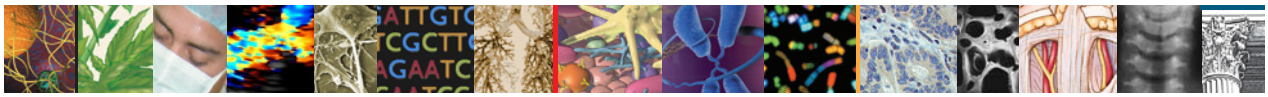

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Perspective

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Scientific Drought, Golden Eggs, and Global Leadership — Why Trump's NIH Funding Cuts Would Be a Disaster

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On March 16, 2017, President Donald Trump submitted his budget titled "America First," with a proposal to cut the 2018 National Institutes of Health (NIH) budget by 18.3%, or approximately $5.8 billion. It is the first time a president has proposed a cut of this magnitude since the NIH received its first appropriation in 1938, with an initial investment of $400,000 in the National Cancer Institute. Since that time, the NIH budget has grown to $32 billion, with nearly 80% being awarded through competitive grants to more than 300,000 investigators at 2500 universities, medical schools, and other research institutions in every state and around the world.

The president's proposal has far-reaching implications for public health, research and drug development, and keeping America at the forefront of innovation. It also threatens young scientists who are the future leaders of academia, biotechnology, and the pharmaceutical industry. "If cuts of such magnitude pass, we will lose a generation of scientists," says Mary-Claire King, a professor of genome sciences and medicine at the University of Washington whose early funding from NIH led to the identification of the *BRCA1* gene and its role in inherited breast cancer. "Scientists doing research in new areas are the most vulnerable and the first who will be let go. We will have a scientific drought, which is even harder to fix than a natural one."

Feng Zhang of the Broad Institute at the Massachusetts Institute of Technology (MIT) and Harvard is an example of a young investigator whose ground-breaking work with colleagues might never have come to fruition without the 5-year NIH Pioneer Award he received. The grant funded the development of a technique for editing the genome, CRISPR-Cas9, deemed the 2015 breakthrough of the year by the American Association for the Advancement of Science. Basic research of this sort has broad implications for science, health, and the further development of new therapeutics by the biotechnology and pharmaceutical industries.

The NIH plays a pivotal role in the U.S. medical innovation sector as the world's largest funder of biomedical research. Companies frequently leverage basic and

clinical research supported by the NIH to develop new therapeutics and technologies. Up to 47% of drugs approved by the Food and Drug Administration (FDA) between 1988 and 2005 benefited in some way from public-sector support.[1] Publicly funded research conducted in academic medical settings and government laboratories has led to the discovery and development of many transformative drugs — those that have the greatest effect on patient care.[2]

"Groundbreaking medical products often arise from NIH-funded work because they involve risk-taking, innovative research that large manufacturers have increasingly avoided," said Aaron Kesselheim, an associate professor of medicine at Brigham and Women's Hospital who has studied the origins of transformative drugs and medical devices. "But many of these products end up being blockbusters, earning the manufacturers that do get involved later in the research process billions of dollars a year in global sales."

Contrary to claims by Director of the White House Office of Management and Budget Mick Mulvaney that Trump's proposal is an "America First budget," leading economists argue that cuts to the NIH will undermine job creation in the life sciences and in research and development that frequently results in highly profitable patents. There is a clear consensus among economists that public-sector funding for scientific research produces high returns (see box), and disruptions in spending can have far-reaching effects that may ultimately undermine the U.S. advantage in science, technology, engineering, and math (STEM). "The U.S. is a leader in biomedical research, but it has active competitors," argues Harvard health economist David Cutler. "The proposed NIH cuts would severely compromise our ability to lead in STEM development."

Pierre Azoulay, a professor at the MIT Sloan School of Management who has studied the contribution of NIH-funded research to the patenting activities of biopharmaceutical firms, estimates that a $10 million investment in research generates two to three new patents, on average.[5] He doubts that the private sector could fill in the gaps that cuts of this magnitude would leave in their wake — "This may well kill the goose that lays the golden eggs."

Beyond the economic ramifications, NIH funding has produced significant health benefits. "There is no question that Americans are living longer in large part due to research that has been funded through the NIH," notes Harold Varmus, a Nobel laureate and professor at Weill Cornell Medicine who directed the NIH from 1993 to 1999. The life expectancy of the average American increased by 8 years between 1970 and 2013 (from 70.8 to 78.8 years), while all-cause mortality decreased by 43% (from 1279 to 730 per 100,000 population), according to the Centers for Disease Control and Prevention. Research advances supported in large part by the NIH have led to reductions in mortality due to the leading causes of U.S. deaths, including cardiac disease, diabetes, stroke, and cancer.

The quality of health care has also advanced under the Agency for Healthcare Research and Quality (AHRQ), a free-standing agency within the Department of Health and Human Services devoted to fostering research to improve health care's quality, safety, and accessibility. Under Trump's budget proposal, the AHRQ would be folded into the NIH, and its $479 million budget would be eliminated. AHRQ-funded research has contributed to a 21% reduction in the rate of hospital-acquired conditions since 2010, averting 3 million adverse events and saving 125,000 lives. The agency estimates that these improvements have generated $28 billion in savings.

The NIH also supports critical global public health efforts, largely coordinated through the Fogarty International Center, a $69.1 million program dedicated to building partnerships between health research institutions in the United States and other countries. The president's budget proposal would eliminate Fogarty altogether. Yet global partnerships are critical for developing effective responses for global epidemics, argues James Curran, professor of epidemiology and dean of the Rollins School of Public Health at Emory University: "Disease, and our understanding of causal factors, knows no geographic boundaries."

International collaborations are essential for surveillance of infectious diseases such as HIV, Ebola, SARS, and influenza and for development of effective treatment and prevention programs. They are also critical for understanding how chronic diseases, such as diabetes and hypertension, can manifest differently in diverse settings, which can lead to new therapeutic discoveries. "Fogarty is catalytic," said Eric Goosby, a former ambassador-at-large and U.S. global AIDS coordinator. "It amplifies the other

Return on Government-Supported Biomedical Research.*

Improved health
NIH-funded research has led to major reductions in deaths from heart disease, stroke, cancer, and infections. Rates of U.S. deaths from all causes dropped by 43% between 1969 and 2013. Long-term research investments such as the Framingham Heart Study and the Diabetes Prevention Program have identified major risk factors for chronic disease and low-cost lifestyle changes that can delay or prevent the onset of illness.

Increased safety and value
Research funded by the Agency for Healthcare Research and Quality (AHRQ) has contributed to lowering the rates of hospital-acquired conditions by 21% since 2010, which translates into 3 million fewer adverse events and 125,000 lives saved. The AHRQ estimates that these improvements have generated $28 billion in savings.

Research and drug development
NIH-funded basic science research fuels the entry of new drugs into the market. NIH-supported research has contributed to the discovery of 153 new FDA-approved drugs, vaccines, and new indications for current drugs in the past 40 years.[3] Examples include the development of zidovudine (AZT) to treat HIV, imatinib to treat chronic myelogenous leukemia, and vaccines for disease prevention (hepatitis B, cervical cancer, and Ebola).

Staying ahead in science, technology, engineering, and math
The United States is the largest funder of biomedical research in the world, but it has active competitors. In 2007, China trained more Ph.D.s in the natural sciences and engineering than the United States.[4] Furthermore, China's investments in research and development are projected to surpass U.S. spending in 2019.

* Information is from the National Institutes of Health, the Agency for Healthcare Research and Quality, and the Organization for Economic Cooperation and Development, unless otherwise noted.

NIH institutes' funding globally, and makes other investments more sustainable, by helping to identify local talent to be trained in clinical, bench, and implementation research, which results in stabilizing regions and responding promptly to outbreaks and epidemics."

The NIH is already operating on a slim margin, with funding that has essentially flat-lined since an expansion period under the Clinton administration when the budget doubled over 5 years. Although the NIH was set to receive an increase of $1 billion to $2 billion in the 2017 fiscal year, which began in October, Congress has been unable to finish its 2017 spending plan. The government has been operating under a continuing resolution that freezes spending at 2016 levels. While the NIH is constrained by the need for annual appropriations, its research grants and contracts are multiyear awards, with most of its budget geared toward recipients of awards from prior years. Yet on March 24, the Trump administration issued an emergency request for an additional spending cut of more than $1.2 billion to the NIH for the current fiscal year.

Most experts agree that cuts of any magnitude will ultimately hamper the scientific enterprise and adversely affect local, national, and global economies, while inhibiting discoveries that are essential for fighting disease worldwide. Scott Stern, a professor of management of technology at MIT, notes that "perhaps more than any other agency in the world, the NIH has fostered the careers of individuals who have gone on to develop meaningful connections in human health outcomes and therapeutic interventions that result in the United States being global leaders. Funding disruptions will have far-reaching effects, destabilizing generative research, and even cuts less than those currently proposed could be devastating. Often, the full impact of a knife wound is only discovered long after you have removed the blade."

Ultimately, the legislative process will determine the 2018 appropriations for the NIH. There has historically been enthusiastic bipartisan congressional support for biomedical research, as evidenced by the passage of the 21st Century Cures Act at the end of 2016. Fiscal year 2017 marks the beginning of proposed 10-year funding (a total of $4.8 billion) for expediting the discovery, development, and delivery of new treatments and cures through the Precision Medicine Initiative, as well as supporting former Vice President Joe Biden's Cancer Moonshot and the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative aimed at improving our understanding of diseases such as Alzheimer's.

Although Republican leaders, including U.S. Senator Roy Blunt (R-MO), chairman of the Senate Appropriations Subcommittee that funds the Department of Health and Human Services, have said that Congress must "continue to firmly establish our federal com-

mitment to NIH," there are no guarantees. Two years ago, Newt Gingrich, former speaker of the House, called for a doubling of the NIH budget, noting in a *New York Times* op-ed that past support had been bipartisan because "health is both a moral and financial issue." Unfortunately, funding for the NIH has struggled to keep up with inflation over the past decade. Especially in light of the recent Republican infighting that led to the withdrawal of legislation to repeal the Affordable Care Act, many observers, recognizing that the GOP is not marching in lock-step, argue that this is a key time for academics to join together and lobby congressional leaders.

Ultimately, the NIH provides the foundation for U.S. competitiveness in driving discovery. It is the U.S. crown jewel, and our medical innovations are among our strongest exports to the world. Undermining this system will deplete medicine and science of the best and brightest minds and lead to a global destabilization with far-reaching impact. It is up to the U.S. Congress to follow through on its mandate and ensure that bipartisan support remains for the NIH to advance science, technology, and medicine in the 21st century.

Disclosure forms provided by the authors are available at NEJM.org.

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Resident Duty Hours and Medical Education Policy — Raising the Evidence Bar

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On March 10, 2017, the Accreditation Council for Graduate Medical Education (ACGME) issued revised common program requirements for residents that go into effect this July. The revisions emphasize the importance of teamwork, flexibility, and physician welfare during training, but all the attention has been (and will no doubt remain) focused on the changes in duty hours. The new rules maintain an 80-hour-per-week cap on residents' work, averaged over 4 weeks, but extend the permissible work shifts for first-year residents from 16 hours to 24 — limits already in place for residents in year 2 and beyond — and permit more within-shift flexibility as long as weekly duty-hour limits are met. What makes this policy change so important is that it seems to reverse direction on the basis of a new approach to developing and using evidence to inform education policy.

For a public largely used to 8-hour workdays and 40-hour workweeks, the old rules seemed stressful enough. Public interest in the topic has been strong since 1984, when an 18-year-old college freshman named Libby Zion died at New York Hospital, ostensibly because she was cared for by overworked and undersupervised residents.[1] A New York State grand jury investigating the case looked beyond the involved physicians and hospital and essentially indicted U.S. graduate medical education for its long hours and lax supervision. Resident duty hours became a focus of the ACGME, and duty-hour policies were introduced, shaped, and reshaped over the subsequent three decades, at first on the basis of opinion, and later supplemented by bits and pieces of evidence.

At the heart of this debate is the concern that residents work-