

# Advancing Gold Standard Science to Address America's Chronic Disease Crisis

National Advisory Council for Nursing Research  
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Director, National Institutes of Health



**NINR Advances  
Real-World Science**

# DISPLACE Study

Turning **proven stroke prevention** into routine care

- **Transcranial Doppler screening** can dramatically reduce stroke risk in children with sickle cell anemia,
- Closing the gap between evidence and care



# Technology-Enhanced Transitional Palliative Care

Supporting rural caregivers through **nurse-led telehealth**

- Rural family caregivers
- Nurse-led support through video visits, phone calls
- Cost-efficient model



# Hypertensive Disorders of Pregnancy and CVD Risk

## Turning pregnancy history into prevention insight

- Women with **high blood pressure during pregnancy** face nearly **double the risk** of developing premature cardiovascular disease within 10 years postpartum.
- All of Us data
- **Replicated findings**

<https://pubmed.ncbi.nlm.nih.gov/41697979/>



# Real-Time Surveillance for Patient Deterioration

## Using nursing data to power clinical AI

- Predictive model “**early warning**” system that analyzes **patterns in nurses' documentation**
  - Risk of death reduced by 36%
  - Hospital stays shortened by 11%,

# Physical Activity and Cognition in People Living with HIV

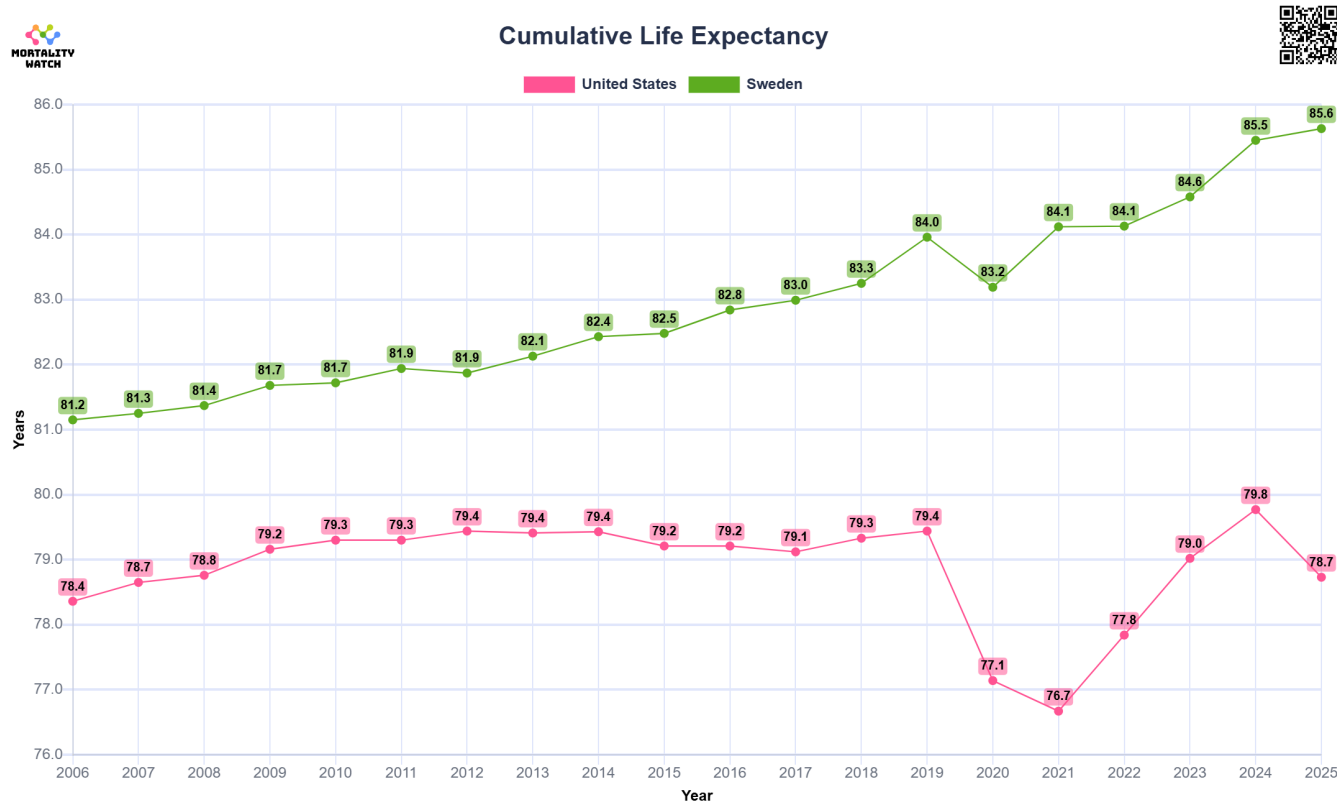
## Finding feasible paths to cognitive health

- **Light physical activity** was the most consistent variable associated with better cognitive outcomes
- Sedentary time was linked to worse executive function
- Higher step counts correlated with better cognitive scores



# Addressing America's Chronic Disease Crisis

# No Improvement in American Longevity for 15 years



**US life expectancy flatlined between 2010 and 2019 and collapsed during the pandemic**

Source: Mortality Watch

<https://www.mortality.watch/explorer/?c=USA&t=le&ct=yearly&e=0&cs=line&df=2001&bf=2011&sb=0&ce=1&m=0&sl=1&lg=0>

# Make America Healthy Again



**Chronic diseases** such as heart disease, cancer, and diabetes are:

- Leading causes of death and disability in the U.S.
- Leading drivers of the nation's \$4.5 trillion in annual health care costs

**NIH's role:** Find better ways to prevent, treat, and cure chronic diseases.



**To make America healthy  
again, we must rethink  
how we do science**

# Why Aren't We Making More Progress?

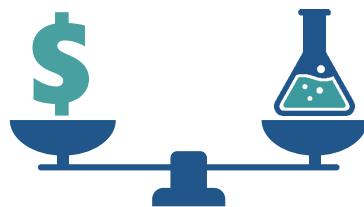
Too much **safe,**  
**incremental science**

Research doesn't  
**replicate**

**Funding**  
**concentrated** in few  
institutions

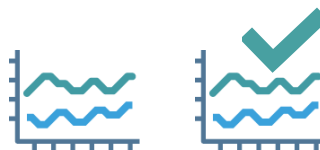
# Solution: Democratizing Science

Too much **safe, incremental science**



**Unified Funding Strategy**

Research doesn't **replicate**



**Replication initiative**

**Funding concentrated** in few institutions



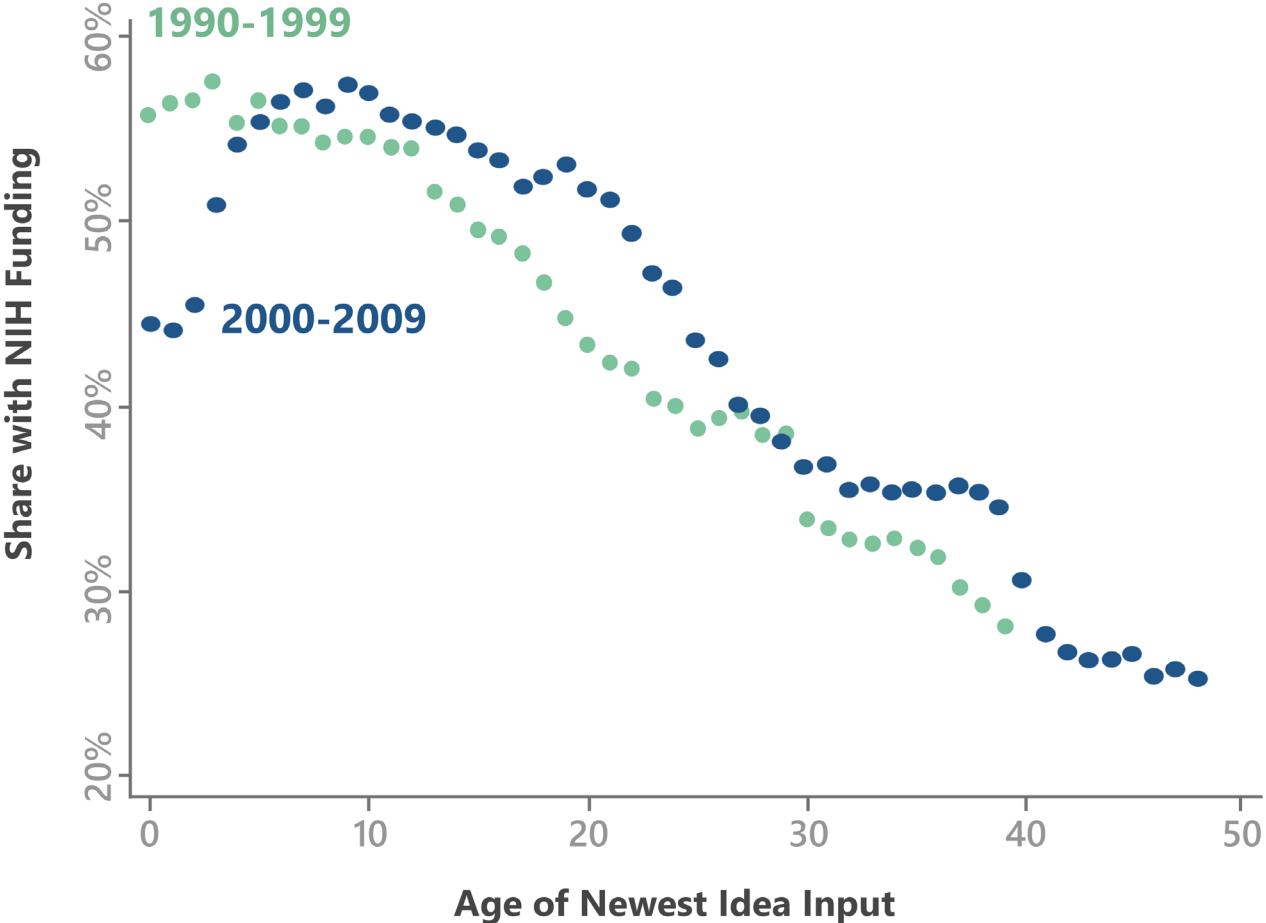
**Competitive infrastructure support**

# Funding Bold Ideas

# Unified Funding Strategy

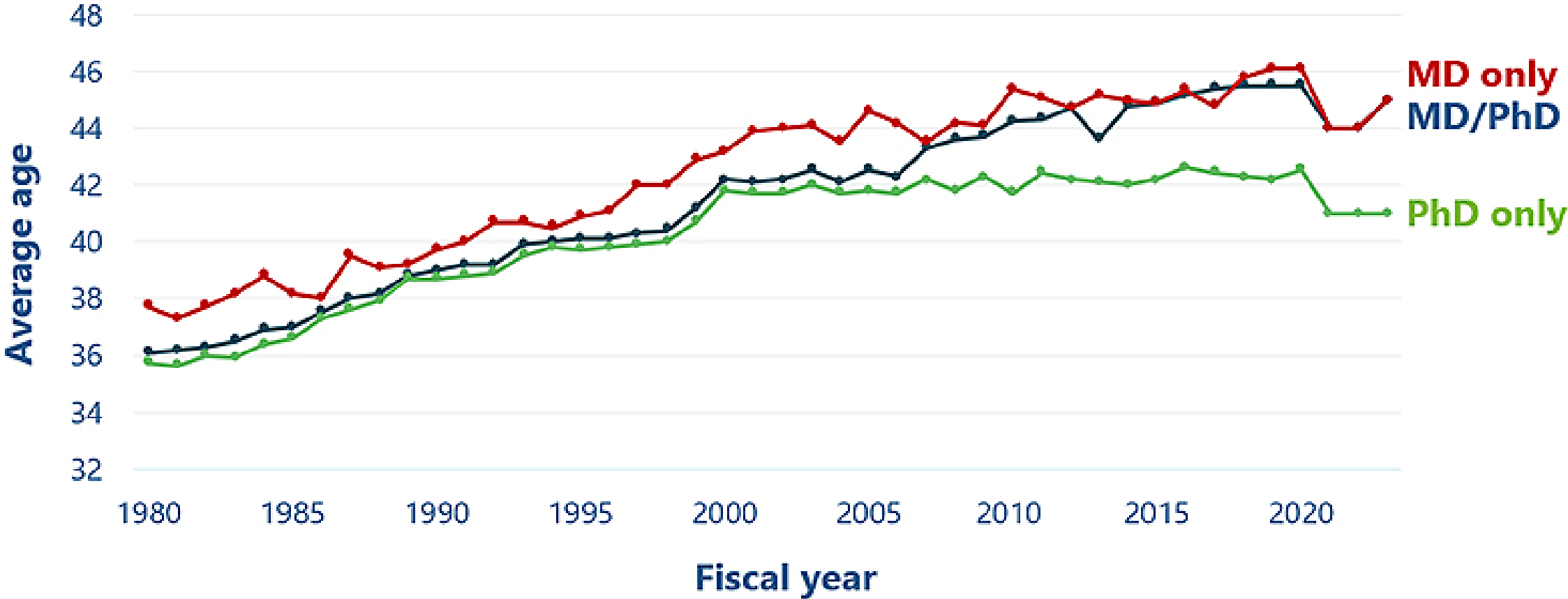
- End pay-lines for selecting projects to fund
- Peer review important + other key factors
- **Goals:**
  - Gives NIH Institutes and Centers flexibility to fund high-risk, high-reward research
  - Align funding with institute missions
  - Prioritize early-career scientists and novel ideas

# Supporting Edge Science



*Packalen and Bhattacharya (2020)  
NIH Funding and the Pursuit of  
Edge Science. PNAS*

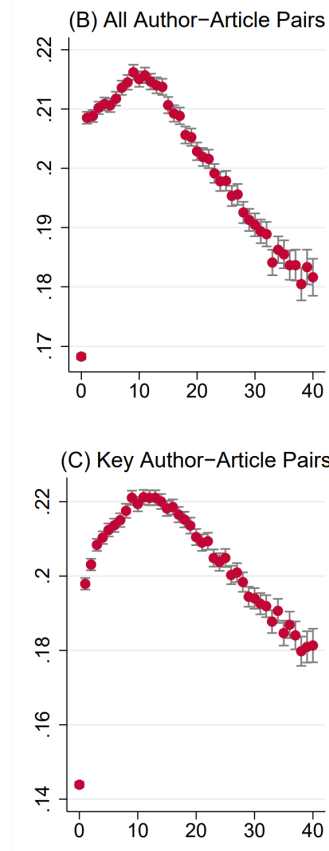
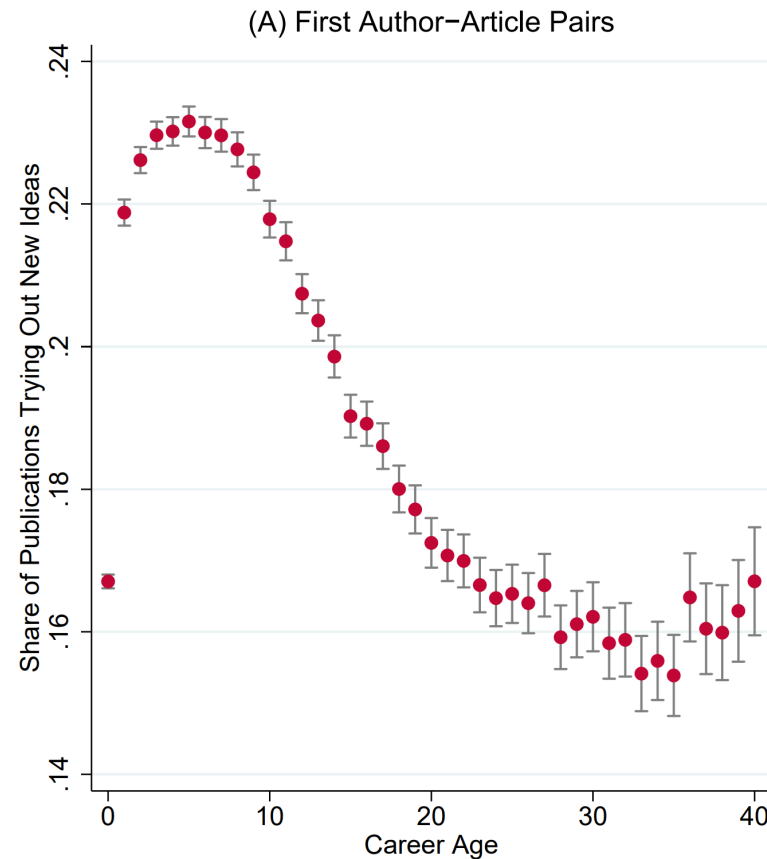
# Average age of first-time R01 (1980-2023)



<https://grants.nih.gov/policy-and-compliance/policy-topics/early-stage-investigators/related-data>  
Garrison HH, Ley TJ. Physician-scientists in the United States at 2020: Trends and concerns. *FASEB J.* 2022;36(5):e22253. doi:10.1096/fj.202200327  
<https://web.archive.org/web/20250404233158/https://nexus.od.nih.gov/all/2024/07/03/continued-support-for-early-stage-investigators-in-fy-2023/>

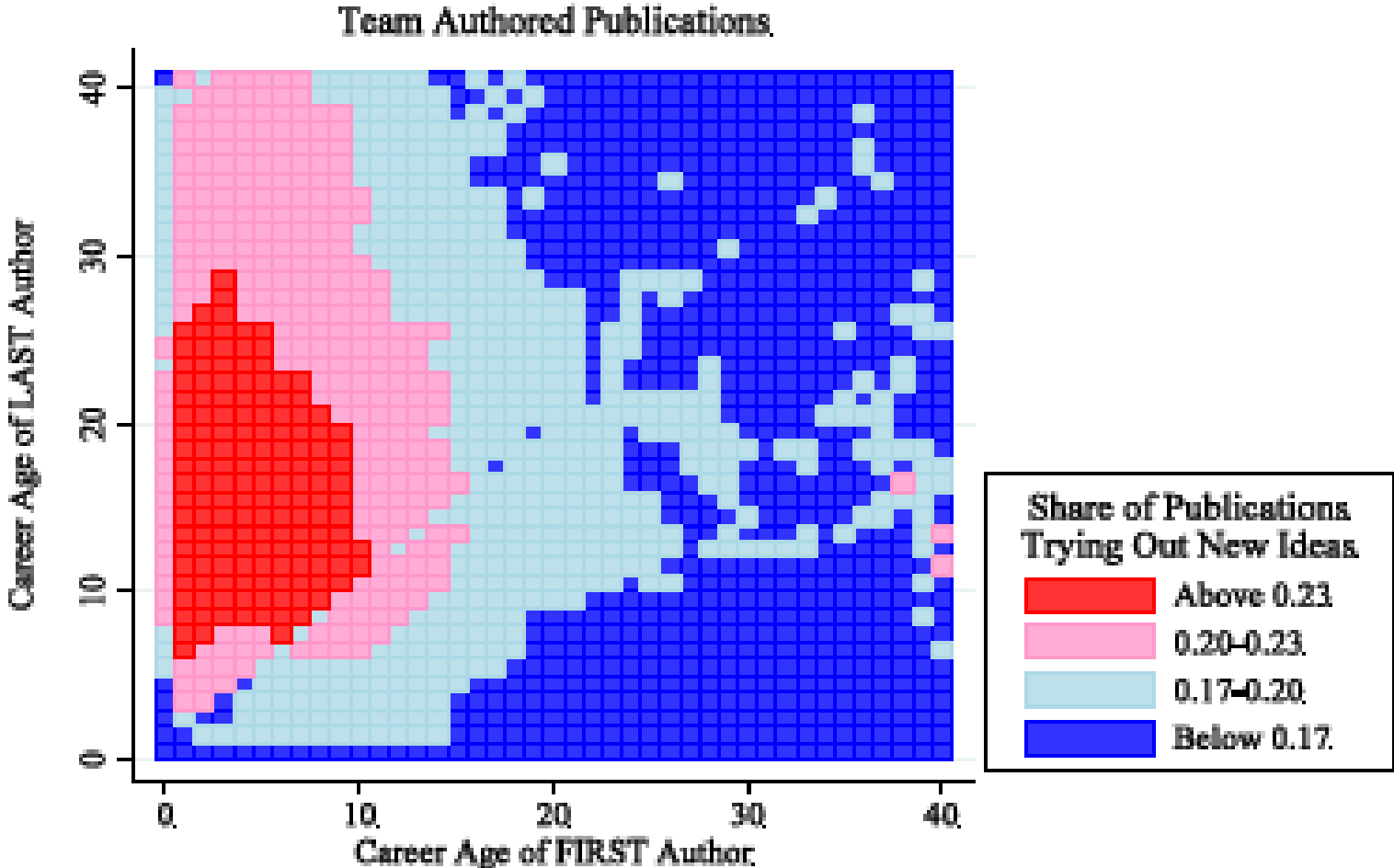
# Early-Career Researchers Contribute a Larger Share of New Ideas

## Team and Solo Authored Publications



*Packalen and  
Bhattacharya (2019)  
"Age and the Trying  
Out of New Ideas."  
Journal of Human  
Capital.*

# Teams of Early Career and Later Career Researchers Most Likely to Try Out New Ideas



The background of the slide features a stack of several white papers, slightly out of focus, with a semi-transparent blue overlay. The papers appear to be documents or reports, with some text and a small yellow mark visible on the top sheet. The overall aesthetic is professional and academic.

# Solving the Replication Crisis

# Replication as the Basis for Truth in Science

## Essay

### Why Most Published Research Findings Are False

John P.A. Ioannidis

#### Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller, when effect sizes are smaller, when there is a greater number and lesser preselection of tested relationships, where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

Published research findings are sometimes refuted by subsequent evidence, with ensuing confusion and disappointment. Refutation and controversy is seen across the range of research designs, from clinical trials and traditional epidemiological studies [1–3] to the most modern molecular research [4,5]. There is increasing concern that in modern research, false findings may be the majority or even the vast majority of published research claims [6–8]. However, this should not be surprising. It can be proven that most claimed research findings are false. Here I will examine the key

The Essay section contains opinion pieces on topics of broad interest to a general medical audience.

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factors that influence this problem and some corollaries thereof.

#### Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a  $p$ -value less than 0.05. Research is not most appropriately represented and summarized by  $p$ -values, but, unfortunately, there is a widespread notion that medical research articles

#### It can be proven that most claimed research findings are false.

should be interpreted based only on  $p$ -values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. “Negative” research is also very useful. “Negative” is actually a misnomer, and the misinterpretation is widespread. However, here we will target relationships that investigators claim exist, rather than null findings.

As has been shown previously, the probability that a research finding is indeed true depends on the prior probability of it being true (before doing the study), the statistical power of the study, and the level of statistical significance [10,11]. Consider a  $2 \times 2$  table in which research findings are compared against the gold standard of true relationships in a scientific field. In a research field both true and false hypotheses can be made about the presence of relationships. Let  $R$  be the ratio of the number of “true relationships” to “no relationships” among those tested in the field.  $R$

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is  $R/(R+1)$ . The probability of a study finding a true relationship reflects the power  $1 - \beta$  (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate,  $\alpha$ . Assuming that  $\epsilon$  relationships are being probed in the field, the expected values of the  $2 \times 2$  table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the  $2 \times 2$  table, one gets  $PPV = (1 - \beta)R/(R - \beta R + \alpha)$ . A research finding is thus

Citation: Ioannidis JPA (2005) Why most published research findings are false. *PLoS Med* 2(8): e124.

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Abbreviation: PPV, positive predictive value

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## IS THERE A REPRODUCIBILITY CRISIS?

A Nature survey lifts the lid on how researchers view the ‘crisis’ rocking science and what they think will help.

BY MONYA BAKER



More than 70% of researchers have tried and failed to reproduce another scientist's experiments, and more than half have failed to reproduce their own experiments. Those are some of the telling figures that emerged from *Nature's* survey of 1,576 researchers who took a brief online questionnaire on reproducibility in research. The data reveal sometimes-contradictory attitudes towards reproducibility. Although 52% of those surveyed agree that there is a significant ‘crisis’ of reproducibility, less than 31% think that failure to reproduce published results means that the result is probably wrong, and most say that they still trust the published literature. Data on how much of the scientific literature is reproducible are rare and generally bleak. The best-known analyses, from psychology<sup>1</sup> and cancer biology<sup>2</sup>, found rates of around 40% and 10%, respectively. Our survey respondents were more optimistic: 73% said that they think that at least half of the papers in their field can be trusted, with physicists and chemists generally showing the most confidence. The results capture a confusing snapshot of attitudes around these issues, says Arturo Casadevall, a microbiologist at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. “At the current time there is no consensus on what reproducibility is or should be.” But just recognizing that is a step forward, he says. “The next step may be identifying what is the problem and to get a consensus.”

Failing to reproduce results is a rite of passage, says Marcus Munafò, a biological psychologist at the University of Bristol, UK, who has a longstanding interest in scientific reproducibility. When he was a student, he says, “I tried to replicate what looked simple from the literature, and wasn't able to. Then I had a crisis of confidence, and then I learned that my experience wasn't uncommon.” The challenge is not to eliminate problems with reproducibility in published work. Being at the cutting edge of science means that sometimes results will not be robust, says Munafò. “We want to be discovering new things but not generating too many false leads.”

#### THE SCALE OF REPRODUCIBILITY

But sorting discoveries from false leads can be discomfiting. Although the vast majority of researchers in our survey had failed to reproduce an experiment, less than 20% of respondents said that they had ever (see ‘A crisis’ in numbers). Our results are strikingly similar to another online survey of nearly 900 members of the American Society for Cell Biology (see [www.nature.com/kbz2b](http://www.nature.com/kbz2b)). That may be because such conversations are difficult. If experimenters reach out to the original revealing too much about their own projects. A minority of respondents reported ever having tried to publish

Sources:  
Baker, M. 1,500 scientists lift the lid on reproducibility. *Nature* 533, 452–454 (2016). DOI: 10.1038/533452a  
Ioannidis JPA (2005) Why most published research findings are false. *PLoS Med* 2(8): e124.

# Replication Crisis: Empirical Basis

nature

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NEWS | 25 April 2025

## Huge reproducibility project fails to validate dozens of biomedical studies

Unique reproducibility effort in Brazil focuses on common methods rather than a field — and prompts call for reform.

By [Rodrigo de Oliveira Andrade](#)

### Falling short

The authors judged a paper's replicability by five criteria, including whether at least half of the replication attempts had statistically significant results in the same direction as the original paper. Only 21% of the experiments were replicable using at least half of the applicable criteria.

The authors also found that the effect size — the magnitude of the observed impact in the experiments — was, on average, 60% larger in the original papers than in the experimental follow-ups, indicating that published results tend to overestimate the effects of the interventions tested.

# Invest in the Science of Replication



Fund replication research



Establish a replication platform



Enhanced visibility through PubMed



New metrics for scientific contribution



# Funding Scientific Excellence Everywhere

# More Equitable Distribution of Funds

Current system concentrates resources at a few institutions

**Research project support**



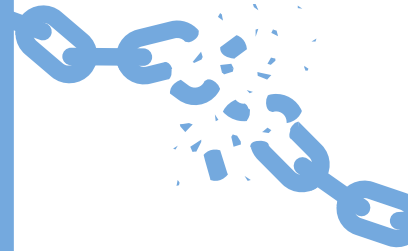
Research grants



**Research infrastructure support**



Infrastructure funding



Thank you



National Institutes of Health

*Turning Discovery Into Health*