

A generation at risk: Young investigators and the future of the biomedical workforce

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A number of distressing trends, including a decline in the share of key research grants going to younger scientists, as well as a steady rise in the age at which investigators receive their first funding, are now a decades-long feature of the US biomedical research workforce. Working committees have proposed recommendations, policy makers have implemented reforms, and yet the trajectory of our funding regime away from young scientists has only worsened. An investigation of some of the major factors and their geneses at play in explaining the increasing average age to first RO1 is presented. Recommendations related to funding, peer review, career paths, and the university-government partnership are provided.

graduate education | biomedical workforce | federal funding | postdoctoral education

It has been almost a decade since the National Academy of Sciences received the report of a blue ribbon panel that had been convened to consider the challenges facing young biomedical researchers in the United States (1). The report described a number of disturbing trends, including a decline in the share of key research grants that were going to younger scientists, a steady rise in the age at which investigators received these grants, and the early hints of an exodus of young minds from the profession. The report also proposed a sweeping set of recommendations, ranging from new research awards for young scientists to expanded mentoring opportunities to enhanced data collection. At least some of these reforms were eventually adopted by the National Institutes of Health (NIH).

Despite these efforts, the trajectory of our science funding away from young scientists has only continued. Consider the following data: the R01 is the leading NIH research grant and a prerequisite to a career as an independent investigator. The average age at which an investigator with a medical degree receives her first R01 or equivalent grant has risen from less than 38 y in 1980 to more than 45 y as of 2013.^a The number of principal investigators for R01s who are 36 y of age or younger has declined from 18% in 1983 to 3% in 2010. Today, more than twice as many R01s are awarded to principal investigators who are over 65 y as are under 36 y, a reversal from only 15 y ago.^b A similar decline can be seen if one looks beyond R01s at all NIH research grants: the percent of all grant funding awarded to scientists under the age of 36 has dropped from 5.6% in 1980 to 1.3% in 2012 (Dataset S1). Each of the above trends has only worsened since the publication of the National Academy of Sciences report in 2004.

The implications of these data for our young scientists are arresting. Without their own funding, young researchers are prevented from starting their own laboratories, pursuing their own research, and advancing their own careers in academic science. It is not surprising that many of our youngest minds are choosing to leave their positions in academic research for careers in industry, other countries, or outside of science altogether (4–6).

The departure of young scientists from the academic biomedical workforce in turn poses grave risks for the future of science. The dangers are many: the gradual evaporation of the pipeline of new discoveries and therapeutics; the loss of a generation of future leaders and mentors in science; a delay in the introduction of greater diversity into the biomedical workforce (7); and finally, the disappearance of scientists at the precise moment in their careers when they so often perform an essential, disruptive role in the science ecosystem. The linkage of youth with major scientific breakthroughs has been confirmed in a wide range of studies (8–10). These are precisely the young minds our science enterprise is now turning away.

The inability to staunch—if not reverse—the above trends stands as an urgent and compelling policy challenge. The salience of scientific discovery to the future of our health, our economy, and our society is profound. All of us, as the current stewards of the US research enterprise, bear a responsibility to sustain and safeguard that enterprise, so that it can provide a platform for the scientists and the science of generations to come.

In this article, I canvass several different explanations for the persistence and rising severity of the problem. Then, I propose a number of policy reforms to provide our

youngest scientists with the support they need to advance their own independent research.

Reasons Young Scientists Are Losing Their Share of NIH Funding

What explains the relative decline in research funding to young scientists? This article mainly considers three possibilities. First is that longer training periods explain the delay in scientists obtaining research grants. Second is that young scientists are disadvantaged in securing grants due to aspects of the grant process that tend to favor systematically incumbent scientists over new entrants. Third is that imbalances in the total costs of federally funded research borne by sponsoring institutions such as universities and research laboratories relative to the NIH have deterred recruitment of young scientists into faculty entry positions, thereby impairing their capacity to compete for research funds.

Training Periods. One leading theory for the rise in the age at which scientists receive their R01 points to longer training periods and the resulting delay in obtaining a faculty position as principal causes. For the most part, scientists are unable to obtain their own

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^aThe number for PhDs has increased from 36 to 42 y during the same period. See Average Age of Principal Investigators with MD, MD-PhD, or PhD at the time of first R01 Equivalent Award from NIH, fiscal years 1980 to 2011 (2).

^bPercentage of NIH R01 Principal Investigators Age 36 and Younger and Age 66 and Older (Fiscal Years 1980 to 2010) (3).

method and scope of the research to the institutions themselves” (19). The system he helped to design is widely regarded as one of the principal drivers of US science innovation and a model for the world (19, 20).

The current approach to national science funding continues to bear all of the hallmarks of his vision of a meritocratic allocation of grants to independent researchers, including through its use of an open and extensive application process, its demand for a clear scientific case for funding based on a showing of prior data and findings, and its reliance on peer review by scientific experts to determine the merits of each proposal and the distribution of funds. Yet, it is notable that as the system has developed over the years, these very same features might very well have left our system vulnerable to incumbency advantage.

For instance, although the complexity of more than 200 pages of federal grant application rules and criteria is designed to ensure a rigorous and full review of proposals, it also can work against the uninitiated such as young scientists, who lack expertise in the application process (21). Moreover, the requirement that a scientist offers preliminary data to obtain an R01 can place young scientists in what one report described as a Catch-22: “They can’t get the NIH R01 funding they need to establish a lab and launch an independent career because NIH reviewers say they don’t have the data to support their grant applications. Yet the preliminary data and proof that experiments will succeed is hard to come by without that very funding” (22). The NIH has sought ways to relax the importance of preliminary data, especially for new investigators, in response to precisely this concern.

One final area that is vulnerable to incumbency advantage is the peer review system itself. An ever expanding number of studies have voiced concern that the NIH open review process is a “networked system” that favors insiders and the familiar and disfavors the unknown and the innovative (23–26). These network effects may be all of the more acute in times of financial pressure, where there may be an even greater tendency to choose principal investigators who had previous success over a risky newcomer. It is important to emphasize here that institutional bias can be entirely inadvertent and unintentional—an extensive body of scholarship shows that a result of bias does not require an explicit intention on the part of the architects or the implementers of public policy to favor one group over another (27–29).

Whether it is one of these three factors or another entirely, an analysis of new NIH success rate data indicates that there is

some variable in the selection process that is leading to a lower likelihood of grants being awarded to young scientists (Dataset S2). I compared the success rate for applications for R01 and equivalent grants of scientists 45 y and younger to the success rate for scientists older than 45 y. The difference was modest but statistically significant: younger scientists had a lower rate of success than established scientists in each of 20 of the last 21 y, by a gap that ranges from 0 to 3%.^d Of course, in addition to the explanation of an incumbency advantage, it is also possible that the proposals of the younger scientists simply have been less worthy of funding by objective measures. Even so, if the success rate for scientists under the age of 45 y had been identical to the success rate of scientists over 45 y, the younger cohort would have received almost 1,000 additional research grants over the last 10 y alone.^e

Cost Shifting to Universities. A final set of explanations for the R01 data involves an increase in the relative cost of research that is borne by universities and other sponsors.

Federally funded research is premised on a compact of shared responsibility between NIH and sponsoring institutions. Research grants such as the R01 do not cover the full costs of research, which can encompass everything from salary and benefits, to infrastructure and core services, to materials and supplies, and to administrative costs, and universities must step in to shoulder the burden that the federal government will not support.^f All said, according to data from the National Science Foundation, the university share of support for all university-based research and development has risen over the last half century from 8.7% in 1962 to 19.4% in 2012 (30). Universities now spend more than \$12 billion of their own funds on research and development, a figure that has more than doubled in the last 12 y.

The costs borne by universities are increasing for several reasons. First is the increased complexity of science and the higher costs of instrumentation in many fields, which has led in particular to a rise in startup packages to young scientists (31, 32). Second is the widening gap between time of entry of faculty and time of receipt of the first R01—the cost of supporting research during this increasing period must be borne by the

university, an expense that is “going to be difficult for institutions to sustain over time” (5). Third is that the federal government has placed a cap on reimbursements for administrative costs that has remained at the same level for more than 20 y, even as regulatory burdens have expanded and become more costly. Finally, the federal government has sought to ration their funding in recent years through steps such as a lowering of the cap on salary recoveries and reductions in the size of grants.

For all of these reasons, universities are finding it necessary to invest more in the research enterprise, and not only at the outset of a faculty member’s career. They must step up at the times that a faculty member faces a funding trough; at the moment when a startup package is exhausted and yet the faculty member is taking on additional responsibilities; and at the stage when a scientist is simply no longer as productive as he or she once was. Institutions such as academic medical centers operate under exceedingly tight revenue margins; financial pressures are intense and are exacerbated by a loss of clinical revenues and broader unpredictability in funding (33). Over time, the ability of some universities to support robust scientific research at all could be jeopardized.

Of course, universities benefit immensely from the investment of the federal government in their research, and ultimately, the decision is theirs as to how and when to direct their own resources to their faculty and students. However, with so much of the federal research investment taking the form of grants to individuals, cash-strapped universities might be led to make choices that are short of ideal for science policy or the biomedical workforce. For instance, over time, universities could shy away from the recruitment of unproven scientists who lack their own funding streams, opting instead for established investigators who have shown that they can attract more consistent support. Although there are certainly many variables at play in the data, there is at least some indication this could be taking place. The Association of American Medical Colleges notes that the average age of medical school faculty has increased over the last 30 y in part because “recruited faculty have not been young enough to offset the overall aging due to continuing (i.e. retained faculty)” (13).

Summary. Our biomedical workforce is a complex ecosystem, and the most persuasive answer is that no single cause is driving the tilt of our science funding regime away from young scientists. The solutions we devise will also need to be similarly diverse. An answer

^dA comparison of the success rates yields $P < 0.001$.

^eThis analysis assumes an increase in appropriations to allow the NIH to lift the success rate of young scientists.

^fThis is at some odds with Alberts et al. (18), who see the treatment of indirect costs of federally funded research as a source of subsidy for other university activities.

set will demand an integrated, systems approach, one that recognizes shared and distributed responsibility for the problem and its fixes. Especially in a world where the precise cause is still uncertain, we should resist the temptation to overreach or overreact, and instead proceed cautiously, through experiments and pilots, in the finest tradition of the very science that we are seeking to support.

In the sections to follow, I explore a number of candidates for this sort of measured reform.

Proposals for Redressing the Funding Barriers Confronting Young Scientists

This section addresses four areas of potential action: (i) strategic reinvestment in scientific research, (ii) reform of the external peer review process, (iii) rebalancing the compact between academia and government; and (iv) developing sustainable career paths for our young scientists.

Reinvestment in Our Science Enterprise.

The story at this juncture is all too familiar. Even after the partial restoration of funds this last year, the NIH has lost more than 20% of its purchasing power since 2003. The success rate for R01s and equivalent grants has dropped from 30% to 17% in this same period. Eighty-one percent of universities report that recent cuts in funding have detrimentally affected their research activities and output, and 47% of scientists have abandoned an area of planned investigation that they considered central to their laboratories' mission (4, 34).

The deflation of NIH funding harms all scientists, but in some respects it injures young scientists all of the more: their own opportunities for funding disappear at the precise moment that positions in other scientists' laboratories vanish and opportunities for mentorship with senior investigators—busy struggling to keep their own R01s—fade away. Therefore, any set of reforms must start with an infusion of appropriations to the NIH, one that is sufficient not only to restore R01s to young scientists but to maintain support for grant mechanisms at all points in the pipeline, so that the young investigators graduate to a supportive funding regime.

At the same time, we need to explore new mechanisms to direct funds to the most talented young scientists. The NIH has tried its hand at new funding streams that are tailored at least in part to young researchers, including the New Innovator Awards (DP2) for exceptionally creative early stage investigators, the Early Independence Awards (DP5) for young scientists to pursue independent research immediately after a terminal degree, and the Pathway to Independence Awards (K99/R00), which combine a mentored research phase

with later, independent research support. These awards tend to share several traits: an emphasis on experimental ideas, a waiver or relaxation of the need for preliminary data, special review sections, and funding for a period long enough to offer stability as scientists launch their careers. The NIH has also established a policy of seeking to achieve comparable success rates for first time and established investigators.

These initiatives are laudable, but they have not solved the problem, and more creative approaches yet will be needed to overcome the structural barriers to young scientists. One new possibility would be to incorporate conditionality into R01s for the unproven, early stage investigator. For instance, the investigator might be required to achieve certain milestones set out in the application and approved by the review panel in an initial phase, and only if the milestones are achieved would the grant complete as a full R01. This staged approach, inspired by the K99/R00 program, would provide a newly structured path to a completed R01 for a young investigator while reducing the downside risk to the agency if the applicant is unable to deliver.

A separate area of reform might involve the conundrum of preliminary data. The NIH has chosen to address this issue by easing the requirement of preliminary data for young investigators: it has created new funding programs that are less reliant on this data, and it has instructed peer reviewers to expect less such data from new investigators seeking R01s.^g Another approach altogether would be to help these investigators to obtain this data, empowering them at the outset to identify the most compelling and successful science. One such mechanism could be a nimble program to provide easily accessible infusions of small amounts of cash for pilot projects, renewable as R01s if the pilots showed promise. Either as a reform of the existing R03 grant mechanism, or an entirely new mechanism on its own, a well-designed program could give rise to a greater sense of experimentation and provide a new stepping stone to the R01 system.^h

^gIn the NIH lexicon, "new" investigators are first-time investigators. Early-stage investigators are new investigators who are within 10 y of completing their terminal research degree or within 10 y of completing their medical residency at the time they apply for R01 grants. Only about 55% of investigators who receive their first NIH grants are at an early stage of their career (35).

^hR03s are relatively small, short-term grants offered by some of the institutes that can be used to run pilot projects. The R03 program faced criticism for being underfunded, nonrenewable, about as burdensome to apply for as an R01, and with only a slightly higher success rate. The program was so flawed as a gateway to preliminary data that the NIH was compelled to issue a notice that "strongly encourage[d]" young scientists not to apply for the R03s, for fear that the program was dissuading them from applying for R01s (36).

Reforming Peer Review. Although the US system of peer review has been a model to the world, it also has come under growing scrutiny, including for the ways in which it could impair access to unknown scientists. This is another facet of science policy that is ripe for reform.

One of the focal points of any reform effort should involve the makeup of review panels and study sections. The difficulty in attracting qualified and experienced senior scientists to sit on review panels was a main area of focus of a recent report on the NIH peer review system, and it endures as an area of concern for observers (23, 37). At least anecdotal evidence suggests that the absence of senior distinguished scientists can be harmful to young scientists, as—paradoxically, perhaps— inexperienced young scientists on panels can be more exacting in their scoring of other inexperienced scientists. The NIH must continue to explore new paths to encouraging senior faculty to serve on review panels.

At the same time, the NIH should take steps to increase the combination and cross-pollination of review panels and study sections. An effort to fuse together new panels and sections with a broader scope and more funds at their disposal not only might be more likely to promote cross-disciplinary research, but in an age of financial austerity, could allow a greater sense of liberty to accept a handful of truly risky ideas. The NIH has experimented with multidisciplinary review panels for its New Innovator Awards, but thus far the NIH appears not to have answered calls to extend that approach more broadly to other awards for young scientists. The NIH also should be encouraged to more actively explore reallocation of resources across institutes and study sections, to permit more investment in emergent and interdisciplinary fields of science, which are also likely to be areas of appeal to the next generation of scientists.

A second topic of possible focus concerns the requirement of consensus among study section members on the ranking of grants. One recent study of peer review concluded that the "decision-by-committee system that predominates social choice at NIH is... deficient in identifying potentially transformative projects" and that the NIH should "establish multiple alternative systems of social choice that would complement the deficiencies of the current system" (25). The NIH has experimented with allowing the vote of a single reviewer to prevail in one of its newer programs (38). An alternative would be to pilot an initiative that removes the best and the worst scores in a review panel. As a practical matter, in a time of scarcity, the applications that are

being funded are those that receive a high score from every reviewer, and a single bad score can doom an applicant's chance. In this environment, deletion of outlier scores may leave more scope for daring proposals that cannot win the consensus of the entire room.

Investing Across a Scientific Career. As discussed earlier, the traditional approach of the US extramural funding regime has been to invest in proposals rather than scientists, a model that could be leading to distortions in how universities allocate their own resources. Some private foundations have opted for a different approach, the Howard Hughes Medical Institute (HHMI) providing the most prominent example. HHMI offers large, 5- to 7-y grants to investigators throughout the United States. The focus of the application is on the potential of the faculty member rather than the merits of a particular research idea, and the grants are typically renewed at least once. One recent study concluded that HHMI investigators produce high-impact papers at a substantially higher rate than similar scientists funded through a model that offers grants to research projects (39).

The NIH itself has edged in a similar direction itself in recent years. For example, the new Pioneer Award Program (DP1) provides grants to scientists for their visionary potential, with the final set of winners chosen through interviews. However, the NIH is awarding only a dozen of these a year, and the winners already tend to be faculty at a university, so the program does not truly address the problem that institutions are forced to shoulder the burden of investing in talented new appointments. The NIH does offer many more Pathway to Independence (K99/R00) awards each year, through which postdoctoral fellows receive a mentored training award that can transition into an independent research grant when they obtain a tenure-track faculty position. However, this program is still premised on a mandatory, detailed research plan at both stages.

Now compare these programs to the Canada Research Chairs initiative, through which the government directed about \$900 million to universities in a single five year period alone to create 2,000 new endowed university faculty chairs. A university is awarded chairs in proportion to their receipt of research funding, and the university is expected to contribute its own support to ensuring the success of the chair. A portion of the chairs is set aside for junior faculty who are deemed to have exceptional research potential, and the faculty enjoy the freedom to shape their research enterprise over time (40). A similar

role for the US government, one that supports faculty not only during their research successes but throughout their career path, could allay the distortions of an overwhelmingly research grant-based approach, while allowing faculty to spend less time on grant applications, and more time on science.

Separately, the NIH could introduce a new program for the experienced scientist who no longer wants to pursue R01s, but feels compelled to do so to stay afloat in an era of fading soft money. This program would provide an opportunity for established scientists to complete their line of study and bring their NIH supported work to an orderly conclusion, while transitioning into a more active mentorship role for other R01 applicants. Notably, the award would also ask the scientist to ease out of the R01 grant pool, freeing up space for the next generation of scientists. The early impact of this proposal might be modest, but it could be most valuable for what it signals: a spirit of renewal and the importance of cycling the scarce resource that is our scientific funding.

Improving Career Paths. To provide a true foundation of support for early-stage scientists, we will need to construct a pathway to a career in the biomedical sciences that is sustainable, humane and fair. By any measure, we have quite a ways to go. A range of studies and analyses continue to find that postdoctoral fellowships are unstable and uncertain; the number of postdoctoral fellows vastly outstrips the number of openings for academic positions; and "current training programs do little to prepare people for anything besides an academic research career" (5, 12, 40).

One area of needed reform is to identify for our entering scientists a diverse set of career options, including a permanent staff scientist career track (5, 18).^l In this regard, a focus on cores facilities at universities may be especially useful: as they are shared resources that are less vulnerable to vagaries in grant funding, the cores are a promising place to build an enduring scientist track for young scientists who do not want, or cannot launch their own research. Much of the effort here will fall to the institutions themselves. However, as with other aspects of the national science infrastructure, this can and should be an area

of shared responsibility. There is acknowledgment even on the part of officials at NIH that the federal government can do much more to encourage and incentivize the development of effective cores (42).

Next, research institutions and policy makers alike must attend in earnest to the length of the postdoctoral period. The very first recommendation of the decade-old National Academy of Sciences report on young scientists was that the federal government impose a 5-y limit on the use of funding mechanisms to support a postdoctoral researcher (1). This recommendation was never implemented. If coupled with a range of other resources for postdocs and staff scientists, including an expansion of K99/R00 awards that bridge training to independent research, this move could have a salutary and substantial impact in weaning our biomedical workforce away from an over-reliance on postdoctoral researchers.^j

Finally, it is still often the case that research institutions require a scientist to obtain an R01 or a similar grant to secure a tenured faculty position. The need for proof of a capacity to obtain outside funding of some sort is understandable, but the weight placed on the R01 may be excessive, particularly in a time of funding constraints. If we truly believe that process is leaning away from young scientists, one remedy is to relax the custom of looking to an R01 as a strict criterion for promotion. Demystifying the R01 could go a long way toward allowing young scientists the breathing room needed for advancement.

Conclusion

Even 10 y ago, the National Academy of Sciences report underscored there had been a "history of concern for these issues, and many previous recommendations have been offered to address them" (1). To its great credit, the NIH has confronted this issue forthrightly.^k However, the trends have endured and even worsened. The persistence of the underlying problem in the face of these concerns distinguishes it from many others. How do we keep this moment of focus from again slipping away?

Over the years, reforms in the United States have been humbled by an absence of resources, data, and monitoring. Recommendations to expand programs for young scientists have been hamstrung by budget

^lEconomic tournament theory tells us that competitions (such as that for a move from a postdoctoral position to a tenure track position) are a useful and effective mode of allocating a scarce resource when reward structures are based on relative rank rather than absolute levels of output. However, the theory also tells us that to achieve optimal results it is critical that the competition be transparent, open, and fair (41).

^jIt would be advisable to extend the 5-y period during periods of family or medical leave.

^kFormer NIH Director Elias Zerhouni, in departing from the NIH in 2008, said of the young scientist conundrum: "I think anybody who thinks this is not the number one issue in American science probably doesn't understand the long-term issues" (35).

constraints (5, 43). Essentially every major task force to touch on these issues in the last decade has lamented the lack of reliable data capture or analysis on which to base its suggestions and assess progress (1, 5, 6, 37). Finally, despite the great care it devoted to the issue, the Bridges to Independence panel disbanded after it published its report, its mandate expired.

Other countries are marshaling the will and resources to invest in the next generation of young scientists. Singapore's Agency for Science, Technology and Research launched an ambitious program to award roughly \$1 million to each of 1,000 top science students (44). China recently announced a multiagency

strategy to cultivate thousands of the country's most talented young scientists over the next 10 y (45).

A solution in the United States will require a comparable commitment on the part of the entire biomedical science ecosystem. An enduring solution to this problem will require enduring attention from a range of stakeholders, including the Congress, the NIH and other federal agencies, institutional sponsors, and private industry. Yet, no single multistakeholder body is responsible for lasting oversight of this issue. Legislators have called for a new report from the National Academy of Sciences on young scientists. I would go further and convene

a standing body to undertake a continuing review of the causes of the problems, the effectiveness of interventions, and press stakeholders into action.

Targeted policy recommendations could have a profound impact on the trajectory of scientific research. Our next generation of scientists, and indeed our next generation of science, demands nothing less.

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