New Physician-Investigators Receiving National Institutes of Health Research Project Grants
A Historical Perspective on the “Endangered Species”

Howard B. Dickler, MD  
Di Fang, PhD  
Stephen J. Heinig, MA  
Elizabeth Johnson, MS  
David Korn, MD

Decades of concerns have persisted about the production of new physician clinical scientists and their success in receiving and sustaining research support by the National Institutes of Health (NIH), no comprehensive analysis documents the experiences of first-time investigators with an MD over a long period.

Objective To ascertain the perseverance and comparative success of physician-scientists competing for NIH research (R01) grants awarded over 40 years.

Design, Setting, and Participants A longitudinal, comparative study of all first-time applicants and recipients of NIH R01 grants between 1964 and 2004 stratified by the principal investigators’ major degrees (MD, PhD, or MD and PhD) and their proposed involvement in research of humans or human tissues.

Main Outcome Measures Number of first- and second-time NIH R01 grant applicants and recipients by academic degree and by research type (clinical vs nonclinical).

Results The annual number of first-time investigators with an MD only as NIH R01 grant applicants remained remarkably stable over 4 decades (41-year mean of 707 [range, 537-983] applicants). Among first-time applicants, those with an MD consistently had less success in obtaining funding (mean annual percentage [MAP], 28%) than either investigators with a PhD (MAP, 31%; \( P = .03 \) vs MD only) or both an MD and a PhD (MAP, 34%; \( P < .001 \) vs MD only and \( P = .002 \) vs PhD only). Among investigators who obtained a first R01 grant, those with an MD were consistently less likely (MAP, 70%) than those with a PhD (MAP, 73%; \( P = .04 \) vs MD only) or those with an MD and a PhD (MAP, 78%; \( P < .001 \) vs MD only and \( P = .007 \) vs PhD only) to obtain a subsequent R01 grant. First-time applicants with an MD were much more likely to propose clinical research (MAP, 67%) than applicants with an MD and a PhD (MAP, 43%) and applicants with a PhD only (39%). First-time applicants with an MD only who proposed clinical research were funded at lower rates than their MD-only counterparts proposing nonclinical research (23% vs 29%, respectively; \( P < .001 \)).

Conclusions From 1964-2004, the number of physician-investigators applying for first R01 grants showed little net change. Physician-investigators consistently experienced higher rates of attrition and failure, even after receiving a first R01 grant, and those proposing clinical research were less successful in obtaining funding than physicians proposing nonclinical research.
nitigate major resources to clinical research training, career development, and shared resources. In 2005, the NIH launched a bold Clinical and Translational Sciences Award program centered on creating academic homes for clinical research in universities and teaching hospitals.8

Concerns about the status of clinical investigation persist and are now exacerbated by the current NIH budget and the prospect of an indeterminate period of flat or diminishing purchasing power by the NIH. In this circumstance, new initiatives become more difficult to sustain both materially and politically.9 Challenging policy and resource allocation decisions loom both for the NIH and the academic medical community.10

This study was undertaken with a conviction that a common and accurate perception of the experience of physician-scientists awarded NIH research grants during the past 40 years could help dispel misunderstanding and inform sounder policy making. Both the health of the environment for physicians conducting hypothesis-generating clinical research and the caliber of their science are reflected in the pool of new physician applicants for NIH traditional research awards and their subsequent success. Accordingly, the following were compared from the earliest available years: the annual numbers of first-time applicants with an MD, a PhD, and an MD and a PhD for traditional NIH research project grants; the relative likelihood of receiving the first grant awards; the likelihood of their applying for and receiving a subsequent NIH award whether successful or not in receiving a first grant; and the fates of these applicants according to whether their grant applications and awards were coded as clinical by the NIH.

METHODS

Data from NIH's Consolidated Grant Applicant File between 1964 and 2004 were analyzed for trends in the annual number of first-time applicants for NIH R01 grants. The analysis was completed in 2006.

The R01 is the US Public Health Service's administrative code designating "[traditional] research grants." As defined by the NIH, "the Research Project (R01) grant is an award made to support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing the investigator's specific interest and competencies, based on the mission of the NIH."11

First-time applicants were individuals who applied for no previous R01 grant, although they may have applied for or received another type of NIH award. Common first awards included R23 or R29 first investigator awards but the latter have been discontinued. Application records for these first-time applicants were then matched by applicants' unique identification numbers to determine whether they subsequently received a first R01 grant either on their original submission or any subsequent revision. Those who received funding for any amendment of that first R01 grant application were counted as successful on their first application.

This same cohort was subsequently analyzed, stratified by success or failure for their first R01 grant application. Analysis was performed for those who failed to have their first R01 grant funded on their first or revised attempts but later applied for a different R01 grant, and principal investigators who received their first R01 grant and later applied for either a competing renewal or second R01 grant. Each application in every analysis was counted only once no matter how many times revised and resubmitted. If any version was funded, that application was considered successful.

Applications and awards were categorized as clinical research if investigators had checked a box in the grant application that indicated the proposed project involved humans or human tissues, unless exemption 4 (involving use of deidentified data or specimens) was checked. This proxy is used by the NIH even though it overestimates the volume of "true" clinical research as defined by many.12 Contamination of clinical with nonclinical application data in this study would tend to minimize any differences observed, so significant differences become even more meaningful. Thus, for the purposes of this study, the proxy is explicit, objective, and instructive.

Regression models with autocorrelated error terms were used to determine the significance of differences in the mean outcomes across the different degree cohorts and across clinical vs nonclinical applications. These models take into account the correlation in the data over time. The models assumed an autoregressive lag 1 correlation model, which implies an exponentially decaying correlation structure as the number of years between measurements increase. Three comparisons were made for each outcome (investigators with an MD vs a PhD, investigators with an MD vs an MD and a PhD, investigators with a PhD vs an MD and a PhD).

To account for multiple comparisons, the P values were adjusted using the conservative Bonferroni correction (each P value was multiplied by 3). Significance was set at a level of .05. All statistical analyses were completed using SAS software version 9.1 (SAS Institute Inc, Cary, NC).

The presence in the Consolidated Grant Applicant File of both an MD and a PhD on an applicant record may indicate a graduate of a dual-degree program such as the NIH Medical Scientist Training Program. Other types of professional health degrees (eg, dentistry, nursing, veterinary medicine, etc, which together comprise a small percentage of Consolidated Grant Applicant File records) have been excluded for clarity of presentation.

RESULTS

First-Time Applicants

The number of investigators with an MD who annually apply for their first R01 grant has remained remarkably stable for the last 30 years (FIGURE 1). The steady decline in applicants with an MD during the late 1960s (from a
Although the percentage of applicants with an MD who failed to obtain funding for their first R01 grant application but who later applied for a different R01 grant (Figure 2), the data again show that a lower percentage of individuals with an MD only (23%) are funded than those with a PhD only (25%; P < .001 vs MD only), who are in turn lower than those with an MD and a PhD (34%; P < .001 vs those with either an MD or a PhD). Separate analyses showed that the difference in obtaining funding between individuals with an MD and those with a PhD was due to a difference in the reapplication rate (P < .001) and not a difference in the success rate among those who reapply (P > .99). For those with an MD and PhD vs either those with an MD or those with a PhD, there were significant differences in rates of both reapplication and success among those who reapply (P < .001 for all comparisons).

Clinical vs Nonclinical Research
Using coding for humans and human tissues as a surrogate marker, the data confirm intuition that physicians are more likely than nonphysicians to pursue clinical research. A mean of 67% of individuals with an MD who apply annually for a first R01 grant application pursue clinical research. The percentage is much lower for physicians who also have a PhD (43%) and for investigators with a PhD only (39%). Nevertheless, because of their greater numbers, more investigators with a PhD submit clinical applications (mean of 60% of applicants proposing clinical re-
search for all years) than those with an MD and those with both an MD and PhD (40%). This ratio was steady over the 21 years analyzed. The total number of applicants whose grants were coded as clinical has averaged 1385 for the 21 years and has risen gradually during that period (from 1311 in 1984 to 1843 in 2004).

Figure 3 shows that the annual percentage of applications by individuals with an MD who are funded for their first R01 grant is on average lower for those who conduct clinical research than those who conduct nonclinical research (23% vs 29%; P<.001). While individuals with an MD and a PhD were more successful than those with an MD only overall, a similar difference in obtaining funding between those performing clinical and nonclinical research was observed (28% vs 35%; P<.001).

When first-time applicants who had received their first R01 grant applied for a second R01 grant, the difference in obtaining funding between clinical and nonclinical research was again substantial: 72% vs 80% (P=.02) for individuals with an MD and 76% vs 86% (P=.003) for individuals with an MD and a PhD (Figure 3). The designation of clinical refers to the first application. Separate analyses of these differences indicated that for individuals with an MD, the difference was due to a lower rate of reapplication (P<.001) but not a difference in the success rate of those who reapply (P=.34). For individuals with an MD and a PhD the opposite was true, with the difference being due to a lower success rate among those clinical investigators who reapply (P=.005) but not to a difference in the rate of reapplication (P=.68).

Among individuals whose applications for a first R01 grant were unsuccessful but who later applied for a different R01 grant, the mean annual percentages of grant recipients were again lower for clinical than nonclinical research (20% vs 27%, P<.001 for those with an MD only; 31% vs 37% for those with an MD and a PhD, P=.45), but for the latter the difference was not significant. The designation of clinical refers to the first application. The difference for those with an MD only was due both to lower rates of reapplication (P<.001) and lower percentages of reapplicants being funded (P=.04).

Finally, how consistently first-time applicants for R01 grants in clinical research pursue clinical research in subsequent R01 grant applications was examined. A strong concordance was found; for example, about 80% of first-time recipients of clinical R01 grants with an MD who apply for a second R01 grant persist with clinical research. A similar concordance exists for nonphysicians and for first-time unsuccessful applicants who reapply for R01 grants.

**COMMENT**

By focusing exclusively on first-time R01 grant applicants and their subsequent success, this analysis has several strengths. It measures specific cohorts of individuals, not the number of applications alone, which is influenced by individuals submitting multiple applications. It examines trends across several decades and thereby avoids focusing on trends during narrow time intervals, which can be aberrant and suggest misleading conclusions. Given the wide variation across the types of projects and awards funded by the NIH, the R01 grants are universally recognized as embodying competitive, meritorious, hypothesis-testing research as discerned by peers, and nearly half (44% in 2004) of the NIH extramural budget supports R01 grants.

Our analysis does not distinguish between R01 grants that were investigator-initiated or invited by specific requests for applications or program announcements, although the vast majority of R01 grants are initiated by the investigator. Although certainly not the sole measure of productive research, receipt of an R01 grant has come to be considered a threshold event launching a career as an independent investigator and is often accorded great weight by institutional appointments and promotions committees. Similarly, the clinical research community recognizes the volume of R01 grant support for clinical investigation as a reliable, measurable signal of the status and vitality of the discipline.

Despite remarkable scientific and funding opportunity, the pool of available physician-investigators has not increased for many decades. Although physician-investigators do not appear in danger of extinction from the R01 grant pool, the growth of this cohort has
certainly been less than nonphysician-investigators. Following the decline in the middle 1960s, the numbers of new applicants have fluctuated within a remarkably steady band for the past 3 decades. Although the percentage of applicants with an MD receiving an award decreased from the early 1960s to the early 1980s, it has generally not declined for the past 2 decades.

The lack of increase in the number of applicants with an MD only contrasts with the increases seen in both applicants with a PhD and applicants with an MD and a PhD, and is discordant with a number of other relevant factors. First, the size of the pool was unresponsive to the approximate doubling in the number of allopathic medical graduates during the 1970s or the increasing physician work force. Although the annual number of allopathic graduates stabilized between 1980 and 2004 at about 15 700 (15 632 in 1980; 15 736 in 2004), during this period there was a substantial increase in physicians with medical degrees from non-US institutions, admitted driven almost exclusively by the needs of the health care delivery system. Second, from 1983 to 2004, inflation-adjusted annual funding for NIH traditional research project grants increased by 148%, the funding per grant adjusted for inflation increased by 36%, the number of these grants increased by 76%, the pace of scientific discovery and its increasing applicability to human disease were unparalleled, and the medical research frontier truly seemed endless—all of which might have been expected to attract physicians into careers in science but did not. Notably, the applicant pool of individuals with an MD did not grow significantly, even during the doubling of NIH funding.

First-time applicants with an MD only for an R01 grant are consistently less persistent and successful than applicants with a PhD or applicants with an MD and a PhD. Throughout the examined interval, first-time applicants with an MD have consistently been less likely than applicants with a PhD or applicants with an MD and a PhD to receive an R01 grant, and less likely, if not funded, to eventually receive a different R01 grant. Even when successful at obtaining a first R01 grant, investigators with an MD are less likely to receive a second R01 grant. Whether applicants were successful or unsuccessful in receiving a first R01 grant, lower re-application rates were a major cause of their diminished likelihood of receiving a subsequent R01 grant. Thus, at every point in the early life cycle of an R01 investigator—first-time applicant, first-time recipient applying for a second R01 grant, or first-time unsuccessful applicant applying for a different R01 grant—investigators with an MD only have generally been less successful than investigators with a PhD or investigators with an MD and a PhD, and more likely to exit the cycle. The attrition rate for investigators with a PhD and investigators with both an MD and a PhD is also high but has been offset by increases in first-time applicants. It is important to underscore that we are observing attrition from the NIH R01 grant pool but not necessarily from research; we have no information on the career choices made by those who leave the R01 grant pool.

Physician clinical researchers are more likely than nonclinical researchers to leave the R01 grant applicant pool. Consistently during the study interval, physician-scientist (MD only or MD and PhD) R01 grant applicants were more successful when they proposed nonclinical projects, consistent with the findings of Kotchen et al. That clinical research applications fare less well than nonclinical applications in the NIH review system. Kotchen et al have observed that the “bias” seems not to be explained by the composition of the study sections, lack of focus in the study section on clinical research topics, or other factors endemic to the system but rather can often be attributed to intrinsic difficulties with the applications, often involving procedural or administrative requirements in studying humans.

Taken together, our results portray remarkably consistent patterns of comparative success across more than 3 decades for physicians and nonphysicians who are first-time R01 grant appli-
cients; are recipients of funding for their first application and then reapply for a second R01 grant; are unsuccessful in their first application but later reapply for a different R01 grant; and are applicants who do or do not conduct clinical research as coded by the NIH.

We agree with others1,4,13,19,21 that physician-scientists bring unique skills, experience, motivation, and perspective to biomedical research. They play an indispensable role, especially in designing and conducting the translational and clinical research by which scientific advancements are brought into medical practice.

An often proposed interpretation of attrition for those with an MD from the R01 grant pool is that physicians have more competitive alternatives to R01 research careers.2,22 Yet, abundant anecdotal evidence indicates that physician-scientists who leave research careers often do so because of insufficient institutional support, a perceived lack of available mentors and role models, and discouragement.23,25 These anecdotes are consistent with our observation that even investigators with an MD who receive their first R01 grant are less likely than their counterparts with a PhD to recompete the grant or apply for another R01 grant.

For medical schools and teaching hospitals, the challenge is to create a more attractive and supportive academic culture that not only attracts and trains but also actively nurtures and sustains clinical and translational scientists. The recent report by the Association of American Medical Colleges Task Force II on Clinical Research24,25 calls on the leadership of academic medical centers to reaffirm translational and clinical research as a core mission. The report urges the establishment of central administrative oversight of shared research facilities and of training programs for physician-scientists that provide protected time for trainees and dedicated time for capable mentors, and that ensures the protected time and access to infrastructure necessary to launch the careers and nurture adequately prepared clinical physician-scientists. Adoption of the report’s recommendations, together with recent NIH program initiatives,7,8 would greatly ameliorate the problems that have impeded development of the robust clinical research enterprise that both unprecedented scientific opportunity and rising public expectations demand.

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Study concept and design: Dickler, Fang, Korn.
Analysis and interpretation of data: Dickler, Fang, Heinig, Johnson, Korn.
Drafting of the manuscript: Dickler, Heing, Korn.
Critical revision of the manuscript for important intellectual content: Dickler, Fang, Heing, Johnson, Korn.
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