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May 2026 | Volume 55, Number 5

Launching a Second Scientific Revolution

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The following is adapted from a speech delivered at a Hillsdale College National Leadership Seminar on April 28, 2026, in Dana Point, California.

AT THE root of the scientific revolution was the idea that there was not and should never be a scientific authority. For centuries, a small number of ecclesiastical powers had decided such questions as whether the moons of Jupiter move. The scientific revolution placed these questions in the hands of a lot of very smart scientists, including those with telescopes. Unfortunately, we find ourselves back in a situation today, as demonstrated a few years ago by the Covid lockdowns, mask mandates, and vaccination requirements, where a relatively small number of people—directors of government agencies like the National Institutes of Health, heads of international agencies like the World Health Organization, and editors of prestigious journals—have the power to say what is true or false in science.



JAY BHATTACHARYA is director of the National Institutes of Health. Prior to serving in that position he was a professor of medicine at Stanford University, where he received both an M.D. and a Ph.D. in economics. He has also served as a research associate at the National Bureau of Economic Research, a senior fellow at the Stanford Institute for Economic Policy Research and at the Freeman Spogli Institute for International Studies, and director of the Stanford Center on the Demography and Economics of Health and Aging. A co-author of the Great Barrington Declaration, his research has been published in economics, statistics, legal, medical, public health, and health policy journals.

A PUBLICATION OF HILLSDALE COLLEGE

But before I go on, I want to make a historical defense of the National Institutes of Health, which I now lead. The history of the NIH is incredible. Almost every modern advance in biomedicine has, at its root, an NIH investment. NIH is, by far, the single largest public funder of biomedical research in the world, providing 85 percent of funding in every single area of biomedicine. The development of heart attack prevention and treatments came out of the NIH. Almost every cancer advance and cancer treatment came out of the NIH. Because of the NIH, we now have advances in the treatment of rheumatoid arthritis that, when I was a medical student in the 1990s, seemed beyond reach. Because of the NIH, we can now treat cystic fibrosis, a terrible disease that used to kill young people in their teens and 20s, allowing those who have it to live full lives. We have not one, but two cures for sickle cell anemia, a disease that primarily affects African-American children. So I am strongly of the view that the NIH is an institution worth saving. It is, however, an institution that has not done its job well in some time.

The mission of the NIH is to fund research that improves the health and longevity of the American people. But when we look at life expectancy in the United States since 2010—and this is not the case in most European countries—we find that there has been no improvement despite the huge investments we have made in

medical research. (See, for instance, the accompanying graph comparing life expectancy over time in the U.S. and Sweden.) If we continue as we have been, the prospect of our children living shorter, less healthy lives than we do is a real possibility. “Make America Healthy Again” can be seen as a political slogan. But it can also be seen as a cry for help from the American people. We have huge chronic disease problems. We can solve them—but we can only solve them if we fix science, which suffers today from three great problems.

THE REPLICATION CRISIS

The first of these problems is the replication crisis. Scientists publish studies today; we hear about their findings on TV, in newspapers, and on podcasts; and we (and even our doctors) take them for granted. But then when other scientists ask the same questions and perform the same experiments, they do not come up with the same results. That means that a lot of the science we (and our doctors) take for granted is not actually true.

Are eggs good for us? I grew up in the 1970s and 1980s, when eggs were considered the next worst thing to poison. I didn’t eat an egg until I was 19, and then it was a tasteless egg white omelet, since only the whites of eggs were considered healthy in the 1990s. But today eggs are considered a superfood! There are so many examples like this, and at the root of the confusion is the replication crisis.

How do we address this? We begin by recognizing the fact that most ideas hatched by scientists do not work or are not true. That is completely normal in science and always has been. John Ioannidis, a former colleague of mine at Stanford and one of the most frequently cited scientists in the world, wrote a paper in 2005 entitled, “Why Most Published Research Findings Are False.” He was correct, and the reason

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for this is that science is hard. That is why it is frustrating to be a scientist—and why, to be a good scientist, an essential requirement is epistemic humility.

We also need to recognize that just because a study is published in a prestigious journal, it does not mean the study is true—not even if it is peer reviewed! Peer reviewers do not double check the data of a study. They just look at it and then accept or reject it. Peer review is not a measure of scientific truth; it is basically a measure of approval by an editor. It is not meaningless, because presumably the editor has some expertise in the subject. But it is in no way a confirmation of truth.

The only effective way for scientists to check one another is through replication. If I write a paper proposing a theory, I will present the experiments that I used to come up with that theory. If I am right, other scientists should be able to replicate those same

experiments and come up with the same answer. That is *narrow* replication. Even better is reproducibility, by which other people use a different method to come up with the same answer to the question. This is how science operated in the past, and we must return to it if science is to regain the public trust.

The NIH can do a lot to achieve this goal. We can do it first by funding replication. And scientists should welcome this. If someone wants to replicate a study I produced, I should not view that as a threat because it might prove me wrong. I should look on it as an honor because replication is a source of advancements in science. If my study turns out not to be true, then maybe we can figure out why. That kind of collaboration is how science advances.

Let me give you an example of something we are doing already. We funded a project called the Autism

Data Science Initiative. The goal is to figure out the causes of the increasing rates of autism. As part of this initiative, we funded replication teams to look at new and promising studies scientists are undertaking to see if they can be replicated.

IN THE 1990S, ABOUT 55 PERCENT OF NIH FUNDED RESEARCH WAS BASED ON NEW IDEAS—ZERO-YEAR-OLD OR ONE-YEAR-OLD IDEAS—AND RESEARCH IN WHICH THE NEWEST IDEAS WERE TEN TO 30 YEARS OLD RECEIVED MUCH LESS FUNDING. AND THAT IS AS IT SHOULD BE. NIH IS SUPPOSED TO FUND IDEAS THAT ARE ON THE BLEEDING EDGE OF SCIENCE. BUT WHAT HAS HAPPENED SINCE THEN—ESPECIALLY SINCE 2000—IS A COLLAPSE IN NIH SUPPORT FOR NEW IDEAS.

In addition to funding replication studies, we have to make it easier to discover whether scientific ideas have been replicated. There is a popular database called PubMed that people use to look up biomedical papers. Currently, when you look up a paper, you can see where it was published and cited but not whether it has been replicated. So the NIH is going to add a replication button, and when users click on it, they will be able to see the related replication studies if any.

SCIENTIFIC STAGNATION

The second problem we need to address is scientific stagnation—the problem that for every dollar we spend on science today, we get far less scientific advancement than we did over the past five decades. Another way of looking at this is that for every additional research paper in biomedicine, there are fewer improvements in health per paper.

In the 1960s, for example, we were making great advances in breast cancer survival per research paper addressing breast cancer. Today, per paper, the advances are dramatically

smaller. We need to keep funding breast cancer research, but we need to make that research more effective. I think this problem can also largely be solved through reforms at the NIH.

First, we must recognize that most scientific papers, far from introducing new ideas, rely on old ideas. I once collaborated on a study that looked at every word and phrase published in biomedicine in 1940 and 1941. When we subtracted all the 1940 words and phrases that were published in 1941, we were left with the ideas introduced in 1941. Doing this for every subsequent year

up to the present produces a kind of history of biomedicine. What we see in that history is that in the 1990s, about 55 percent of NIH funded research was based on new ideas—zero-year-old or one-year-old ideas—and that research in which the newest ideas were ten to 30 years old received much less funding. And that is as it should be. The NIH is supposed to fund ideas that are on the bleeding edge of science. But what has happened since then—especially since 2000—is a collapse in NIH support for new ideas.

In addition to this, the average age at which scientists receive their first NIH grant has risen from the mid-30s in 1980 to the mid-40s today. This is not a good development, given that younger scientists are the most likely to have new ideas. In a 2019 paper, Mikko Packalen and I showed that the probability of trying out new ideas declines monotonically with career age. The great theoretical physicist Max Planck once said that new scientific discoveries triumph only because “their opponents eventually die.” We have to make sure that is not true if we are going to reverse scientific stagnation.

To address this problem, the NIH needs to adopt something like the Silicon Valley financing approach, in which young people attract investors and start their own firms. Even if those firms fail, they often do so in a productive way—a way that pays off when investors bank on those smart young people again based on a useful discovery made through the failure. Similarly, the NIH needs to start funding ideas on the bleeding edge of science—ideas that may not work but that offer the greatest chance of advancing science.

The NIH receives about 100,000 funding applications each year, out of which only eight to ten percent are approved. In recent years, the winners have been chosen by scientific reviewers who score each application based on two factors: (1) the strength of the proposed methods and (2) the innovation involved in the proposal. Looking at the results of this process, the overall score has correlated very strongly with the methods score, and innovative ideas have been left by the wayside. To fix this, the NIH is replacing that process (called the payline method) with a new approach called the Unified Funding Strategy. The scientists who review applications will now be empowered to approve projects on the bleeding edge of science—projects that may very well not work but that will produce a fundamental advance in biomedicine if they do.

As a result, we will have a portfolio of projects that may all fail but that will have a much greater potential to solve type 1 diabetes, reduce the mortality rate from breast cancer, and prevent heart disease. Funding decisions will not be judged by how many projects succeed, but by whether and how they improve the health of Americans.

FUNDING CONCENTRATION

The third problem to be addressed is the fact that about one third of all NIH grant money goes to about 20 institutions, despite the fact that there are

excellent scientists all across the country. In order to make the kinds of advances that lead to better health for Americans, we have to empower young and innovative scientists wherever they are. If they have a new and promising idea, we should be funding them.

The reason the NIH has such a concentrated funding portfolio is largely a matter of economics. Scientists who receive NIH grants need to have access to labs with expensive equipment, such as electron microscopes, that make their research possible. For this reason, when the NIH awards grants, they cover both direct costs—for the research studies themselves—and indirect costs for facility or lab expenses. This gives scientists a strong incentive to work at institutions that have great facilities, where it is often the case that priority lab access is given to older rather than younger scientists. And scientists who do not work at these institutions have much less of a chance to secure NIH funding due to the lack of high-quality labs where they teach.

Our solution to this problem is to sever the link in the NIH grants between the direct money for research and the indirect money for facilities. Institutions outside of the top 20 will be able to compete for facilities support, leading to a dynamic market. The number of institutions that receive NIH money will increase, and funds will go to wherever the best scientists are. This will supercharge science across the country because NIH seed money attracts other investments.

We can solve the nation's health problems if we establish gold standard science. When I say gold standard science, I mean science that is replicable, at the bleeding edge, and supports scientists with new and promising ideas wherever they are. Achieving these goals will amount to launching a second scientific revolution. ■