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Sustaining Independent Careers in Vision Research: **Demographics and Success in Second R01 Attainment** Among Clinician–Scientists from 1985 to 2019

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Purpose: To evaluate the success of ophthalmology and optometry clinician-scientists in obtaining a second R01 (renewal or new) and factors associated with this success, including gender, clinical specialty, degree, institution, and bench versus non-bench research.

Methods: First-time National Eye Institute (NEI) R01 awardee data from 1985 to 2014 (N = 234) were analyzed to calculate second R01 success rates. Only R01 awards to ophthalmology or optometry clinician-scientists were included. Demographic data were obtained from clinicians with first-time NEI R01 funding spanning from 1962 to 2019 (N = 386). We obtained information regarding time span of the first R01, year of second R01, institution, and project title on the National Institutes of Health (NIH) Research Portfolio Online Reporting Tool, Expenditures and Results (RePORTER) database, and additional measures of gender, clinical specialty, and degree by performing Internet searches.

Results: Overall, from 1985 to 2014, 62.8% of ophthalmology or optometry clinicianscientists were awarded a second R01; at 5 years after receipt of the first R01 (the typical length of an R01), only 3.9% received their second R01. None of the factors examined (temporal cohort, gender, clinical specialty, degree, institution, or bench vs. non-bench research) was significantly associated with successful attainment of a second R01.

Conclusions: We found an overall success rate of 62.8% for receiving a second R01, but 5 years after the first R01 an attainment rate for a second R01 of only \sim 4%.

Translational Relevance: Our study provides insight on significant leaks in the clinician-scientist pipeline and raises questions of how stakeholders should support this important group of individuals at the intersection of clinical medicine and biomedical research.

Introduction

Clinician-scientists play a vital and unique role in academic medicine. They have undergone advanced clinical and research training and have a unique ability to bridge medical discoveries to patient care and traverse the "valley of death": the gap between laboratory-based research and clinical application.^{1,2} Despite their value, clinician-scientists are becoming an endangered species, which is evident in the decades-long trend of the declining share of federal funding awarded to clinicians for biomedical research.³ Many reasons are thought to underlie this unsettling trend, including the increasing medical school debt burden, reduced exposure to hypothesis-driven

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research during medical training, the hypercompetitive environment of grant review, and declining clinical revenues that threaten both the clinicians' time to pursue research and the academic medical center's commitment to clinician–scientists.⁴ Indeed, only about 11% of medical school graduates plan careers that incorporate research in a significant way,⁵ and clinician–scientists are especially scarce among ophthalmologists.⁶

The National Institutes of Health (NIH) Mentored Clinical Scientist Research Career Development (K) Award program constitutes the major pathway through which clinician–scientists develop independent research careers in academic medicine. Individual K awards are associated with a 24.1%increase in the likelihood of obtaining the first R01,⁷ which is important, as an R01 is the goldstandard grant awarded to independent principal investigators and is generally needed for promotion in the tenure track at research-intensive universities.⁵

However, obtaining a first R01 does not necessarily ensure continuation in the pipeline. Data on funding trends according to career stage show that those who have obtained one (and only one) R01, Early Established Investigators (EEIs), are declining, making up a smaller proportion of NIH-funded investigators and falling out of the pipeline most precipitously.⁸ Given these trends, an important question arises: How successful are EEI ophthalmology and optometry clinician-scientists at securing a second R01? Prior studies that analyzed the transition from a K award to an R01 examined the transition from mentored to non-mentored status. Most K awardees are also known as Early Stage Investigators (ESIs), in that they have not successfully been awarded an R01 or R01-equivalent NIH award and are within 10 vears of the end of their postgraduate clinical training. ESIs who apply for their first R01 are "prioritized for funding." In practice, this means that ESIs are funded at payline (percentile scoring thresholds that qualify for funding) levels at which non-ESI applicants would not be funded.⁹ However, after receipt of their first R01, ESI status is withdrawn and this handicap is no longer available. Here, in the largest study hitherto conducted on nearly 400 EEIs in vision research, spanning the longest time period analyzed to date, we characterize the demographics (1962-2019) and the success rates (1985–2014) of ophthalmology and optometry clinician-scientists in obtaining a second R01. This study highlights barriers that may contribute to the shortage of clinician-scientists in ophthalmology and optometry and provides insight on strategies to support this group of biomedical researchers.

Methods

Data Source and Population

National Eye Institute (NEI) R01 awardees were identified using the NIH's online Research Portfolio Online Reporting Tool, Expenditures and Results (RePORTER) database, searching for R01 award recipients from the NEI from 1985 to 2019. Only R01 awards to ophthalmology or optometry clinician-scientists were included. Clinician-scientists were identified by educational degrees, as determined from websites and scientific publications. We defined ophthalmology clinician-scientists as individuals having an MD degree and who completed a residency in ophthalmology. Optometry clinician-scientists were defined as individuals with an OD degree. Subjects that could not be determined to satisfy the criteria of an ophthalmology or optometry clinician-scientist were not included in the study. Scientists were divided into temporal cohorts based on year of first year of apparent R01 funding: pre-1985, 1985 to 1994, 1995 to 2004, 2005 to 2014, and 2015 to 2019.

Measures

Information determined directly from the NIH RePORTER database included the recipient's name, year and time span of first R01, year of second R01, institution, and project title. From this information, additional measures were determined, including gender, clinical specialty, whether the research was bench or non-bench science, and institutional funding tier. Gender was determined by two independent reviewers who categorized individuals as male or female based on gender-specific pronouns on websites and scientific publications. Clinical specialty for ophthalmologists was determined by fellowship training as identified on websites. Research projects were categorized as bench or non-bench based on the title of the grant and abstract if available. Non-bench research was considered clinical research, clinical trials, or human subjects research without evidence for in vitro (animal models, primary cells or cell-line-based or molecular biology) work. If there was evidence for genetic sequencing in these studies, or animal models, primary cells, or cell-line-based or molecular biology, it was considered bench research. Roughly 5% to 10% of cases were ambiguous for either bench or non-bench. Institutions were categorized into three tiers based on NIH funding of the ophthalmology department using the Blue Ridge Institute for Medical Research.¹⁰ If individuals changed institutions between their first and

second R01, institution was determined based on the institution where they were when they obtained their second R01. Ranking was determined based on level of funding. For institutions not listed in the guide, rank was determined by adding all the funding obtained from the NEI in 2019 using the NIH RePORTER database, and that funding value was used to place the institution within the Blue Ridge Reference Rankings. Tier 1 encompassed ranks 1 to 30; tier 2, ranks 31 to 60; and tier 3, rank > 60.

Main Outcome

The main outcome was whether or not a clinician– scientist obtained a second R01 from all NIH sources (including non-NEI), defined as a renewal or a new R01. Renewals were defined as second R01s with the same serial number as the first; non-renewal, second R01s were defined as R01s with different serial numbers from the first.

Statistical Analyses

Descriptive statistics evaluating scientists' characteristics among different temporal cohorts was performed using counts, percentages, and χ^2 tests. Kaplan-Meier survival analysis was performed to evaluate the time to obtaining a second R01, comparing between temporal cohorts as well as by a scientist's gender, institutional funding tier, degrees, specialty, and type of research. Differences in achieving second R01 funding were evaluated using log-rank tests. Multivariate logistic regression models were constructed to evaluate predictors for achieving second R01 funding. Variables considered included a scientist's temporal cohort, gender, degree types, institutional tier, and specialty and whether the first R01 research was bench or non-bench. For both Kaplan–Meier and regression analyses, only the temporal cohorts who had obtained their first R01 between 1985 and 2014 were included because the NIH RePORTER database includes information dating back to only 1985. Thus, only those who continued to receive R01 funding more recently than 1985 had any information about funding prior to 1985; therefore, it was not possible to accurately determine the timing of the first and second R01 in the earliest cohort. The 2015–2019 cohort was also excluded from these analyses, as most individuals are still being funded on their first R01 and not enough time has elapsed to ascertain their success in obtaining a second R01. For survival analysis, individuals were censored at the number of months of time elapsed from their first R01 or until receipt of their second R01 (e.g. at their number of follow-up months). There

were no other criteria for censoring, such that anyone who received a first R01 would be forever eligible to experience the outcome of obtaining a second R01. Because we could not know whether individuals were actively applying for second R01s, we could not censor based on that criteria. This is consistent with how previous studies have handled censoring.^{11,12} All analyses were performed using Stata 12 (StataCorp, College Station, TX). P < 0.05 was considered to be significant.

Consent and Ethical Approval

This study adhered to the tenets of the Declaration of Helsinki. Because this work was based on search of a public online database, this study was deemed exempt by the University of Michigan institutional review board.

Results

Table 1 shows the demographic characteristics of ophthalmology and optometry clinician–scientists who are NEI R01 recipients. We identified 386 ophthalmology (n = 340, 88.1%) and optometry (n = 46, 11.9%) clinician–scientists.

Pre-1985, 5.98% of R01 awardees were female. The proportion of females then increased through the years, from 11.70% (1985–1994) to 31.43% in the most recent cohort (P < 0.001, χ^2 test) (Fig. 1A). Pre-1985, the proportion of individuals with MD–PhD degrees was 7.69%, but this percentage increased to 42.86% for the period 2015 to 2019 (P < 0.001, χ^2 test) (Table 1, Fig. 1B).

The distribution of R01 recipients' clinical specialties is also shown in Table 1 and Figure 1C. The percentage of clinicians practicing general ophthalmology was 21.37% (n = 25) pre-1985, but this percentage decreased to 5.71% (n = 2) for the period 2015 to 2019. There was an increase in the proportion of clinicians specializing in glaucoma, from 14.53% pre-1985 (n =17) to 37.14% (n = 13) for the period 2015 to 2019 (P = 0.032, χ^2 test). In addition, cornea and retina specialists have made up a consistently high proportion of R01 recipients, between 20% and 30% each. The proportion of bench versus non-bench research has remained relatively constant, with 70% to 80% of R01-funded research being bench (P = 0.254, χ^2 test) (Table 1, Fig. 1D).

To assess the impact of institution on the acquisition of funding, we categorized institutions into one of three funding tiers based on level of NIH funding

Table 1. Demographics of R01 Awardees

	n (%)				
	Pre-1985	1985–1994	1995–2004	2005–2014	2015–2019
Characteristic	(<i>N</i> = 117)	(N = 94)	(N = 60)	(N = 80)	(<i>N</i> = 35)
Gender					
unkown	110 (94.02)	82 (87.23)	46 (76.67)	56 (70)	24 (68.57)
unidentified	7 (5.98)	11 (11.70)	13 (21.67)	23 (28.75)	11 (31.43)
		1 (1.06)	1 (1.67)	1 (1.28)	
Degree					
MD	88 (75.21)	52 (55.32)	24 (40)	28 (35)	17 (48.57)
MD–PhD	9 (7.69)	26 (27.66)	20 (33.33)	36 (45)	15 (42.86)
MD + other	4 (3.42)	6 (6.38)	9 (15)	5 (6.25)	1 (2.86)
OD + other	16 (13.68)	10 (10.64)	7 (11.67)	11 (13.75)	2 (5.71)
Specialty					
General	25 (21.37)	15 (15.96)	8 (13.33)	12 (15)	2 (5.71)
Cornea	25 (21.37)	16 (17.02)	10 (16.67)	16 (20)	7 (20)
Glaucoma	17 (14.53)	14 (14.89)	10 (16.67)	13 (16.25)	13 (37.14)
Pediatrics/strabismus	7 (5.98)	9 (9.57)	5 (8.33)	5 (6.25)	1 (2.86)
Retina	20 (17.09)	28 (29.79)	20 (33.33)	25 (31.25)	10 (28.57)
Oculoplastics	0 (0)	1 (1.06)	1 (1.67)	3 (3.75)	0 (0)
Neuro-ophthalmology	1 (0.85)	2 (2.13)	1 (1.67)	3 (3.75)	0 (0)
Unknown	14 (11.97)	4 (4.26)	1 (1.67)	3 (3.75)	2 (5.71)
Other	8 (6.84)	5 (5.32)	4 (23.53)	0 (0)	0 (0)
Research category					
Wet	87 (74.36)	67 (71.28)	48 (80)	54 (67.5)	28 (80)
Dry	30 (25.64)	27 (28.72)	12 (20)	26 (32.5)	7 (20)
Funding tier ^a					
1	71 (60.68)	55 (58.51)	34 (56.67)	52 (65)	25 (71.43)
2	27 (23.08)	23 (24.47)	11 (18.33)	19 (23.75)	6 (17.14)
3	19 (16.24)	16 (17.02)	15 (25)	9 (11.25)	4 (11.43)
Obtained second R01					
Yes	110 (94.02)	61 (64.89)	46 (76.67)	40 (50)	3 (8.57)
No	7 (5.98)	33 (35.11)	14 (23.33)	40 (50)	32 (91.43)

^aInstitutions were categorized into three tiers based on NIH funding of the ophthalmology department using data from the Blue Ridge Institute for Medical Research and the NIH RePORTER database. Tier 1, ranks 1–30; tier 2, ranks 31–60; tier 3, ranks > 60.

of the ophthalmology department in 2019 (Table 1, Fig. 1E). The majority of individuals came from the top tier (n = 237, 62.4%). Eighty-six individuals (22.3%) came from tier 2, and 63 individuals (16.3%) came from tier 3.

Next, we examined how successful NEI R01 awardees were in obtaining a second R01. For the 1985–1994, 1995–2004, and 2005–2014 cohorts, 63% (61/94), 76.67% (46/60), and 50% (40/80), respectively, were successful at obtaining a second R01 (Table 1, Fig. 1F). The length of time of the first R01 was also examined. For the 1985–1994, 1995–2004, and 2005–2014 cohorts, the median length was 47, 59, and

59 months, respectively (Fig. 2A); for those who did obtain a second R01, the median time from the start of the first R01 to that of the second R01 was 48, 60, and 59 months, respectively, for these three cohorts (Fig. 2B). We investigated the proportion of investigators who achieved their second R01 at various timepoints using Kaplan–Meier survival analysis. Including all cohorts, at 60 months (5 years), 3.9% had been awarded a second R01; at 121 months (10.1 years), 50% had received an R01; and at 180 months (15 years), 69.4% had achieved a second R01. There was no significant difference among the temporal cohorts in achieving the second R01

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Figure 1. Demographics of R01 awardees. Graphs indicate (A) gender, (B) degree, (C) specialty, (D) bench versus non-bench research, (E) institution, and (F) attainment of second R01 in temporal cohorts.

 $(P = 0.8069, \log-rank)$ (Fig. 3A). Other characteristics that were also not significantly associated with successful attainment of a second R01 included gender $(P = 0.6365, \log-rank)$ (Fig. 3B), institutional funding tier $(P = 0.4202, \log-rank)$ (Fig. 3C), type of research $(P = 0.0986, \log-rank)$ (Fig. 3D), degree $(P = 0.7240, \log-rank)$, and clinical specialty $(P = 0.5355, \log-rank)$. The demographics of second R01 awardees and non-awardees are shown in Supplementary Table S1.

We also investigated predictive factors for obtaining a second R01 in a multivariable logistic regression model, including cohort, gender, degree, specialty, institutional funding tier, and type of research (Table 2). There were no factors significantly predictive of obtaining second R01 funding. Similarly, log-rank analysis looking at factors associated with time to second R01 among only successful awardees also did not reveal any significant predictors (Supplementary Fig. S1).

Discussion

For clinician-scientists who are independent principal investigators, success in academic medicine is marked by sustained R01-equivalent funding. Our report represents the largest study of clinicians with







Figure 3. Kaplan–Meier survival curves for months to second R01 after first R01. Curves are stratified according to (A) cohort, or year that the first R01 was obtained; (B) gender; (C) tier of institution; or (D) whether the first R01 research was bench or non-bench science.

Table 2.Predictive Factors in Attainment of SecondR01

Outcome	Odds Ratio	95% CI
Gender		
Male	Ref.	Ref.
Female	0.96	0.45-2.05
Research category		
Wet	Ref.	Ref.
Dry	0.57	0.29–1.11
Degree		
MD	Ref.	Ref.
MD-PhD	1.23	0.62–2.44
MD + other	0.74	0.25–2.18
OD + other	1.04	0.19–5.79
Temporal cohort		
1985–1994	Ref.	Ref.
1995–2004	1.72	0.79–3.75
2005–2015	0.55	0.28-1.08
Funding tier ^a		
1	Ref.	Ref.
2	0.76	0.37–1.56
3	0.58	0.27–1.26
Specialty		
General	Ref.	Ref.
Cornea	1.19	0.24–5.90
Glaucoma	1.32	0.26–6.74
Pediatrics/strabismus	0.96	0.17-5.53
Retina	0.84	0.18–3.83
Oculoplastics	0.69	0.07–7.28
Neuro-ophthalmology	1.06	0.11–10.33
Unknown	0.35	0.05–2.74
Other	3.07	0.24-38.88

^aInstitutions were categorized into three tiers based on NIH funding of the ophthalmology department using data from the Blue Ridge Institute for Medical Research and the NIH RePORTER database. Tier 1, ranks 1–30; tier 2, ranks 31–60; tier 3, ranks > 60. Ref.: reference population.

independent, federal funding of vision research (N = 386) to date. Our study also analyzed longest time span of ophthalmology and optometry EEI clinician–scientist demographic data, from 1962 to 2019. To our knowledge, this work is also the first to have explored the subsequent independent, federal grant funding rates and demographics of ophthalmologists or optometrists *after* they have obtained their first R01.

First-time R01 clinician–scientist applicants are frequently ESIs who benefit from special considerations in selection for funding, a benefit that is removed after attainment of a first R01.⁹ Not surprisingly, data show that from 1995 to 2015 individuals who had already received a first R01 (EEI applicants) suffered the steepest decline in R01 success rates.⁸ A major goal of our study was to obtain baseline data of success rates of ophthalmologist and optometrist clinician– scientists who are EEIs. In addition, we sought to identify strategies for sustaining R01 funding.

Among ophthalmology and optometry clinicianscientists who were first-time R01 awardees, the percentage of female clinician-scientists increased from 5.98% pre-1985 to 31.43% for the period 2015 to 2019. This could reflect the parallel increase in the percentage of female ophthalmologists and/or an increase in interest in research careers among women. Analysis of ophthalmic subspecialties showed that the majority of R01 recipients specialized in cornea, glaucoma, or retina. Few individuals in oculoplastics (<5%), neuro-ophthalmology (<5%), or pediatrics/strabismus (<10%) were represented. Further, the percentage of general ophthalmologists decreased to 5.71%, but the percentage of glaucoma specialists increased to 37.14% in the period 2015 to 2019. It would be interesting to investigate factors related to the increase in glaucoma specialists and how they might be applied to other specialties to increase their representation among R01-funded clinicianscientists. Among US members in the American Academy of Ophthalmology, 47.1% are in general ophthalmology, 16% in retina, 7.6% in glaucoma, 7.1% in cornea/external disease, 5.4% in pediatric ophthalmology and strabismus, 5% in oculofacial plastics, and 2.5% in refractive surgery, and 2.6% other and 6.7% unknown/declined to state.¹³ Thus, there is an enrichment of fellowship-trained ophthalmologists represented among R01-funded clinical scientists, which has also been reported previously.¹⁴

A higher proportion of ophthalmology and optometry first-time R01 clinician-scientists in recent cohorts have a PhD degree in addition to an MD. This could reflect a decreased propensity for MD-only individuals to pursue research, or it could reflect successes of MD– PhD programs in fostering the growth of clinicianscientists. We believe that supporting programs that expose medical students and residents to vision research will be important to refreshing the clinicianscientist pipeline.

The majority of clinician-scientists who received their first R01 were faculty from universities that comprise the top two NIH funding tiers. Still, 10% to 20% of ophthalmology and optometrist EEIs were from the third NIH funding tier. Future initiatives to support clinician-scientists should include factors aimed at lesser NIH-funded academic medical centers.

Bench research trended toward predicting second R01-funding success, but this was not statistically

significant. Studies that identify factors related to the dominance of bench research and the value that individuals and/or institutions place on it over nonbench research may provide insights into this trend in vision research. One possibility for this trend could be that non-bench researchers may have more mechanisms for funding that are non-NIH or non-R01 based, such as industry clinical trials.

Investigation of the second R01 funding rates showed that 76.67% (46/60) of individuals were successful at obtaining a second R01 in the 1995–2004 cohort compared to 50% (40/80) in the 2005–2014 cohort. The more limited time that the 2005–2014 cohort had to obtain a second R01 likely played a role in this apparent decrease, but it could also reflect the trend in the decline of EEIs overall.

From 1985 to 2014, 62.8% (*n* = 147) of ophthalmology or optometry clinician-scientists were awarded a second R01. At 5 years after receipt of the first R01 (the typical length of an R01), only 3.9% received their second R01, although among those who did receive a second R01 the median time to receive a second R01 was within 5 years. This is slightly better retention than has been reported for the K award to first R01 in ophthalmologists previously, which was closer to 50%.^{11,12} However, it is still unsettling that almost 40% of individuals who might have expected to sustain R01 funding did not receive a second grant. None of the factors examined (gender, degree, clinical specialty, funding tier, bench versus non-bench research, cohort period) was a significant predictor of success in obtaining a second R01. We believe that this loss of individuals represents a significant dropoff, especially considering that these individuals and their sponsors have already invested considerable time and resources toward career development, such as PhD degrees, K awards, and the first R01. The average age of the recipient of a first R01 is 42 to 45 years.¹⁵ when one would already be mid-career in other professions; however, the first R01 award represents the first step in a career as an independent investigator. This loss of individuals furthers the notion that clinicianscientists, especially in ophthalmology and optometry, are an endangered species. A study that analyzed all of the NIH award applicants who received their first R01 similarly showed challenges in retention, as 30% to 50%of those who received their first R01 dropped out from the program within 5 years of the initial award, either because they did not submit a second R01 application or because subsequent applications were not selected for funding.¹⁶

When our study results are considered in the context of the results of a seminal study that determined the proportion of clinician-scientists with NEI K awards who obtain their first R01 grant, we arrive at a somewhat clearer, more longitudinal picture of the precarious current position and worrying future of ophthalmologist clinician-scientists. This study found that, of 128 ophthalmologists (optometrists excluded) who received K08 or K23 awards from the NEI from 1996 to 2010, 62 (48%) received their first R01 award.^{11,12} Of the 140 ophthalmologists and optometrists who received their first R01 from 1995 to 2014, 86 (61%) received their second R01. Although our study is distinct in that we included optometrist clinician-scientists but did not assess whether ophthalmology and optometry EEIs had obtained a K award, we would estimate that less than one-third of ophthalmology K awardees receive a second R01. When viewed from this perspective, there appear to be massive leaks from the clinician-scientist pipeline, as some 7 in 10 of clinician-scientist K awardees are not likely to obtain their second R01.

Our data raise sobering questions for clinicianscientists, department chairs, foundations, and philanthropists, as well as the NEI and NIH. Because only 3.9% of ophthalmology and optometry clinicianscientists receive their second R01 5 years after the start of initial R01 funding, how should stakeholders support this group? Should department chairs set aside bridge or retention funding during initial hire or during receipt of the R01 by the clinician-scientist? Because startups for clinician-scientists are usually lower than for PhD scientists,¹⁷ should ophthalmology and optometry departments and schools increase startup packages during initial hire of the clinicianscientist? Should the NEI offer mechanisms like the National Cancer Institute's R37 MERIT Award,¹⁸ which funds the initial R01-level grant for 7 rather than 5 years, for a subset of meritoriously scored first-time R01s from ESIs, some of whom are ophthalmology and optometry clinician-scientists?

There are several limitations of this study. We focused our outcomes on receipt of the second NIH R01. We did not assess other major federal grants, such as U10 NIH grants, Veterans Affairs grants, and private foundation grants, because these are not easily accessible in a publicly available database and some were not offered at the time of the earliest analyzed cohort. We also did not assess receipt of other NIH grants, such as R21 and R03 grants, because they provide much lower levels of funding. Finally, the modest sample sizes may limit the power of subgroup analyses.

Taken together, these results support the idea that interventions are needed during the first R01, as a high proportion of investigators are precipitously dropping out of the pipeline. Identifying factors that can help promote success at the much more poorly understood

EEI career stage will be critical to ensuring the survival of clinician–scientists.

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