POLICY ARTICLE

SCIENCE FUNDING

What if NIH had been 40% smaller?

Replaying history with less NIH funding shows widespread impacts on drug-linked research

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The US National Institutes of Health (NIH) has enjoyed unusually consistent support from the US government since its expansion after World War II (*1*). Continued support is less certain. For much of 2025, new and competitive grants at NIH were more than 40% below the levels that had been disbursed by the same date in the preceding year (*2*). Meanwhile, the president's proposed budget for discretionary spending called for a 39.3% cut to NIH for fiscal year (FY) 2026 (*3*). To help understand the effects of such large cuts to funding, we leveraged new data and measures to consider an alternative history: If the permanent NIH budget had been 40% smaller, how would that have affected the medicines we enjoy today? Results suggest that such large cuts could affect a large share of drug approvals.

In recent decades, biomedical innovation has contributed to marked health improvements in the United States (*4*). A large share of these gains can be attributed to advances in medical technology, and the largest single funder of biomedical research in the world over this period has been NIH. NIH funding levels are of global importance because scientific knowledge circulates across borders, and drug developers depend on research backed by many sources. Against this backdrop, the president's budget proposes substantial reductions to NIH appropriations, with no offsetting increases at other biomedical research agencies, and broader reductions across federal research and development (R&D).

The ultimate NIH budget for FY2026 (which begins 1 October 2025) will depend on congressional action, and the effect on grant funding will hinge on how any reductions are allocated (for example, intramural versus extramural research, institute by institute, and direct versus indirect costs). Although the proposed FY2026 decrease would be unprecedented in the agency's postwar history, proposals for large reductions are not new. In 2017, for example, the president's budget proposed an 18% reduction to NIH. Because such proposals recur, evidence on their potential consequences remains relevant. Estimating those consequences is difficult, however, when contemplated changes lie well outside the historical range of appropriations. Recently, when asked to assess how large NIH reductions would affect drug development, the Congressional Budget Office reported that its data and methods did not permit an estimate.

CREATING AN ALTERNATIVE HISTORY

Although we cannot, of course, literally replay history, we can identify which grants in any given year fell in the bottom 40% of the funding priority queue. These are proposals that likely would not have been funded under a reduced NIH budget. In the remainder of this article , we call these "at-risk" grants. We examined the actual output of at-risk grants to assess which drugs, if any, are linked to research funded by such grants. If few advances are connected to at-risk grants, it would suggest that a 40% NIH budget cut might have had limited consequences for drug development, implying less cause for concern about current proposed reductions. Conversely, if medical advances are frequently connected to at-risk grants, it would indicate that future cuts may also carry substantial costs.

To perform this analysis, we proceeded in two steps. First, we used data on grant-level priority scores to identify the funded grants that would have been cut had the NIH budget been 40% smaller in each year. Priority scores were assigned by peer review study sections that evaluated grant applications. Second, we linked these at-risk grants to new molecular entities (NMEs) approved by the US Food and Drug Administration (FDA). NMEs are drugs that contain a new active ingredient. We linked at-risk grants to NMEs using

Share of linked drugs under different criteria

Compared with patents that directly acknowledge NIH funding, a much higher share link to NIH indirectly through citations.

	ANY NIH FUNDING	AN "AT-RISK" GRANT
Directly acknowledged by at least one patent	40 (7.18%)	14 (2.5%)
Connected to at least one patent-to-paper citation	331 (59.4%)	286 (51.4%)
Connected to at least 25% of patent-to-paper citations	204 (36.6%)	65 (11.7%)

The denominator consists of the 557 drugs with at least one preapproval Orange Book patent approved by the FDA between 2000 and 2023. There are 271 (48.6%) drug approvals that do not cite any at-risk NIH research. Of this set, 94 (16.9%) are associated with patents that do not reference any scientific publications; a further 132 (23.7%) have patents that do reference scientific publications, but none of these publications acknowledge NIH grant support. Last, 45 approvals (8.1%) have patents that do reference scientific publications that acknowledge NIH grant support, but none of these grants would disappear under our hypothetical 40% cut.

both a direct and indirect approach. The direct approach looks for drugs whose patents explicitly acknowledge support from an at-risk grant, and the indirect approach looks for drugs whose patents cite academic research that acknowledges support from an at-risk grant.

We identified at-risk grants using the actual scores received by NIH grants, which were provided to one of the authors for the 1980 to 2007 period. At NIH, grant applications are funded according to two key factors: the priority score and the institute responsible for potentially funding it. Broadly speaking, each NIH institute funds the applications it is assigned in order of priority scores until its budget is exhausted (*5*). Because we have information on a grant's score and its assigned institute, we could closely recreate this rank ordering and identify which applications would not have been funded, had the budget been 40% smaller.

Indicators of importance of approved drugs

Two levels of approved drugs' connection to at-risk grants are shown, reflecting how many connected publications disappear under a 40% cut to the NIH budget.

	AT LEAST ONE CITED PUBLICATION DISAPPEARS			AT LEAST 25% OF THE CITED PUBLICATIONS DISAPPEAR		
	Not at risk (n = 271)	At risk (n = 286)	Δ	Not at risk (n = 492)	At risk (n = 65)	Δ
Mean cited publications	3.61	35.39	31.78**	20.82	13.17	−7.65
Mean NIH-linked cited pubications	0.32	9.93	9.62**	5.13	6.20	1.07
Mean cited at-risk publications	0.00	5.46	5.46**	2.62	4.23	1.61†
Granted priority review (%)	41	60	20**	50	55	5
Approval year	2011.52	2014.27	2.74**	2012.89	2013.28	0.39
Total patent value (US$ millions)	271.02	504.23	233.21**	388.91	580.13	191.22

n = 557 drugs approved since 2000 with 2668 preapproved patents (average patents per drug = 4.8, median = 4, minimum = 1, and maximum = 34). P values corresponding to two-tailed t tests of equality for the outcomes between at-risk and not-at-risk drug approvals are indicated (†$P < 0.10$, **$P < 0.01$). Patent value comparison is based on a subset of 329 approvals, corresponding to public firms (196 approvals for which at least one cited publication would disappear, 32 approvals for which at least 25% of the cited publications would disappear).

Next, we linked these at-risk grants to FDA-approved drugs. We started with a simple and direct approach. The Bayh-Dole Act requires patent-holders who received government funding to add a "government-interest statement" to their patents and report their patents back to the funding agency. We could use these statements and reporting data to identify drugs with patents that acknowledge funding from specific NIH grants. This data is imperfectly reported, but we built on Ouellette and Sampat (*6*), who combine several distinct sources to correct for various omissions. These authors identified all patents listed in the FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations (commonly called the "Orange Book") that link to public sector funding. Starting with the subset of these patents emanating from NIH extramural funding, we determined the specific grants supporting the patents and which of these were at-risk grants. Not all drug patents are created equal: Secondary patents, which cover ancillary aspects of drugs rather than the core active ingredient, are sometimes viewed as more peripheral (*7*). To limit the influence of late-filed secondary patents, although we do not explicitly categorize patents, we focused our analyses on patents applied for before a drug was approved.

Our focus on NMEs limits the scope of our analysis to small-molecule drugs. As a result, we excluded a wide range of important medical advances that may also build on NIH-funded research. These include vaccines, gene and cell therapies, and other biologic drugs; diagnostic technologies and medical devices; as well as innovations in medical procedures, patient care practices, and surgical techniques. Our work relies on the patents that protect medical advances, which we linked to NIH-funded research in various ways. This was enabled by the Orange Book patent-listing requirements for small-molecule drugs that do not apply to biologic drugs or other medical technologies. Our analysis therefore provides a focused lens on one type of medical innovation that could be affected by NIH budget cuts.

Direct linkages

Because of the long lags involved between fundamental research (mostly but not exclusively performed in academia) and drug development investments from the private sector (*8*), the sample covers 21st-century drug approvals. Of the 557 drugs that were approved between 2000 and 2023, we found that 40 (or 7.1%) drugs have at least one patent that directly acknowledges NIH extramural funding. Of this set, 14 acknowledge funding from an at-risk grant (see the first table). These include Cerdelga (generic name Eliglustat, approved by the FDA in 2014), the first once-a-day pill for Gaucher disease type 1, an inherited disorder in which fatty material builds up in the liver, spleen, and bones; the drug lets many patients avoid lifelong intravenous enzyme infusions while keeping their organ size and blood counts stable.

By focusing on drug patents that directly acknowledge NIH grant support, we isolated a set of drugs for which there is strong evidence that a specific grant contributed to their development. However, this approach understates the importance of publicly funded research by overlooking the indirect ways that publicly funded research supports innovation. Less than 10% of drugs approved since 1985 list government-funded patents in the Orange Book (*6*), whereas surveys of laboratory managers indicate that public-sector science informs more than 40% of industrial drug R&D projects (*9*).

Indirect linkages

Compared with drug patents that directly acknowledge government funding, a much higher share of drug patents are linked to public sector research indirectly through citation trails. We used citation information to identify drug patents that cite NIH-funded research, rather than NIH funding directly (*10*). This approach allowed us to identify drugs that reference NIH-funded publications but excluded drugs that may have built on NIH-funded research through more circuitous pathways, such as citing research that itself builds on NIH-funded research, or drugs that were developed by private-sector researchers trained with NIH funding that leave no citation trail.

We found frequent links between NIH funding and downstream pharmaceutical research. Of the 557 drug approvals in our sample, 331 (59.4%) have a patent that cites at least one research publication acknowledging NIH support. Indeed, more than half of approved drugs (286, or 51.4%) are linked to at-risk research—research funded by grants that would have been cut under a 40% budget reduction. A flagship example is Gleevec (imatinib, approved in 2001), the first BCR-ABL kinase inhibitor, which transformed chronic myeloid leukemia from a fatal illness into a manageable condition and whose foundational patents ultimately trace back to NIH-funded work on the BCR-ABL oncoprotein (*11*).

A citation linkage between a drug and research can reflect a range of relationships: The cited work may have been pivotal to the drug's development; or contributed background knowledge, methodological tools, or general scientific context; or been cited as part of a pat-

ent strategy but not crucial to the patented invention. On average, each drug that is linked to at-risk research in our sample cites 35 research publications. As such, the loss of any single cited publication in our alternative-history counterfactual scenario should not be interpreted as evidence that the drug could never have been developed in its absence. To identify drugs that are more reliant on NIH-funded work, we also report a stricter threshold: We classified a drug as highly linked to at-risk research if at least 25% of its citations go to at-risk research.

Since 2000, 65 of 557 new drug approvals (11.7%) are highly linked to at-risk research. This portfolio likewise contains several widely used therapies. Tarceva (erlotinib, approved in 2004) was the first epidermal growth factor receptor (EGFR)–targeted agent to demonstrate a clear overall-survival benefit in advanced non–small-cell lung cancer, adding roughly 2 months in the pivotal BR.21 trial (*12*). Emtriva (emtricitabine, approved in 2003) soon became a backbone nucleoside in combination antiretroviral therapy and, as part of Truvada, anchored the first FDA-authorized HIV preexposure prophylaxis regimen in 2012. At least 25% of the citations to research publications made by these two drugs goes to research funded by at-risk grants.

BENEFITS ARE WIDE AND DIFFUSE

Our three approaches yielded different estimates of the proportion of drugs connected to at-risk grants. If we imagine retroactively reducing the NIH budget by 40%, one important question arises: Which specific drugs might not have been developed as a consequence? Answering this question is challenging, and we can only confidently identify a small subset of drugs—specifically, the 14 whose patents explicitly acknowledge support from NIH grants that would have lost funding.

But another question is simply, which drugs reference science funded by at-risk grants? We found that the preapproval patents in 51% of FDA-approved drugs cited research produced by at-risk grants. We take this as a rough indicator that the benefits of research funded by NIH grants that are not funded in our alternative-history scenario is widespread and diffuse, even if we cannot say with certainty whether the development of any specific drug would be unaffected, delayed, or impossible without the specific research publication it cites (see the supplementary materials for details on the interpretation of citations). Our last estimate sits somewhere in between these two questions; it helps to identify drugs that more heavily cite at-risk research.

Last, we examined the types of drugs that would be affected by the funding cut we considered. Although our illustrative cases show that some grant-linked drugs are clearly important, we conducted a more systematic assessment using two metrics: FDA priority-review designation (a proxy for scientific and societal value) and abnormally high stock-market returns (a proxy for private value as judged by investors).

Our first approach examined whether drugs linked to at-risk research are more likely to receive priority review from the FDA. Established in 1992, the priority review system accelerates evaluation for drugs that "if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications" (*13*). Drugs linked to at-risk research are more likely to receive priority review than unlinked ones (60% versus 41%, statistically significant at the 1% level). For drugs "highly linked" to at-risk publications, the same result holds qualitatively (55% versus 50%), but the difference is not statistically significant (see the second table).

Our second approach used estimates of how the stock market values a patent on the basis of changes in a firm's market value around the time of a patent grant (*14*). Applying this to drug patents from the 329 approvals associated with publicly traded companies, we found that drugs linked to at-risk research are more valuable on average than unlinked ones. Overall, we found no evidence that drugs linked to at-risk research or grants are less valuable or impactful than other drugs under any definition of linkage.

These results are consistent with the claim that large cuts to NIH's permanent budget in the past would have resulted in substantially fewer medical innovations than we enjoyed in our actual history. In some narrow cases, we can point to specific drugs that directly relied on NIH grants unlikely to be funded by NIH under a much smaller budget. But the benefits of NIH research in general are wide and diffuse. A very large number of advances—roughly one in two during the 21st century—are linked to NIH grants that are cut in our counterfactual scenario. We also found no evidence that linked drugs are less impactful, on the basis of our proxies for clinical and economic impact, than drugs that are not linked to at-risk grants.

In some ways, our analysis understates the extent to which medical advances are connected to NIH research. Our data on NIH priority scores stops in 2007, so we did not observe whether recent drugs are linked to at-risk grants beyond that time period. Neither did we observe second-order connections, when an NIH-funded scientific discovery enables additional research that in turn leads to drug development. Nor did we observe connections to medical advances beyond small-molecule drugs. Last, we were unable to identify the (likely many) scientists whose careers would have been cut short without NIH support during their doctoral and postdoctoral studies. Even so, in the largest sample of medical advances for which we have good data (post-2000 small-molecule drug approvals), we found extensive connections between medical advances and research that was funded by grants that would have been cut if the NIH budget was sharply reduced. Assuming that the near term resembles the recent past, our analysis indicates that substantial NIH budget cuts—including those implemented at the funding margin—could curtail research linked to a large share of potential drug approvals. □

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SUPPLEMENTARY MATERIALS

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