Preprint – This study has not been peer-reviewed yet.

Modeling the Impacts of Budget Reductions at the U.S. NIH on Research and Innovation

Zeynep Hasgul[1]; Hannah Lee[1]; Mohammad S. Jalali[1,2,*]

[1]MGH Institute for Technology Assessment, Harvard Medical School, Boston, MA
[2]Sloan School of Management, Massachusetts Institute of Technology, Cambridge, MA

*Corresponding author. Email: msjalali@mgh.harvard.edu

Abstract: Stable public funding underpins biomedical innovation, yet the U.S. research system remains vulnerable to swings in federal budgets. We developed BRIDGE (Biomedical Research Investment Dynamics and Growth Evaluation), a simulation model linking NIH funding to new drug approvals, workforce dynamics, and scientific output. Using 47 longitudinal data measures from 1995-2024, validated against historical trends and projecting outcomes through 2050, we examined multiple funding trajectories, including stable growth, flat budgets, large reductions, and later restorations. Results show that across scenarios, even temporary disruptions create lasting setbacks for drug development, researcher training, and basic science. Later funding increases cannot repair the damage for decades, with persistent losses in capacity and output that highlight how fragile the system is to short-term shocks and why stable public investment is essential for long-term innovation.

Teaser

NIH funding cuts create setbacks in research and drug innovation that persist for decades, even when budgets rebound.

Introduction

Federal funding plays a central role in setting the trajectory of biomedical research in the U.S. and, as the world's largest funder, shapes scientific progress worldwide. The National Institutes of Health (NIH) has long been the cornerstone of U.S. biomedical investment, funding research, training, and infrastructure while guiding priorities, norms, and capacity across the system (*1*–*3*). Its budget, however, has periodically been subject to political and economic pressures. Such pressures raise concerns about the continuity of research programs and the broader infrastructure and workforce that underpin the U.S. biomedical research enterprise (*4*, *5*).

A growing body of evidence has shown that these investments support innovative science, help train the next generation of researchers, and catalyze collaborations with industry that lead to therapeutic development (*1*, *6*, *7*). For example, decades of NIH-funded work on the Human Genome Project led to immunotherapy, named "breakthrough of the year" in 2013 (*8*, *9*). Ongoing initiatives, such as the BRAIN Initiative and NIH-supported antibiotic resistance research, could accelerate treatments for Alzheimer's and help avert projected deaths from resistant infections (*10*–*12*). These areas often lack commercial investment, given uncertain returns and long timelines. At the same time, their broad public benefit makes public support essential.

While the value of government research spending is occasionally questioned, studies consistently demonstrate that NIH funding yields significant returns in the form of new knowledge, improved health outcomes, and long-term economic benefits (*13*, *14*). In 2024, NIH funding supported about 408,000 jobs and generated $94.6 billion in new economic output nationwide, an estimated return of

$2.56 for every dollar awarded (*15*). Research also shows that even temporary shifts in NIH funding produce magnified downstream effects due to multi-year grant obligations (*16*). A study that looked at the potential scale of proposed NIH budget cuts found that if the agency's long-term funding had been about 40% lower, high-risk NIH-funded research linked to more than half of modern drug discoveries (286 of 557, or 51.4%) approved between 2000 and 2023 would have been at risk (*17*).

What remains less understood, however, is how different funding paths—such as sustained reductions, stagnation, or later restoration—shape the long-term impacts on the biomedical research system, and what this means for preventing or mitigating disruption to innovation. Understanding the likely impacts of budget reductions raises critical questions: How will the contraction affect the size and composition of the biomedical research workforce? What are the likely consequences for the pace of scientific discovery, translational progress, and therapeutic innovation? And if a large-scale cut is reversed, how quickly and to what extent can the system recover?

To address these questions, this study develops a dynamic simulation model of the biomedical research ecosystem—BRIDGE (Biomedical Research Investment Dynamics and Growth Evaluation)—grounded in historical data and prior empirical insights into funding trajectories, workforce shifts, and innovation outcomes. A systems modeling approach is well-suited for capturing how changes in policies ripple through components of an ecosystem, especially when delays, accumulations, and feedback loops are involved. These mechanisms are common in large-scale adaptive systems. They capture time-lagged and feedback-driven effects that retrospective or regression-based analyses may miss. Rather than extrapolating past trends, the model generates projections from the way elements within the biomedical system interact over time, allowing shifts such as slower therapeutic development or changes in workforce composition to emerge from the system's structure.

While the model incorporates a range of upstream and midstream processes, including training, workforce dynamics, and research outputs, our primary outcome is novel drug approvals since it is a measurable and policy-relevant proxy for downstream biomedical innovation. This focus does not imply that NIH funding serves only drug development; rather, the model is designed to reflect how public investment in basic and translational research enables innovation, including but not limited to therapeutics. We simulate a period of reduced NIH budget, along with alternative scenarios in which funding returns to pre-cut levels at varying speeds.

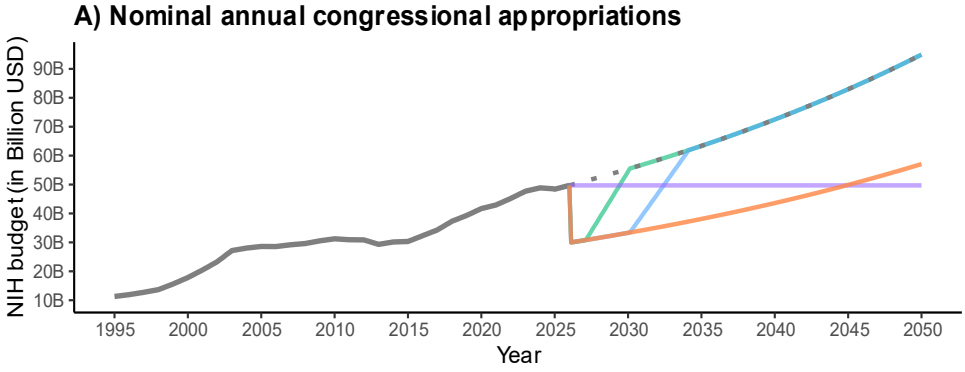
The model integrates 47 longitudinal data measures from 1995 to 2024, is validated against historical benchmarks, and projects outcomes through 2050. Full model details and validation procedures are provided in the supplementary materials.

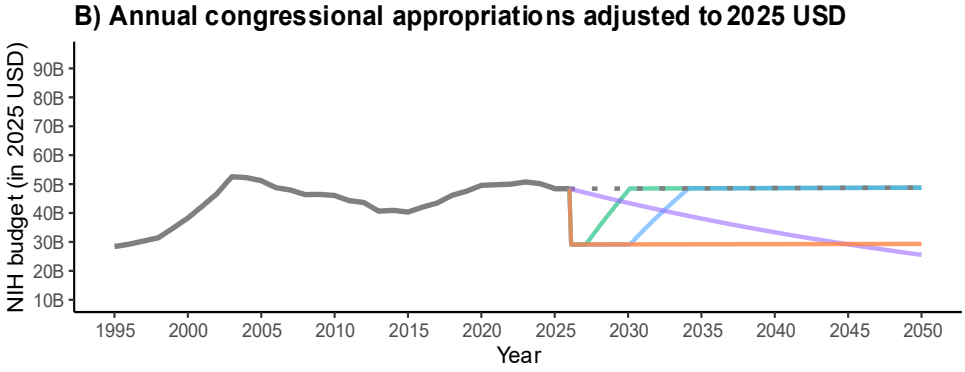
Simulated NIH Budget Scenarios

We examined several counterfactual scenarios for post-2026, shown in Figure 1. In the "baseline" scenario, appropriations grow with inflation, keeping purchasing power constant over time. In the "no-increase" scenario, appropriations remain fixed with no further growth. In the "cut" scenario, funding is reduced by 40% in 2026, after which appropriations grow with inflation from the reduced base.

In addition, in the "restore" scenarios, funding is also reduced by 40% in 2026 but then gradually returns to the baseline trajectory through steady nominal annual increases, beginning either one year after the cut (2027, the "1-year restore" case) or four years after the cut (2030, the "4-year restore" case). These timings reflect two plausible policy paths: one in which funding is adjusted within the current administration, and another in which changes occur under a future administration. The pace and scale of these restoration scenarios are comparable to the historical doubling era, where the NIH budget increased in unadjusted dollars from about $14 billion to $27 billion between 1998 and 2003 (*18*).

In the baseline scenario, the nominal NIH appropriations are assumed to continue to rise, as has often been the case historically (see Figure 1-A), following the annual increase of 2.7% beyond 2025, based on the forecast of the Biomedical Research and Development Price Index (BRDPI). The BRDPI, provided by the Department of Commerce's Bureau of Economic Analysis, measures annual changes in the cost of supplies and workforce necessary for conducting biomedical research (*19*). The BRDPI is routinely cited in annual congressional appropriations discussions as a benchmark for justifying budget increases, making it a relevant and policy-aligned measure for modeling future appropriations (*20*). Because research costs typically rise faster than general consumer prices, BRDPI offers more accurate comparisons than the consumer price index, the most widely used measure of inflation. Hence, we used BRDPI to adjust budget projections in constant 2025 USD as key model inputs to estimate the number of research projects the NIH budget could support, and in turn, other downstream outcomes. Figure 1 presents both nominal (panel A) and BRDPI-adjusted (panel B) values reported in constant 2025 USD. The figure shows that while nominal funding increases, the inflation-adjusted (real) value may decline over time if appropriations do not keep pace with rising research costs.





Scenarios	Description 2026 budget → post-2026 annual growth rate → budget restore path
Baseline	Purchasing power constant 2025 + 2.7% → 2.7% → no restore
No-increase	Budget constant, purchasing power gradually declines Baseline → 0% → no restore
Cut	Immediate budget decline baseline - 40% → 2.7% → no restore
1-year restore	Budget restoration begins in the same administration baseline - 40% → 2.7% → restore starts in 1 year, reaches baseline in 2031
4-year restore	Budget restoration delayed to the next administration baseline - 40% → 2.7% → restore starts in 4 years, reaches baseline in 2034

Fig. 1: Annual NIH congressional appropriations, nominal (A) and adjusted to 2025 USD using Biomedical Research and Development Price Index (B), historical (1995-2025) and projected (2026-2050). Note: Scenarios include: baseline (dashed line); no-increase (purple line); cut (orange line); and restoration to baseline level after one year (green) and four years (blue). The two restore scenarios have a four-year ramp. All values are adjusted using the Biomedical Research and Development Price Index (BRDPI), which accounts for inflation specific to biomedical research; as a result, nominally constant appropriations appear as a decline in real terms over time.

Additionally, as a supplementary test, we examined an extreme case in which, following four years of sustained cuts, the NIH budget doubles in nominal terms in fiscal year 2030, and then grows annually at the rate of BRDPI. This scenario is not intended as a realistic forecast but as a test to examine how quickly the system could recover under extreme conditions, illustrated in the supplementary materials.

Projections of the Simulated Scenarios

Using historical data on NIH appropriations, workforce composition, research outputs, and innovation indicators, the model closely replicated observed trends from 1995 to 2024 with a mean absolute percentage error of 10.5% across series. Model fit is shown in the supplementary materials. Here, we first report projections for the size and composition of the workforce, followed by research outputs and drug innovation, and conclude with economic implications and robustness checks.

Figure 2 presents the projected outcomes in raw numbers, while percentage differences are plotted in the supplementary materials. Panel (a) shows the number of principal investigators (PIs), including early-stage and established researchers with active NIH grants. The number of PIs has remained largely stagnant since 2009. Under the baseline scenario (dashed line), it is projected to remain near current levels with only a slight decline, whereas in the no-increase scenario (purple line), the number of PIs declines gradually at first, then more rapidly, reaching 46% below the baseline by 2050. Under the cut scenario (orange line), the number of PIs declines sharply, reaching a low point within 9 years at 50% below the baseline. It then recovers slightly but remains 36% below the baseline by 2050. In the 1-year restoration scenario (green line), the number of PIs also drops sharply but begins a gradual recovery once funding is restored. However, the recovery is not symmetrical: the decline is rapid, while the rebound is slower, returning to baseline in about 20 years. The 4-year restoration scenario (blue line) follows an overall similar trend.

Panel (b) shows that postdoctoral researchers have increased in previous years. Under the baseline scenario, growth is projected to continue but at a slower rate. In the no-increase scenario, the number of postdocs is projected to decline, reaching about 31% below the baseline by 2050. The cut scenario results in a faster initial decline, with the number of postdoctoral researchers falling to about 33% below the baseline at its lowest point in 13 years, before recovering slightly to 31% below baseline by 2050. In both the 1-year and 4-year restoration scenarios, the number of postdoctoral researchers also declines sharply after the initial cut, reaching lows of 12% and 25% below baseline in 5 and 7 years, respectively. However, postdoctoral numbers rebound more quickly than the PI count, returning to near-baseline levels in 12 and 14 years, respectively.

Panel (c) shows that the number of doctoral students in science, engineering, and health has overall risen steadily in recent decades. Under the baseline scenario, enrollment is projected to continue increasing, but at a slower rate after 2036. In all other scenarios, the number of doctoral students is projected to remain above 2025 levels, though the levels vary relative to the baseline. By 2050, the number of doctoral students is projected to be 7% below baseline in the no-increase scenario and 15% below baseline in the cut scenario. In the 1-year and 4-year restoration scenarios, the declines are milder, at 5% and 9% below baseline, respectively, yet recovery still does not return the number of doctoral students to baseline.

Additionally, panel (d) presents NIH-supported fundamental research publications. The number of papers has not increased since peaking around 2010, and under the baseline scenario, this stagnation is projected to continue. In the no-increase scenario, a slow decline begins after one year and accelerates after 2030, reaching 61% below baseline by 2050. Under the cut scenario, the number of publications drops sharply and by 2050 reaches levels last observed in 1996, approximately 70% below baseline. In

the 1-year and 4-year restoration scenarios, publications fall to lows of 28% and 44% below baseline in 10 and 12 years, respectively, before getting back on a recovery track. However, recovery is slow, and by 2050, counts remain 9% and 18% below baseline, respectively.

Finally, panel (e) shows the annual number of FDA-approved novel drugs. Under the baseline scenario, approvals remain near current levels, with a slow decline beginning after about a decade. The no-increase scenario follows a similar trajectory until 2035, after which the decline becomes more pronounced, resulting in 27% fewer annual approvals by 2050. Under the cut scenario, the decline is earlier and sharper, with approvals falling to about 44% below baseline by 2050. In the 1-year and 4-year restoration scenarios, approvals also decline and reach the lows of 13% and 22% below baseline by 2050, respectively.

As panel (f) illustrates, lower approvals lead to a cumulative shortfall in novel drugs between the time of cut, 2026, and 2050. Specifically, the total number of approvals falls from 2,199 in the baseline scenario to 2,114 in the no-increase scenario, which is about a 4% decline. In the cut scenario, with 1,998, the cumulative approvals fall 9% short of baseline. In the 1-year restoration scenario, cumulative approvals reach about 2,117, representing a 4% drop from the baseline, while in the 4-year restoration scenario, they total around 2,066, reflecting a 6% decline.

Translating these novel drug shortfalls into approximate foregone economic value, we estimate losses of about $0.20-$0.88 trillion (median: $0.54 trillion) for the no-increase scenario; $0.48-$2.08 trillion (median: $1.28 trillion) for the cut scenario; $0.20-$0.85 trillion (median: $0.52 trillion) for the 1-year restoration scenario; and $0.32-$1.38 trillion (median: $0.85 trillion) for the 4-year restoration scenario. These figures are expressed in 2025 dollars and should be viewed as rough estimates, intended to illustrate the potential order of magnitude rather than provide precise valuations. Even under an extended scenario where the NIH budget initially follows the cut trajectory but begins to recover after four years—doubling by fiscal year 2030 (an unprecedented increase)—the novel drugs still recover slowly. Cumulative approved novel drugs may not offset the baseline trajectory until around 2062, reflecting a lag of 36 years. Similar inertia is observed across other outcomes, underscoring how delayed or uneven funding recovery can leave lasting gaps in research capacity and outputs. We visualize the results of this extended scenario in the supplementary materials.

We report the ranges of estimated parameters and uncertainty intervals for the projected outcomes in the supplementary materials, showing that the overall trends remain similar across a plausible range. We also present several intermediate outputs, including the application success rate, principal investigators disaggregated by career stage, total faculty counts, the number of clinical trials, the industry research workforce, and other related measures.

Overall, these projections suggest that even temporary reductions in the NIH budget can generate long-lasting effects across the complex system that underpins U.S. biomedical research. We developed an online simulator, available at mj-lab.mgh.harvard.edu/nih-budget-simulator. This tool allows users to interact with the model to examine additional scenarios and explore a wider range of outcomes beyond what we can report here.

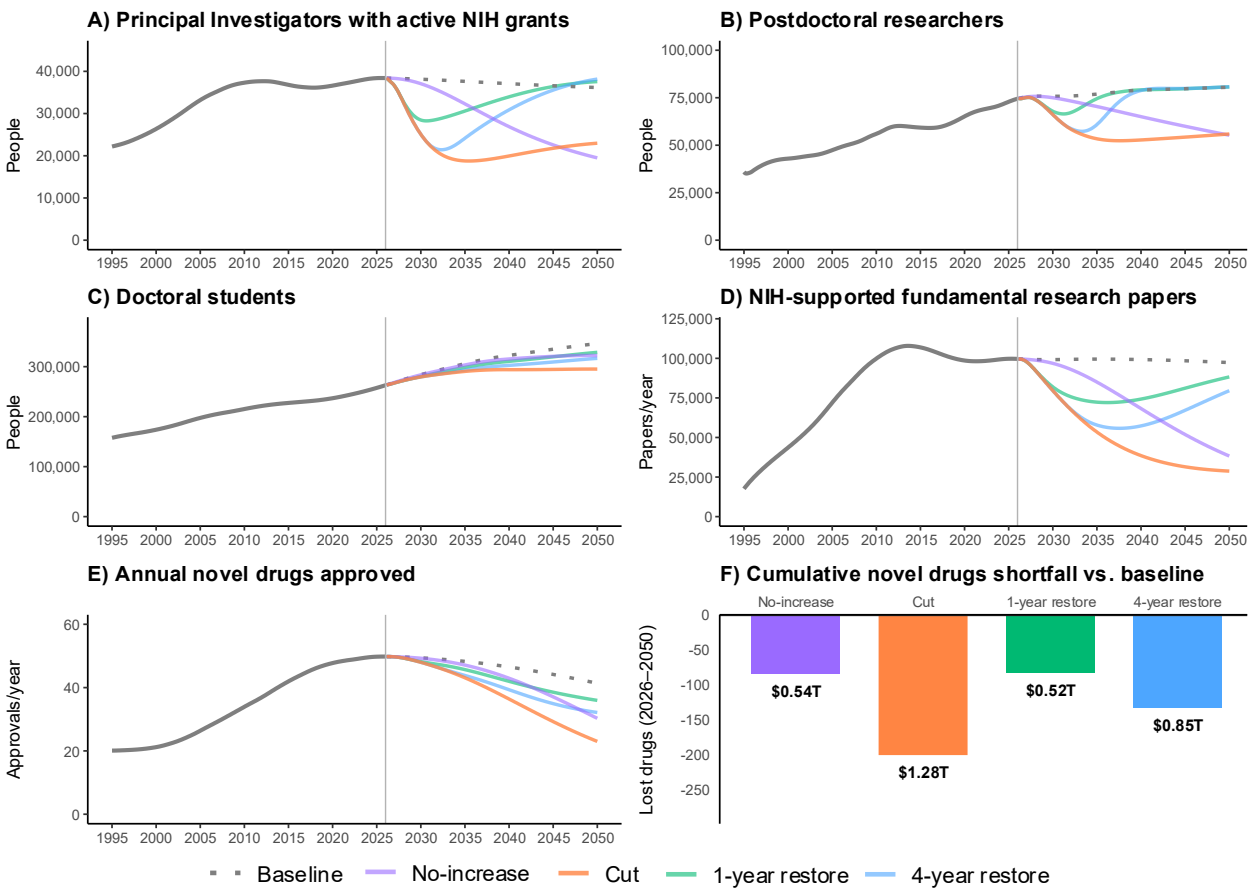


Fig. 2: Projected impacts of NIH funding trajectories on the U.S. biomedical research system (1995-2050). Scenarios include: baseline (dashed line); no-increase (purple line); cut (orange line); and restoration to baseline level after one year (green) and four years (blue). Vertical line indicates the initial year for scenario analysis.

Discussion

This study examines how changes in NIH funding may reshape the U.S. biomedical research system under different scenarios. It is the first data-driven, system-level model calibrated to historical data from 1995 to 2024, and projecting through 2050, linking changes in appropriations to long-term shifts in research workforce development and capacity, and the innovation pipeline. More broadly, the results illustrate how different trajectories of NIH funding—growth with inflation, stagnation, sudden reductions, or restoration—can lead to markedly different outcomes over both short- and long-term horizons. These findings are intended not only to highlight potential risks but also to provide a framework for anticipating outcomes and a decision-support tool to buffer the research ecosystem against volatility.

Overall, our results suggest that NIH funding cuts can have compounding, multi-layered effects, not only reducing the immediate number of grants or workforce participants but also weakening the interdependencies that sustain long-term innovation. For example, fewer research grants reduce mentoring opportunities, which slows workforce development; fewer early-stage studies delay clinical trials, which then bottleneck downstream drug development. These effects are not isolated but reinforcing, revealing how the NIH functions as a keystone actor in the broader U.S. innovation system.

Although the NIH nominal budget historically rose, once adjusted for biomedical research inflation, the effective budget has been stagnating. As a result, several measures, including the number of

researchers, fundamental research papers, and annual FDA approvals of novel drugs, have either already peaked or are projected to peak soon. Beyond those inflection points, our projections show a gradual long-term decline even if the real budget (adjusted for inflation) remains constant. The risks are even more pronounced if the nominal budget remains constant, as that implies the real budget will be decreasing in the upcoming years. In that scenario, the erosion of purchasing power accelerates the decline across all key indicators. Sudden, large-scale budget reductions add another layer of challenge, with the potential to trigger cascading disruptions across the biomedical research ecosystem, reducing the number of doctoral researchers, limiting institutional research capacity, and suppressing downstream innovation.

For instance, a funding cut of 40% in 2026 would reduce the NIH budget to approximately 2015 levels in nominal terms (i.e., without adjusting for inflation), which is equivalent to levels seen nearly three decades ago (1996-1997) when adjusted for inflation. The scale of the proposed 40% cut is so substantial that, everything else being equal, it would not even be sufficient to cover existing active grant commitments, let alone fund any new awards. This raises a policy challenge: when budgets shrink to merely cover existing commitments, the system effectively stalls, leaving little to no room for new ideas, investigators, or approaches to enter the biomedical system in the U.S.

After such a large cut, even when funding is restored to pre-cut levels, the recovery is slow and often incomplete (i.e., key measures like new fundamental research papers and annual FDA approvals of novel drugs remain below baseline trajectories). This reflects the time it takes to rebuild training infrastructure, rehire and sustain faculty, and re-establish institutional capacity to produce research outcomes. Once lost, many of these do not simply spring back. The lag between workforce loss and reconstitution is particularly important, as it means a large number of researchers may be diverted to other sectors. Delays in early-stage research also create ripple effects that slow the development of clinical advances and reduce the long-term flow of commercial innovation, specifically FDA-approved novel drugs. These results align with earlier findings that even modest cuts led to clinical trial delays, lab closures, and disrupted career trajectories for trainees and staff (*16*, *21*).

Even when modeling an optimistic, unprecedented rebound, where the NIH budget remains at the reduced level for four years and is then doubled in 2030, the system shows signs of prolonged disruption. This highlights the inertia and fragility of the biomedical research pipeline: once disinvestment has occurred, even dramatic reinvestment may not fully restore lost ground. Notably, cumulative FDA drug approvals still lag the baseline trajectory by about 36 years. Delays in workforce replenishment, research program ramp-up, and long-cycle innovation processes mean that missed opportunities in the early years compound over time.

Additionally, debates around NIH funding occasionally include concerns about inefficiency, redundancy, or workforce saturation. One may question whether all NIH-supported research or training is equally impactful, or whether some degree of reallocation or streamlining could improve the overall efficiency of the system. Similarly, concerns about an oversupply of publications or the limited number of long-term research or faculty positions for doctoral students are not new (*22*). But such concerns reflect questions of strategic alignment, how talent and funding are matched to long-term national goals, rather than a simple problem of too much research activity. Addressing these challenges calls for targeted adjustments in funding priorities, workforce development, and institutional incentives, not broad reductions in overall support. Uniform funding reductions do not distinguish between high-impact and low-impact projects, or between fields with saturated vs. underserved talent pipelines. Even modest but sustained cuts can erode the workforce across academia and industry, reduce institutional flexibility, and limit the system's ability to respond to emerging needs. In that sense, the issue is not just how much is cut, but how indiscriminately.

Other sources of research support, including industry and philanthropy, play important roles but are insufficient to fully replace the functions of NIH funding. While some substitution is possible, it would require fundamentally different priorities and incentives to close such a gap. NIH plays a central role in supporting early-stage, long-horizon research that often lacks clear commercial incentives (e.g., mechanistic studies of disease pathways or development of novel research methods). In contrast, industry tends to invest in late-stage development with shorter time-to-market and clearer returns (*23*, *24*). Also, philanthropic funding, while important, is comparatively small and typically focused on specific conditions or populations. Even if private investment increased in response to public disinvestment, the result could be narrower therapeutic targeting, reduced emphasis on basic science, or cost shifts to consumers and payers. These dynamics are important but beyond the scope of this model.

Our findings align with the growing body of research indicating that reductions in NIH funding have system-wide impacts. In 2013, the NIH faced a $1.55 billion (5%) budget cut, leading to fewer research grants and widespread disruption across all research programs (*25*). The immediate disruptions signaled broader effects: many researchers were forced to halt clinical trials, lay off staff, and abandon projects, resulting in lost opportunities for treatment development and delays in potentially life-saving therapies (*26*). Additionally, researchers have estimated that a 33% cut in NIH funding would be associated with a 15.3% decline in patents associated with new drugs, suggesting a proportional reduction in the pipeline of novel therapies (*6*, *27*). A preliminary macroeconomic analysis has similarly projected that a 50% reduction in NIH R&D spending could reduce U.S. GDP by approximately 3.7% over the long run (*28*).

Policy Implications

Our findings have implications for policy decisions beyond the current funding cycle. First, budget cuts can generate increased workforce attrition and underused infrastructure, such as laboratory facilities, shared research cores, or national data platforms, that are expensive to maintain and vulnerable to obsolescence as global standards evolve. Such dynamics may slow the pace of discovery, reduce long-term health gains, and shift U.S. positioning in global science, as countries with more stable public investment may attract top talent and accelerate innovation. Indeed, if early-career researchers lose trust in the stability of federal science funding or opt for more stable, non-research careers, the long-term talent pipeline may narrow, with downstream effects that take decades to correct. This may also deter prospective students from pursuing research careers altogether, shrinking the pipeline before talent even enters it. Second, abrupt disruptions to public funding may compromise the system's ability to respond to future national needs. For example, reduced investment in early-stage research today may limit the pool of expertise available to respond to future crises, including pandemics, antimicrobial resistance, or climate-related health threats.

Third, the effects of reductions are not symmetric: the damage from reductions occurs quickly, while recovery is slow and incomplete. Periods of funding instability may shift how institutions plan and prioritize long-term research investments, favoring short-term, lower-risk projects that can yield quicker returns. This strategic conservatism could further suppress breakthrough innovation, particularly in foundational science, where payoffs are inherently long-term and less certain. In this way, short-term austerity may lead to long-term stagnation, compounding the very economic and health burdens that scientific research is intended to alleviate. Fourth, our results caution against assuming that later surges in funding can readily compensate for earlier cuts. The model illustrates how scientific output is not immediately responsive to financial inputs: it must be cultivated, retained, and protected over time.

Finally, the impacts of large-scale budget cuts on novel drug approvals translate into potential present-value economic losses in the range of several hundred billion to over a trillion dollars (2025 USD) by

2050, depending on the cut scenario. These losses are substantial relative to the fiscal savings from the budget reduction, reflecting how disinvestment in biomedical research can generate long-lasting and disproportionate reductions in innovation output.

We provide a decision-support tool (through a user-friendly, online dashboard) for policymakers considering tradeoffs in fiscal planning, enabling exploration of both short-term budget savings and long-term innovation impacts.

Study Limitations

This model is designed to capture the key mechanisms linking NIH funding to workforce capacity, research activity, and novel drug development, but it does not represent every factor that could influence the biomedical landscape over the next 25 years. For example, shifts toward medical devices or diagnostics, advances in artificial intelligence-enabled care, regulatory changes, or global shifts in research priorities could alter drug approvals independently of NIH investment. These dynamics are outside the present scope.

Beyond these scope boundaries, the model has several specific limitations. While the model integrates historical data and estimates, it includes simplifications. It does not explicitly represent how universities might shift internal priorities, restructure grant portfolios, or adapt staffing models in response to external shocks. The model uses novel drug approvals as a primary outcome to represent downstream innovation, but it does not capture other important public health impacts of NIH-funded research, such as diagnostics or behavioral interventions. The model also does not distinguish workforce diversity or equity impacts, nor does it account for regional or institutional disparities, both of which may worsen under funding contractions and compound disparities in training, career advancement, and research opportunities across communities. Moreover, all projections assume that other key institutions, such as the FDA, continue operating as usual; however, these entities may also be impacted by budget cuts, and such ripple effects were not modeled in this analysis.

Despite these limitations, the model offers a transparent, focused foundation for assessing long-term impacts of NIH budget cuts. No single model can address every question in a complex system, and overly comprehensive models often sacrifice clarity and usefulness (*29*). By concentrating on core structural relationships, this model provides a flexible base for future extensions and more targeted policy analysis.

Taken together, our findings underscore that the biomedical research ecosystem is sensitive not only to how much funding it receives, but also to how predictably and consistently that funding is delivered. When support is withdrawn suddenly, the effects can extend across generations of training, discovery, and application. Recovery is possible, but it could take multiple decades, and some opportunities might never return. Finally, while focused on NIH, these findings may generalize to other large-scale public research institutions, highlighting the broader risks of destabilizing national science infrastructures.

Materials and Methods

Model Development

We developed a simulation model to capture the interdependent processes through which NIH research funding influences workforce composition and capacity, and downstream innovation. We chose a system dynamics modeling approach due to its strength in representing feedback, delays, and cumulative effects in complex, interdependent systems like research funding and innovation pipelines (*29*).

The model is conceptually grounded in theories of public sector retrenchment and draws on frameworks from innovation economics and science and technology policy, as discussed in our prior research (*5*). This foundation reflects a body of empirical research documenting the relationship between NIH funding and scientific productivity, translational activity, and long-term innovation outcomes (*1*, *2*, *6*, *7*). It also incorporates lags between funding changes and measurable system responses, consistent with prior studies of biomedical research and development trajectories (*14*, *30*).

Figure 3 presents a schematic overview of the model, organized into four sections: NIH-funded research grants, the academic research workforce, the industry workforce, and the biomedical innovation pipeline. The model tracks how publicly funded research investments move through the biomedical ecosystem, supporting academic researchers, some of whom later enter industry, and shaping flows of people across training, faculty appointments, and exits. It focuses specifically on research and development (R&D) roles, excluding those not engaged in research. Innovation emerges from fundamental research (basic research that reveals mechanisms of biology, disease, or behavior) supported by NIH, which is often long-term, infrastructure-focused, and non-commercial, as well as from applied research led by industry, resulting in outputs such as publications, clinical trials, and Food and Drug Administration (FDA)-approved novel drugs (*24*).

Arrows in the figure are labeled as positive or negative to reflect whether connected variables move in the same or opposite direction. The model includes several feedback loops that reflect real-world system behavior. For example, when NIH funding declines, grant application success rates fall, leading to more grant submissions since funding is a requirement to conduct fundamental research, which in turn further reduces grant application success rates—closing a reinforcing, vicious loop. Consequently, as more time is spent writing grants, researchers have less time available for conducting research, reducing overall knowledge production.

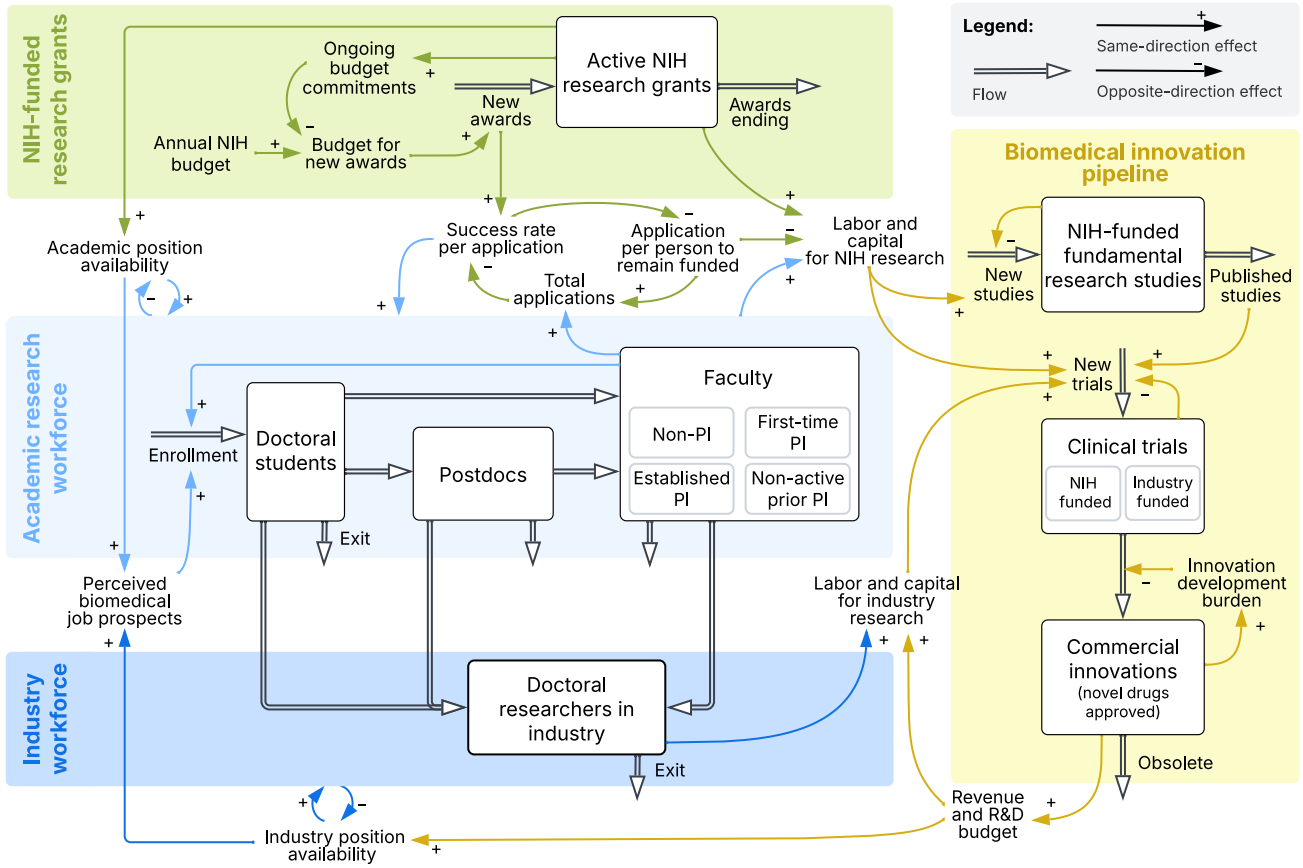


Figure 3: Overview of the model capturing the U.S. biomedical research ecosystem, encompassing NIH-funded research grants, academic and industry workforce, and biomedical innovation pipeline

Note: Stocks, represented by rectangular boxes, indicate accumulations. Transitions, or flows, to the stocks are shown with double-lined arrows. Single-lined arrows represent relationships between variables, with arrowheads indicating the direction of the effect. A plus sign denotes that two variables move in the same direction (e.g., an increase in one leads to an increase in the other and vice versa for the case of a decrease), while a minus sign denotes an inverse relationship (e.g., an increase in one leads to a decrease in the other). These relationships form feedback loops that drive the behavior of the model.

The model also includes balancing feedback loops, such as when increased academic position availability draws more researchers into the academic workforce, which then reduces the number of open positions and slows further inflow into the workforce. In addition, when perceived biomedical job prospects in academia and industry decline, fewer individuals enroll in doctoral programs. Another balancing feedback loop captures how the accumulation of commercial innovations contributes to an overall innovation development burden, reflecting how each new novel drug tends to be harder to develop due to increasing scientific, regulatory, and translational complexity. Although learning and efficiency gains can partially offset these challenges over time, historical patterns suggest the growing development burden has been the dominant force. As therapeutic frontiers advance, subsequent innovations face diminishing returns, higher efficacy standards, and greater biological uncertainty, making development slower and more complex. The model also links faculty availability to doctoral enrollment, recognizing that without sufficient faculty to teach and supervise, programs may reduce admissions. Additional feedback effects and loops are also presented in the figure. Together, the model mechanisms illustrate how shifts in funding and capacity can cascade across sectors and influence long-term innovation.

Projected Outcomes

The primary outcome is the commercial innovations, measured through the annual number of FDA-approved novel drugs. These approvals refer specifically to new molecular entities and original biologics that contain active ingredients not previously approved in the U.S., in any form or combination, and that receive marketing authorization for the first time. Using the drug approval as a proxy for biomedical innovations, consistent with prior research on biomedical innovation (*14*, *30*), we report the cumulative shortfall in approved novel drugs by 2050 compared to the baseline. To explain the projections of novel drug approval, we report several other outcomes, including early-career and established principal investigators (PI) funded by NIH, total doctoral students and postdoctoral researchers in science, engineering, and health, and NIH-supported fundamental knowledge output measured in published papers.

Additionally, to provide an illustrative sense of the potential magnitude, we translated the projected shortfall in each scenario into an approximate estimate of foregone economic value. We used an inflation-adjusted per-drug net social value, with an upward adjustment to account for the higher average value of novel approvals, yielding a range of roughly $5.1-$21.9 billion (2025 USD) per novel drug (see supplement for details). Future losses were discounted to present value using a 3% annual rate.

Data Inputs and Model Calibration

As presented in Table 1, the model includes 47 longitudinal datasets from 1995 to 2024, where available. Of these, 35 were used as calibration targets, such that unknown parameters were estimated by optimizing the model to closely replicate these historical patterns. The remaining 12 time series were used as external historical data inputs, meaning they were directly fed into the model (e.g., NIH congressional appropriations) as they reflect outside conditions or policy decisions that the model takes as given rather than trying to predict. See more details in the supplementary materials.

We primarily drew from the Research Portfolio Online Reporting Tools of the NIH to inform model parameters of the NIH budget and grant awards characteristics. Then, we derived workforce statistics (i.e., graduate students, postdoctoral appointees, and doctorate-holding individuals in R&D) using the surveys conducted by the National Science Foundation's National Center for Science and Engineering Statistics. These include the Survey of Graduate Students and Postdoctorates in Science and Engineering (GSS), the Survey of Earned Doctorates (SED), and the Survey of Doctorate Recipients (SDR). The GSS is a comprehensive survey of U.S. academic institutions that grant research-based graduate degrees; institutions provide data with consistent, near-complete coverage on graduate students and postdoctoral researchers in science, engineering, and health fields. The SED is a census of all individuals earning research doctorates from U.S. institutions each year, with response rates typically exceeding 90% (*40*). The SDR surveys a representative sample of U.S.-trained doctorate recipients exceeding a hundred thousand individuals to track career trajectories and workforce outcomes, with response rates generally above 70% (*41*). Together, these surveys offer nationally representative data on the U.S. scientific workforce with direct relevance to biomedical research fields.

We also used population estimates and projections by the U.S. Census Bureau to generate age-cohort-based estimates of enrollment potential in the academic pipeline. In addition, we used NIH ExPORTER to extract detailed project-level data, including PI identifiers, which allowed us to construct cohorts of PIs over time. We linked NIH grant identifiers to associated PubMed publications to analyze research outputs over time. Finally, we used various data sources to estimate parameters for the biomedical innovation pipeline, including active clinical trials registered on ClinicalTrials.gov and new drug approvals from the FDA. Further details are presented in the supplementary materials.

Table 1: Time series data used in the model

Time series data	Sources	Years	Unit
A) Calibration data targets (35 time series)			
NIH budget and Research Project Grants			
(1) Annual competing research project grant budget	NIH RePORT (*42*)	1995-2023	USD/year
(2) Annual noncompeting research project grant budget	NIH RePORT (*42*)	1995-2023	USD/year
(3) Annual new grant approvals	NIH RePORT (*42*)	1995-2024	Grant/year
(4) Active research project grants	NIH RePORT (*42*)	1999-2024	Grant
(5) Annual research project grant applications	NIH RePORT (*42*)	1995-2023	Grant/year
(6) Annual number of competing investigators	NIH RePORT (*42*)	1995-2023	People/year
(7) Research project grant success rate	NIH RePORT (*42*)	1995-2023	%
R&D Workforce in Academia and Industry			
(8) Annual doctoral enrollment	NSF GSS (*39*)	1995-2023	People/year
(9) Doctoral students in science, engineering, and health	NSF GSS (*39*)	1995-2023	People
(10) Annual new doctoral attainment	NSF SED (*40*)	1997-2023*	People/year
(11) New doctorate recipients with commitments to a postdoc position	NSF SED (*40*)	1997-2023*	People/year
(12) New doctorate recipients with commitments to an academic position	NSF SED (*40*)	1997-2023*	People/year
(13) New doctorate recipients with commitments to an industry position	NSF SED (*40*)	1997-2023*	People/year
(14) New doctorate recipients with no definite commitments to academia or industry positions	NSF SED (*40*)	1998-2023*	People/year
(15) Post doctorates	NSF GSS (*39*)	1997-2023*	People
(16) Total doctorate holders in R&D in academia	NSF SDR (*41*)	1999-2023*	People
(17) Total doctorate holders in R&D in industry	NSF SDR (*41*)	1999-2023*	People
(18) First-time PIs with active grants	NIH ExPORTER (*43*)	1995-2024	People
(19) Established PIs with active grants	NIH ExPORTER (*43*)	1995-2024	People
(20) Prior PIs without active grants	NIH ExPORTER (*43*)	1995-2024	People
(21) Annual new PIs awarded their first project grants	NIH ExPORTER (*43*)	1995-2024	People/year
(22) Annual new PIs awarded multiple project grants	NIH ExPORTER (*43*)	1995-2024	People/year
(23) Annual first-time PIs receiving another grant before the first one ends	NIH ExPORTER (*43*)	1995-2024	People/year
(24) Annual first-time PI who has a funding gap after the first grant ends	NIH ExPORTER (*43*)	1995-2024	People/year
(25) Annual established PI who has a funding gap after the grant ends	NIH ExPORTER (*43*)	1995-2024	People/year
(26) Annual prior PIs without active grants receiving a new award	NIH ExPORTER (*43*)	1995-2024	People/year
Biomedical Research and Innovation Pipeline			
(27) Publications per NIH grant	NIH ExPORTER (*43*)	1995-2021	Paper/grant
(28) Annual new NIH-funded fundamental research papers	Extracted from PubMed based on (*44*)	1995-2024	Paper/year
(29) Annual new NIH-funded clinical trial registrations	ClinicalTrials.gov (*45*)	2000-2024	Trial/year
(30) Active NIH clinical trials	ClinicalTrials.gov (*45*)	2000-2024	Trial
(31) Annual new industry-funded clinical trial registrations	ClinicalTrials.gov (*45*)	2000-2024	Trial/year
(32) Active industry clinical trials	ClinicalTrials.gov (*45*)	2000-2024	Trial
(33) Annual novel molecular entity and biologics approvals	FDA CDER (*46*, *47*)	1995-2024	Approval/year
(34) Cumulative novel molecular entity and biologics approvals	FDA CDER (*46*, *47*)	1995-2024	Approval/year
(35) Annual pharmaceutical industry R&D expenditure	PhRMA surveys (*48*)	1995-2023	USD/year
B) External Data Inputs (12 time series)			
NIH budget and research project grants			
(1) NIH congressional appropriations	NIH Budget Office (*49*)	1995-2025	USD/year
(2) Biomedical R&D Price Index	NIH Budget Office (*19*)	1995-2030	%
(3) Percent of applications from established contacts PIs	NIH RePORT (*42*)	1998-2024	%
(4) Percent first-time contact PI among annual competing PIs	NIH RePORT (*42*)	1995-2024	%

Time series data	Sources	Years	Unit
R&D Workforce in Academia and Industry			
(5) Population and projections for the 18-year-old cohort	Census (*50–54*)	1995-2050	People
(6) Median time to doctoral degree	NSF SED (*40*)	1995-2023*	Year
(7) Percent of primarily NIH-supported doctoral students	NSF GSS (*39*)	1995-2023	%
(8) Percent of primarily NIH-supported postdoctoral appointees	NSF GSS (*39*)	2000-2023	%
(9) Percent of established active PIs with single grants	NIH ExPORTER (*43*)	1995-2024	%
Research and Innovation Pipeline			
(10) Percent of NIH and industry trials to all clinical trials	ClinicalTrials.gov (*45*)	1995-2023	%
(11) Percent NIH grant recipients in fundamental research	NIH Special Reports (*42*)	2009-2022	%
(12) Percent NIH grants for fundamental research	NIH Special Reports (*42*)	2009-2022	%

Acronyms: NIH, National Institutes of Health; RePORT, Research Portfolio Online Reporting Tools; NSF, National Science Foundation; GSS, Survey of Graduate Students and Postdoctorates in Science and Engineering; SDR, Survey of Doctorate Recipients; SED, Survey of Earned Doctorates; FDA, Food and Drug Administration; CDER, Center for Drug Evaluation and Research; PhRMA, Pharmaceutical Research and Manufacturers of America; R&D, research and development; PI, Principal investigator.
*Data were not available every year in the given interval.

Model Assessment and Reproducibility

We conducted several tests, including extreme conditions testing, model boundary analysis, and comparison of simulated trends to historical data using mean absolute percentage error (*55*). For sensitivity analysis, using Markov Chain Monte Carlo, we ran 2 million simulations, discarding the first 1 million as burn-in, and then retained 1 million samples from the joint posterior distribution of the model parameters. From these, we randomly drew 10,000 samples to estimate model parameters and report 95% projection intervals for each outcome and scenario.

The model was created in Vensim version 10. Model assumptions and details are documented in the supplementary materials. As this study relied exclusively on publicly available, aggregated data, approval from the Institutional Review Board was not needed.

References and Notes

1. D. Li, P. Azoulay, B. N. Sampat, The applied value of public investments in biomedical research. *Science* **356**, 78–81 (2017).
2. A. A. Toole, Does Public Scientific Research Complement Private Investment in Research and Development in the Pharmaceutical Industry? *The Journal of Law and Economics* **50**, 81–104 (2007).
3. N. Gaind, How the NIH dominates the world's health research — in charts. *Nature* **639**, 554–555 (2025).
4. S. Galea, K. Bibbins-Domingo, The Value of Academic Health Research. *JAMA* **333**, 1039–1040 (2025).
5. M. S. Jalali, Z. Hasgul, Potential Tradeoffs of Proposed Cuts to the US National Institute of Health. *JAMA Health Forum* **6**, e252228 (2025).
6. P. Azoulay, D. Li, J. S. G. Zivin, B. N. Sampat, Public R&D Investments and Private-sector Patenting: Evidence from NIH Funding Rules. *Rev Econ Stud* **86**, 117–152 (2019).
7. B. N. Sampat, F. R. Lichtenberg, What are the respective roles of the public and private sectors in pharmaceutical innovation? *Health Aff (Millwood)* **30**, 332–339 (2011).
8. J. Couzin-Frankel, Breakthrough of the year 2013. Cancer immunotherapy. *Science* **342**, 1432–1433 (2013).
9. Testimony on the Fiscal Year 2014 Budget Request before the Senate Committee, *National Institutes of Health (NIH)* (2015). https://www.nih.gov/about-nih/who-we-are/nih-director/fiscal-year-2014-budget-request.
10. J. O'Neill, Antimicrobial resistance: tackling a crisis for the health and wealth of nations, *Rev. Antimicrob. Resist.* (2014). https://cir.nii.ac.jp/crid/1370857593729357568.
11. Testimony on the Fiscal Year 2016 Budget Request before the Senate Committee, *National Institutes of Health (NIH)* (2015). https://www.nih.gov/about-nih/who-we-are/nih-director/fiscal-year-2016-budget-request.
12. Testimony on the Fiscal Year 2018 Budget Request before the Senate Committee, *National Institutes of Health (NIH)* (2017). https://www.nih.gov/about-nih/who-we-are/nih-director/fiscal-year-2018-budget-request.
13. J. D. Buxbaum, M. E. Chernew, A. M. Fendrick, D. M. Cutler, Contributions Of Public Health, Pharmaceuticals, And Other Medical Care To US Life Expectancy Changes, 1990-2015. *Health Affairs* **39**, 1546–1556 (2020).
14. E. Galkina Cleary, M. J. Jackson, E. W. Zhou, F. D. Ledley, Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. *JAMA Health Forum* **4**, e230511 (2023).
15. United for Medical Research, "NIH's Role in Sustaining the U.S. Economy" (2024); https://www.unitedformedicalresearch.org/wp-content/uploads/2024/03/UMR-NIHs-Role-in-Sustaining-the-US-Economy-2024-Update.pdf.
16. R. C. Larson, N. Ghaffarzadegan, M. G. Diaz, Magnified Effects of Changes in NIH Research Funding Levels. *Serv Sci* **4**, 382–395 (2012).
17. P. Azoulay, M. Clancy, D. Li, B. N. Sampat, What if NIH had been 40% smaller? *Science* **389**, 1303–1305 (2025).
18. B. N. Sampat, Doubling Down: Will Large Increases in the NIH Budget Promote More Meaningful Medical Innovation? *J Law Med Ethics* **51**, 21–23.
19. Office of Budget, National Institutes of Health, Price Indexes. https://officeofbudget.od.nih.gov/gbipriceindexes.html.
20. National Institutes of Health (NIH) Funding: FY1996-FY2025. https://www.congress.gov/crs-product/R43341.

21. The Postdoc Queue: A Labour Force in Waiting - Andalib - 2018 - Systems Research and Behavioral Science - Wiley Online Library. https://onlinelibrary.wiley.com/doi/abs/10.1002/sres.2510.
22. R. C. Larson, N. Ghaffarzadegan, Y. Xue, Too Many PhD Graduates or Too Few Academic Job Openings: The Basic Reproductive Number R0 in Academia. *Syst Res Behav Sci* **31**, 745–750 (2014).
23. E. Budish, B. N. Roin, H. Williams, Do firms underinvest in long-term research? Evidence from cancer clinical trials. *Am Econ Rev* **105**, 2044–2085 (2015).
24. M. Mazzucato, *The Entrepreneurial State: Debunking Public Vs. Private Sector Myths* (Penguin Books, 2018).
25. M. McCarthy, Sequester to force $1.5bn cut in NIH budget. doi: 10.1136/bmj.f3707 (2013).
26. C. Printz, Federal budget woes continue to imperil cancer research. *Cancer* **119**, 4055–4056 (2013).
27. D. M. Cutler, E. Glaeser, Cutting the NIH—The $8 Trillion Health Care Catastrophe. *JAMA Health Forum* **6**, e252791 (2025).
28. I. Gonzalez Garcia, J. Montecino, V. Ramaswamy, "Preliminary Estimates of the Macroeconomic Costs of Cutting Federal Funding for Scientific Research" (report, Institute for Macroeconomic and Policy Analysis, 2025); https://doi.org/10.57912/28746446.
29. J. Sterman, *Business Dynamics: Systems Thinking and Modeling for a Complex World* (Irwin/McGraw-Hill, 2000).
30. E. Galkina Cleary, J. M. Beierlein, N. S. Khanuja, L. M. McNamee, F. D. Ledley, Contribution of NIH funding to new drug approvals 2010–2016. *Proceedings of the National Academy of Sciences* **115**, 2329–2334 (2018).
31. Translational Science Spectrum, *National Center for Advancing Translational Sciences* (2025). https://ncats.nih.gov/about/about-translational-science/spectrum.
32. N. Ghaffarzadegan, J. Hawley, A. Desai, Research Workforce Diversity: The Case of Balancing National versus International Postdocs in US Biomedical Research. *Syst Res Behav Sci* **31**, 301–315 (2014).
33. D. L. Herbert, A. G. Barnett, P. Clarke, N. Graves, On the time spent preparing grant proposals: an observational study of Australian researchers. *BMJ Open* **3**, e002800 (2013).
34. K. Gross, C. T. Bergstrom, Contest models highlight inherent inefficiencies of scientific funding competitions. *PLOS Biology* **17**, e3000065 (2019).
35. M. E. Blume-Kohout, J. W. Clack, Are Graduate Students Rational? Evidence from the Market for Biomedical Scientists. *PLOS ONE* **8**, e82759 (2013).
36. K. D. S. Fernald, P. C. Förster, E. Claassen, L. H. M. van de Burgwal, The pharmaceutical productivity gap - Incremental decline in R&D efficiency despite transient improvements. *Drug Discov Today* **29**, 104160 (2024).
37. J. W. Scannell, A. Blanckley, H. Boldon, B. Warrington, Diagnosing the decline in pharmaceutical R&D efficiency. *Nat Rev Drug Discov* **11**, 191–200 (2012).
38. R. E. Santerre, J. A. Vernon, Assessing Consumer Gains from a Drug Price Control Policy in the U.S. Social Science Research Network 666346 [Preprint] (2005). https://papers.ssrn.com/abstract=666346.
39. National Center for Science and Engineering Statistics (NCSES), "Survey of Graduate Students and Postdoctorates in Science and Engineering: Fall 2023" (NSF 25-317, U.S. National Science Foundation, Alexandria, VA, 2025); https://ncses.nsf.gov/surveys/graduate-students-postdoctorates-s-e/2023.
40. National Center for Science and Engineering Statistics (NCSES), "Doctorate Recipients from U.S. Universities: 2022" (NSF 24-300, National Science Foundation, Alexandria, VA, 2023); https://ncses.nsf.gov/pubs/nsf24300.

41. National Center for Science and Engineering Statistics (NCSES), "Survey of Doctorate Recipients: 2023" (NSF 25-321, U.S. National Science Foundation, Alexandria, VA, 2025); https://ncses.nsf.gov/surveys/doctorate-recipients/2023.
42. RePORT (Research Portfolio Online Reporting tools), *National Institutes of Health*. https://report.nih.gov/.
43. National Institutes of Health, NIH Research Portfolio Online Reporting Tools (RePORTER): Exporter. https://reporter.nih.gov/exporter.
44. B. E. Steinberg, N. M. Goldenberg, G. D. Fairn, W. M. Kuebler, A. S. Slutsky, W. L. Lee, Is basic science disappearing from medicine? The decline of biomedical research in the medical literature. *The FASEB Journal* **30**, 515–518 (2016).
45. U.S. National Library of Medicine, National Institutes of Health, ClinicalTrials.gov. https://clinicaltrials.gov/.
46. U.S. Food and Drug Administration (FDA), Summary of NDA Approvals & Receipts, 1938 to the present. *FDA* (2024).
47. C. for D. E. and Research, Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals. *FDA* (2025).
48. PhRMA, 2024 PhRMA Annual Membership Survey. https://www.phrma.org/resources/2024-phrma-annual-membership-survey.
49. NIH — Office of Budget —Appropriations History by Institute/Center (1938 to Present). https://officeofbudget.od.nih.gov/approp_hist.html.
50. U. C. Bureau, Population Projections, *Census.gov*. https://www.census.gov/programs-surveys/popproj.html.
51. U. C. Bureau, National Population by Characteristics: 2020-2024, *Census.gov*. https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html.
52. U. C. Bureau, National Population by Characteristics: 2010-2019, *Census.gov*. https://www.census.gov/data/tables/time-series/demo/popest/2010s-national-detail.html.
53. U. C. Bureau, National Intercensal Datasets: 2000-2010, *Census.gov*. https://www.census.gov/data/datasets/time-series/demo/popest/intercensal-2000-2010-national.html.
54. Index of /programs-surveys/popest/tables/1990-2000/national/totals. https://www2.census.gov/programs-surveys/popest/tables/1990-2000/national/totals/.
55. Y. Barlas, Formal aspects of model validity and validation in system dynamics. *System Dynamics Review* **12**, 183–210 (1996).
56. Appropriations History by Institute/Center (1938 to Present), *National Institutes of Health: Office of Budget*. https://officeofbudget.od.nih.gov/approp_hist.html.
57. M. T. Nietzel, As The Demographic Cliff Looms, How Far Will College Enrollment Fall?, *Forbes*. https://www.forbes.com/sites/michaeltnietzel/2024/12/11/as-2025s-demographic-cliff-looms-how-far-will-college-enrollment-fall/.
58. U.S. postdoctoral careers in life sciences, physical sciences and engineering: Government, industry, and academia | PLOS One. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0263185.
59. W.-Y. Chang, Y. Wang, M. Lynn, D. Foley, "Labor Force Transitions of U.S.-Trained Doctoral Scientists and Engineers: Findings from a New Longitudinal Panel" (NSF 22-327, National Center for Science and Engineering Statistics (NCSES), Alexandria, VA; National Science Foundation, 2022); https://ncses.nsf.gov/pubs/nsf22327.
60. NOT-OD-25-068: Supplemental Guidance to the 2024 NIH Grants Policy Statement: Indirect Cost Rates. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-25-068.html.
61. K. W. Boyack, P. Jordan, Metrics associated with NIH funding: a high-level view. *J Am Med Inform Assoc* **18**, 423–431 (2011).

62. C. for D. E. and Research, New Molecular Entity (NME) Drug and New Biologic Approvals. *FDA* (2025).
63. C. for D. E. and Research, NDA and BLA Calendar Year Approvals. *FDA* (2025).
64. U.S. Food and Drug Administration (FDA), NDA and BLA Approval Times. *FDA* (2019).
65. Pharmaceutical Research and Manufacturers of America. https://phrma.org/about.
66. Budget, *National Institutes of Health* (2024). https://www.nih.gov/about-nih/what-we-do/budget.
67. M. A. P. M. da Silva, Cobb–Douglas R&D production function, appropriability and opportunity: effects on R&D, technological progress and knowledge sharing. *Economics of Innovation and New Technology* **32**, 1069–1086 (2023).
68. Federal Reserve Bank of Minneapolis, Inflation Calculator. https://www.minneapolisfed.org/about-us/monetary-policy/inflation-calculator.

Acknowledgments: We thank Aaron Kesselheim and Adam Raymakers of the Program on Regulation, Therapeutics, and Law for their comments on an earlier draft. We also thank Mariya Andreeva, Larissa Calancie, Doris Chang, Alina Denham, Catherine DiGennaro, Huiru Dong, Joshua Ghosh-Groen, Anvita Guttikonda, Ashish Kumar, Lam Shao Wei Sean, Celia Stafford, Erin Stringfellow, Wayne Wakeland, and Junlai Zhang, who reviewed earlier versions of this report and shared constructive feedback.

Funding: None

Author contributions:

Conceptualization: ZH, MSJ

Methodology: ZH, HL, MSJ

Investigation: ZH, HL, MSJ

Visualization: ZH

Supervision: MSJ

Writing – original draft: ZH, MSJ

Writing – review & editing: ZH, HL, MSJ

Competing interests: Authors declare that they have no competing interests.

Data and materials availability: All data are available in the main text or the supplementary materials.

Preprint statement: This draft paper is intended for review and comments only. It is not intended for citation, quotation, or other use in any form.

Supplementary Materials

Materials and Methods

Supplementary Text

Figs. S1 to S22

Tables S1 to S3

References (*56–68*)

Supplementary Materials for

Modeling the Impacts of Budget Reductions at the U.S. NIH on Research and Innovation

Zeynep Hasgul[1]; Hannah Lee[1]; Mohammad S. Jalali[1,2,*]

*Corresponding author. Email: msjalali@mgh.harvard.edu

The PDF file includes:

Materials and Methods
Supplementary Text
Figs. S1 to S22
Tables S1 to S3
References (*56–68*)

Contents

1. Data Sources 21

1.1. NIH Budget and Research Project Grants 21

1.2. R&D Workforce in Science, Engineering, and Health 22

Doctoral students 22

Doctorate recipients and future commitments 23

Postdoctoral appointees 23

Total academic and industry researchers 24

Transitions out of academia and the industry workforce 25

Principal investigators 25

Fraction of NIH-supported academic workforce 26

1.3. Biomedical Research and Innovation 27

Fraction of NIH grants in fundamental research 27

NIH supported fundamental research papers 27

Publications per grant 27

Clinical Trials 28

Novel Drug Approvals 28

Research and Development Expenditure of the U.S. Pharmaceutical Industry 28

2. Model Overview 29

3. Model formulation and assumptions 32

3.1. NIH-funded research grants 32

3.2. R&D Workforce in Science, Engineering, and Health 36

3.3. Biomedical Research and Innovation 40

3.4. Economic value associated with novel drug approvals 43

4. Model Fit and Estimated Parameters 45

5. Additional Results: Percent Changes, Intermediate Outcomes, Extreme Case, and Uncertainty 49

1. Data Sources

This section details the data collection process and data analysis methods used for the sources provided in Table 1 of the article. Descriptions are grouped into three categories: 1) NIH Budget and Research Project Grants, which covers federal appropriations, grant budgets, applications, and awards; 2) R&D Workforce in Science, Engineering, and Health, which tracks doctoral students, postdoctoral researchers, faculty, and industry researchers; and 3) Biomedical Research and Innovation, which captures outputs such as publications, clinical trials, and novel drug approvals.

All data are reported in the project's online repository, available at: github.com/MJ-LAB-Harvard/BRIDGE-model

1.1.NIH Budget and Research Project Grants

We draw most of the data related to the NIH budget and grants from NIH's RePORT (*42*), which provides publicly accessible datasets organized by specific Report ID numbers within the Data Book. Each Report ID corresponds to a unique dataset, enabling direct reference to the underlying data we report below for reproducibility.

We used the NIH Office of Budget's Data Tables for History of Congressional Appropriations for NIH (i.e., the specific amount of funding allocated to the NIH by Congress) (*56*). The annual noncompeting and competing budget is derived from the NIH Data Book Report ID: 226, where we noted the budget amount for Research Project Grants (RPG). To help interpret purchasing power changes over time, we incorporated the NIH Office of Budget's 2025 Biomedical Research and Development Price Index (BRDPI) values, which track inflation specific to R&D activities (*19*).

We obtained data on the number of RPG applications, application success rates, and annual new grant approvals from NIH Data Book Report ID: 20. The number of active NIH awards was sourced from Report ID: 207. The total number of applicants was obtained from Report ID: 164, which provides annual counts of all investigators applying for RPGs, regardless of whether they were funded.

We distinguish between two groups of applicants for the RPGs: first-time and established contact principal investigators. Established-contact PIs are applicants who have previously received NIH funding and thus have an established history of contact with the NIH grant system. This group includes investigators with prior awards who continue to submit additional applications. By contrast, first-contact applicants are those applying to NIH to become a PI for the very first time. Although the data for number of applications by investigator type is not available across all RPGs, the R01 series from the NIH Data Book Report ID: 136 provides disaggregated information on applications from each group. We used these data to estimate the percentage of applications submitted by established-contact PIs and, by extension, the share from first-contact applicants. Applying these percentages to overall RPG application totals allowed us to estimate the number of applications attributable to each group.

We further incorporated NIH Data Book Report ID: 167, which reports the number of supported competing awards by career stage of investigator. These data were used to estimate the proportion of applicants who are established-contact PIs, under the assumption that the distribution of awards by career stage reflects the underlying distribution of applicants and that this relationship remains stable over time. This assumption is supported by the Report ID: 166, which shows that the funding rate difference between career stages has remained relatively consistent across years.

Taken together, these sources allowed us to construct estimates of (1) the number of applicants by composition (first-contact versus established-contact PIs), (2) the number of applications by composition, which then allowed us to estimate the average number of applications submitted per person within each group over time.

1.2.R&D Workforce in Science, Engineering, and Health

Most of the data on the workforce in the model are drawn from the National Science Foundation's (NSF) National Center for Science and Engineering Statistics.

These include the Survey of Graduate Students and Postdoctorates in Science and Engineering (GSS), the Survey of Earned Doctorates (SED) (*40*), and the Survey of Doctorate Recipients (SDR) (*41*). The GSS collects institution-reported counts from U.S. academic institutions that grant research-based graduate degrees; institutions provide data with consistent, near-complete coverage on graduate students and postdoctoral researchers in science, engineering, and health fields (*39*). These include disciplines, such as physical sciences, life sciences, mathematics and computer sciences, psychology, all engineering fields, public health, clinical medicine, and pharmacy. The SED is a census of all individuals earning research doctorates from U.S. institutions each year, with response rates typically exceeding 90% (*40*). The SDR surveys a representative sample of U.S.-trained doctorate recipients exceeding a hundred thousand individuals to track career trajectories and workforce outcomes, with response rates generally above 70% (*41*). Together, these surveys offer nationally representative data on the U.S. scientific workforce with direct relevance to biomedical research fields. We limited the workforce to individuals located in the U.S. during the time of data collection.

Doctoral students

To derive data on doctoral students, we used NSF's GSS. For this analysis, we restricted the total number of graduate students to those enrolled full-time, as most of the key indicators, such as first-time enrollment, are reported for full-time students. We included all students within GSS coverage who were enrolled in science, engineering, or health disciplines. We note that in the GSS, trend breaks occasionally occur due to changes in methodology, coverage, or classification. In such cases, we used the recent year values provided by NSF rather than attempting to splice old and new series. Where data prior to 2017 did not include separate counts for master's versus doctoral students, we applied a consistent estimation method: calculating the average share of doctoral students from 2017–2023 and using that proportion to estimate values for 1995–2016.

Additionally, to place workforce trends in a broader demographic context, we incorporated population estimates and projections from the U.S. Census Bureau to generate age-cohort–based estimates of the potential enrollment pool in the academic pipeline (*50–54*). We focused on the cohort aged 18 years and applied a four-year lag to approximate the point at which individuals would typically become eligible for doctoral study following undergraduate education. The inclusion of demographic projections was incorporated, given the decline in U.S. birth rates during and after the 2008 financial crisis. This drop in births is expected to produce a corresponding reduction, also called the "enrollment cliff," in the size of entering classes beginning in the late 2020s (*57*).

Using the GSS public data tables, we derived the doctoral student enrollment (inflow) from Table 1-5b. *First-time status among full-time graduate students in science, engineering, and health, by degree level: 1975–2023*. According to NSF, this includes all students newly enrolled for credit in a graduate degree program in the fall, including those with prior graduate enrollment or existing graduate or professional degrees. The number of doctoral students (stock) was derived from Table 1-5a. *Enrollment intensity of graduate students in science, engineering, and health, by degree program: 1975–2023*, which enumerates total full-time doctoral enrollments regardless of entry year.

Doctorate recipients and future commitments

Using SED, we obtained the annual number of research doctorate recipients from U.S. academic institutions, focusing on science and engineering fields, including health sciences. Available for selected years only, we used Table 1-6. *Research doctorate recipients, by trend broad field of doctorate and citizenship*, which reflects the doctoral attainments or the outflows from the stock of doctoral students. Furthermore, SED *Table 1-12, Median years to research doctorate* provides information on time to degree, which has declined over the time horizon of our model. In years 2018 and 2023, the SED distinguished between years since initial graduate enrollment and years since entry into a doctoral program, with the difference (about 1.5 years) reflecting the typical duration of a master's program; we applied this adjustment retroactively to earlier years to maintain comparability. For years without direct observations, values were interpolated linearly between survey points. This approach allowed us to capture the exogenous downward trend in time to degree more accurately (declining from 7.2 years in 1993 to 5.7 years in 2023). These harmonized measures allowed us to estimate doctoral inflows (new enrollees), the stock of students in training, and outflows (degree completions), with the residual values representing attrition through exit without completion. As the accounted data in the model captures doctoral enrollment (inflows), the stock of doctoral students, and doctoral attainments (outflows), the remaining share reflects attrition without completion.

Additionally, the SED allowed us to obtain data on our model's outflow of doctorate recipients into specific career stages. Using Table 2-6. *Employment sector of research doctorate recipients with definite postgraduation commitments for non-postdoc employment in the U.S., by trend broad field of doctorate: Selected years, 1993–2023*, we obtained the number of research doctorate students of science and engineering fields who secured positions in academia and industry or business—categories we broadly interpret as representing project grant investigators and those employed in industry, respectively. Similarly, we obtained the doctorate recipients who committed to postdoctoral training plans using Table 2-3. *Postgraduation plans of research doctorate recipients with definite commitments, by trend broad field of doctorate* and the doctorate recipients with no definite postgraduation commitment, using Table 2-1. *Postgraduation commitment of research doctorate recipients, by trend broad field of doctorate: Selected years, 1993–2023*. In addition, the SED reports commitments to government or nonprofit sector positions, as well as other employment. For the purposes of our model, we combined these government, nonprofit, and no-commitment and other categories into a single group representing pathways outside academia and industry.

Unlike many statistics collected by the GSS, the SED surveys all graduate students without distinction of enrollment intensity. In other words, our outflow data includes all doctoral students (both full- and part-time), whereas our stock data focuses on full-time students. We recognize this mismatch between the two sources; however, we consider the impact minimal, as part-time doctoral students have consistently accounted for less than 13% since 2017. Therefore, no adjustment was applied to reconcile this difference.

Postdoctoral appointees

Following the same approach used for graduate students, we identified all postdoctoral appointees in the science, engineering, or health fields from NSF's GSS public data tables (*39*). Specifically, we used Table 1-1. *Graduate students, postdoctoral appointees, and doctorate-holding nonfaculty researchers in science, engineering, and health: 1975–2023*, to obtain the total number of postdoctoral appointees.

The inflow into postdoctoral roles was estimated from the SED, using Table 2-1. *Postgraduation commitment of research doctorate recipients, by trend broad field of doctorate: Selected years, 1993–2023*. From this table, we selected doctorate recipients who had committed to enter a

postdoctoral position at the time of degree completion. These counts represent individuals with definite postdoctoral commitments, regardless of whether the position was in academia, government, industry, or other research settings.

While there are no consistent time series tracking outflows from postdoctoral positions or their direct transitions into academia or industry, the SDR provides information on the average duration of postdoctoral appointments. These duration data serve as an indirect basis for estimating the timing of sector transitions. From SDR Table 77. *U.S.-residing doctoral scientists and engineers on postdoc appointments*, by selected demographic characteristics and broad field of doctorate, we see that out of 23,450 postdoctoral appointees in 2023, 18,800 had earned their doctorate within the previous five years (*41*). This indicates that the majority of postdocs remain in such positions for fewer than five years, with the median duration around three years.

For further insight into postdoctoral career outcomes, we used the findings of Denton et al. (2022) (*58*), who linked SED and SDR records for respondents completing the SED between 2009 and 2018 and participating in the SDR in 2013, 2015, and/or 2017. They reported that 33% (n=792) of physical sciences and engineering postdocs, and 35% (n=862) of life sciences postdocs, transitioned to industry positions after a postdoc in academia. These proportions, combined with average postdoc duration estimates, inform postdoc-to-industry and postdoc-to-academia transitions.

Total academic and industry researchers

To obtain the total number of researchers currently in either an academic or industry setting, we utilized NSF's SDR for the selected years available. The SDR provides biennial, nationally representative data on U.S.-residing individuals with research doctorates, including detailed information on their employment sector, employer type, and primary and secondary work activities.

To begin, we obtained the total number of doctorate recipients residing in the U.S. whose primary or secondary work activity is any research and development (R&D) using Table 15-1. *U.S.-residing employed doctoral scientists and engineers, by fine field of doctorate and primary or secondary work activity: 2023.* For earlier years, we used the corresponding tables from prior SDR releases, with many values obtained from archived SDR reports to ensure consistent time series coverage.

To determine the number of academic researchers, we selected doctorate recipients whose primary or secondary work was R&D in a 4-year educational institution. These counts were obtained from Table 23. *U.S.-residing employed doctoral scientists and engineers in 4-year educational institutions, by broad field of doctorate, primary work activity, and secondary work activity: 2023,* and the equivalent tables for previous years. We note that the *4-year educational institutions* category in the SDR includes researchers employed in universities, 4-year colleges, and affiliated research centers, as well as those working in university-based hospitals and medical schools.

For industry researchers, we applied two approaches depending on the availability of detail. For 2017 and later, we used Table 26-2. *U.S.-residing employed doctoral scientists and engineers*, by selected demographic and employment-related characteristics, primary work activity, and sector of employment, and Table 26-1. *U.S.-residing employed doctoral scientists and engineers*, by selected demographic and employment-related characteristics, primary or secondary work activity, and sector of employment, to determine the share of total R&D activity occurring in the for-profit sector. For years before 2017, these sectoral fractions were not available, so we applied the average ratios from the post-2017 period to earlier years. The number of industry researchers was calculated as the for-profit share of total R&D after subtracting academic researchers from the total R&D workforce.

All counts cover doctorate recipients in the science, engineering, and health fields as defined in the SDR classification system. By considering both primary and secondary R&D activities, we ensured that researchers who conduct R&D as part of a mixed portfolio of responsibilities (e.g., research combined with teaching or administration) were included in our estimates for people contributing to biomedical innovations.

Transitions out of academia and the industry workforce

While there is no consistent longitudinal time series that tracks exits from academia and industry specifically, we can draw on related surveys to approximate attrition rates for doctoral recipients in the science, engineering, and health. For example, according to the 2023 SDR (Table 32-2), the involuntarily out-of-field rate for U.S.-residing doctoral scientists and engineers in science occupations was 2.1% (*41*). This reflects individuals who reported being unable to work in their trained field due to job market, structural, or personal constraints. Using the 2015–2019 SDR longitudinal panel subsample, we estimated retirement rates for doctoral scientists and engineers under age 65. Calculations suggest annual retirement rates in the range of ~2.5%–6.8% (e.g., 2.5% for 2015, 4.3% for 2017, and 6.8% for 2019) (*41*).

Beyond workforce exits, the 2015–2019 SDR longitudinal panel subsample also provides insights into mobility between academia and non-academic sectors (*59*). Among the science, engineering, and health doctorate holders, an estimated 745,400 remained employed in all three survey waves (2015, 2017, 2019). Employment sectors were classified into two broad categories: academia and non-academia (government, for-profit, self-employed, nonprofit). Over these 4 years, data show that while the majority of researchers remain in their original sector, there is a net outflow from academia. Specifically, 13,350 researchers exited academia by 2019 (5,100 transitioning from academia → academia → non-academia, and 8,250 academia → non-academia → non-academia). By contrast, 7,000 researchers entered academia over the same period (2,750 moving from non-academia → non-academia → academia, and 4,250 non-academia → academia → academia). The net change indicates that academia lost approximately 6,350 researchers over four years, which translates to an average annual net loss of about 1,590 researchers per year to non-academic sectors.

Principal investigators

We analyzed publicly available granular RePORTER Project Data from NIH ExPORTER (*43*), which includes funded projects from all NIH Institutes and Centers. Each annual file contains award information for every grant active in that fiscal year, including unique project identifiers, unique principal investigator (PI) identifiers, funding institute or center, activity code, application type, project start and end dates, and other administrative data related to the awarded project. For this study, we compiled all available project-level data from the NIH RePORTER Project Files for fiscal years 1985-2024.

Our focus is mainly on Research Project Grants, defined by the NIH as activity codes: DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R16, R21, R22, R23, R29, R33, R34, R35, R36, R37, R50, R55, R56, R61, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, SI2, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, U34, and U3R. We restricted the dataset to research project grants by filtering for a predefined set of activity codes and the organizational codes for NIH Institutes and Centers that fund these awards. From each record, we retained the core project number, PI identifier(s), application type, project start and end dates, and fiscal year. The purpose of this processing was to transform the annual award records into a longitudinal PI-year cohort for quantifying both the size of the active PI states (stocks) and the year-to-year movements of investigators into, out of, and between states (flows).

The dataset was restructured to yield unique PI-project-year records, and unique identifiers were used to determine each PI's first grant and second grant event, the latter defined as either a competitive renewal of the first grant or a new parent grant. Career timelines for each PI were constructed from their first to last recorded year, with annual active status determined by continuous sequences of active years between start and end dates. In the model, we classified PI-stages into one of four career states 1 (see Model Overview).

An established PI is defined as a PI who, after their first award, has either (1) obtained a second research project grant before the active grant from their first award period ended, (2) received more than one grant in the first application cycle, or (3) accumulated more than 5 years of continuous active funding as a first-time awarded PI. This threshold was chosen to be longer than the typical five-year duration of an NIH R01 award (*60*). The intent was to capture investigators who sustained an award beyond a single standard cycle, indicating successful renewal or continuation of support. Renewals or new parent grants can be identified in the data using CORE_PROJECT_NUM patterns and APPLICATION_TYPE codes (e.g., Type 2 for competitive renewals). However, in our analysis of the data, we observed that some first-time awards extended well beyond five years without being coded as a second grant or competitive renewal. Because our calculations use actual PROJECT_START and PROJECT_END dates, these cases were visible in the data even when renewal codes were absent. We therefore applied a ≥6-year continuous funding threshold to classify such long-running first awards as established. Lastly, a PI may also experience a period without active funding (becoming non-active) before receiving a second grant and thus meeting the established investigator definition. Once a PI meets either criterion, they are considered established for all subsequent years in which they hold at least one active research project grant.

Stocks were calculated as the number of unique PIs in each state per year. We then defined transitions between these states to capture patterns such as new entries, losses of funding, promotions from first-time to established status, returns to funding, and multi-grant first-year entrants. Flows captured the number of investigators moving from one state to another in a given year. We compiled project-level data for fiscal years 1985-2024 to more accurately capture the number of unique PIs granted for the first time. We then used the numbers from 1995 to 2024.

Fraction of NIH-supported academic workforce

For doctoral students, the GSS provides annual counts of graduate students by primary source of financial support. Using Table 1-7. *Detailed primary source of federal support for full-time graduate students in science, engineering, and health: 1975–2023*, we identified the number of students whose primary source of support was federal funding from the NIH.

For postdoctoral researchers, comparable time series were not available in the current GSS data tables, so we used counts of federally funded postdoctoral appointees from archived GSS reports. In GSS Fall 2020 Table 3-4. *Detailed primary source of federal support for postdoctoral appointees in science, engineering, and health, by broad field: 2020* (*39*), NIH-funded postdoctoral fellows represented 60.2% of all federally funded postdoctoral appointees. Due to the absence of equivalent NIH-specific fractions for other years, we applied this value as a constant multiplier to the total number of federally funded postdoctoral appointees for all years in our analysis.

For faculty researchers, only PIs with active NIH research project grants are considered directly supported by NIH funding in our model. First-time PIs are, by our definition in the model, funded by a single active award. For established PIs, we estimated the fraction holding only a single active NIH grant at a given time by compiling and analyzing all available project-level data from the NIH RePORTER Project Files for fiscal years 1985–2024. This approach parallels

the methodology used for first-time PIs and allowed us to determine the share of the established PI pool with direct NIH support in any given year.

In the model, these NIH-supported fractions are applied to estimate the number of individuals in each workforce category (doctoral students, postdoctoral researchers, and PIs) who would lose their current NIH funding under changes in active award counts or budget allocations to capture individuals exiting their current NIH-supported role.

1.3.Biomedical Research and Innovation

Fraction of NIH grants in fundamental research

The NIH Special Reports and Current Issues Report Archive includes a report titled "*Trends in NIH-Supported Basic, Translational, and Clinical Research: FYs 2009–2022*" (*42*). Our definition of *fundamental* research aligns with NIH's definition of *basic* research projects, defined as research that involves scientific exploration, which can reveal mechanisms of biology, disease, or behavior (*31*). From this report, we obtained disaggregated data on the number of basic research projects and applied projects supported by NIH per year. The data also includes unique PI information and the classification of the grants they work on as basic or applied, allowing us to estimate the fraction of NIH researchers in basic sciences. We assume the NIH-funded trainees would have the same fraction as the PIs.

NIH supported fundamental research papers

We obtained annual numbers of published fundamental research papers using PubMed that were funded by NIH. To do so, we employed a search strategy adapted from previously published work in the basic sciences (*44*), with the addition of the filter 'NIH[Grants and Funding]' to restrict results to NIH-funded studies. We filtered annual results using: (cellular* [Title/Abstract] OR cell[Title/Abstract] OR animals[Title/ Abstract] OR Biologic Markers[mh] OR mice OR Polymorphism[mh] OR pathway[Title/Abstract] OR mechanism[Title/ Abstract] OR cytokine[Title/Abstract] OR signal transduction [mh] OR animal[mh] NOT clinical trial[Publication Type] NOT editorial[Publication Type] NOT Case Reports[Publication Type] NOT Practice Guideline[Publication Type] NOT Comment[Publication Type]) AND (NIH[Grants and Funding]).

Publications per grant

We used two publicly available NIH ExPORTER datasets: the NIH RePORTER Project Data and the NIH RePORTER Publication Link Tables (*43*). The project data contain records for every NIH-funded project active in a given fiscal year, including unique project identifiers, activity codes, project start and end dates, and the administering NIH Institute or Center. The publication link tables provide mappings between individual funded projects and the peer-reviewed articles that acknowledge support from those projects.

We replicated an approach previously published to explore metrics associated with NIH funding with more recent data (*61*). We restricted the analysis to RPGs by filtering the project data for a predefined set of NIH activity codes corresponding to RPG mechanisms (e.g., R01, R21, P01) and organizational codes identifying NIH Institutes and Centers that fund these mechanisms. All available annual CSV files from 1985 onward were imported and merged into a single dataset. Then we linked the project dataset to the publication data via the project number, producing a merged table in which each grant was associated with its linked publications.

From the linked dataset, we calculated the total number of publications produced under each grant, the grant's duration in years, and the average number of publications per year. We also extracted the grant start year to allow analysis by cohort. Finally, we aggregated results by start year, computing the mean publications per grant per year for each cohort and the number of

grants initiated in that year. This allowed us to examine trends over time in publication productivity relative to the grant start year.

Clinical Trials

We identified annually active registered clinical trials from ClinicalTrials.gov by applying the following filters: "Study start date on or before 12/31/[year]," "Study completion date on or after 01/01/[year], and location being the U.S. This approach captures trials that were active during the specified year. Among these, we further filtered for trials with NIH funding and with industry funding and recorded the corresponding annual counts. We repeated the same process to obtain the inflow of annual new clinical trials, using filters simply for the location being the U.S. and "Study Start Date from 01/01/[year] to 12/31/[year]."

Novel Drug Approvals

We collected data on annual Novel Drug Approvals, defined as medications that have not previously been approved by the FDA, either as single-ingredient drugs or as components of combination products, and have not been marketed in the U.S. These approvals are granted by the FDA's Center for Drug Evaluation and Research (CDER), which oversees a wide range of drug products. This includes New Molecular Entities (NMEs), which contain parts of drug molecules responsible for their therapeutic effect that have not been approved in any form. CDER also approves original Biologics License Applications (BLAs), which are complex therapies derived from living organisms and include products such as monoclonal antibodies, therapeutic proteins, and enzymes (*62*, *63*). To establish a baseline for cumulative innovations, we compiled historical FDA approval archives to extend our series as far back as possible. Since our model measures innovations relative to the simulation's initial year, it was necessary to construct an accurate cumulative count of total innovations prior to this point. For NMEs and biologics, consistent annual approval data are available beginning in 1985. Before 1985, FDA records did not provide systematic counts of novel biologics. For these earlier years, we therefore relied exclusively on NMEs, aggregating annual approvals of new molecular entities back to the 1940s, when FDA approval requirements became formally codified in regulation. By merging these sources, we created a continuous historical series of cumulative NMEs and biologics extending to 1995. This ensures that the model's innovation stock is anchored in observed data, capturing both the rise of novel biologics in the modern era and the longer trajectory of NMEs (*46*, *47*). We also sourced median novel drug approval times from the FDA (*64*).

Research and Development Expenditure of the U.S. Pharmaceutical Industry

To capture R&D expenditure by the industry, we utilized annual surveys of Pharmaceutical Research and Manufacturers of America (PhRMA) member companies (*48*). PhRMA is a trade association that represents major biopharmaceutical research companies in the U.S. (*65*).

2. Model Overview

This section describes the detailed structure of the model, including how the variables are interconnected in each model section. As shown in **Figure S1**, the model consists of three sections: (1) NIH-funded research grants, (2) academic and industry research workforce, and (3) biomedical innovation pipeline.

All model and data files are reported in the project's online repository, available at: github.com/MJ-LAB-Harvard/BRIDGE-model

Stocks, represented by rectangular boxes, indicate accumulations. Transitions, or flows, to the stocks are shown with double-lined arrows. In the first sector, NIH-funded research grants are represented as a stock where each year new ones are approved through the inflow and previous ones are timed out through the outflow.

In the workforce component, NIH-funded research grants support the academic research workforce, impacting the flows from doctoral students to postdoctoral researchers, faculty positions, and exits. Faculty researchers are categorized into four groups: non-PIs (faculty without prior NIH grants), first-time PIs (receiving their first NIH grant), established PIs (with active NIH grants and additional awards beyond the initial grant), and non-active prior PIs (with past but not current awards, who may return to active PI status in the future). Exits represent movement out of the U.S. research workforce, including shifts to non-research roles, moving outside the country, retirement, or other forms of departure from research activities. Some doctoral degree recipients can transition into industry, where the model captures those engaged in industry's research and development (R&D) roles.

The model also captures how NIH-funded research grants, in combination with academic and industry workforce dynamics, drive innovation, specifically novel drugs. It represents the sequential nature of the biomedical innovation pipeline while incorporating time lags. Outputs from fundamental research provide the foundation for applied research, which can then lead to the approval and commercialization of new drugs. The fundamental research reflects the scientific investigations aimed at understanding biological mechanisms (e.g., cellular pathways and protein targets, among others) that can inform therapeutic development. The model uses the number of scientific publications as a proxy for fundamental research output. Applied research translates basic scientific knowledge through clinical trials, which ultimately, in part, turn into novel drug approvals. Inputs to applied research come from both academia and industry. The final output is represented by novel drug approvals, which are most often carried out by the industry.

As shown in **Figure S1**, the model includes feedback loops. A feedback loop is called reinforcing when the initial change is amplified, where an initial increase leads to changes in the following variables, ultimately, increasing the starting variable in the same direction, or an initial decrease results in a further decrease. A feedback loop is called balancing when an initial increase in a variable affects the following variables, ultimately causing the variables in the loop to counteract that increase, bringing the system to stability. Several balancing (B) and reinforcing (R) feedback loops structure the interactions among NIH-funded research grants, the research workforce, and the biomedical innovation pipeline.

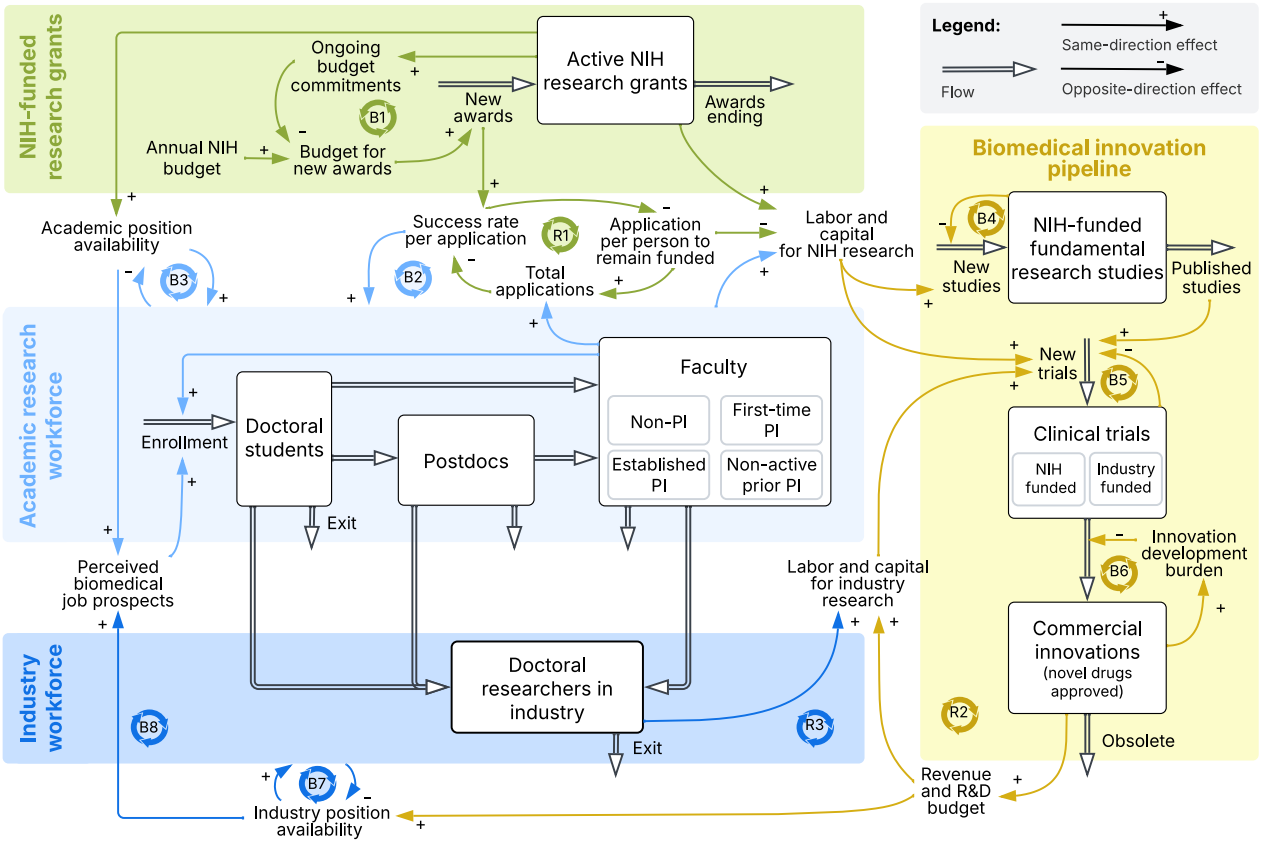


Figure S1: Overview of the model and feedback loops.

Note: Single-lined arrows represent relationships between variables, with arrowheads indicating the direction of the effect. A plus sign denotes that two variables move in the same direction (e.g., an increase in one leads to an increase in the other and vice versa), while a minus sign denotes an opposite relationship (e.g., an increase in one leads to a decrease in the other and vice versa). These relationships may also form feedback loops.

The budget commitments loop (B1) begins when the number of active NIH research grants increases. As more grants are sustained over multiple years, a larger share of the NIH budget is obligated to the ongoing commitments. This leaves fewer funds available for new awards in the next budget cycle, which slows the growth of future grant numbers.

This funding dynamic directly influences the number of principal investigators (PIs). For instance, rises in NIH awards increase the application success rate, allowing more researchers to become PIs, which ultimately expands the applicant pool. However, with more PIs submitting proposals in subsequent cycles, the pool of applications increases, leading to decreases in application success rate, closing the feedback loop. Reduced chances of securing funding prompt some PIs to leave the system, which decreases competition and stabilizes both PI numbers and application pressure.

The academic research workforce is also shaped by the academic position availability loop (B3). As PI numbers grow, more faculty positions are filled. Once most positions are occupied, opportunities for new PIs diminish, which slows the rate at which new investigators enter the system. Together, B2 and B3 balance the PI population with available funding and positions, creating a coupled set of feedback mechanisms that link budget constraints to workforce capacity.

Additionally, as fundamental and applied research activity grows in NIH-funded projects, the demand for labor and capital in NIH-funded projects rises. However, with more people and resources tied up in ongoing work, fewer are available to take on new projects, which slows the pace of further NIH-funded research (B4). A similar capacity effect occurs in the industry sector:

as applied research expands, it draws more labor and capital into current projects, reducing the availability of personnel for new industry-led studies. This limitation on available capacity acts as a natural brake on the rate at which new applied research projects can be launched (B5).

Growth in commercial innovations, i.e., novel drugs approved, increases the complexity and resources required for the next generation of novel drug discoveries. Over time, this slows the pace of subsequent drug development and reduces the number of new approvals, balancing the overall rate of commercial innovation (B7). Increases in the availability of industry R&D positions attract more doctoral students, postdocs, and faculty into industry roles. However, as more people transition into industry, the remaining pool of researchers available to fill additional positions shrinks, slowing further expansion (B8). Moreover, as more industry jobs become available, enrollment in doctoral programs rises as students see stronger career prospects in industry. Over time, this larger pool of trained researchers, along with postdocs and faculty, feeds more people into industry positions, which gradually fills the available roles. As positions become occupied, the number of open industry jobs declines, slowing further workforce growth (B9).

Finally, falling application success rates lead researchers to submit more applications per person to improve their chances. The resulting rise in proposal volume further pushes down the success rate, reinforcing the cycle and making it progressively harder to secure funding (R1). In the academic system, higher enrollment in doctoral programs eventually leads to a larger faculty body, which expands the system's capacity to admit and train more students. This growth in training capacity reinforces the ability to grow the academic workforce when conditions are favorable (R2). In industry, a larger pool of doctoral researchers enables more research projects, which drive further innovation and ultimately increase the R&D budget. A larger budget supports even more industry positions, feeding back into the continued growth of the industry research workforce (R3).

3. Model formulation and assumptions

This section describes how the model is operationalized and the key underlying assumptions in each part in further detail. The description is organized into four parts: (1) NIH Budget and Research Project Grants, which covers funding, application and grant dynamics; (2) R&D Workforce in Science, Engineering, and Health, which tracks career stages and transitions across academia and industry; (3) Biomedical Research and Innovation, which captures outputs along the research pipeline from fundamental discoveries to novel drug approvals; and (4) Economic value associated with novel drug approvals.

3.1. *NIH-funded research grants*

The model estimates the total number of NIH-funded research grants each year using historical data as input. Grants are represented as a stock, with new awards as the inflow and grant endings as the outflow, as presented in **Figure S2**. Exogenous historical data are used to estimate how much of the NIH budget translates into grants, and grant duration is partially calibrated to determine the rate at which grants end. The estimated number of grants serves as an input for other downstream outcomes, including the size of the research workforce and scientific outputs.

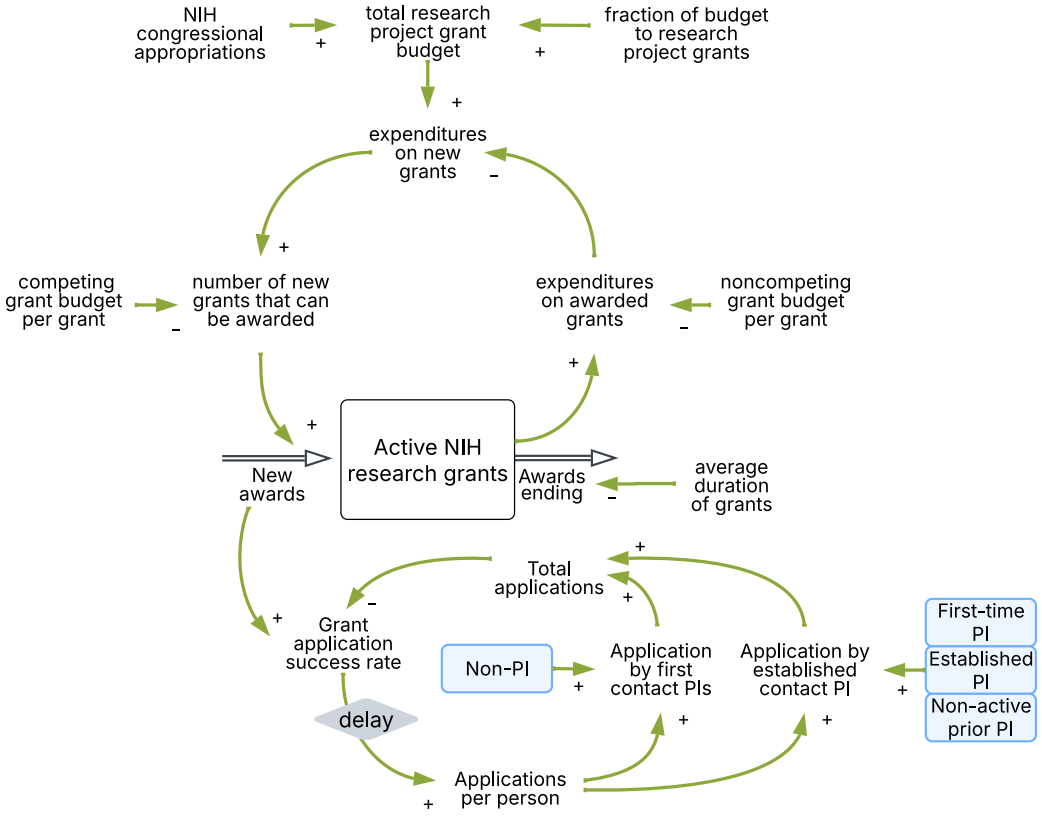


Figure S2: Overview of the model focusing on NIH-funded research grants

Future projections of the NIH budget are based on the Biomedical Research and Development Price Index (BRDPI), which measures annual changes in the cost of supplies and workforce necessary for conducting biomedical research. Historical BRDPI values are shown in **Figure S3**, panel A, and the projected annual increase in costs from 2025 to 2030 is 2.7 percent (*19*). We continue this value into future projections. Historical nominal NIH appropriations are shown in **Figure S3**, panel B, and are projected into the future under the baseline assumption that the nominal budget will continue to increase, as has often been the case historically. We assume an annual nominal increase of 2.7 percent, consistent with BRDPI forecasts. All nominal budget values are then adjusted to constant 2025 USD using the BRDPI multiplier shown in **Figure S3**,

panel C, which has a value of 1 in 2025 and earlier and later years calculated using annual changes presented in panel A. This results in the adjusted budget series presented in panel D.

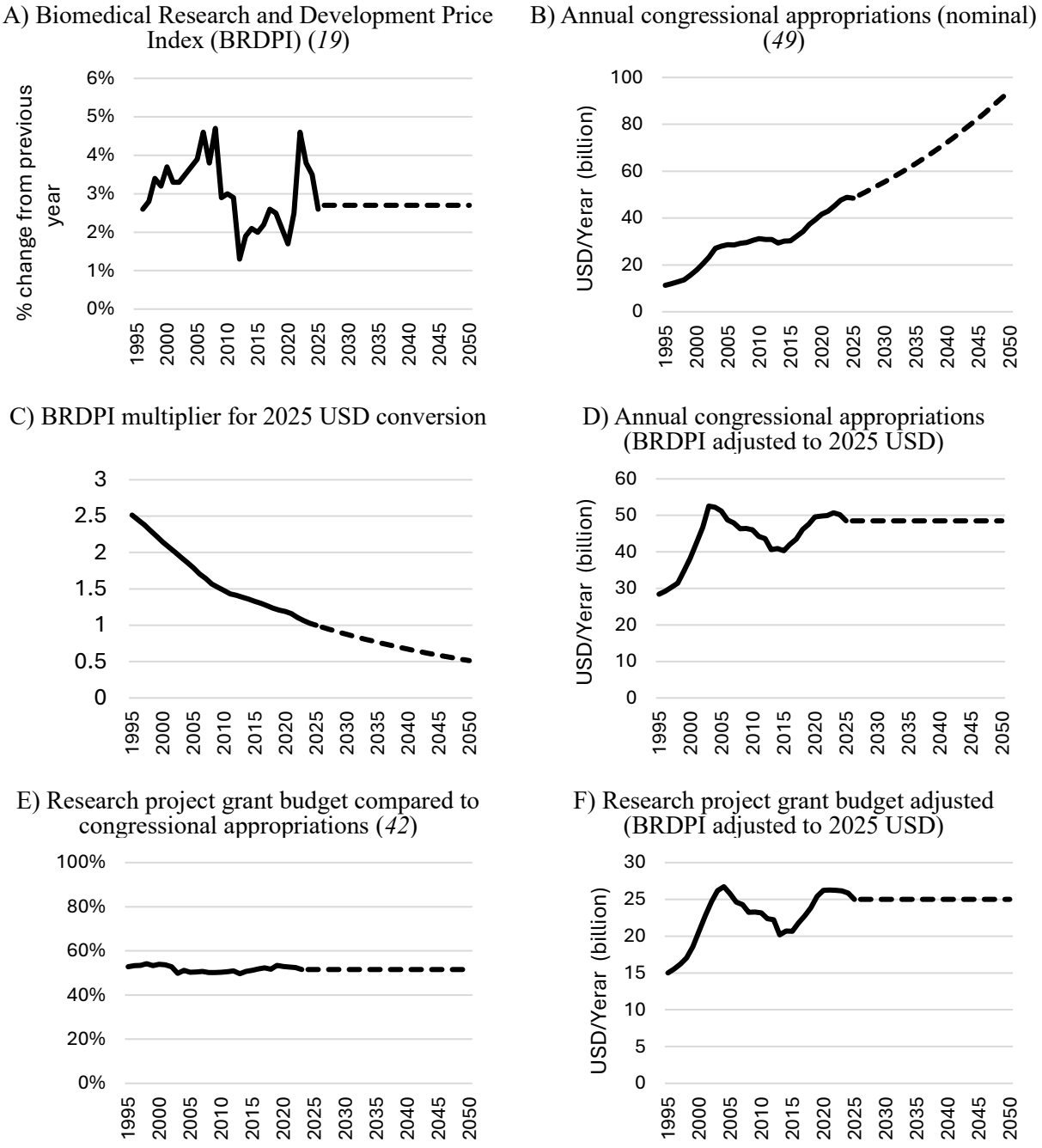


Figure S3: Historical trends and projections for the Biomedical Research and Development Price Index (BRDPI), U.S. congressional appropriations, and research project grant budgets, shown in both nominal and BRDPI-adjusted 2025 USD, along with the proportion of appropriations allocated to research project grants.
Note: Solid lines indicate historical data, and dashed lines indicate projections.

The NIH budget supports a wide range of activities, including its own staff and administration, training programs, research infrastructure, small business grants, and both intramural and extramural research. Our model focuses on extramural research, which is primarily funded through competitive research project grants (RPGs) awarded to more than 2,500 research institutions nationwide (*66*). As shown in **Figure S3**, panel E, the share of the NIH budget allocated to RPGs has historically been stable at approximately 50 to 55 percent. The model assumes this proportion remains constant going forward, using the most recent year of available data as the baseline, i.e., 51.5%. We multiply this number by adjusted annual appropriations and use the research project grant budget adjusted in Panel F.

The RPG budget consists of two components: competing grants, which are newly awarded through a competitive review process, and non-competing grants, which represent renewals of prior funding commitments. The stock in **Figure S2** is the pool of active multi-year grants that continue to receive annual funding until the end of their award period. These ongoing commitments form the non-competing budget, reducing the flexibility of each new budget cycle. To determine the portion of the budget available for new grants each year, the model first subtracts the estimated funding required to support existing active grants. The stock of active grants is calibrated in the model and multiplied by exogenous historical data on non-competing award size per active grant, given in **Figure S4**, panel A, as nominal USD values. Similar to the projections in **Figure S3**, these values are extended into the future with a 2.7 percent annual increase in line with BRDPI forecasts, with BRDPI-adjusted 2025 USD values shown in **Figure S4**, panel B.

The remaining budget, after subtracting the non-competing component, is divided by the average size of a competing grant to determine how many new awards can be made. Historical competing grant sizes are calculated from data and presented in **Figure S4**, panel C (nominal USD) and **Figure S4**, panel D (BRDPI-adjusted 2025 USD). Future competing grant sizes are projected to grow by 2.7 percent annually, consistent with BRDPI forecasts. This structure produces estimates of both new and active RPGs over time.

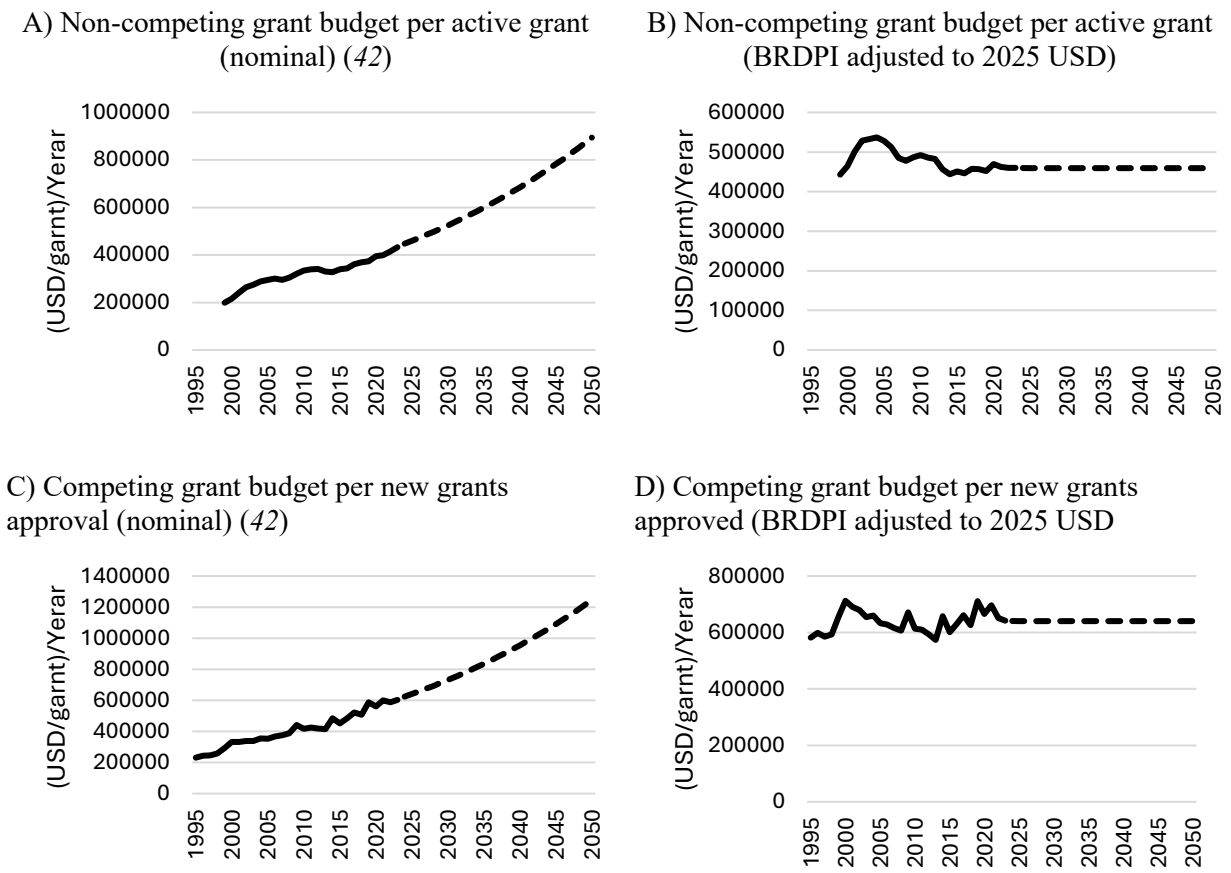


Figure S4: Historical data and projections for competing and non-competing grant budgets per award, shown in nominal and Biomedical Research and Development Price Index (BRDPI)-adjusted 2025 USD.
Note: Solid lines represent historical values; dashed lines represent projected values.

After estimating the number of annual new RPGs from the NIH budget, we calculate the grant success rate as the ratio of awards to total applications. To compute applications, we distinguish between two applicant groups: first-contact and established-contact principal investigators. Established-contact PIs are those who have previously received NIH funding and thus already have an established history of engagement with the NIH grant system. In the model structure, this group corresponds to first-time PIs, established PIs, and prior PIs without an active award (see Section R&D Workforce in Science, Engineering, and Health for details). By contrast, first-contact applicants are those applying to NIH to become a PI for the first time, which in the model corresponds to non-PI faculty.

To operationalize this structure, we multiply the number of individuals in each relevant workforce stock by the fraction of that group who submit an application in a given year. This yields the number of applicants from each category. We then differentiate applications from each group by incorporating estimates of the number of applications per person. The application per person is not a fixed parameter. We capture a feedback loop from the application success rate. As success rates fall, applicants need to submit more proposals per person to remain funded, while higher success rates ease pressure and reduce submissions. This feedback between success rate and application behavior is explicitly captured in the model, with parameters calibrated to historical data.

In the historical data, total applicants and total applications per year are available (see Data Input section). To separate these totals into first-contact and established-contact groups, we applied

historical input time-series data that report the fractions of NIH RPG applications and applicants by group, as shown in **Figure S5**. For years beyond the historical record, the projections assume that the most recent trend continues, as fractions in those years are fairly flat.

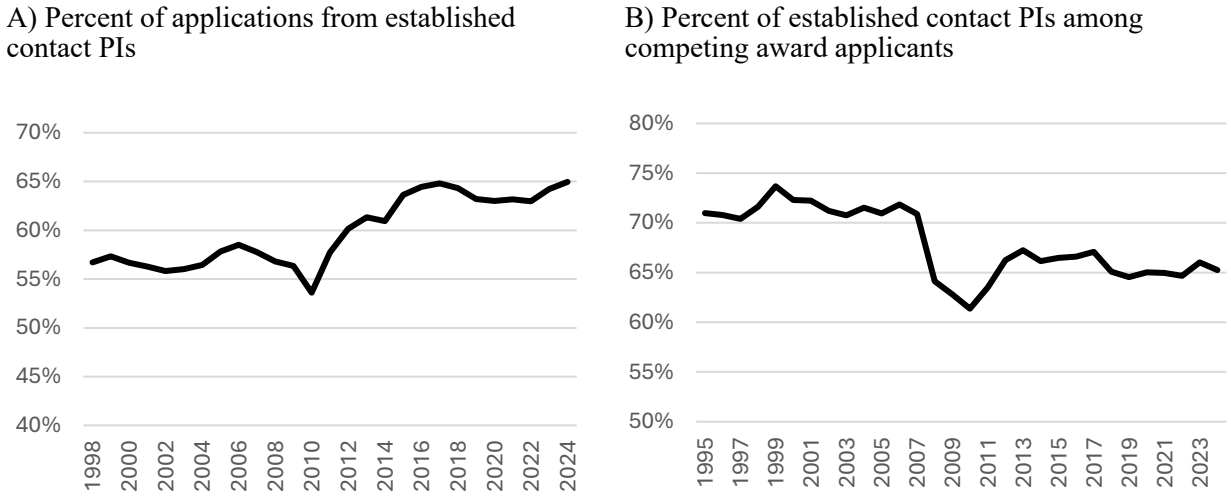


Figure S5: Historical input time-series data used to estimate fractions of NIH research project grant applications and applicants by first-time and established contact PIs. These data were used as multiplicative factors with the total number of research project grant applications and applicants.

*3.2.*R&D *Workforce* in Science, Engineering, and Health

A detailed overview of the workforce component of the model is presented in **Figure S6**. This section of the model tracks the states and transitions of doctoral researchers within both academic and industry settings, showing how shifts in career stages and resource constraints shape the workforce composition over time.

The figure shows several interconnected effects across the research workforce. Importantly, the central variables, shown in circles in **Figure S6**, are not fixed constructs; they are endogenous elements that change within the model as other effects evolve, capturing the dynamic nature of the system. This approach better represents how the dynamics unfold in the real world and increases the credibility and viability of future projections.

One set of dynamics captures how changes in grant success rates influence the flows of researchers between different funding and career stages. Another mechanism reflects how the availability of academic positions impacts the transition of doctoral students and postdoctoral researchers into faculty roles. Similarly, in the industry, the number of available positions shapes transitions from academia into industry. Both academic and industry position availabilities feed back into the system, influencing enrollment. Total job availability also influences upstream outflow from early career stages that reflect exits from the biomedical research workforce.

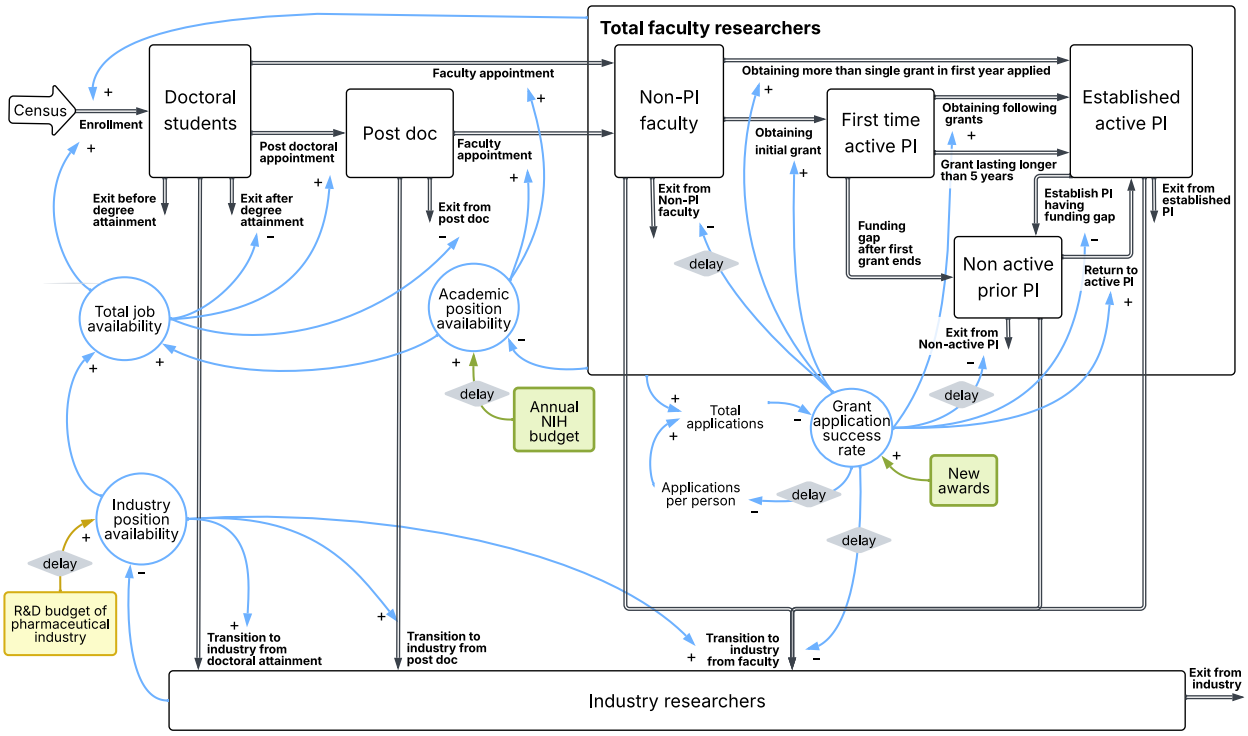


Figure S6: Overview of the model focusing on the research workforce

The model begins with doctoral student enrollment, which is informed by census data to capture broader demographic trends presented in **Figure S7**, panel A. In addition to this external driver, two endogenous feedback loops (i.e., faculty availability and job availability) also influence enrollment rates. Total job availability plays a critical role in shaping enrollment behavior, but its effects unfold with a delay. Prospective students and trainees do not immediately adjust their decisions in response to labor market shifts; rather, they perceive changes in job prospects gradually, and their career choices adjust over time. On the other hand, exits from the research workforce after degree attainment can happen without such delay. When research jobs are not available, individuals can take non-research roles and leave the biomedical research workforce.

To estimate the number of individuals completing their doctoral degrees, we draw on the historical trend in median years to degree, as presented in **Figure S7**, panel A. For years without directly reported values, we interpolate linearly between available data points. For future years beyond the historical record, we carry forward the most recent observed value, consistent. The decline in time-to-degree is treated as an exogenous input to the model, reflecting a broader structural trend that we do not attempt to endogenously capture.

After doctoral training, the model traces career flows into faculty, postdoctoral appointments, and industry researchers. Postdoctoral researchers represent a transitional stage, where individuals may later move into faculty positions or enter industry, depending on position availability and funding conditions. If total job availability is insufficient, some individuals may also exit the research system entirely, taking on non-research roles, much like the attrition observed after degree attainment.

In the model, the dynamics of career flows into future positions are both driven and controlled by the number of available positions in each category. When more positions are available in a given sector, more individuals are drawn toward that career path. This may reflect higher compensation, greater perceived stability, or even social influence, as people observe their peers choosing similar paths. In this way, we consider that the availability itself can act as a driver of career choices.

On the control side, available positions act as a limiting factor. Within each career path (i.e., faculty, postdoctoral, or industry), positions decrease when new entrants are hired and increase when individuals exit, creating a natural balancing mechanism. This ensures that the flow of people into each category cannot exceed the capacity defined by existing opportunities.

Growth in the number of available research positions is further shaped by funding conditions. In academia, growth is tied to the NIH budget, while in industry it is driven by the R&D budget. These financial resources expand or constrain opportunities by influencing the creation of new positions. However, the effects of funding are not immediate. Institutions and companies require time to adjust staffing levels, so shifts in funding translate into job market changes only after a delay. The model also incorporates an asymmetrical delay in capacity adjustment. When perceived funding availability decreases, hiring freezes are implemented quickly, placing immediate limits on new opportunities. By contrast, when funding improves, the response is slower. Institutions take more time to expand their positions.

Once individuals transition to a faculty position, the model captures career transitions by the grant application success rate. The pathway begins with non-PI faculty, a diverse group that includes many researchers who may never obtain an NIH grant. Importantly, this pathway is highly variable across fields. In many health-related disciplines in the U.S., where faculty positions are heavily dependent on external funding ("soft money"), failure to secure grants can lead to exit from academia. By contrast, in some other fields, like engineering, faculty members may remain in their roles without ever receiving NIH support. Since the model tracks all doctoral holders in science, engineering, and health fields, all individuals remain part of the system. Even if they retire without ever receiving NIH funding, as their training and background are relevant to potential biomedical researchers, they are included in the overall pool of non-PI faculty.

Within the non-PI faculty group, a fraction attempts to secure their initial NIH grants. Using data on first-time applicants, the model estimates the proportion who try. Some succeed and advance into the stage of first-time active PIs. Others may get discouraged after repeated unsuccessful attempts and eventually transition into the industry or leave research altogether. For the effect of perceived grant success rate on such exits, the model accounts for a delay.

Securing initial funding allows faculty to transition into the first-time PI stage. Those who successfully obtain subsequent grants then move forward into established PI status (see Data section for detailed definition), whereas those who experience funding lapses risk becoming non-active prior PIs. In the model, the first-time PI stage is assumed to be short-lived and transitional, with no exits from academia occurring during this phase. Transitions out of the research workforce, whether into industry or complete exits from academia, are assumed to take place either before individuals reach this stage or after they progress beyond it. Within this framing, the first-time PI stage functions primarily as a brief gateway.

Established PIs can remain in their positions with sustained funding, but they also face the possibility of transitioning into the non-active PI category if they lose grant support. Once in the non-active PI pool, individuals may remain there for extended periods without exiting academia. Some of these non-active PIs may eventually return to active PI status by successfully securing new grants, while others may leave the academic research workforce altogether. Non-active PIs, much like non-PI faculty, represent a heterogeneous group. They may remain in this category long-term. For this reason, the model continues to track them as part of the research workforce, even if they do not hold funding. This ensures that the system captures their potential re-entry.

The model also incorporates feedback around the grant application success rate. Transitions into the first-time PI and established PI stages are immediately impacted by changes in success rates, while established PIs are impacted by a delay, as in the short term, they hold multi-year grants, creating a buffer effect when their funding lapses. Exits from academia or transitions to industry

also occur with delays, as they depend on how faculty perceive long-term opportunities rather than immediate outcomes.

In addition, the model captures the reinforcing cycle that emerges when success rates decline. Lower success rates lead faculty to submit more applications per person in an effort to improve their odds of getting funded and sustain their positions, which drives up the total number of applications. This behavioral adjustment, however, does not occur instantaneously. Instead, it unfolds with a delay, as investigators first perceive lower success rates and then gradually increase their submission activity in response. This increasing number of applications, in turn, reduces the success rate even further, reinforcing the competitive pressure.

The workforce section of the model is parameterized to include all individuals in science, engineering, and health fields. This reflects the fact that individuals such as doctoral students and post doctorates who are not currently funded by NIH can still progress through the pipeline and, upon reaching faculty status, may apply for NIH grants and become PIs. Hence, to estimate NIH-specific outcomes (such as NIH-funded fundamental research and clinical trials), we scale these broader stocks by the fraction supported by NIH presented in **Figure S7**, panel C (doctoral students) and panel D (postdoctoral researchers). On the faculty side, only first-time PIs and established PIs with active NIH grant stocks are considered the NIH-supported workforce.

In the event of a funding reduction, the model assumes that individuals dependent on a single grant are immediately affected, with their position status shifting accordingly. This includes all first-time PIs by definition and a fraction of established PIs who hold only one active NIH grant at a time, as shown in **Figure S7**, panel E. The impact on workforce stocks is calculated based on the number of grants per capita in each category: if a given fraction of grants is terminated, the same fraction of individuals in the corresponding stock is assumed to be affected. This operates by reducing doctoral student enrollment and completion, eliminating postdoctoral positions, for the proportion and pushing faculty from active PI to non-active PI status. The model also accounts for the interdependence between academic and industry employment. As more individuals exit academia due to the loss of NIH support, they seek industry positions. This increased competition reduces the availability of industry research roles, pushing additional individuals out of the research workforce altogether when demand exceeds available positions. In this framework, we do not prioritize placement by career stage (doctoral student, postdoc, or faculty) when industry positions are limited. Instead, we assume that each group competes within its respective level of opportunities, and if overall research positions are not available, individuals exit into non-research employment or retire.

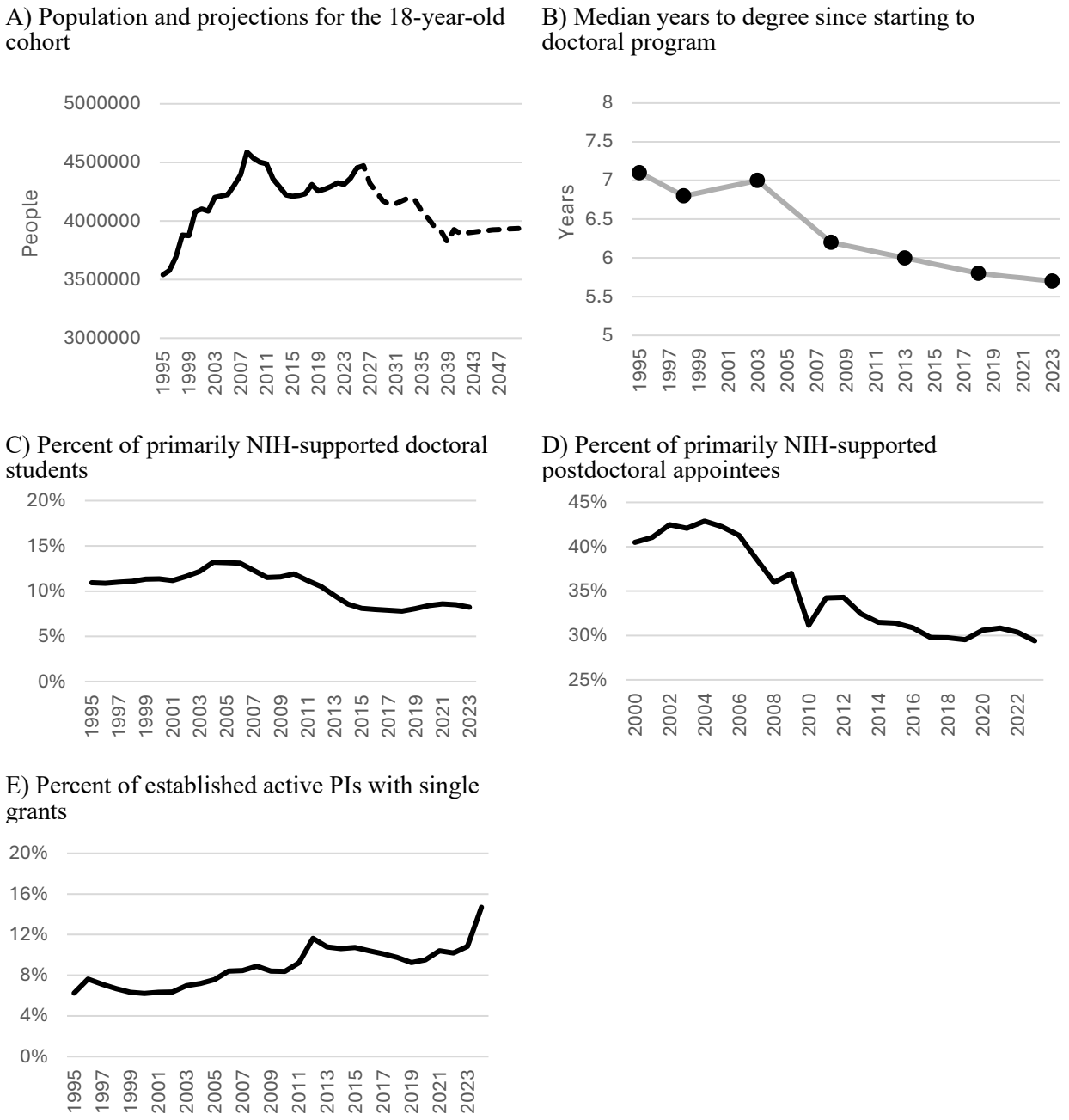


Figure S7: Historical input time-series data for 18-year-old age cohort from U.S. Census data, and to the fraction of the workforce supported by the NIH.

Note: Solid black lines represent historical values; dashed line represents projected values; grey line represents interpolated values between years of data.

3.3.*Biomedical* Research and Innovation

We model research output under two broad categories: fundamental research and applied research. **Figure S8** presents fundamental research funded by NIH and applied research funded by both NIH and industry, which then results in commercial innovations (measured as approved novel drugs). To capture outputs in each category, we adopt a framework based on the Cobb-Douglas production function (*67*), which models output as a function of capital and labor inputs while considering output elasticities to capital and labor.

For NIH-funded fundamental research, the capital input is defined as the number of active grants in basic sciences. These active grants are derived from the NIH Budget and the research grants section described earlier. This is multiplied by the fraction of NIH research grants in basic sciences. These broader trends, drawn from external sources (see Data section), are used as input time series as shown in **Figure S9**, panel A. For years prior to and beyond the historical record, projections assume continuation of the most recent trend, consistent with the observed stability of these fractions at both the start and end of the available series.

The labor input includes NIH-funded principal investigators, postdoctoral researchers, and doctoral students engaged in basic sciences. To construct these labor measures, we draw on the researcher sections described previously and then scale them by exogenous time-series data on the fraction of researchers funded by NIH and the fraction of NIH researchers working in basic sciences as shown in **Figure S9**, panel B. For years prior to and beyond the historical record, the same trend continuation assumption is applied. The model does not attempt to explain why the shares of NIH grants or researchers dedicated to fundamental research have declined over time; these are treated as exogenous trends that directly feed into the model's capital and labor inputs as multipliers.

An asymmetric delay is applied to represent how workforce changes affect productivity. When new researchers enter the workforce, it typically takes longer for them to get onboarded and become productive. By contrast, when the workforce shrinks, the decline in research capacity occurs more rapidly, as individuals exiting the workforce immediately reduce available labor. This asymmetry captures real-world lags in training, integration, and productivity, while reflecting the faster impact of attrition.

In addition to the size of the workforce, the model also incorporates the availability of researchers to conduct research as part of the labor input. Researcher availability is treated as an endogenous factor that adjusts with workload and funding dynamics. As the number of ongoing projects per person increases, or as investigators devote more time to preparing and submitting grant applications, the amount of time available for research activities decreases. This reduction in effective labor availability constrains the initiation of new projects, as researchers have less capacity to launch additional work, and eventually lowers the rate of research output, reflected in fewer publications over time.

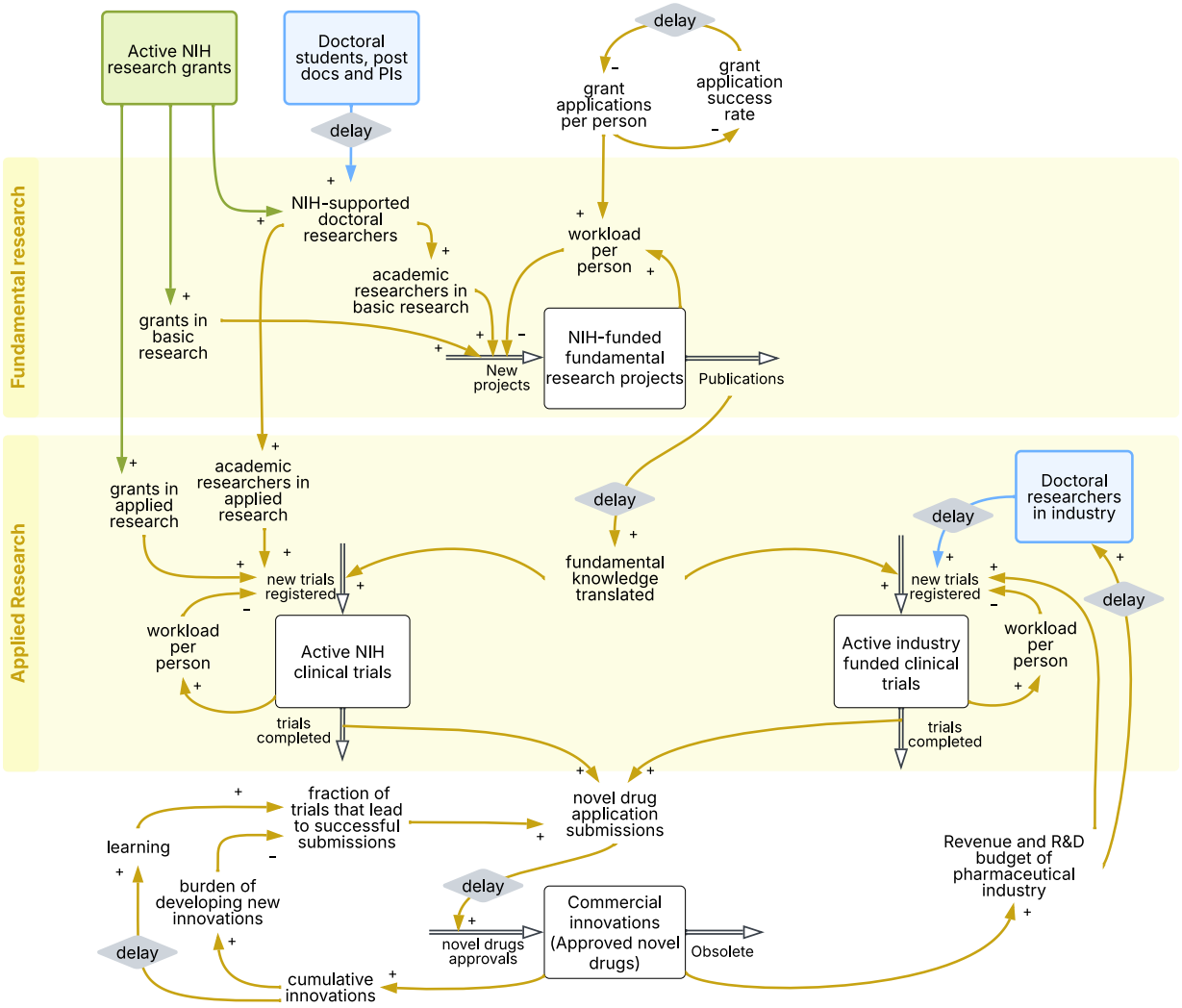


Figure S8: Overview of the model focusing on the innovation pipeline

For NIH-supported applied research, the model captures capital and labor inputs in a parallel way to fundamental research. In both fundamental and applied research sides, the model is calibrated using historical data to estimate the elasticities of capital and labor as well as the overall productivity factor, given the feedback loops described.

On the industry side, the capital input is defined as the R&D budgets of pharmaceutical companies, which are in turn tied to commercial innovations and industry revenue. These R&D budgets are captured endogenously, with delays that reflect the time lag between commercial products and subsequent reinvestment into research. The labor input comes from the pool of doctoral researchers employed in industry, again derived from the workforce section. The number of available positions for these researchers depends on R&D budgets, which shape industry workforce capacity with a delay. As with fundamental research, researcher availability is treated as a constraint on effective labor. When researcher are engaged in ongoing clinical trials, their availability to launch new ones decreases.

Additionally, in both NIH and industry applied research, the model also captures the dependence of applied research on fundamental research outputs, with a delay structure. This dynamic reflects empirical evidence from prior studies showing that many approved medications can be traced back to NIH-funded fundamental research publications, such as those identifying novel biological targets (*30*). Thus, fundamental research outputs indirectly feed into applied research productivity, linking the two categories into a pipeline. Once applied research progresses are

completed, only a fraction of completed trials succeed in producing a novel drug, with additional regulatory delays introduced by application review and FDA approval.

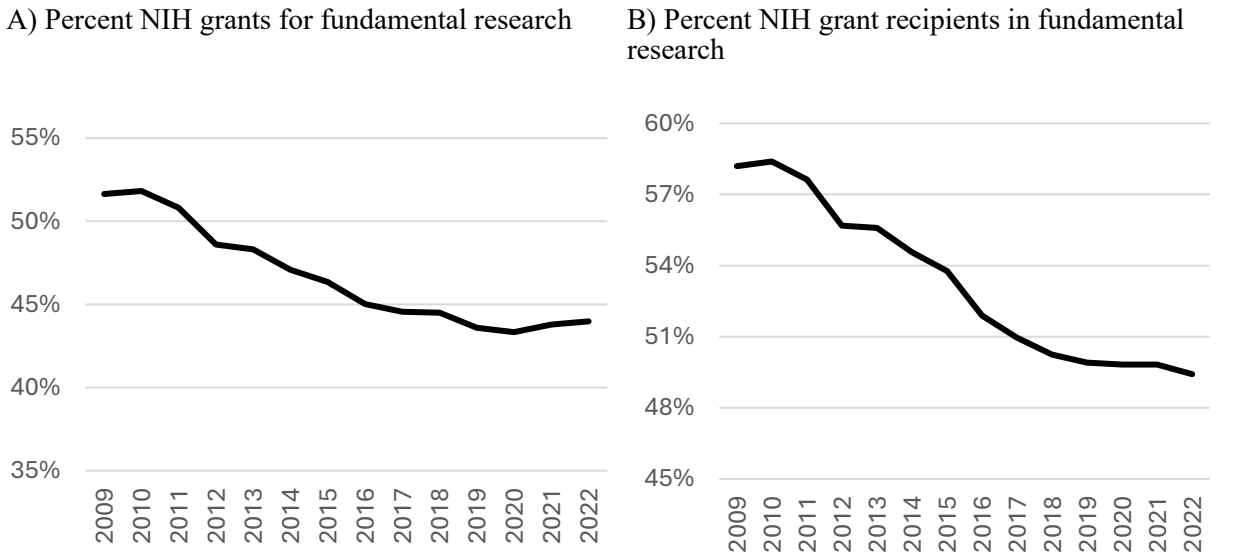


Figure S9: NIH-support for fundamental research as a share of all grants and investigators.

Novel drug approvals introduce new layers of complexity into the discovery landscape. Each approved drug expands the knowledge frontier but simultaneously raises the bar for subsequent innovations, as unmet needs shift to more difficult problems and biological targets become increasingly complex. As a result, the resources and effort required for future drug discovery increase. To balance this effect, the model incorporates a learning mechanism, whereby each wave of drug approvals can generate new knowledge and technological capabilities that eventually enhance future discovery. However, this learning is subject to a delay, as new methods and insights take time to diffuse and become broadly usable. The interplay between these two opposing forces (growing discovery difficulty and delayed learning) slows the overall pace of novel drug development, consistent with prior research (*14*, *30*).

3.4.*Economic value* associated with novel drug approvals

To estimate the economic value associated with novel drug approvals, we began with Santerre and Vernon's estimate (*38*) of $0.9-$3.9 billion in net social value per new drug (2000 USD), which reflects consumer surplus for all newly approved drugs, not just novel drugs. We adjusted these values to 2025 dollars using the U.S. Consumer Price Index (CPI-U) (*68*), yielding approximately $1.7-$7.3 billion per drug.

Then, to approximate the economic costs specifically attributable to novel drugs, we examined the historical ratio of novel to all drug approvals. Since 1995, which marks the beginning of the model's time horizon, there have been roughly three total drug approvals for every novel drug approval (*46*, *47*) as shown in **Figure S10**. This ratio reflects the broader mix of approvals, including both novel and non-novel drugs, and provides a basis for linking novel drug discovery to overall approval activity. To build confidence in this estimate, we also examined approval patterns from earlier years. We observed that the ratio exhibited little variation over time, reinforcing the stability of the relationship between novel and total drug approvals. We applied this ratio to Santerre and Vernon's per-drug values and adjusted accordingly to isolate the portion attributable to novel drugs.

We multiplied per-drug values by the projected changes (shortfall or surplus) in novel drug approvals for each scenario and calculated both the undiscounted total (constant 2025 USD) and the present value (PV) using a 3% annual discount rate, performing the calculation on a year-by-year basis and summing across the projection period (2026-2050).

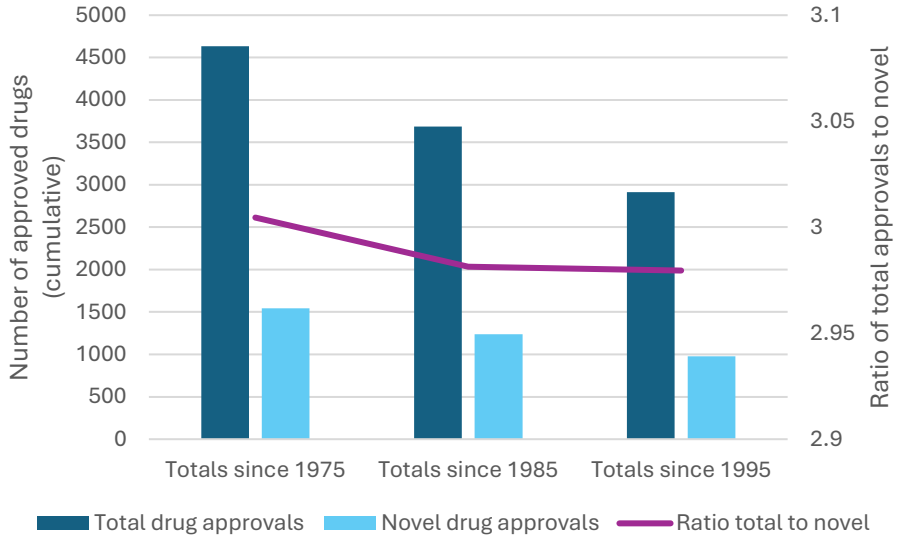


Figure S10: Comparison of total and novel drug approvals and their ratio

4. Model Fit and Estimated Parameters

The model simulates historical years and uses optimization to estimate unknown parameters in order to match the historical patterns.

Figure S11 shows model alignment with historical data for NIH budget components. Given the ample data and only two unknown parameters for this section of the model (specifically, the stock of active NIH grants in **Figure S2**), a close match to data is expected; such alignment does not raise concerns about overfitting.

Figure S12 shows model outputs compared to historical data across the other time series, assessing how well the model reproduces observed trends for estimated parameters. Data for the calibration targets are reported in Table 1 of the main text, which includes 36 data sources. Several of these measures were further disaggregated for visualizations, yielding a total of 40 calibration targets reported in this section.

Table S1 summarizes the model calibration fit metrics, reporting an overall Mean Absolute Percentage Error of 10.5% and Mean Percentage Error of -1.1%.

Finally, the estimated parameters and their ranges by the MCMC calibration are reported in **Table S2**.

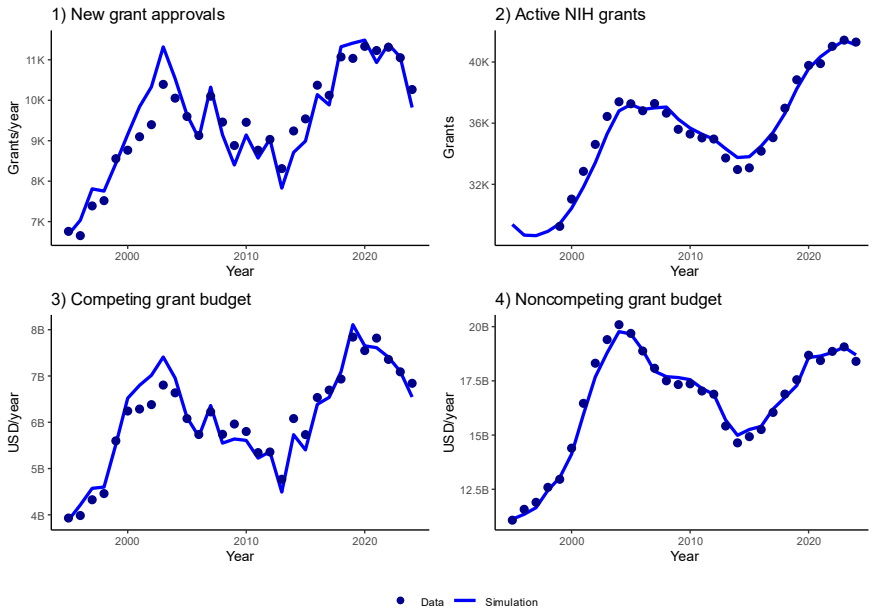


Figure S11: Model alignment with historical data on NIH budget and research project grants

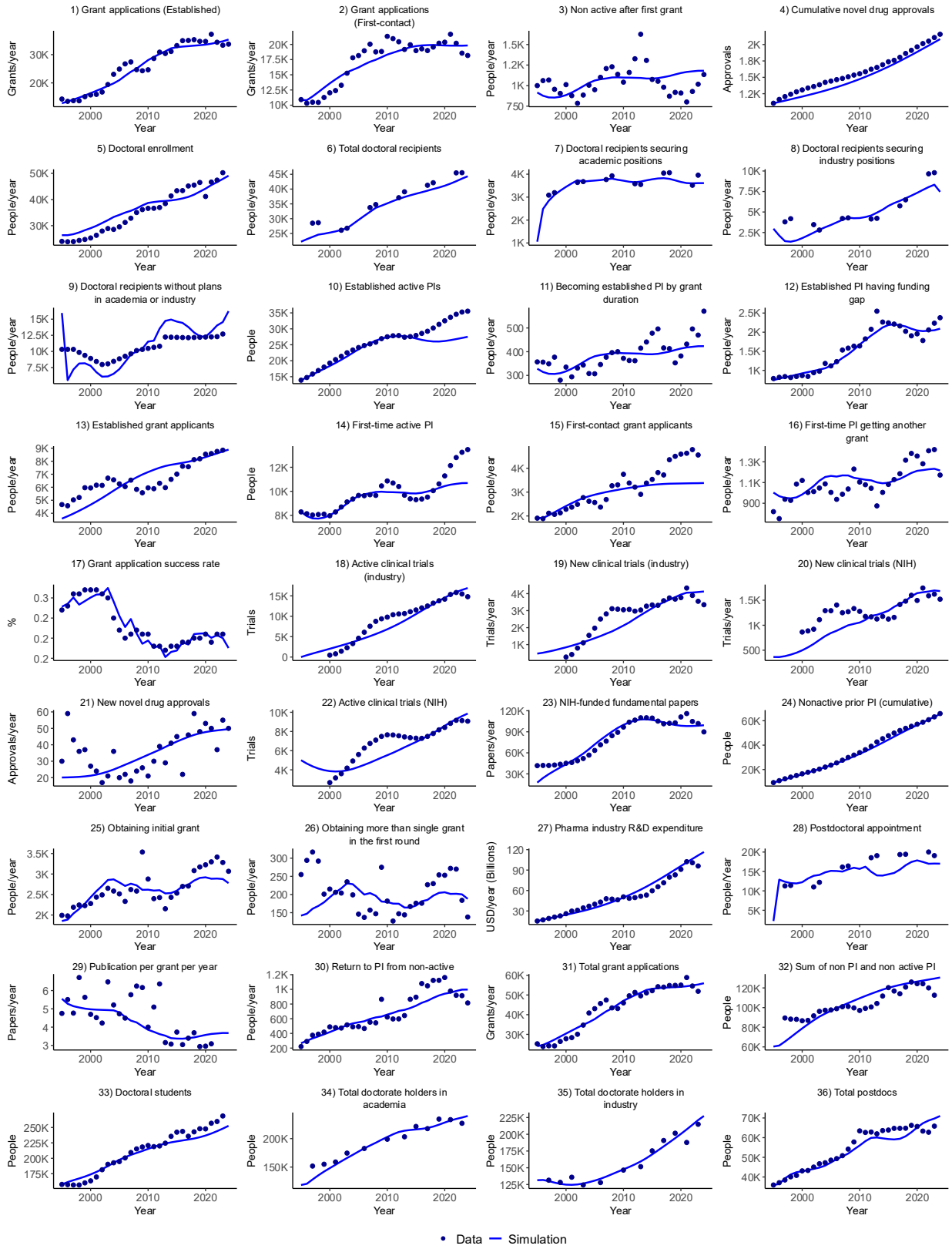


Figure S12: Model fit to historical data for calibrated parameters

Table S1: Model calibration fit metrics on historical data

Plot no.	Time series	MAPE *(Mean Absolute Percentage Error)*	*MAE (Mean Absolute Error)*	MPE *(Mean Percentage Error)*	*Pearson r*	*Theil's U²*
S11.1	New grant approvals	3.6%	333.5	0.5%	1.0	0.7
S11.2	Active NIH grants	1.3%	445.0	-0.1%	1.0	0.5
S11.3	Competing grant budget	3.6%	2.2E+08	0.5%	1.0	0.5
S11.4	Noncompeting grant budget	1.3%	2.2E+08	-0.2%	1.0	0.3
S12.1	Grant applications (Established)	6.1%	1560.7	-1.2%	1.0	1.2
S12.2	Grant applications (First-contact)	7.5%	1237.8	0.1%	0.9	1.4
S12.3	Non-active after the first grant	13.9%	143.8	2.5%	0.2	1.4
S12.4	Cumulative novel drug approvals	5.3%	81.7	-5.3%	1.0	2.3
S12.5	Doctoral enrollment	8.7%	2813.9	5.1%	1.0	1.6
S12.6	Total doctoral recipients	5.3%	1861.2	-5.3%	1.0	0.7
S12.7	Doctoral recipients securing academic positions	3.8%	139.7	-2.0%	0.9	0.5
S12.8	Doctoral recipients securing industry positions	19.6%	947.8	-12.6%	0.9	1.0
S12.9	Doctoral recipients without plans in academia or industry	16.5%	1713.3	0.0%	0.9	4.8
S12.10	Established active PIs	6.7%	2054.2	-6.4%	0.9	4.1
S12.11	Becoming an established PI by grant duration	10.4%	41.2	-1.4%	0.6	1.2
S12.12	Established PI having funding gap	6.4%	106.0	-1.2%	1.0	0.9
S12.13	Established grant applicants	13.2%	781.8	-1.2%	0.8	2.5
S12.14	First-time active PI	5.1%	571.8	-3.1%	0.9	2.3
S12.15	First-contact grant applicants	11.5%	424.3	-4.4%	0.9	2.3
S12.16	First-time PI getting another grant	10.1%	106.1	3.3%	0.7	1.2
S12.17	Grant application success rate	6.3%	0.0	0.3%	0.9	1.1
S12.18	Active clinical trials (industry)	39.2%	1359.7	17.9%	0.9	2.2
S12.19	New clinical trials (industry)	29.8%	485.8	4.4%	0.9	2.2
S12.20	New clinical trials (NIH)	17.5%	207.1	-11.1%	0.8	2.2
S12.21	New novel drug approvals	27.6%	8.8	3.3%	0.5	1.0
S12.22	Active clinical trials (NIH)	14.3%	883.3	-6.9%	0.9	3.1
S12.23	NIH-funded fundamental papers	10.5%	6425.6	-3.5%	1.0	1.4
S12.24	Nonactive prior PI (cumulative)	2.6%	975.6	-2.6%	1.0	0.7
S12.25	Obtaining initial grant	8.5%	235.1	-0.4%	0.7	1.1
S12.26	Obtaining more than single grant in the first round	22.3%	48.1	-2.6%	-0.2	1.4
S12.27	Pharma industry R&D expenditure	9.2%	5.0	1.6%	1.0	1.5
S12.28	Postdoctoral appointment	14.6%	2415.3	-5.2%	0.8	2.0
S12.29	Publication per grant per year	14.8%	0.8	-3.7%	0.6	0.9
S12.30	Return to PI from non-active	12.7%	94.6	-1.0%	0.9	1.2
S12.31	Total grant applications	5.6%	2159.9	0.5%	1.0	1.1
S12.32	Sum of non-PI and non-active PI	7.5%	7423.0	0.7%	0.9	2.2
S12.33	Doctoral students	3.5%	7487.7	-1.0%	1.0	1.6
S12.34	Total doctorate holders in academia	4.3%	7723.6	-2.2%	1.0	0.7
S12.35	Total doctorate holders in industry	4.0%	6576.9	0.2%	1.0	0.6
S12.36	Total postdocs	4.3%	2580.9	-2.2%	1.0	1.8
	Mean across time series	**10.5%**	**NA**	**-1.1%**	**NA**	**NA**

Table S2: Estimated parameters and 95% projection ranges

Variable name	Mean and 95% projection range	Variable name	Mean and 95% projection range
base grad school leave rate	1.1e-03 (1.0e-04, 3.4e-03)	NIH initial clinical trials	4,973.4 (4,905.2, 5,000.0)
base doctoral enrollment	26,790.0 (25,663.9, 27,796.4)	avg grant duration	3.9 (3.8, 4.0)
base post doc duration	4.2 (3.5, 5.0)	avg time to become obsolete	18.7 (10.6, 25.0)
post doc transition to faculty fraction	6.8e-01 (6.1e-01, 7.3e-01)	initial grants	28,978.8 (27,592.7, 30,140.9)
strength of job availability on post docs to go to academia	2.6e-02 (1.0e-04, 8.9e-02)	initial non PI faculty researchers	46,821.5 (39,880.2, 54,831.2)
avg time in industry research positions	22.5 (19.6, 25.9)	initial prior PI	12,571.3 (10,000.0, 17,201.5)
base rate to receive initial awards	9.3e-02 (5.8e-02, 1.2e-01)	base rate for funding gap after first grant	1.1e-01 (1.0e-01, 1.2e-01)
base rate to receive following awards	1.6e-01 (1.2e-01, 2.0e-01)	base rate for established PI funding gap	1.3e-02 (1.0e-02, 1.8e-02)
base publication per grant per year	13.2 (8.8, 18.8)	base rate for established PI by grant duration	3.9e-02 (3.7e-02, 4.2e-02)
fraction of trials that succeed	3.3e-02 (2.3e-02, 4.3e-02)	base rate for return to PI	3.5e-02 (2.1e-02, 5.9e-02)
trial per grant per year	1.7e-02 (1.0e-02, 2.6e-02)	base established PI industry transition rate	1.2e-04 (1.0e-04, 1.6e-04)
trials per billion USD investment	8.7 (5.4, 13.0)	base established PI exit rate	4.8e-04 (1.0e-04, 1.4e-03)
post doc position utilization	9.2e-01 (8.6e-01, 9.5e-01)	base non PI faculty exit rate	1.2e-01 (1.0e-01, 1.4e-01)
faculty capacity utilization	9.4e-01 (9.3e-01, 9.5e-01)	base prior PI exit rate	7.2e-03 (1.0e-04, 2.3e-02)
industry capacity utilization	9.0e-01 (8.4e-01, 9.4e-01)	applications per first time PI	5.1 (3.7, 6.1)
initial commercial innovations	216.8 (112.4, 365.8)	applications per established PI	3.0 (2.0, 4.3)
initial industry clinical trials	10.1 (1.0, 31.3)	fraction of established contacts that apply	1.0e-01 (8.8e-02, 1.2e-01)
post doc position growth rate	3.1e-01 (2.6e-01, 3.6e-01)	fraction of potential first time contacts that apply	4.3e-02 (3.7e-02, 5.1e-02)
academic position growth rate	1.5e-01 (1.4e-01, 1.6e-01)	scaling factor to adjust multi PI grants with both first time and established PIs	1.0 (9.7e-01, 1.1)
industry position growth rate	1.7e-02 (1.3e-02, 2.1e-02)	first time PI grant success rate strength	7.4e-02 (1.0e-04, 2.7e-01)
avg trial duration industry	4.8 (4.2, 5.7)	established PI grant success rate strength	1.9e-01 (1.0e-04, 4.3e-01)
NIH avg trial duration	7.1 (6.3, 8.0)	base rate to receive multiple awards at first year	1.2e-02 (7.4e-03, 1.8e-02)
commercial innovation strength on positions	3.0 (2.9, 3.0)	strength of NIH funding on first time PI faculty to receive multiple awards	1.0 (7.1e-01, 1.3)
strength of commercial innovation on investment	1.9 (1.3, 2.8)	strength of grant availability on having funding gap	1.1 (8.4e-01, 1.3)
fundamental research strength on clinical research	7.2e-01 (5.0e-01, 9.3e-01)	strength of NIH funding on non active PI faculty exit	2.2e-02 (1.0e-04, 7.3e-02)
strength of perceived job prospect on enrollment	1.2 (8.2e-01, 1.7)	strength of grant application workload on productivity for NIH researchers	6.0e-01 (2.2e-01, 9.0e-01)
strength of job availability on new grads going to industry	5.4e-01 (2.7e-01, 8.9e-01)	strength of active commitments on productivity	1.9e-01 (1.2e-02, 4.7e-01)
strength of faculty position availability on faculty placement from doctoral	1.8e-01 (1.4e-03, 3.4e-01)	strength of grant availability on becoming nonactive after first grant	9.9e-03 (1.0e-04, 3.7e-02)
strength of job availability on duration	5.1e-01 (5.4e-02, 1.1)	strength of trainer availability on enrollment	1.1e-01 (1.0e-01, 1.3e-01)
strength of NIH funding on non PI faculty to leave research	9.8e-03 (1.0e-03, 3.1e-02)	strength of complexity on new innovations	3.0 (2.9, 3.0)
strength of grant availability on PI career start	5.9e-01 (3.4e-01, 7.7e-01)	strength of learning	7.2e-01 (1.0e-04, 2.4)
strength of grant availability on career establishment	3.1e-01 (3.5e-02, 6.6e-01)	delay for learning	20.3 (1.0, 35.0)
strength of established faculty transition to industry	2.9 (2.8, 3.0)	publication delay	8.4 (6.4, 10.0)
faculty availability strength on fundamental research	1.3 (8.1e-01, 1.7)	fundamental research translation delay	5.1 (5.0, 5.4)
trainee availability strength on fundamental research	4.9e-01 (1.0e-03, 1.4)	academia funding strength on positions	6.3e-03 (1.0e-04, 2.2e-02)
faculty availability strength on clinical research	1.4e-02 (1.0e-03, 4.1e-02)	post doc funding strength on positions	2.3 (1.7, 3.0)
trainee availability strength on clinical research	1.6e-02 (1.0e-03, 5.0e-02)	strength of NIH funding on receiving follow up awards	1.8e-01 (2.0e-02, 3.8e-01)
strength of workload on productivity	8.8e-03 (1.0e-03, 2.7e-02)	initial NIH supported fundamental studies	111,774.7 (36,027.8, 257,450.2)
strength of industry researcher availability on clinical research	3.4e-02 (1.0e-03, 1.2e-01)	strength of post doc position availability on post doc placement from doctoral	3.0 (2.9, 3.0)

5. Additional Results: Percent Changes, Intermediate Outcomes, Extreme Case, and Uncertainty

In this section, we present four sets of supplementary findings. First, we report percent changes in outcomes under the scenarios described in the main text, relative to the baseline. Second, we provide key model outcomes together with extended intermediate outputs not included in the main text. Third, we show the budget trajectory and results for extreme cases under the extended scenarios. Fourth, we report uncertainty ranges across scenarios.

The projected percentage changes in key outcomes under the no-increase, cut, and cut-restore scenarios relative to the baseline are shown in **Figure S13**.

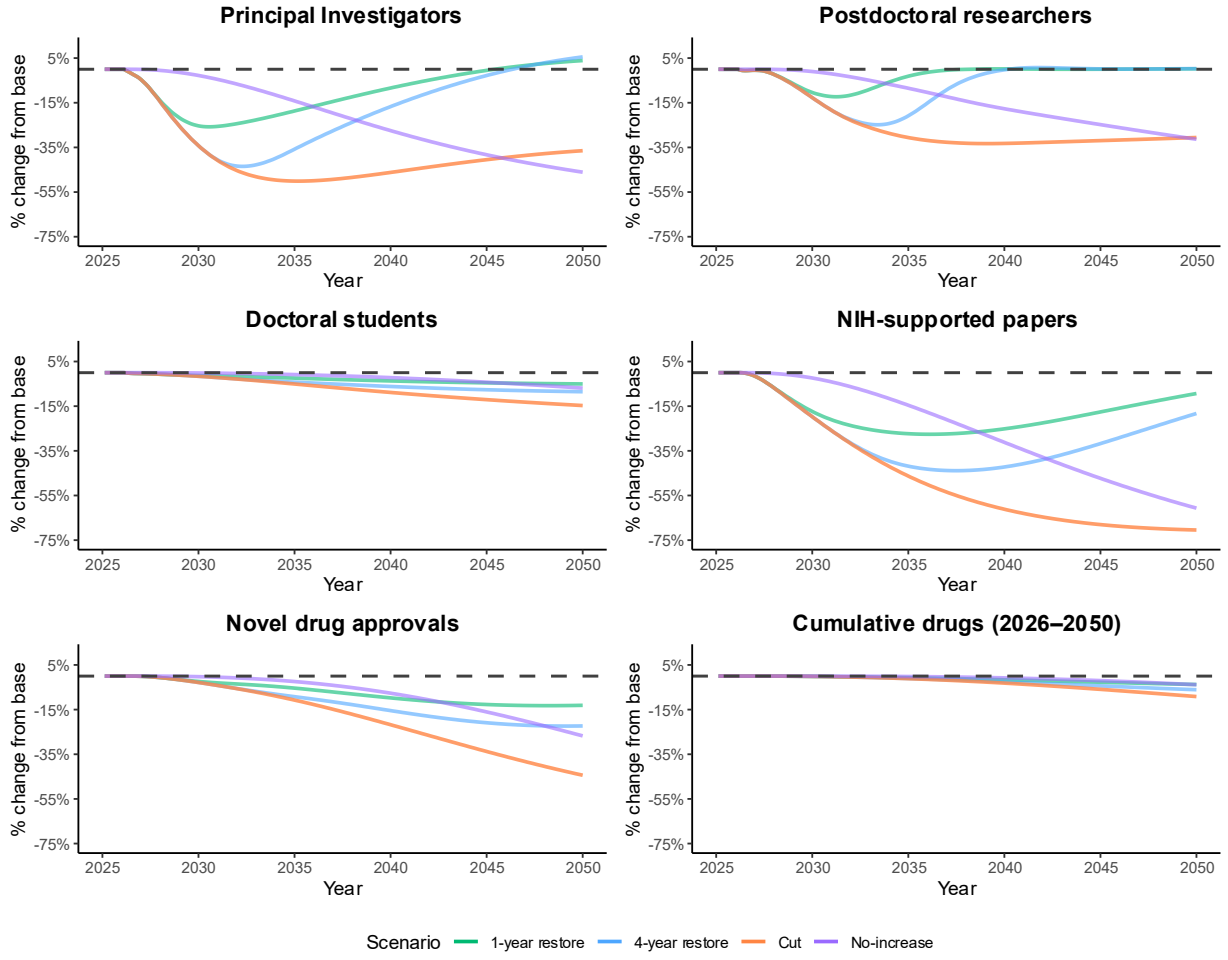


Figure S13: Percent changes from baseline for the outcomes of interest.

Scenarios include: no-increase (purple line); cut (orange line); and restoration to baseline level after one year (green) and four years (blue). The dashed line represents no change from baseline with 0%.

The extended set of intermediate outputs is summarized in **Table S3** and organized into three categories: grant outcomes (e.g., application success rates and number of awards), workforce outcomes (e.g., principal investigators by career stage, total faculty counts, and industry workforce), and innovation outcomes (e.g., clinical trials funded by NIH or industry). Results are shown as raw numbers for the baseline case and as percent changes under alternative scenarios at four time points, representing short-, medium-, and long-term horizons.

Table S3: Extended outcomes for baseline and percent changes from baseline for the scenarios. Color coding is applied within each outcome row to represent the relative magnitude of change over time and across scenarios. Green indicates increases and red indicates decreases.

		Baseline				No-increase				Cut				1-year restore				4-year restore			
	Year	2027	2030	2040	2050	2027	2030	2040	2050	2027	2030	2040	2050	2027	2030	2040	2050	2027	2030	2040	2050
Grant outcomes	Total grant applications	59433	60930	65919	70315	0.3%	3.0%	-2.0%	-11.6%	10.4%	5.7%	-27.7%	-25.0%	10.4%	0.8%	-14.0%	-8.0%	10.4%	5.7%	-24.3%	-14.8%
	Application success rate	16.9%	16.7%	15.4%	14.5%	-7.7%	-19.4%	-35.4%	-45.3%	-85.7%	-45.1%	-16.8%	-19.8%	-85.7%	29.1%	16.2%	8.7%	-85.7%	-45.1%	32.1%	17.4%
	New grant awards	10071	10169	10174	10174	-7.4%	-17.0%	-36.7%	-51.7%	-84.2%	-42.0%	-39.9%	-39.9%	-84.2%	30.1%	0.0%	0.0%	-84.2%	-42.0%	0.1%	0.0%
	Active NIH grants	39205	39061	39054	39054	-0.9%	-7.6%	-29.4%	-46.1%	-23.2%	-39.0%	-39.9%	-39.9%	-23.2%	-13.6%	0.0%	0.0%	-23.2%	-39.0%	0.0%	0.0%
Workforce outcomes	Doctoral students (SEH)	268479	284054	322542	346139	0.0%	-0.1%	-2.2%	-6.9%	-0.4%	-1.6%	-8.8%	-14.7%	-0.4%	-1.3%	-3.7%	-5.0%	-0.4%	-1.6%	-6.2%	-8.5%
	Post doctorates	75423	75773	79007	80519	0.0%	-1.0%	-17.7%	-31.4%	-0.4%	-12.7%	-33.2%	-30.6%	-0.4%	-10.4%	0.2%	0.2%	-0.4%	-12.7%	-0.3%	0.3%
	First-time PIs with NIH grants	10449	10358	10191	10035	-0.1%	-2.6%	-10.2%	-14.4%	-8.5%	-19.7%	-6.7%	-5.0%	-8.5%	-10.9%	4.5%	3.1%	-8.5%	-19.7%	8.8%	5.9%
	Established PIs with NIH grants	27905	27775	26888	26129	0.0%	-2.9%	-34.0%	-58.3%	-3.1%	-39.6%	-61.2%	-48.6%	-3.1%	-30.7%	-13.3%	4.2%	-3.1%	-39.6%	-26.4%	5.4%
	Total PIs (first and established)	38354	38133	37079	36164	-0.1%	-2.8%	-27.5%	-46.1%	-4.6%	-34.2%	-46.2%	-36.5%	-4.6%	-25.3%	-8.4%	3.9%	-4.6%	-34.2%	-16.7%	5.5%
	Total faculty	172622	175819	184410	191545	0.0%	-0.5%	-7.9%	-16.2%	-0.3%	-11.5%	-23.7%	-21.0%	-0.3%	-9.1%	-9.0%	-4.6%	-0.3%	-11.5%	-15.8%	-8.7%
	Doctoral researchers in industry	238076	244344	245382	220452	0.0%	0.0%	-0.4%	-3.2%	0.0%	0.0%	-2.0%	-8.9%	0.0%	0.0%	-1.2%	-4.3%	0.0%	0.0%	-1.8%	-6.7%
Innovation outcomes	Fundamental research papers (NIH)	99416	99195	99229	97330	0.0%	-2.4%	-31.2%	-60.7%	-1.5%	-19.7%	-61.2%	-70.5%	-1.5%	-17.4%	-25.2%	-9.3%	-1.5%	-19.7%	-42.2%	-18.3%
	Clinical trials (Industry)	18046	18821	18627	15528	0.0%	0.0%	-6.2%	-27.0%	0.0%	-0.7%	-21.6%	-49.4%	0.0%	-0.6%	-12.9%	-19.1%	0.0%	-0.7%	-19.1%	-31.0%
	Clinical trials (NIH)	10332	10557	10866	10910	0.0%	-1.6%	-20.2%	-46.1%	-1.5%	-14.2%	-43.1%	-60.1%	-1.5%	-10.5%	-11.9%	-12.6%	-1.5%	-14.2%	-21.7%	-22.2%
	Annual novel drug approvals	50	49	47	41	0.0%	-0.3%	-7.7%	-26.8%	-0.1%	-2.9%	-21.8%	-44.4%	-0.1%	-2.4%	-9.8%	-13.1%	-0.1%	-2.9%	-15.5%	-22.3%
	Cumulative drug approvals	1128	1276	1758	2199	0.0%	0.0%	-0.8%	-3.9%	0.0%	-0.1%	-3.1%	-9.2%	0.0%	-0.1%	-1.6%	-3.8%	0.0%	-0.1%	-2.6%	-6.1%

Acronyms: NIH, National Institutes of Health; SEH, Science, Engineering, and Health; PI, Principal Investigator.

In addition to scenarios presented in the main text, we evaluated an aggressive growth scenario to analyze the rebound time. In the aggressive growth scenario, following four years of the cut scenario (40% cut), the NIH budget doubles in nominal terms in fiscal year 2030, and then grows annually at the rate of inflation. For this scenario, we present the nominal and BRDPI-adjusted budget in **Figure S14**. Outcomes of interest for the same scenario and their percent changes over time are presented in **Figure S15** and **Figure S16**, respectively.

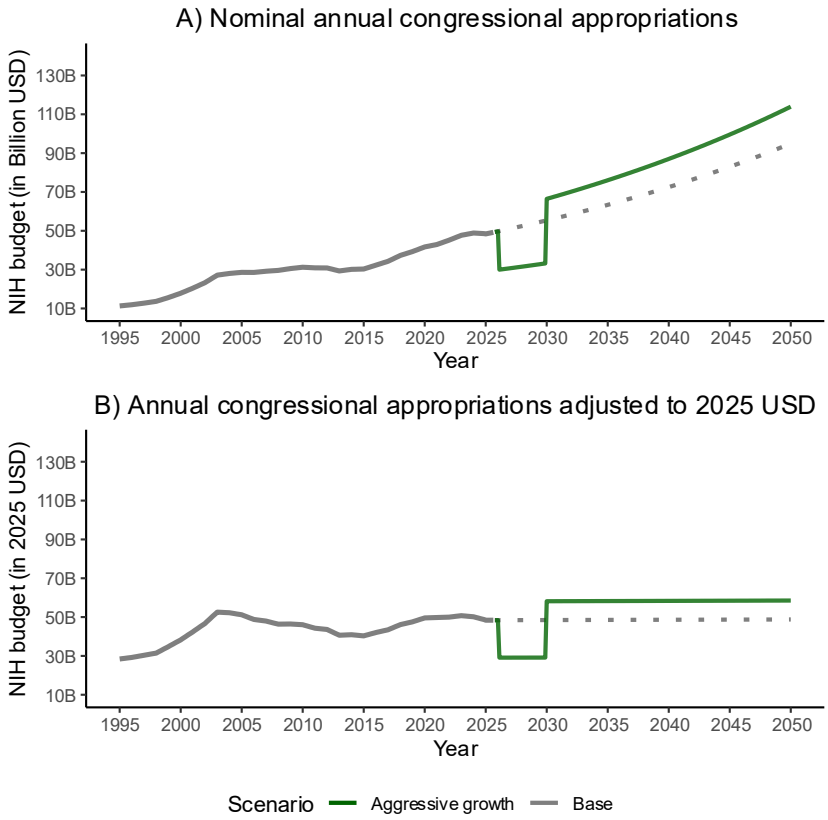


Figure S14: Annual NIH congressional appropriations, nominal (A) and adjusted to 2025 USD using Biomedical Research and Development Price Index (B), historical (1995-2025) and projected (2026-2050) under the aggressive growth scenario (green), in constant 2025 USD

Scenarios include: historical (grey line); baseline (grey dashed line); aggressive growth scenario (green); All values are adjusted using the Biomedical Research and Development Price Index (BRDPI), which accounts for inflation specific to biomedical research; as a result, nominally constant appropriations appear as a decline in real terms over time.

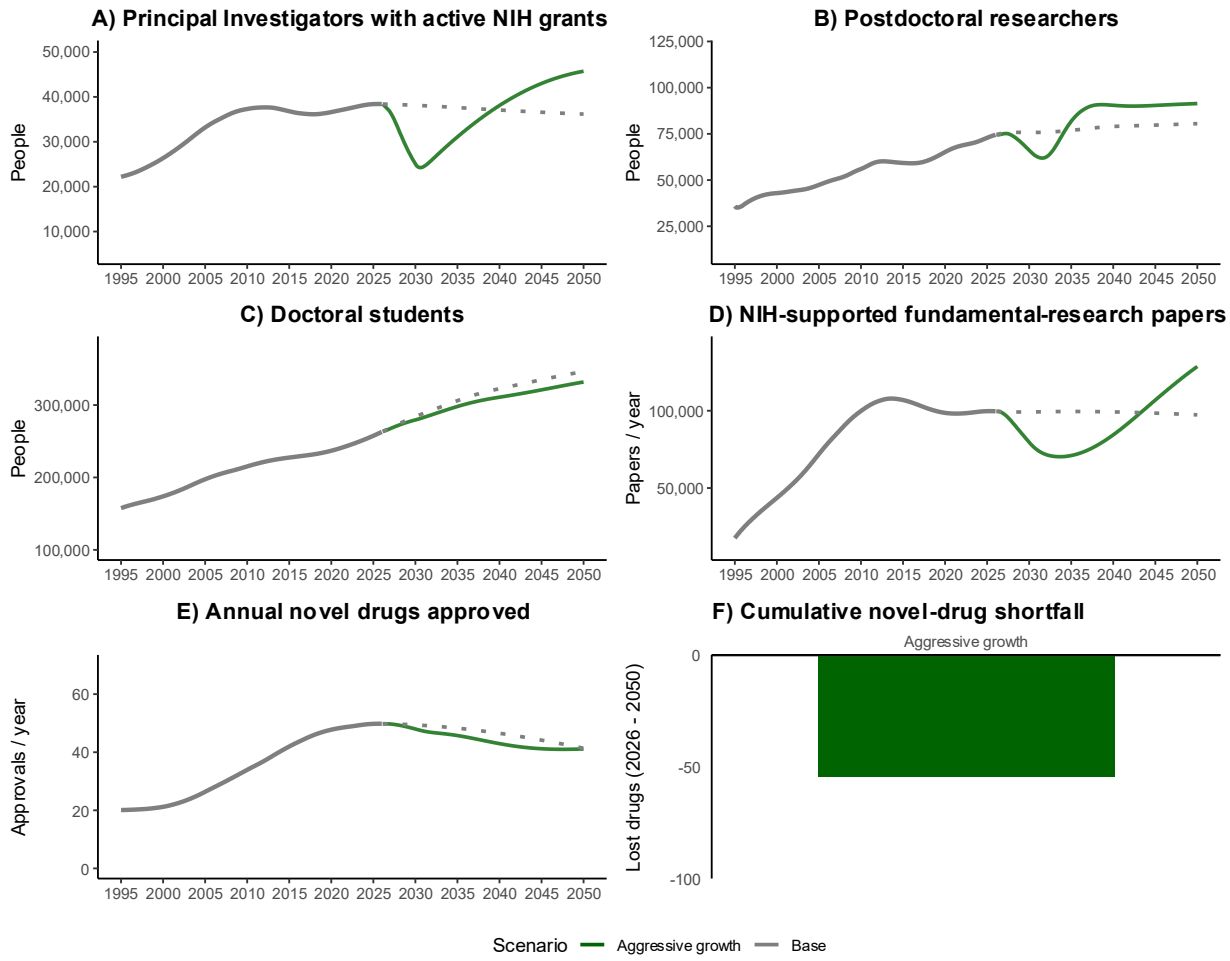


Figure S15: Projected impacts of NIH funding trajectories on outcomes of interest in the aggressive growth scenario, 1995-2050.

Note: Scenarios include: baseline (grey line); aggressive scenario (green)

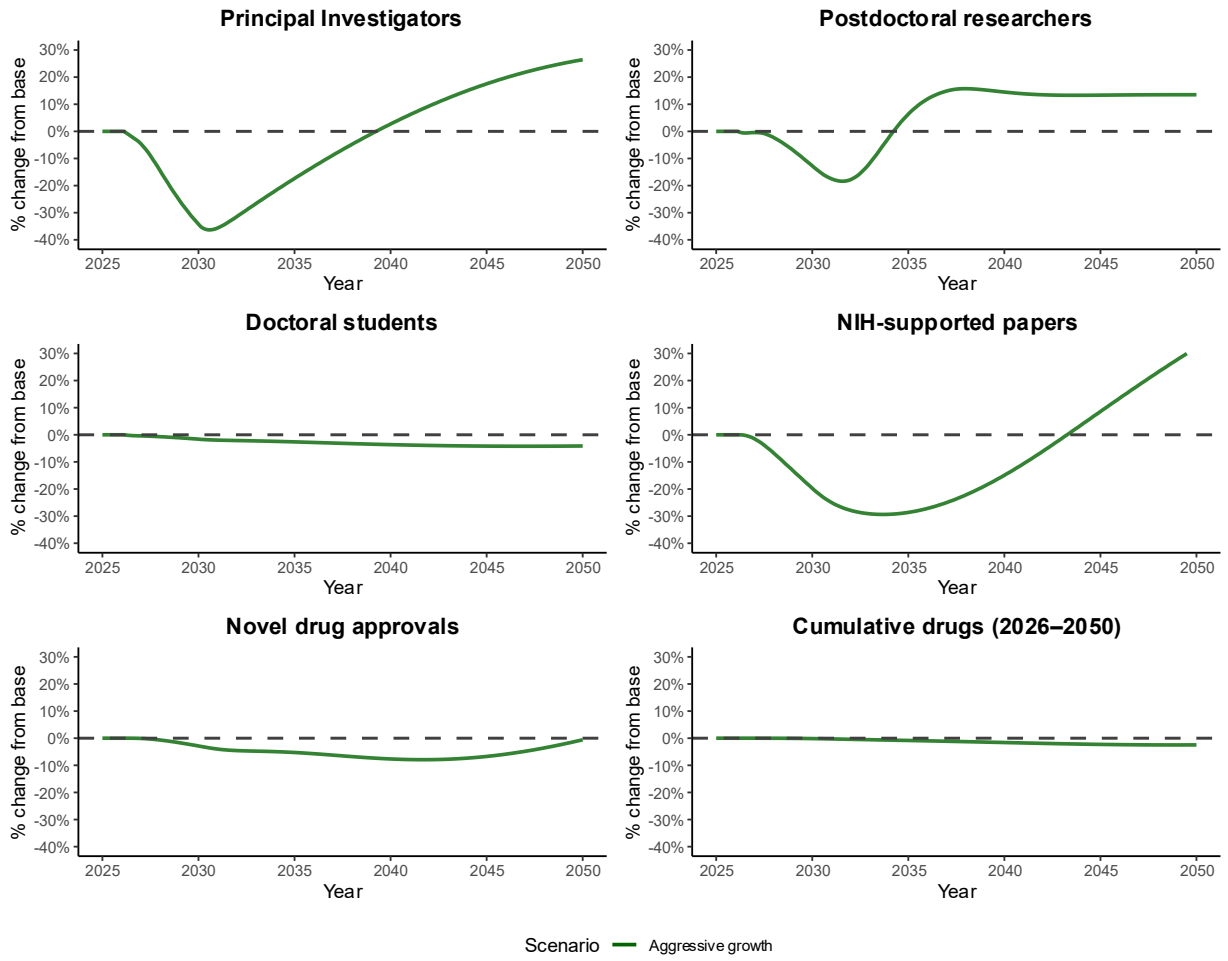


Figure S16: Percent changes from baseline for the outcomes of interest in the aggressive growth scenario.

Note: The dashed line represents no change from baseline with 0%.

Using the MCMC parameter distributions reported in **Table S2**, we conducted sensitivity analyses for the outcomes reported in the main text. The outcomes examined include principal investigators with active NIH grants, postdoctoral researchers, doctoral students, NIH-supported fundamental research papers, and annual drug approvals. The projections with uncertainty ranges for six scenarios are shown in six plots: baseline (grey, **Figure S**), no-increase (purple, **Figure S**), budget cut (orange, **Figure S**), restoration to baseline after one year (green, **Figure S**), restoration to baseline after four years (blue,**Figure S**), and an aggressive scenario (dark green,

Figure S).

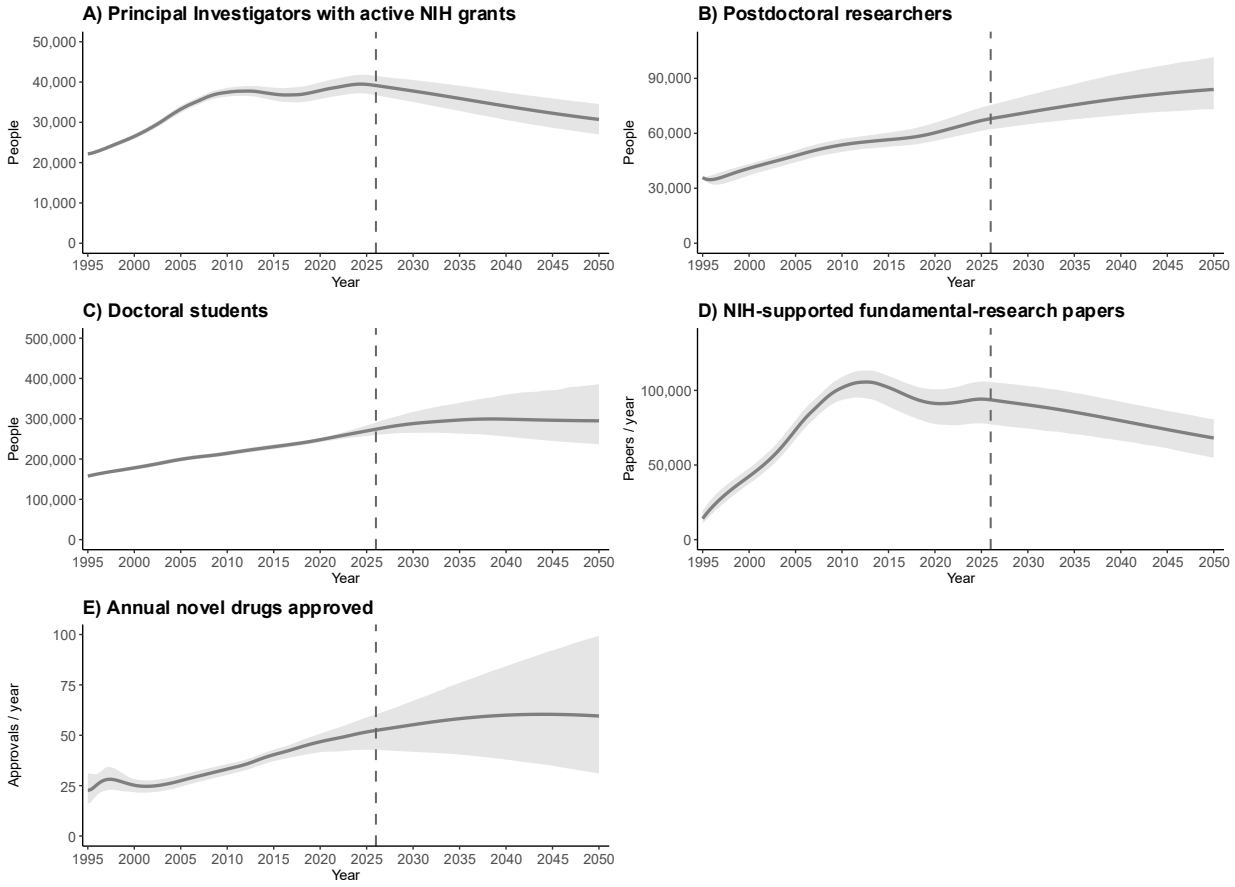


Figure S17: Baseline scenario, 95% projection intervals

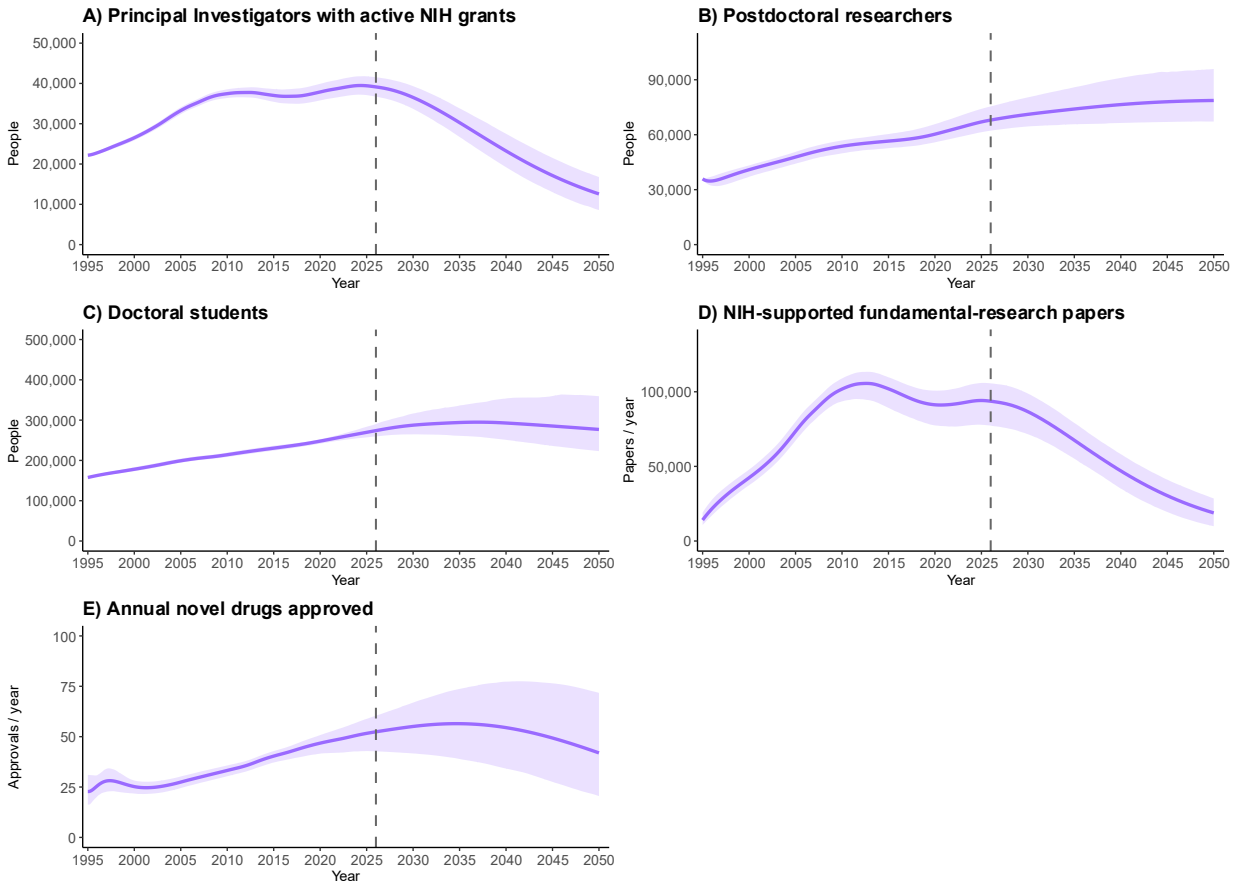


Figure S18: No-increase scenario, 95% projection intervals

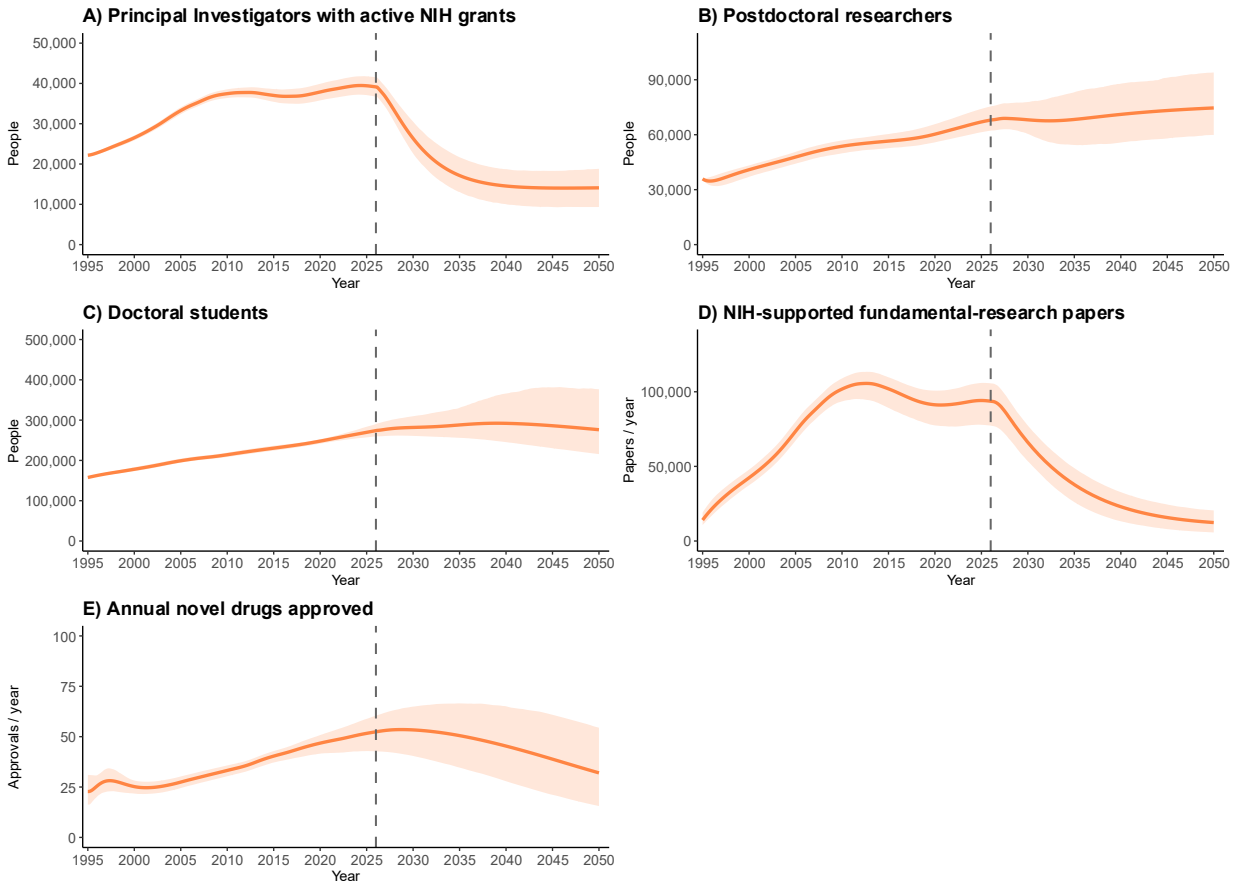


Figure S19: Cut scenario, 95% projection intervals

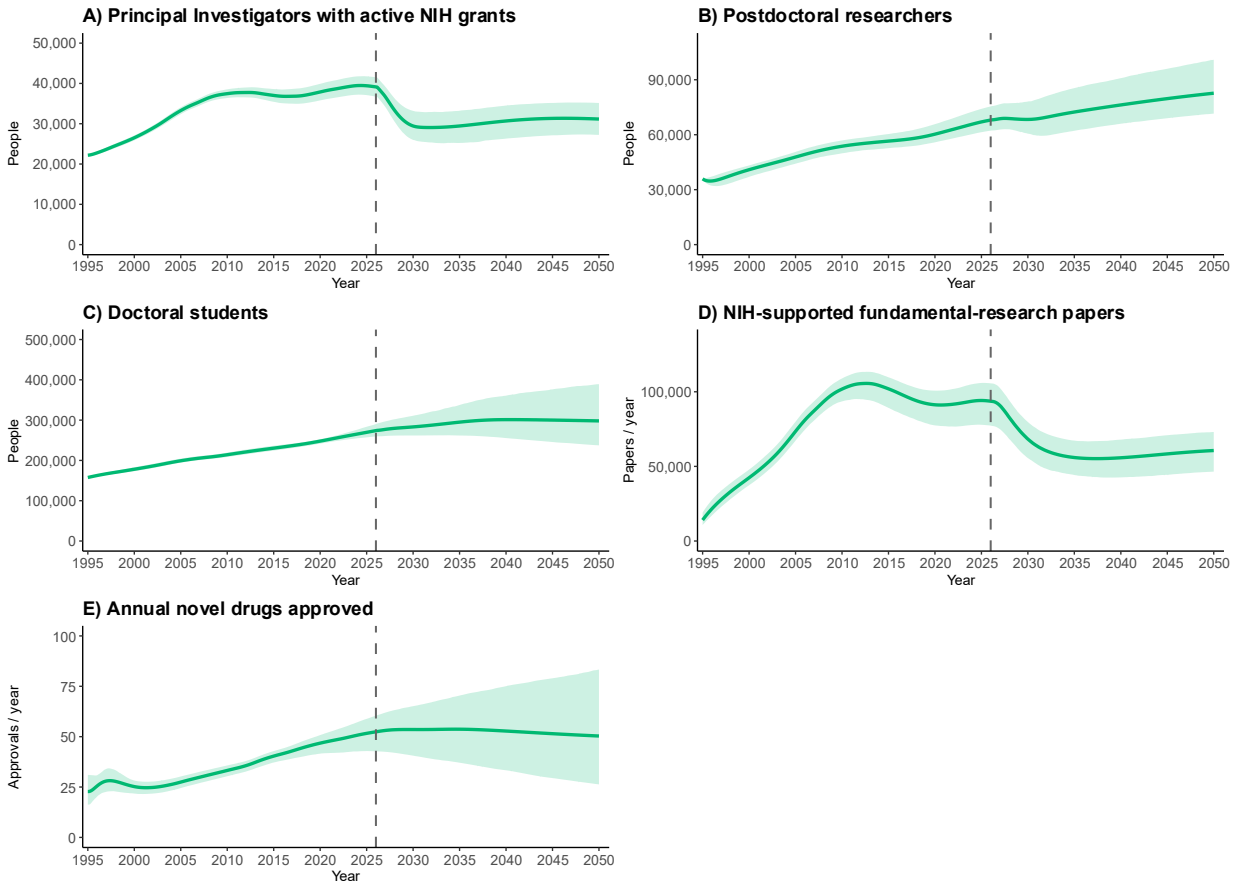


Figure S20: 1-year restore scenario, 95% projection intervals

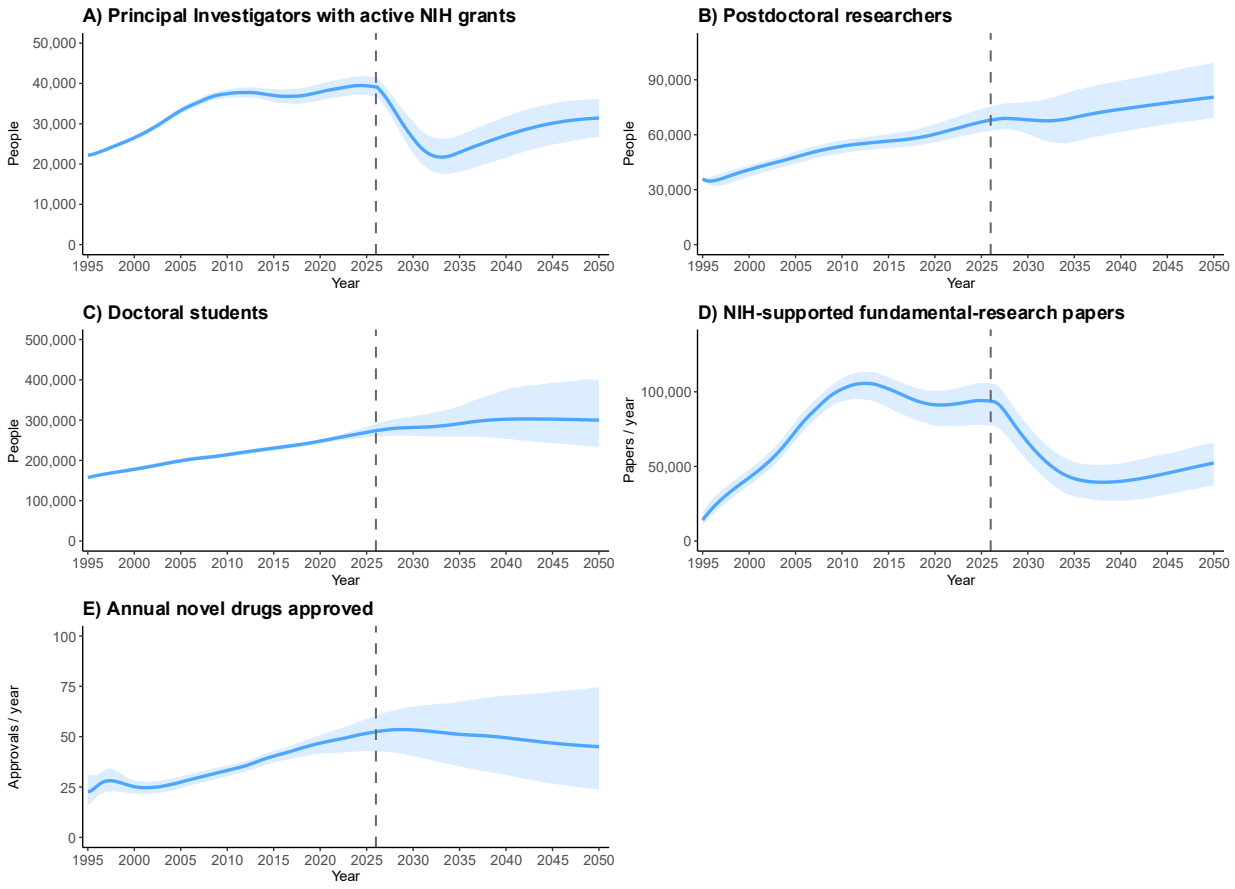


Figure S21: 4-year restore scenario, 95% projection intervals

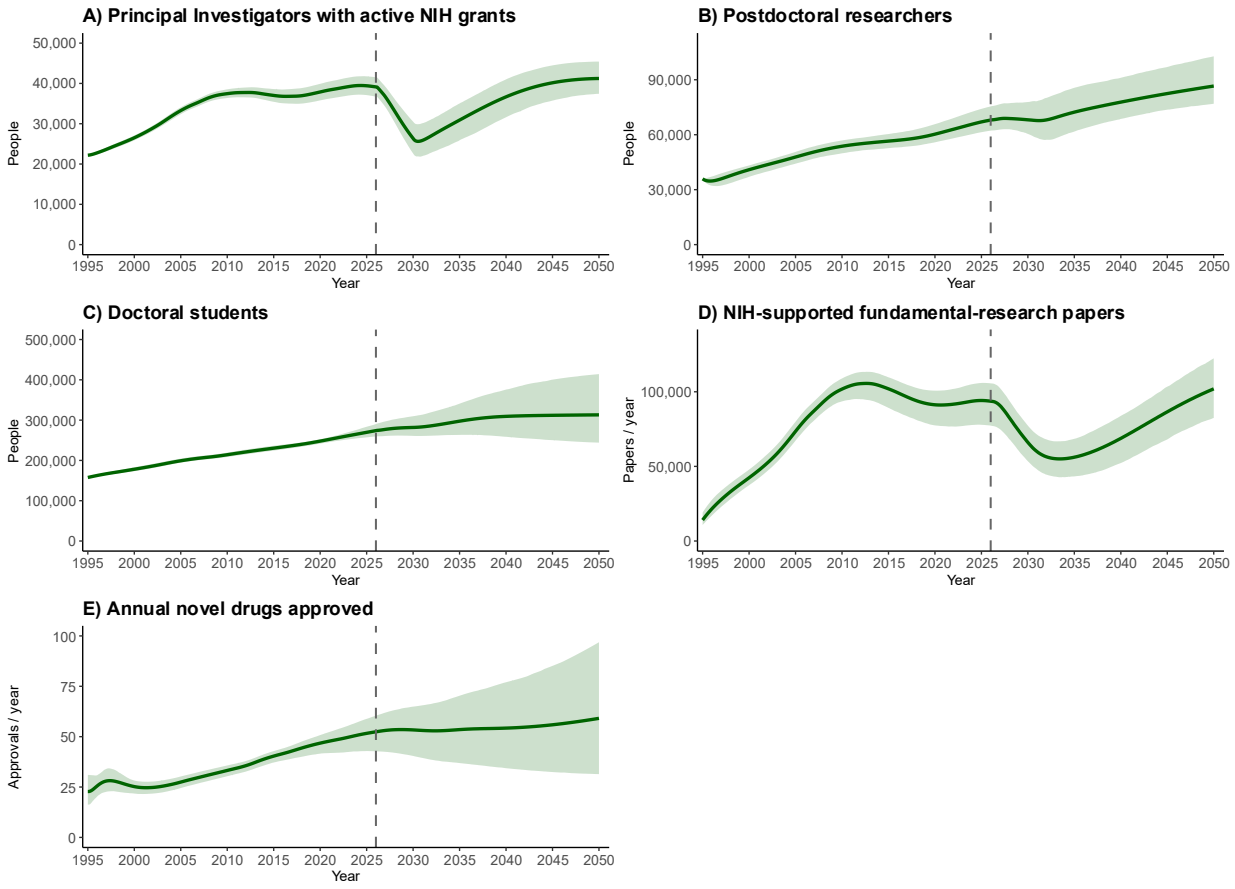


Figure S22: Aggressive growth scenario, 95% projection intervals