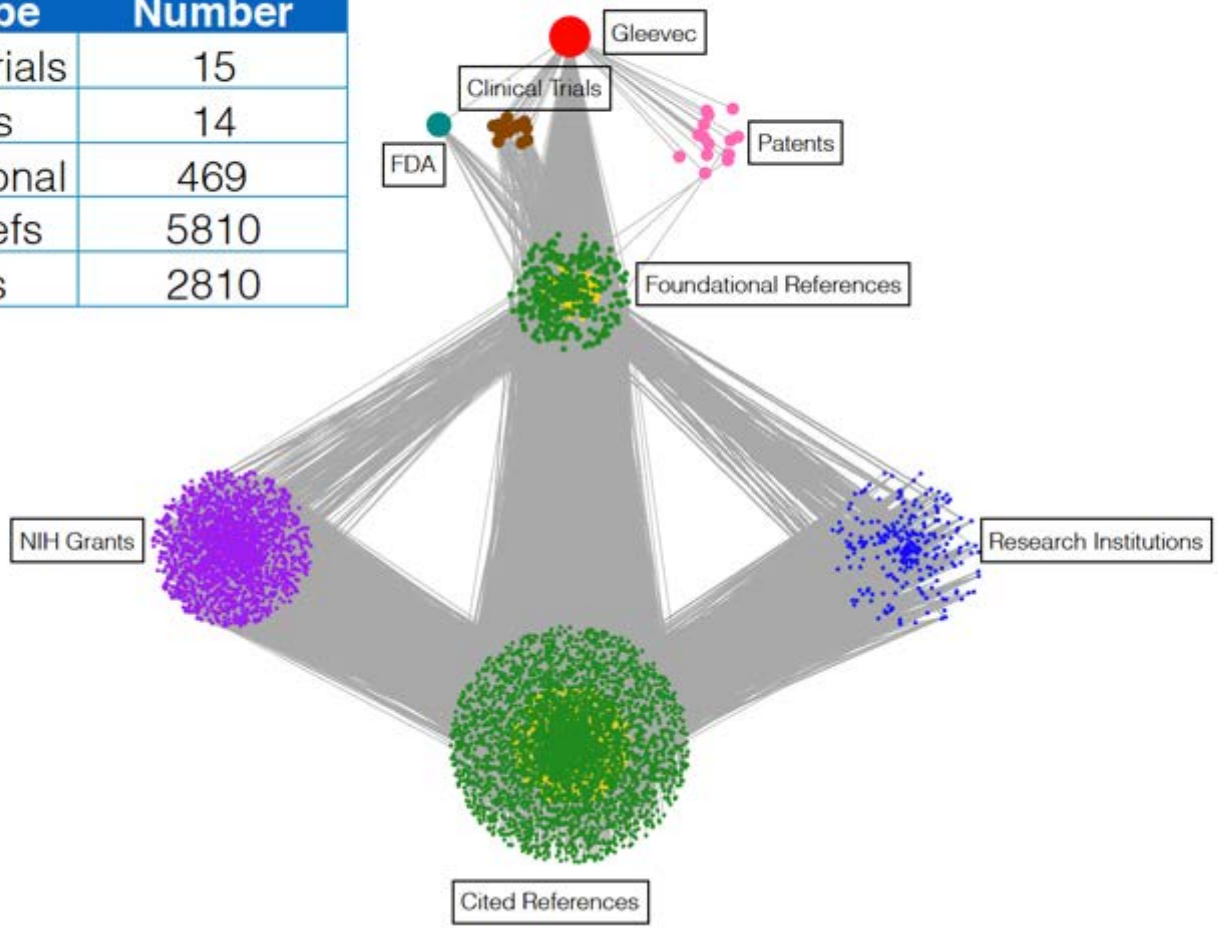
Sanders Williams R et al. Cell 2015;163:21-23



A Data-Based Outcome Story

Gleevec

Nodetype	Number
Clinical Trials	15
Patents	14
Foundational	469
Gen2 Refs	5810
Grants	2810



Thanks Jim Onken, Brian Haugan, George Chacko, Shixin Jiang, Samet Keserci, Alex Pico, and Lindsay Wan

Putting It All Together

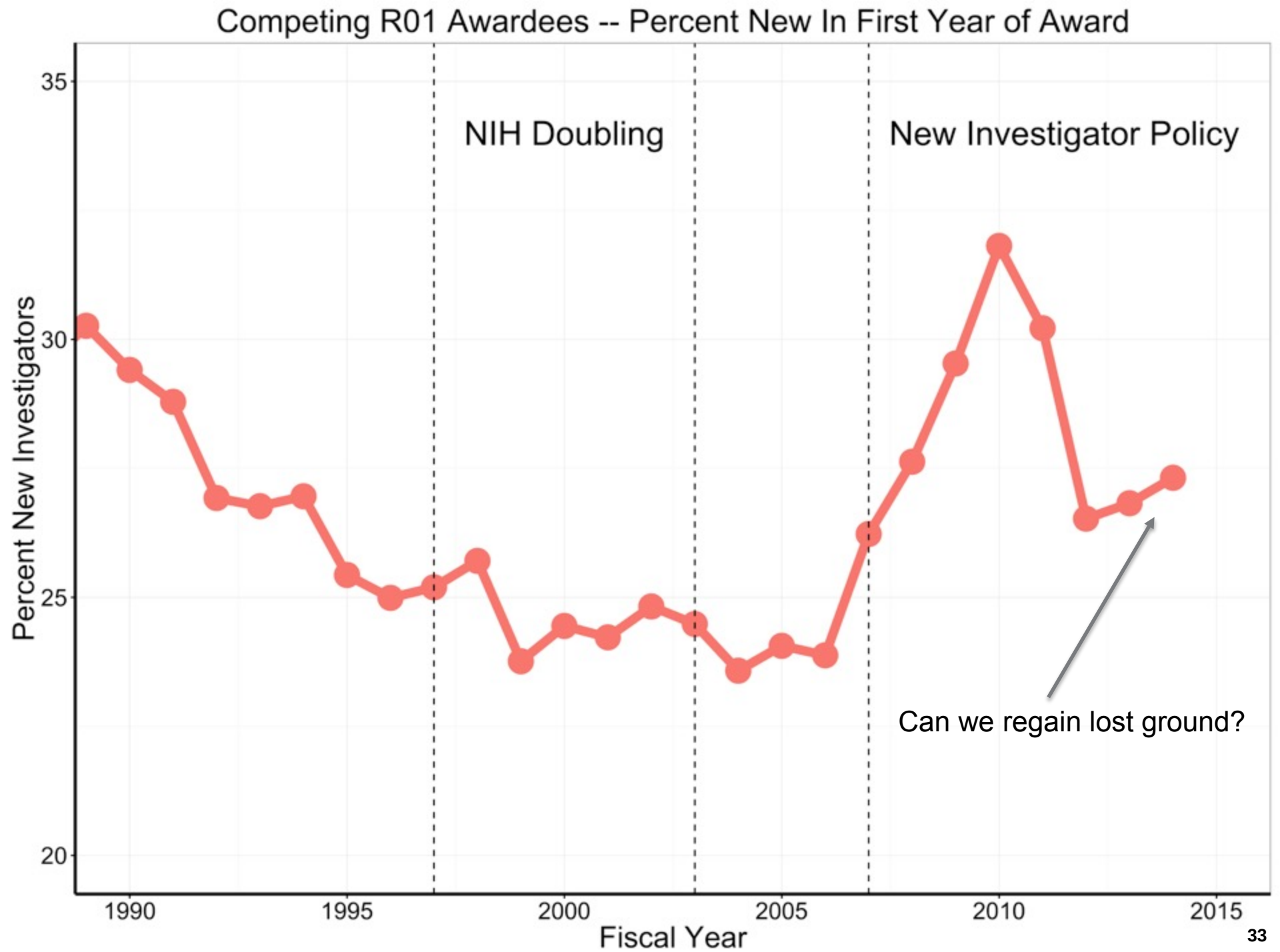
- Input
  - Focus on investigators as well as grants
    - New and **mid-career** investigators
  - Other tools: total budgets, RCI
- Output
  - Diminishing returns
    - Growing evidence within NIH system
    - Opportunities to fund more investigators

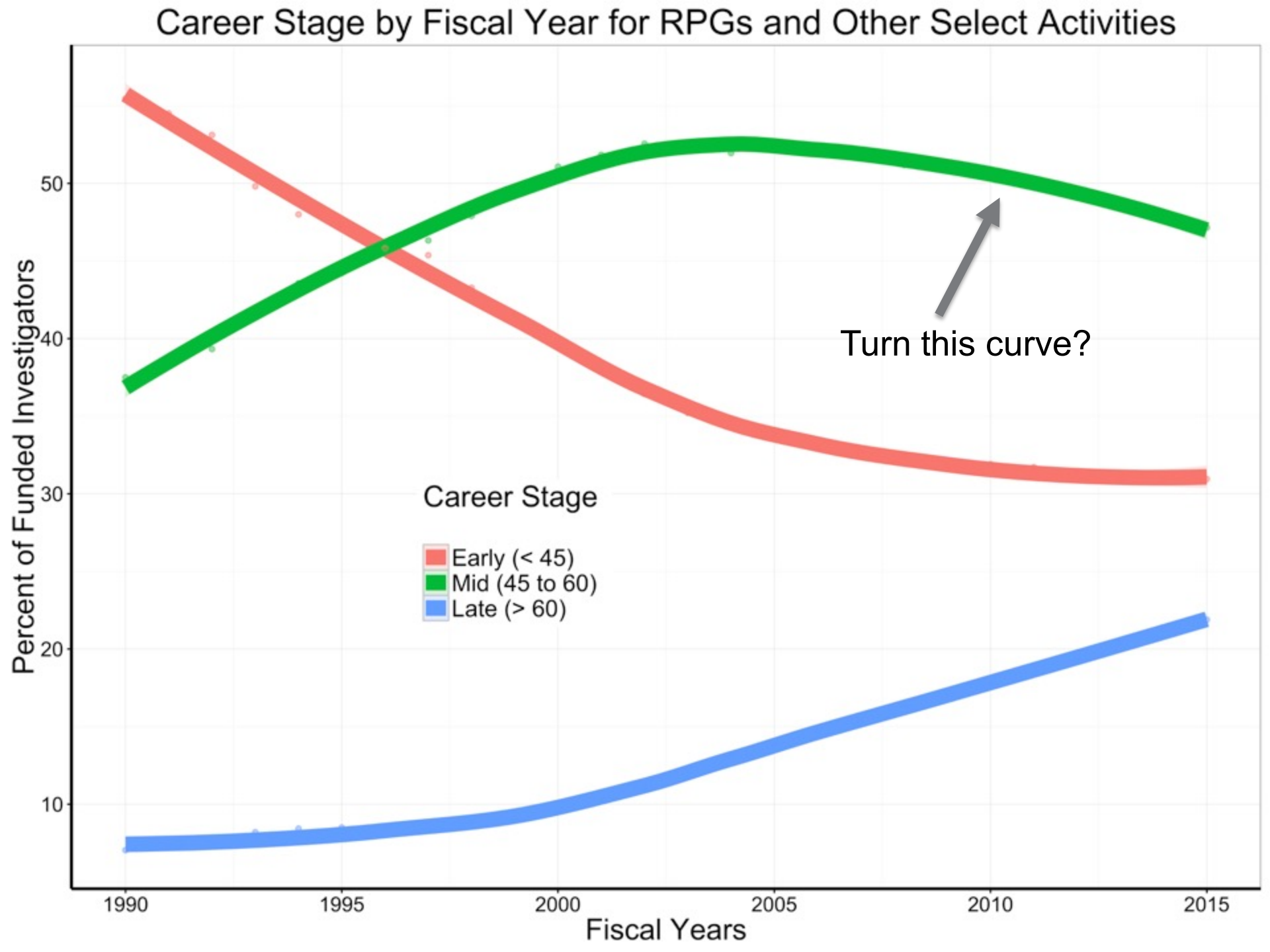
Prior Policy Lever: New Investigators

"New investigators are the innovators of the future - they bring fresh ideas and technologies to existing biomedical research problems, and they pioneer new areas of investigation. Entry of new investigators into the ranks of independent, NIH-funded researchers is essential to the health of our country's biomedical research enterprise."

Sally Rockey, PhD

http://grants.nih.gov/policy/new_investigators/history.htm


Competing R01 Awardees -- Percent New In First Year of Award
NIH Doubling
New Investigator Policy
Can we regain lost ground?
Percent New Investigators
35
30
25
20
1990
1995
2000
2005
2010
2015
Fiscal Year


Career Stage by Fiscal Year for RPGs and Other Select Activities
Percent of Funded Investigators
50
40
30
20
10
1990
1995
2000
2005
2010
2015
Fiscal Years
Turn this curve?
Career Stage
Early (< 45)
Mid (45 to 60)
Late (> 60)

Closing Thoughts

- Unstable system with hyper-competition
- Hurting early- & mid-career faculty most
- Inefficient with diminishing returns
- Possible to fund more investigators
  - Especially early- and **mid-career**
- New tools to measure input, output

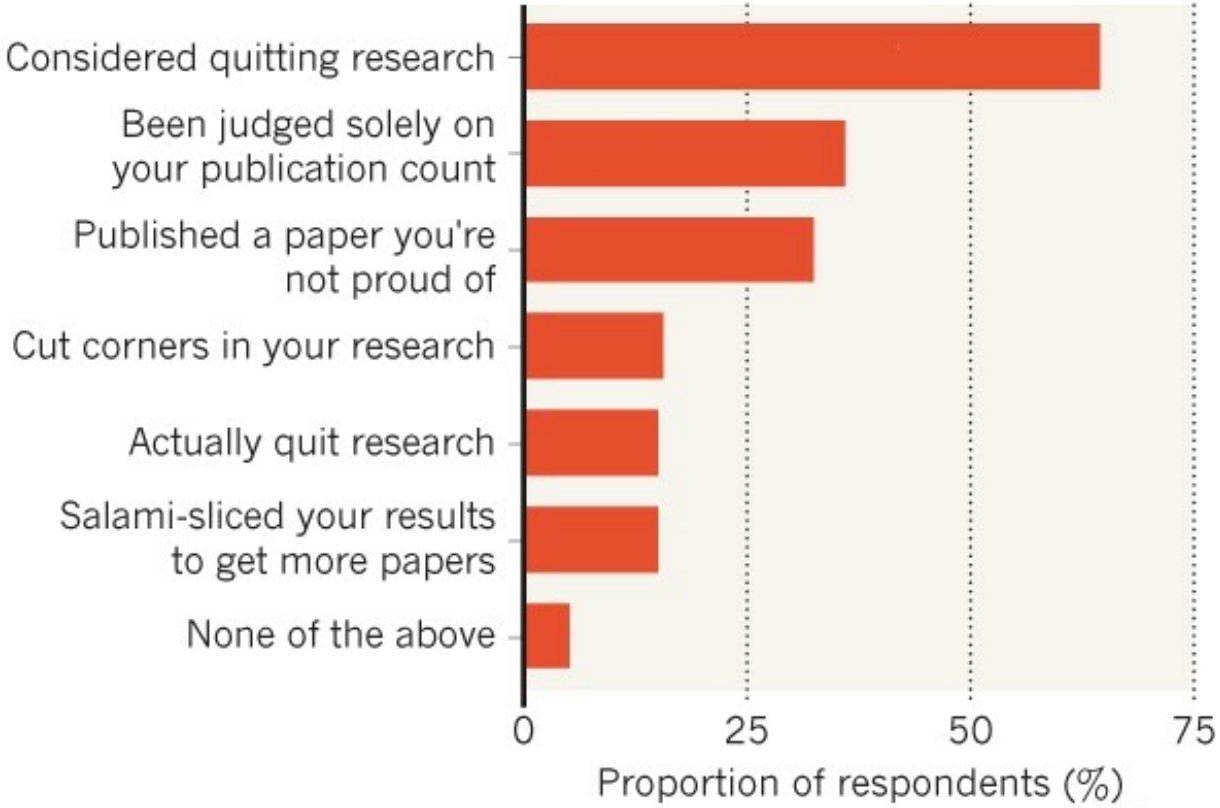
Appendix Material

The Mood Outside Is Grim

SHOULD I QUIT?

Almost two-thirds of *Nature*'s readers say they have considered quitting research; 15% have actually quit.

Poll question:
Have the challenges of research ever meant that you have ... (8,820 responses)



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Numbers of Researchers: A Different Metric

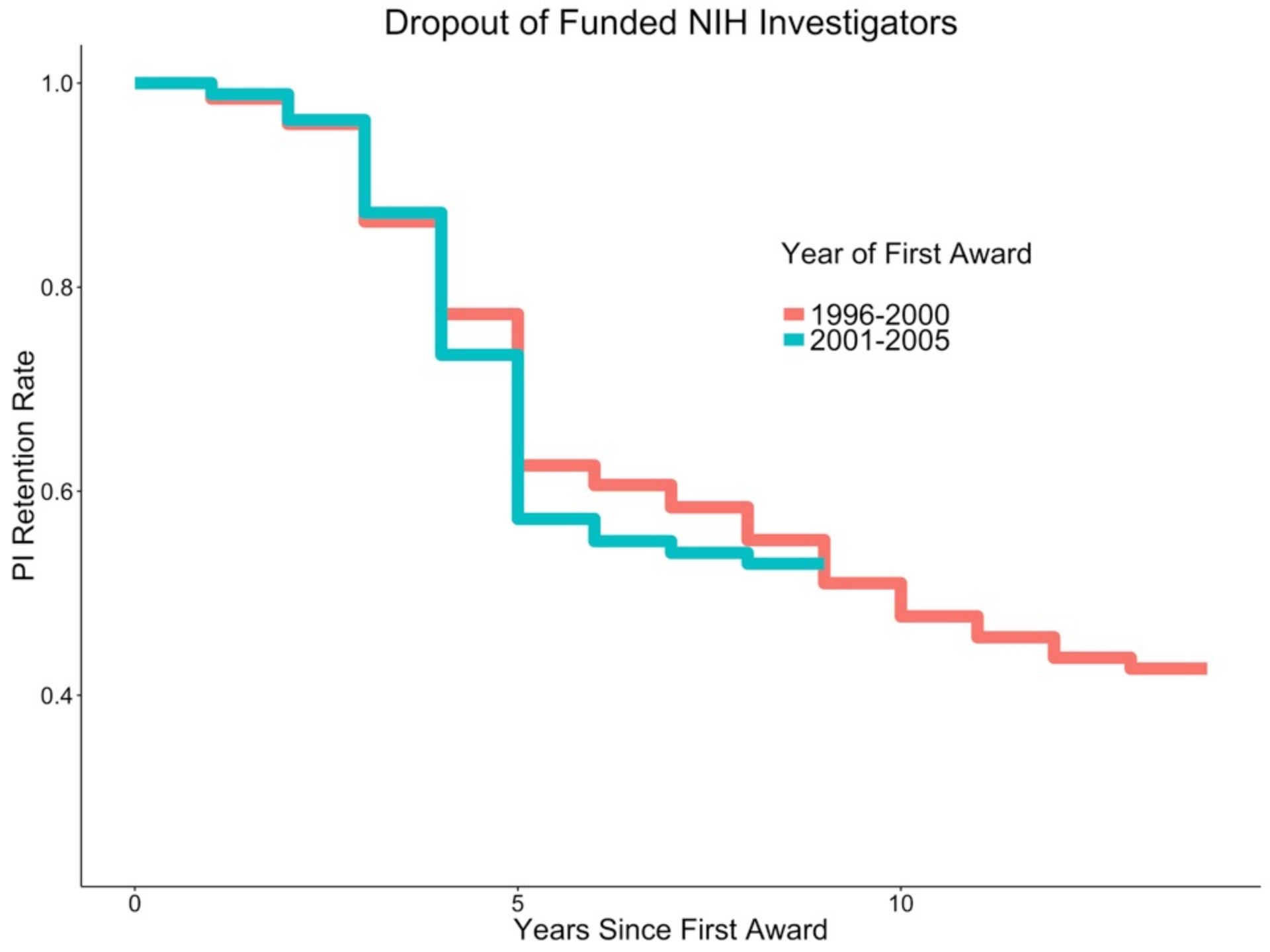
Maximizing the return on taxpayers' investments in fundamental biomedical research

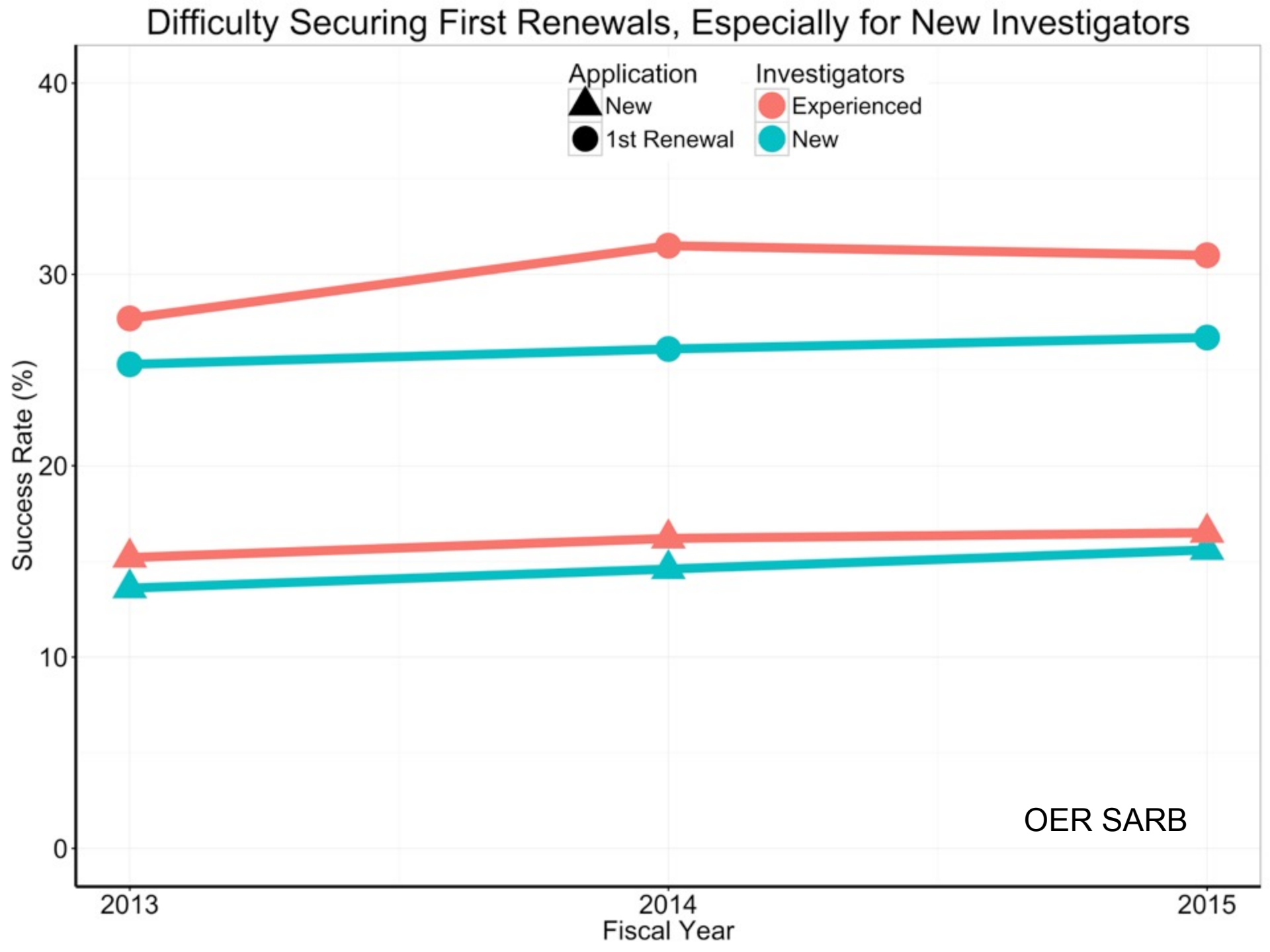
Jon R. Lorsch
National Institute of General Medical Sciences, National Institutes of Health, Bethesda, MD 20892

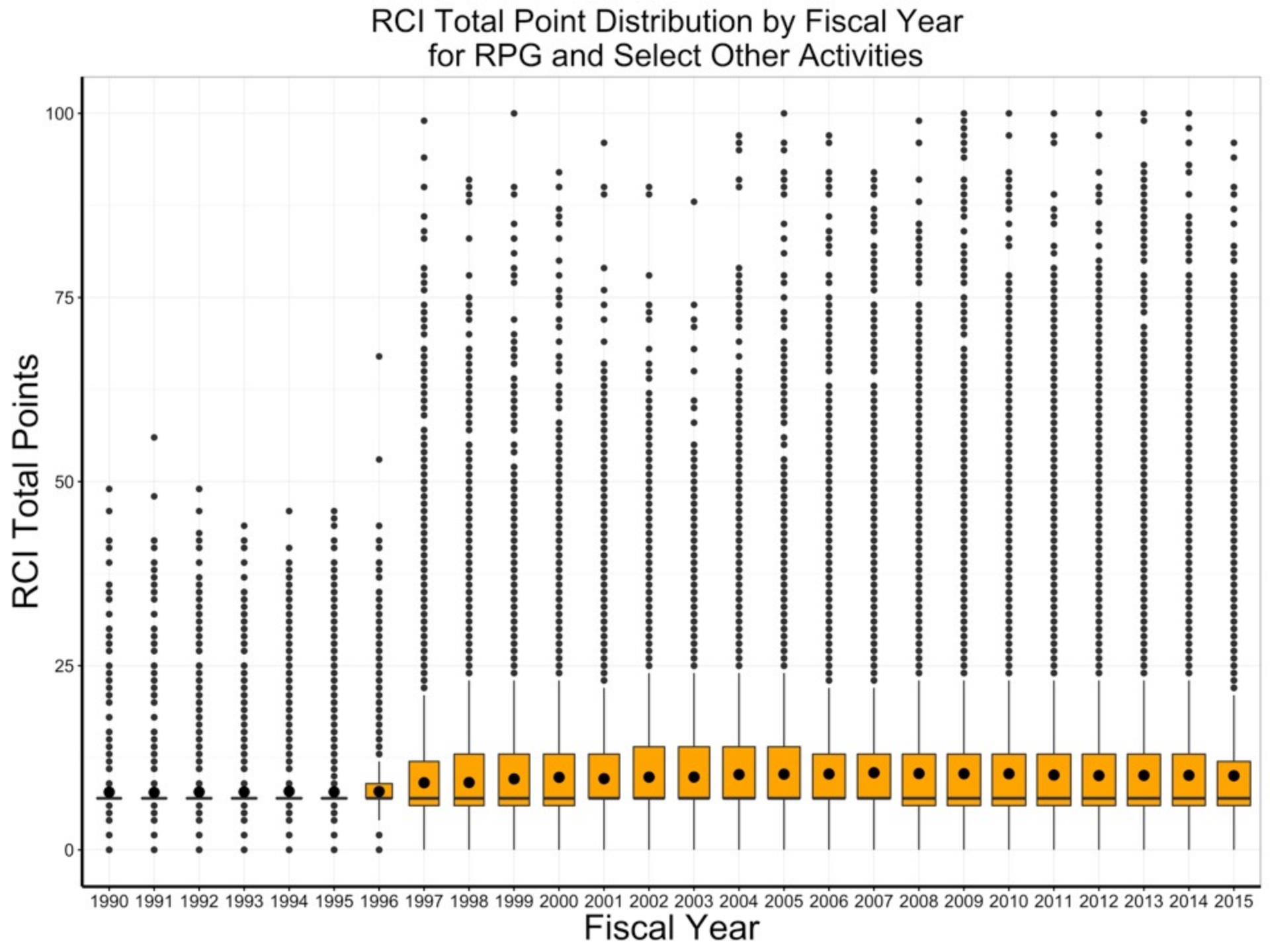
Changing our funding metric

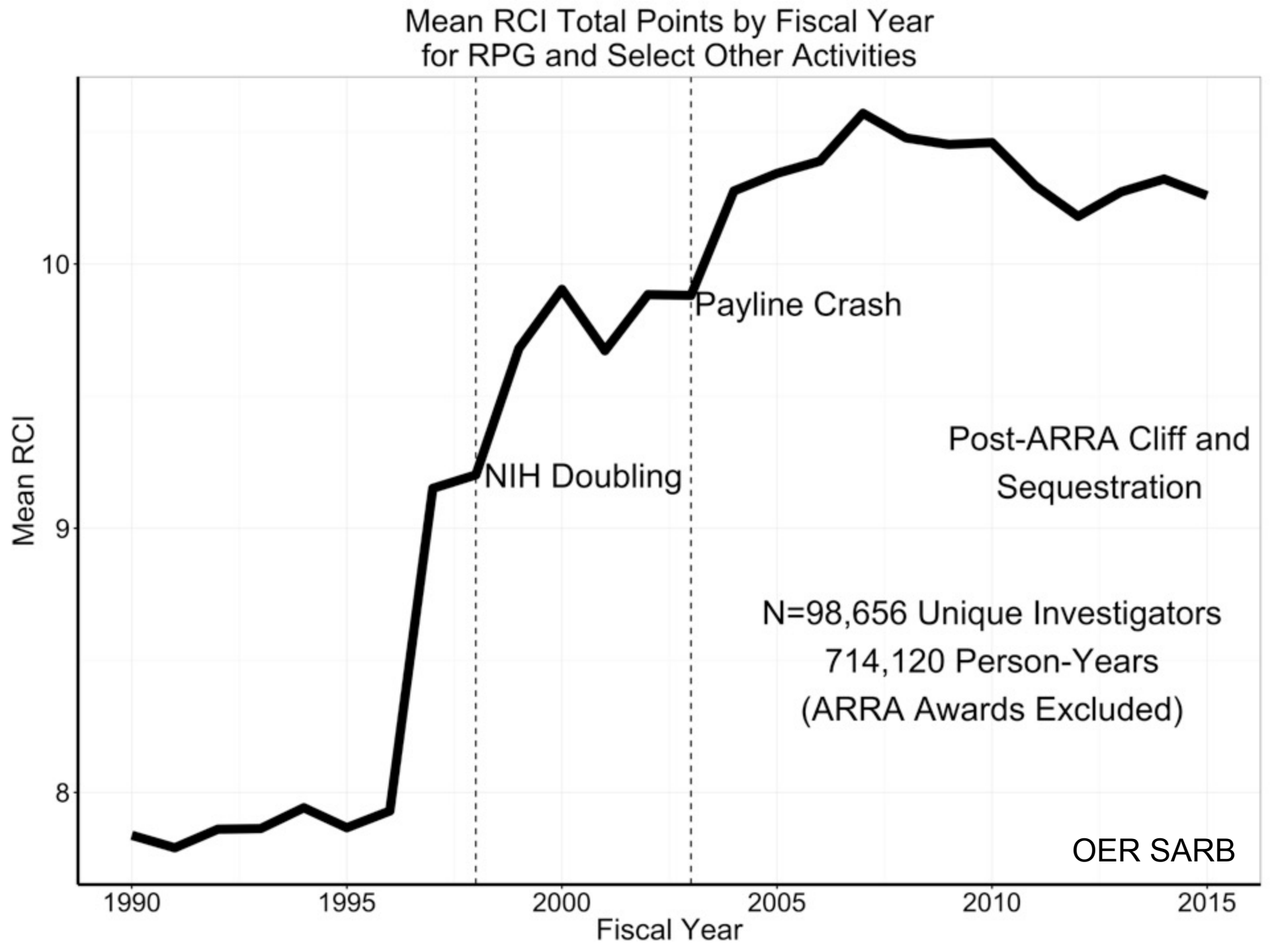
"A question that at first glance may seem trivial but is, I believe, a significant one is whether our key metric for how… we invest in … research should be the number of grants we award or ***the number of investigators we support***."

Lorsch JR. Mol Biol Cell 2015;26:1578-82

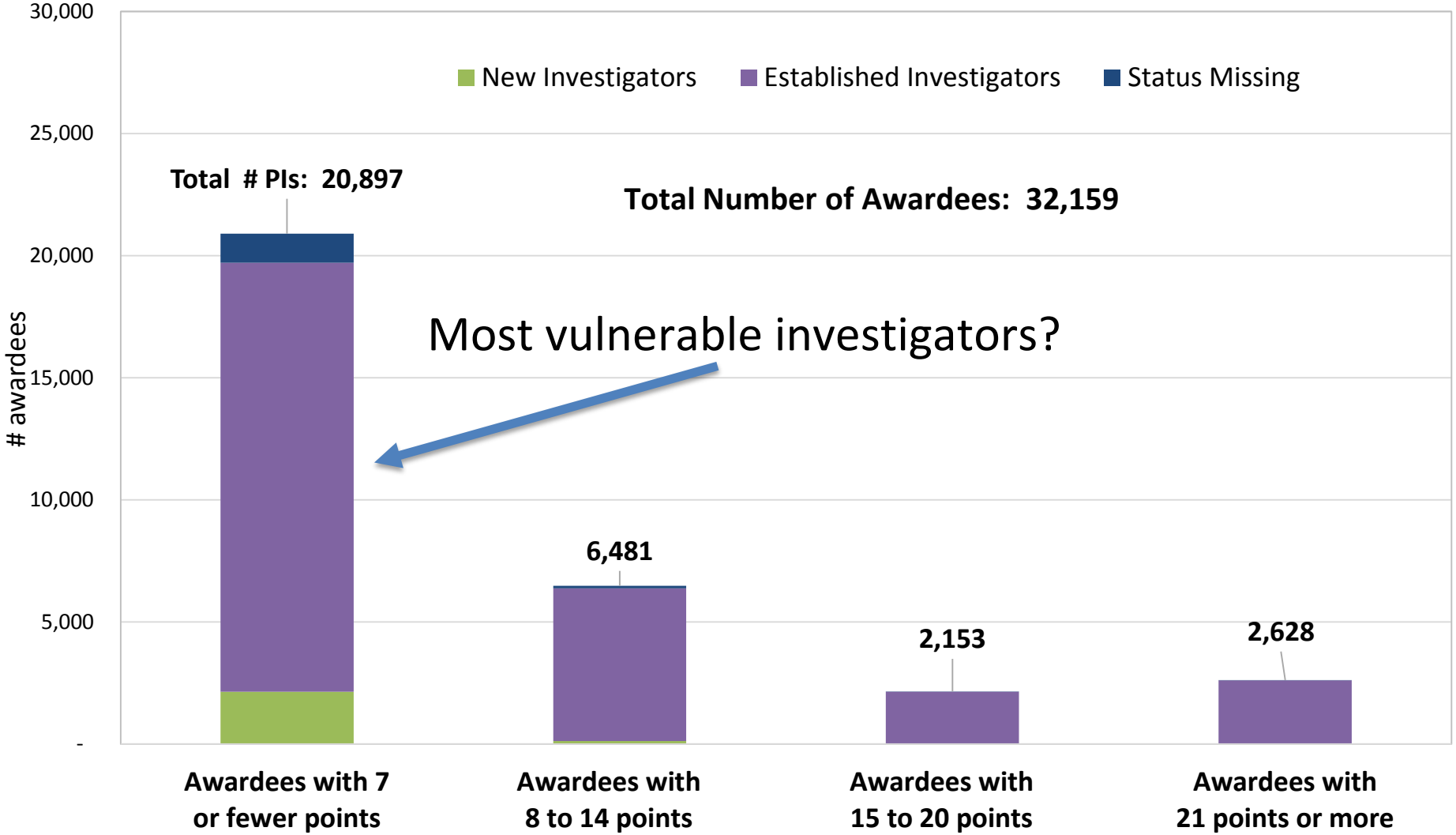

Dropout of Funded NIH Investigators
PI Retention Rate
1.0
0.8
0.6
0.4
0
5
10
Years Since First Award
Year of First Award
1996-2000
2001-2005


Difficulty Securing First Renewals, Especially for New Investigators
Application
New
1st Renewal
Investigators
Experienced
New
Success Rate (%)
40
30
20
10
0
2013
2014
2015
Fiscal Year
OER SARB

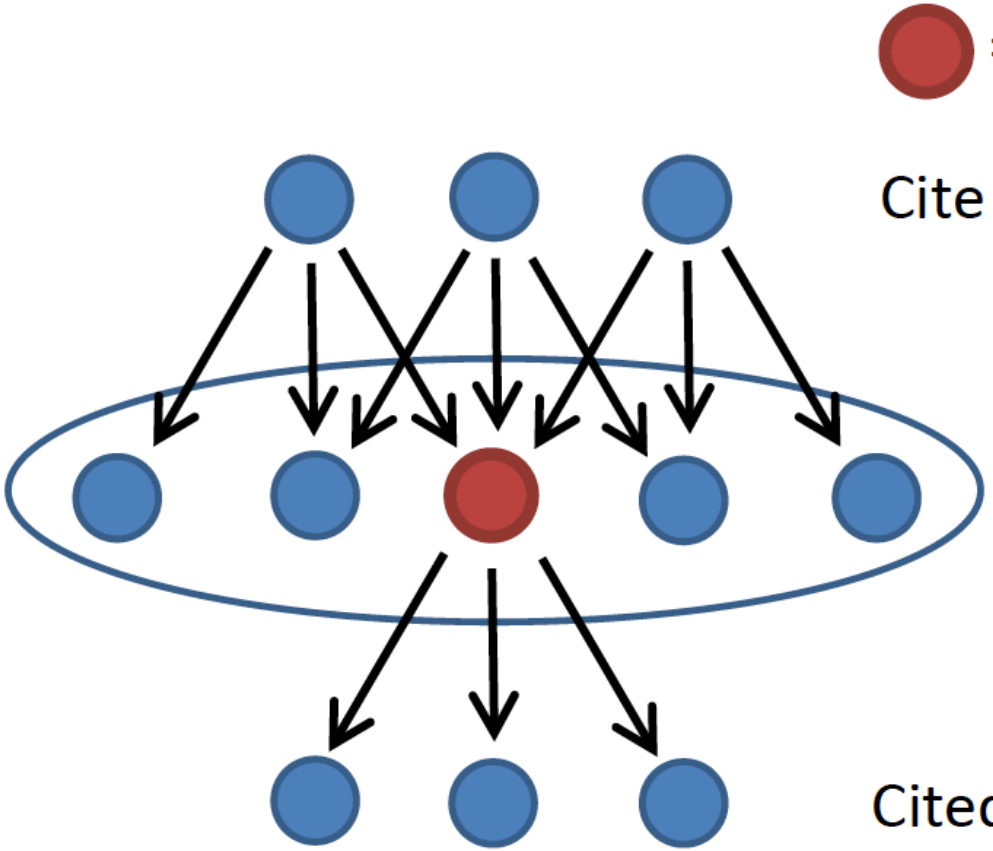

RCI Total Point Distribution by Fiscal Year
for RPG and Select Other Activities
RCI Total Points
100
75
50
25
0
1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Fiscal Year


Mean RCI Total Points by Fiscal Year
for RPG and Select Other Activities
Mean RCI
10
9
8
1990
1995
2000
2005
2010
2015
Fiscal Year
NIH Doubling
Payline Crash
Post-ARRA Cliff and
Sequestration
N=98,656 Unique Investigators
714,120 Person-Years
(ARRA Awards Excluded)
OER SARB

Distribution by Investigator Status



Relative Citation Ratio



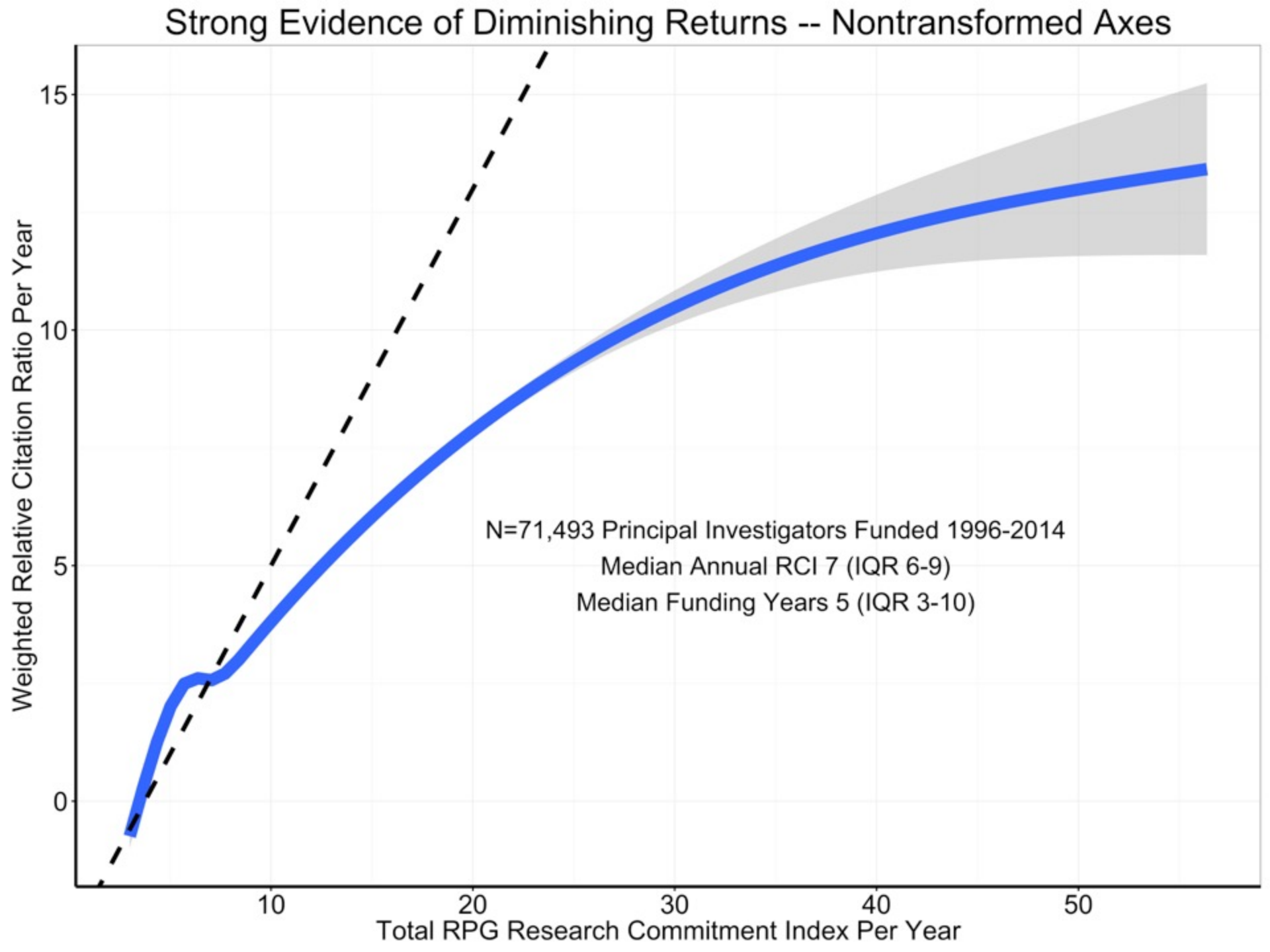
= Article of interest

Cite the article of interest

Co-cited with article of interest:
the co-citation network

Cited by the article of interest

NIH Office of Portfolio Analysis
PLoS Biology (September 6, 2016)


Strong Evidence of Diminishing Returns -- Nontransformed Axes
Weighted Relative Citation Ratio Per Year
15
10
5
0
10
20
30
40
50
Total RPG Research Commitment Index Per Year
N=71,493 Principal Investigators Funded 1996-2014
Median Annual RCI 7 (IQR 6-9)
Median Funding Years 5 (IQR 3-10)

Funding and Mentorship: OPA Analyses

Early Stage Investigator (ESI) data

- Definitions
  - ESI applicant: PI submitting at least one competing RPG ESI application in FY2015-FY2016
  - ESI awardee: PI submitting at least one RPG ESI application that was funded in FY2015-FY2016
- All publications in each ESI biosketch were computationally extracted and matched to a PubMed ID
- For each successfully matched PubMed ID, disambiguation analysis and manual curation was used to confirm the link between each ESI name and author name

Linking ESI mentees to mentor PIs

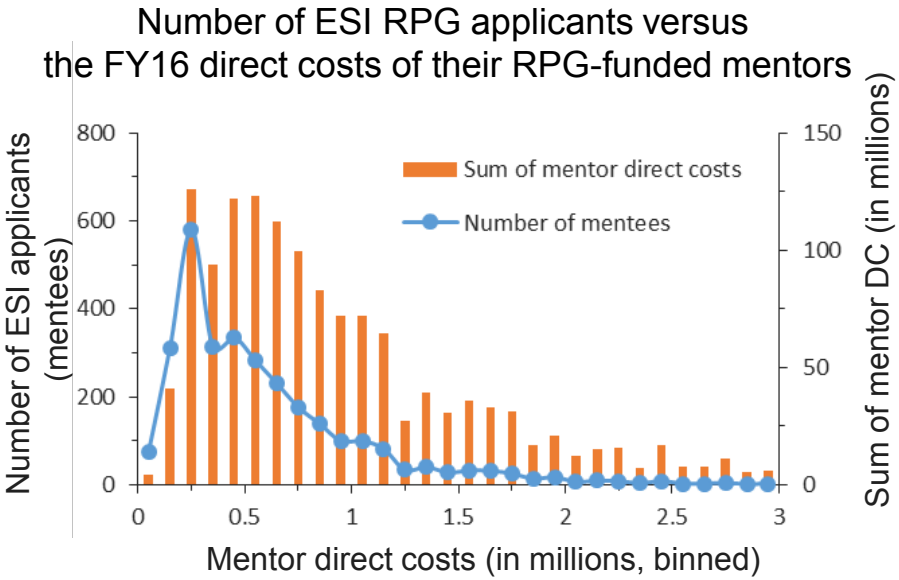
- For each confirmed ESI PubMed ID, matches between the last author and an FY2016 RPG PI were identified
- A PI was considered a mentor of an ESI if both scientists were co-authors on at least two papers that had the mentor as last author; as above, disambiguation analysis and manual curation were used to confirm matches
- If an ESI had multiple applications, the corresponding ESI-mentor links were de-duplicated

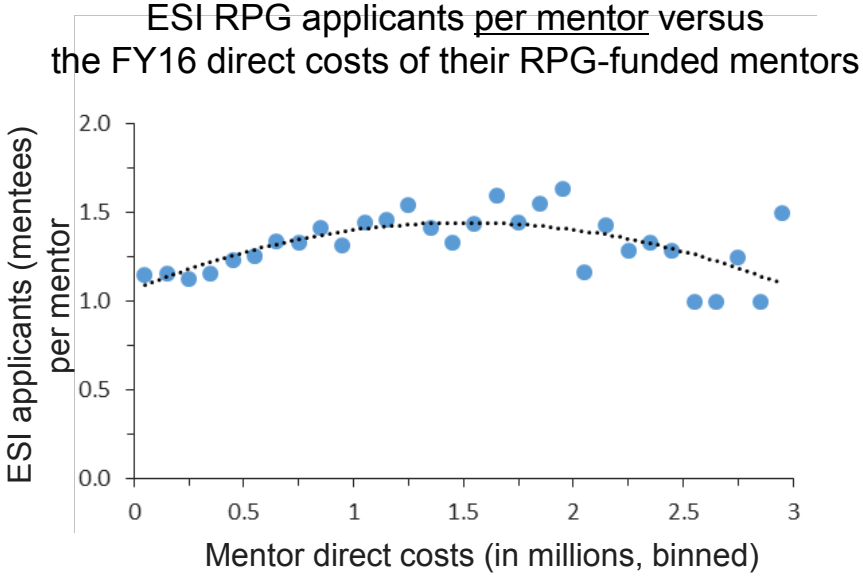
Determining mentor funding

- A mentor's total dollar amount is the sum of FY2016 direct costs for all RPGs linked to the mentor's PI ID
- For projects with subprojects, dollar amounts are apportioned to each subproject PI
- For multi-PI grants, dollar amounts are split evenly between PIs

Thanks to George Santangelo and OPA

No linear relationship between funding level of mentors and the number of ESI applicants that they train





National Institutes of Health
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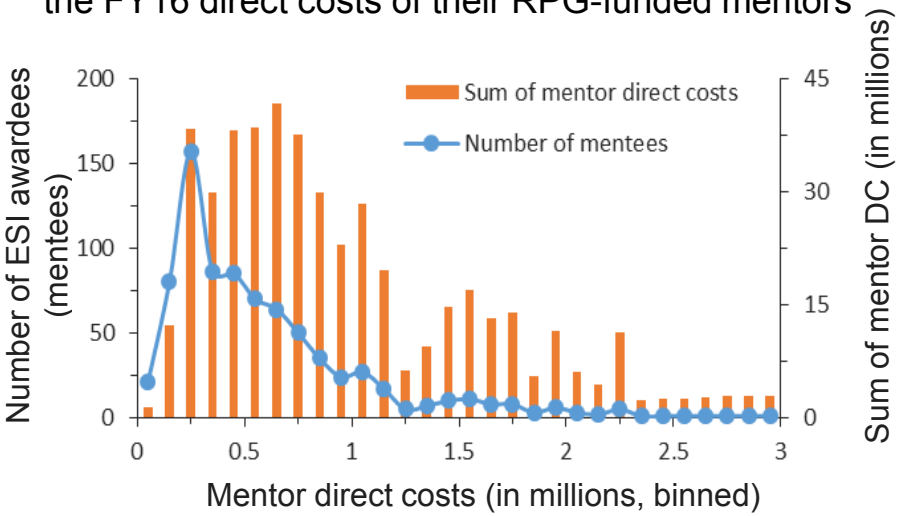
Thanks to George Santangelo and OPA

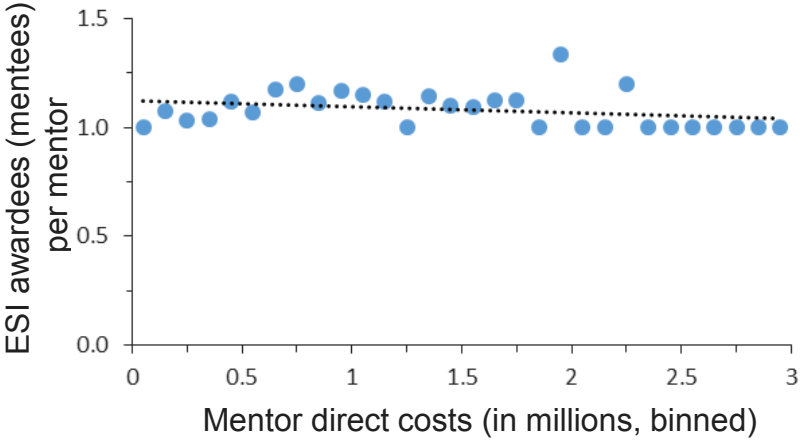
National Institutes of Health
Office of Extramural Research

No relationship between funding level of mentors and the number of ESI awardees that they train

Number of ESI RPG awardees versus
the FY16 direct costs of their RPG-funded mentors



ESI RPG awardees per mentor versus
the FY16 direct costs of their RPG-funded mentors



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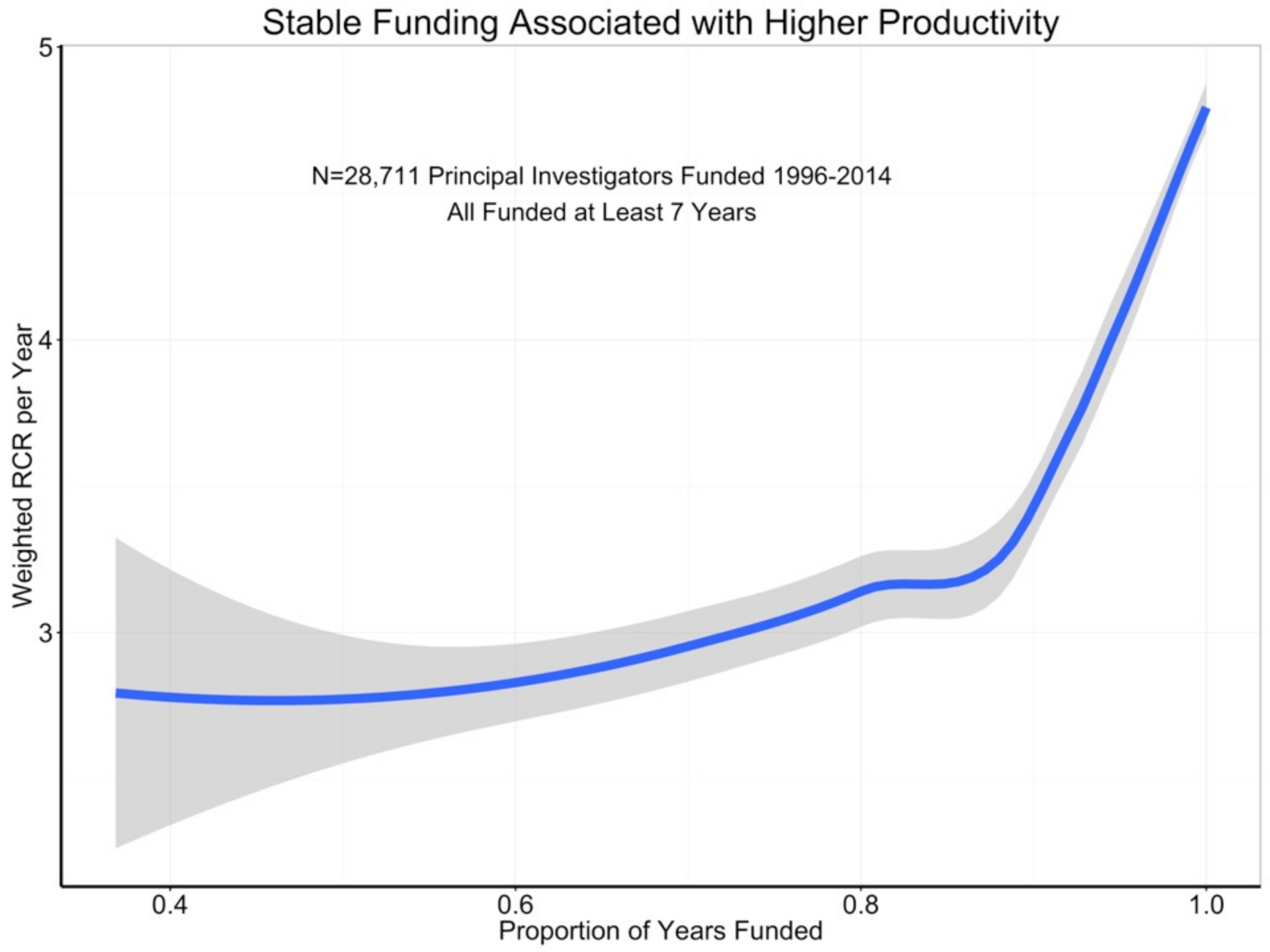
NIH National Institutes of Health
Office of Extramural Research

Thanks to George Santangelo and OPA


Stable Funding Associated with Higher Productivity
N=28,711 Principal Investigators Funded 1996-2014
All Funded at Least 7 Years
Weighted RCR per Year
5
4
3
0.4
0.6
0.8
1.0
Proportion of Years Funded

NEWS FEATURE

YOUNG SCIENTISTS
A *Nature* special issue
nature.com/youngscientists

YOUNG, TALENTED AND FED-UP

BY KENDALL POWELL

Scientists starting labs say that they are under historically high pressure to publish, secure funding and

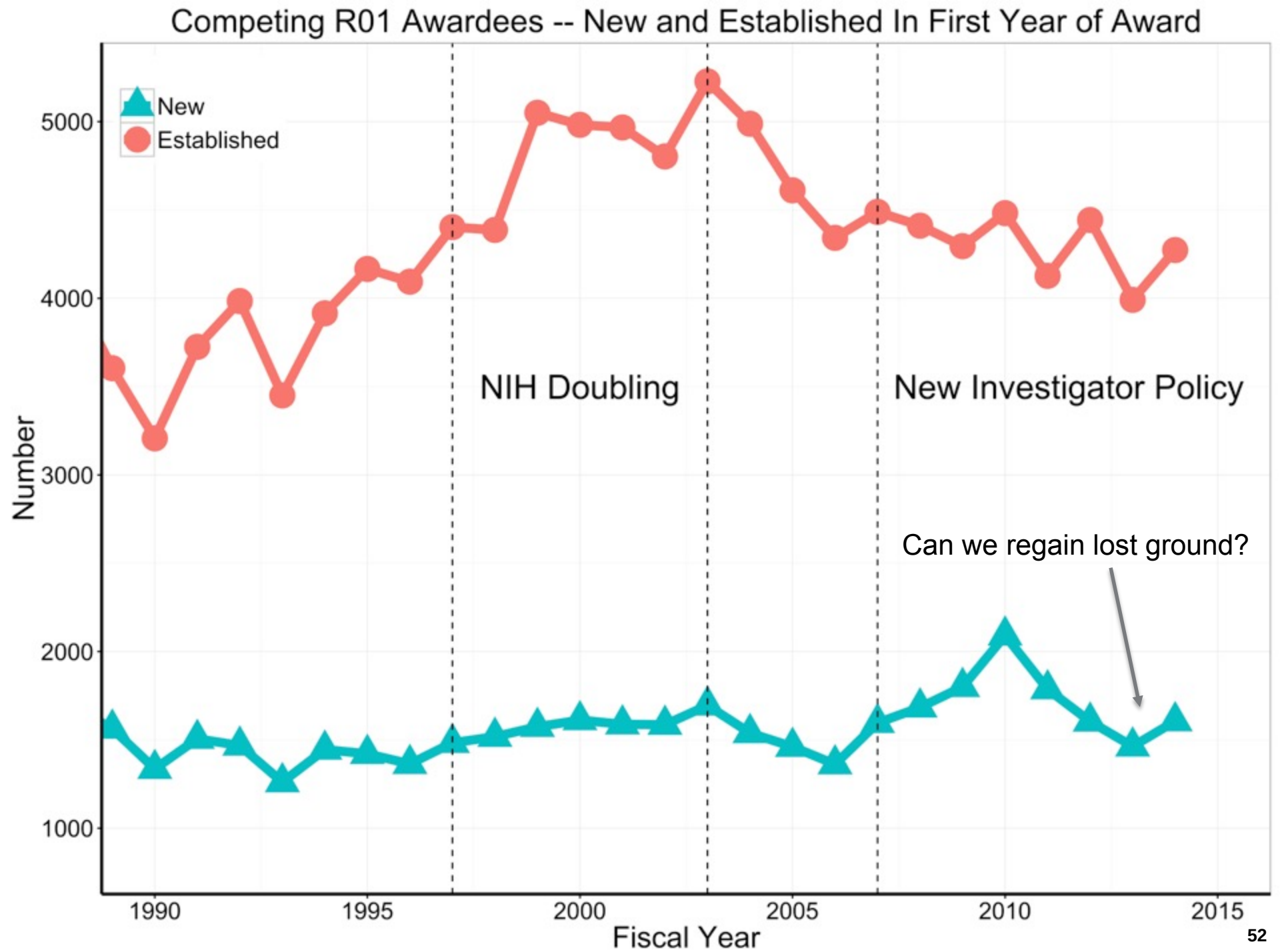
Martin Tingley was coming undone. It was late autumn 2014, just over a year into his assistant-professor job at Pennsylvania State University in State College, and he was on an eight-hour drive home after visiting his wife in Boston. He was stressed, exhausted and close to tears. As the traffic zipped 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

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

The RCI Point Schedule

Activity Code	Single PI point assignment	Multiple PI point assignment
P50, P41, U54, UM1, UM2*	11	10
Subprojects under multi-component awards	6	6
R01, R33, R35, R37, R56, RC4, RF1, RL1, P01, P42, RM1, UC4, UF1, UH3, U01, U19, DP1, DP2, DP3, DP4	7	6
R00, R21, R34, R55, RC1, RC2, RL2, RL9, UG3, UH2, U34, DP5	5	4
R03, R24, P30, UC7	4	3
R25, T32, T35, T15	2	1


Competing R01 Awardees -- New and Established In First Year of Award
New
Established
5000
4000
3000
2000
1000
Number
NIH Doubling
New Investigator Policy
Can we regain lost ground?
1990
1995
2000
2005
2010
2015
Fiscal Year