

## Initial Outcomes for the NHLBI K99/R00 Pathway to Independence Program in Relation to Long-Standing Career Development Programs Implications for Trainees, Mentors, and Institutions

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**S**ufficient history now exists to assess the National Institutes of Health Pathway to Independence Award (K99/R00), first offered in 2007 to support the career development of biomedical researchers. The success of K99 (Mentored Phase of the K99/R00) principal investigators in obtaining subsequent grant support was compared with that of principal investigators supported by the long-standing K08 (Mentored Clinical Scientist Research Career Development Award) and K23 (Mentored Patient-Oriented Research Career Development Award) programs. For cardiovascular K awards initiated in fiscal years 2007 to 2009, K99 principal investigators were more successful in obtaining subsequent grant support than the other groups. Although a bibliometric analysis showed similar publication quality for all groups, the K99 group was most persistent in applying for the next grant. Possible implications of these findings for all K Award principal investigators, their mentors, and institutions are presented.

The National Institutes of Health (NIH) supports a variety of career development or K awards to facilitate the careers of promising investigators through mentorship, salary support, resources, and protected research time with the broad objective of maintaining a skilled cadre of independent biomedical researchers.<sup>1</sup> There are several K mechanisms, and each NIH Institute or Center offers those that best support its mission. Assessments of the entire K program both within<sup>2,3</sup> and across NIH Institutes or Centers<sup>1</sup> and external reviews by working groups of the Advisory Committee to the Director of NIH<sup>4</sup> have shaped the

overall structure and performance of K Award programs to achieve a diverse and highly productive research workforce.

Recently, we have investigated outcomes for the most prevalent mentored K Awards within the portfolio of the Division of Cardiovascular Sciences (DCVS) of the National Heart, Lung, and Blood Institute (NHLBI). K08 (Mentored Clinical Scientist Research Career Development Award), K23 (Mentored Patient-Oriented Research Career Development Award), and K99/R00 (Pathway to Independence Award) grants awarded in fiscal years 2007 to 2009 (and now completed) were examined to determine the success of the recipients in obtaining subsequent NIH funding. Within this cohort, the sample of newly instituted K99/R00 awards is the earliest within our portfolio that is large enough to give a meaningful assessment. Similar numbers of K08 and K23 grants were awarded in the same time period. Although these awards have different objectives and serve different communities, our recent experience for cardiovascular investigators supported by K08 and K23 grants conforms to expectations based on previous findings across the NIH. In addition, this early snapshot of the K99/R00 program suggests that it is at least as effective as the long established programs in launching young investigators into independent careers.

Funding histories for K08, K23, and K99 (mentored phase of the K99/R00) applicants included in this analysis were obtained from the Query View Report (QVR) system, an internal NIH database. For determining the K Award success rates, any initial submission and the resubmission in the same fiscal year were considered a single application. Records for 139 K08 applications, 142 K23 applications, and 182 K99 applications were examined.

The subsequent grant history of each K Award principal investigator (PI) was found in QVR, which includes applications to the NIH, the National Library of Medicine, the United States Agency for Healthcare Research and Quality, and the United States Department of Veterans Affairs. For each PI, we found the characteristics of new grants awarded since receiving the K grant, the number of submissions and years to get funding after the K grant, and the total number of both successful and unsuccessful submissions. For this part of our analysis, any resubmission of a revised application was counted as a submission. Grant submissions eligible for funding through FY2015 were tallied. Thus, the history for each investigator covered a period of 5.2 to 7.6 years from the start of the K Award. For each K PI, we determined sex, degrees held, and whether the PI changed institutions during the K grant. Although NIH collects aggregate racial-ethnic and age

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**Nonstandard Abbreviations and Acronyms**

<b>DCVS</b>	Division of Cardiovascular Sciences
<b>K01</b>	Mentored Research Scientist Career Development Award
<b>K08</b>	Mentored Clinical Scientist Research Career Development Award
<b>K23</b>	Mentored Patient-Oriented Research Career Development Award
<b>K99</b>	mentored phase of the K99/R00
<b>K99/R00</b>	Pathway to Independence Award
<b>NHLBI</b>	National Heart, Lung, and Blood Institute
<b>PI</b>	principal investigator
<b>QVR</b>	Query View Report
<b>R00</b>	independent phase of the K99/R00
<b>R01</b>	Research Project Grant

data, this information for individual PIs is not included in the QVR database and was not analyzed.

The publications attributed to each funded K Award were found in QVR and then linked to a database used by DCVS previously<sup>5,6</sup> to assess research productivity and impact. This database provides a publication percentile normalized to subject category.<sup>7</sup> An article with the greatest number of citations merits a percentile of 0, whereas one with the least citations receives a percentile of 100.

### Baseline Data

For the study cohort, DCVS awarded 56 K08 grants, 53 K23 grants, and 53 K99 grants with an overall success rate of 37%. Although the rates for different awards varied, the differences were not significant (Online Table I). More than 92% of the PIs completed the entire project period of their grants (Online Table I). PIs who did not complete the program are not analyzed further, so our primary outcome is subsequent grant success when all of the originally committed resources are expended to support the career development of an investigator. For K99 PIs, completion meant that both the mentored K99 phase of 1 to 2 years and the independent R00 phase of the grant of 3 years were done. The transition from the K99 to the R00 phase requires the PI to achieve a tenure-track assistant professorship or equivalent appointment and is subject to an internal review by NHLBI. Taking account of the K99-to-R00 transition and no cost extensions, the duration of most K99/R00 programs is 4.5 to 6 years. K08 and K23 applicants may ask for 3 to 5 years of support, with the vast majority choosing 5 year programs that also may increase to 6 years with no cost extensions. K08 and K23 PIs generally have a faculty appointment of instructor or higher at the start of the award with the expectation that they will advance to an independent tenure-track equivalent position during the K project period. K08, K23, and R00 PIs remain eligible for consideration as early-stage investigators, which conveys an equal advantage to all groups over established investigators in competing for an NIH Research Project Grant (R01). Most K99 PIs have PhDs, while all of the K08 and K23 PIs have clinical credentials, with the majority holding MDs but some with degrees in Clinical Psychology, Pharmacy, or Physical Therapy. All groups include at least one PI with both a clinical and a research doctorate (MD/PhDs in the majority of cases), but

the proportions differ significantly (Online Table I). The sex distributions for the K08 and K23 groups are similar to those reported previously across the NIH,<sup>1</sup> and the K99 results are midway between these results (Online Figure I). Both NIH-wide data<sup>1</sup> and a report from the National Cancer Institute<sup>2</sup> show that the sex balance of funded K grants matches the balance of the applicant pool. Although the ages of the PIs in this analysis were not available in QVR, the 2011 NIH-wide report<sup>1</sup> found that the median age of K Award applicants was 37, with no difference between clinician-scientists (K08 or K23 applicants) and PhDs (most K01 [Mentored Clinical Scientist Research Career Development Award] applicants).

### Success at Getting the Next Grant After a K Award

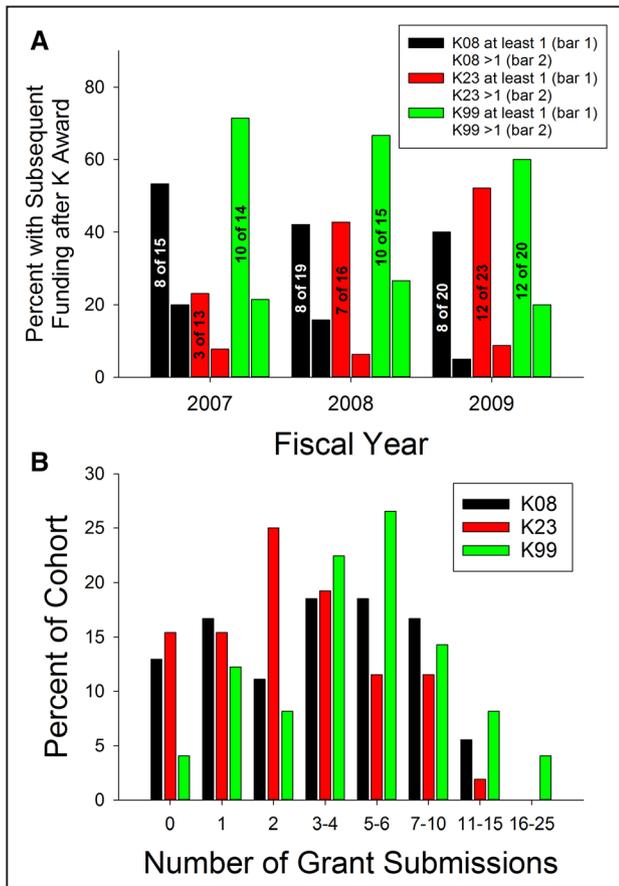
Figure A shows the percent of K Award PIs who obtained subsequent funding from any grants included in QVR for each fiscal year. K08 and K99 PIs funded in 2007 had the greatest success in getting a subsequent grant consistent with having the most time to submit applications. However, small sample sizes may account for the opposite pattern for the K23 group. Some PIs obtained more than 1 grant after the K in all groups, and 60% or more of the K99 PIs were successful for each year in contrast to the K08 and K23 groups where no more than 53% achieved subsequent funding for any year. The aggregate success rates over all years to receive at least one grant were 44.4% for K08 PIs, 42.3% for K23 PIs, and 65.3% for K99 PIs. These rates differed significantly ( $P=0.039$ , Chi-squared test).

### Source of Funding for the Next Grant After a K Award

The NHLBI portfolio of K Awards has overlap with the missions of other NIH Institutes or Centers and government agencies, and some of our K PIs have garnered grants from one or more of these sources. All are considered positive outcomes as shown in Online Tables II and III. On average, each K99 PI competed successfully for 0.898 grants of any kind, whereas this yield was 0.593 grants for each K08 PI and 0.519 grants for each K23 PI, with an overall significant difference ( $P<0.03$ , Kruskal–Wallis test). The first grant after the K was not always an R01, but rather an R01 was the second or third grant after the K. R01s account for 76%, 57%, and 79% of the grants awarded to K08, K23, and K99 PIs, respectively. Overall, R01s were granted to 40.7% of the K08 PIs, 26.9% of the K23 PIs, and 57.1% of the K99 PIs. These rates differed significantly ( $P<0.01$ , Chi-squared test).

### Time and Number of Submissions Needed to Gain Subsequent Funding

About 3 submissions and 4.5 years were needed to receive a first grant of any kind, with no differences between the K groups (Table). Similarly, PIs who eventually received an R01 grant took  $4.59\pm 1.42$  years, with no difference between groups. Table also shows that unsuccessful K08 and K23 PIs submitted less frequently than their funded counterparts, while an opposite pattern occurred for the K99 group. However, these trends did not differ significantly.



**Figure. A**, Percent of K Award principal investigators (PIs) that competed successfully for one or more subsequent grants (left bar in each group) or obtained more than one additional grant (right bar in each group). **B**, Distributions of K Award PIs based on the number of grant applications submitted after the K shown on the abscissa.

### K Award Productivity

Bibliometric data assessed research productivity (Table). The median journal impact factor was highest for the K08 group and was greater than the value for the K23 group. However, K23 PIs published more papers per capita than did the K08 PIs. The median normalized percentiles, median citations per article, and the median best normalized percentile for each PI did not differ between groups.

### Persistence in Seeking Funding After a K Award

Figure B shows the distributions of all submissions for funding after the K, regardless of outcome. Notably, 29.6% of K08 and 30.8% of K23 PIs submitted only once or not at all compared with 16.3% of the K99 PIs. The median numbers of submissions was 3.5 for K08 PIs, 2.0 for K23 PIs, and 5.0 for K99 PIs and differed significantly ( $P < 0.01$ , Kruskal–Wallis test).

The interpretation of our findings is limited by the heterogeneity between groups. Specifically, K99 PIs are predominantly PhDs. In contrast, K08 PIs are clinician scientists pursuing basic research aligned with their clinical specialty, and K23 PIs are clinicians engaged in patient-oriented research, with some holding research doctorates in addition to

their clinical credentials. K99 applicants also had a lower but not statistically different success rate than the other groups in getting K funding (Online Table I), underscoring systematic differences in how each group was selected. Finally, other factors, such as racial and ethnic differences,<sup>8</sup> not available in the QVR database were not explored. Previous assessments of K award outcomes<sup>1,2</sup> avoid the heterogeneity inherent in comparing different K mechanisms by comparing successful and unsuccessful applicants for a single K award in a narrow region on either side of the pay line where there is insufficient power to discriminate scientific merit. Our results are preliminary, and the sample size is too small for this approach.

Unlike the 2011 report on Individual Mentored K Awards Program<sup>1</sup> that covers all of NIH, our analysis is restricted to grants made by a single Division (DCVS) within NHLBI and reflects the culture of the cardiovascular research community. In addition, we report on K grants awarded more recently than those in the 2011 report.<sup>1</sup> K08 and K23 Award success rates from the DCVS groups of 42.5% and 38%, respectively, are less than the respective rates of 48% and 41% found previously across the NIH.<sup>1</sup> The K99 award was not offered before 2007, but its PIs are predominately PhDs in the basic sciences and can be compared with K01 PIs that are also predominately PhDs. Similar to the K08 and K23 results, the K99 success rate of 29.7% is more selective than the K01 rate of 40% reported in the NIH-wide study.<sup>1</sup> Although all of these differences are potential confounders, comparing our recent findings in relation to previous data provides several insights.

The overall success rate for our sample of K08 and K23 PIs of 42% to 45% to obtain a grant of any kind after the K is less than the 53% to 57% range reported previously for a subset of K08 and K23 PIs across the NIH.<sup>1</sup> In contrast, the R01 success rates of our K08 and K23 PIs of 40.7% and 26.9%, respectively, exceed the respective NIH-wide rates of 32% and 18%.<sup>1</sup> Impressively, 65.3% of the K99 PIs in our sample achieved some form of subsequent funding and 57.1% of them received one or more R01 grants. Both rates exceed respective rates of 50% and 27% for a subset of K01 PIs across the NIH in the 2011 report,<sup>1</sup> and both rates differ from the K08 and K23 results in the present study. Thus, the K99/R00 program seems to be more effective than the established mentored K award programs. However, some K08 and K23 PIs may have achieved positive outcomes that are not tallied in the QVR database, such as funding from professional societies, private foundations, pharmaceutical companies, or roles as subproject PIs on large-center grants.

Among PIs who attain funding after the K, there were no differences to suggest that the K99 awardees were better prepared or more skilled than the other groups. Successful applicants from all groups achieved their next grants after similar numbers of submissions and years after their K start dates. In addition, the K99 group was not superior to the other groups by any of the bibliometric measures.

The only significant trend that paralleled the outcomes for the different K groups was the greater persistence of the K99 group compared with the others in submitting grants (Figure B). This trend likely results in part from differences in the

**Table. Performance Metrics of Career Development Awardees**

Outcome	K08	K23	K99/R00	P Value*
Years from K award start date (mean±SD)				
To next grant	4.27±1.66	4.28±1.63	4.76±1.59	0.404
Number of submissions (mean±SD)				
For successful applicants to get the next grant	3.04±1.63	2.68±1.70	3.31±2.31	0.656
Unsuccessful applicants	2.23±2.30	2.10±2.19	3.65±3.77	0.312
Bibliometrics† (median values)				
Normalized percentile for all articles	25.24	29.49	27.62	0.495
Citations per article	7	6	7	0.293
Journal impact factor for all articles	5.218	3.991	4.600	0.001
Articles per PI	3	6	4	0.001
Best normalized percentile of the PI	15.29	6.54	13.79	0.125

K08 indicates Mentored Clinical Scientist Research Career Development Award; K23, Mentored Patient-Oriented Research Career Development Award; K99/R00, Pathway to Independence Award; and PI, principal investigator.

\*P value for difference between groups (Kruskal–Wallis Test).

†Only first- and senior-authored articles attributed to K Award funding that report new research findings are included. Reviews, letters, commentaries, and editorials are excluded.

study populations. During the K project period, the vast majority of K08 and K23 PIs maintain clinical effort outside of the required 75% research training effort. When their K grants end, unfunded clinician-scientists generally must increase their clinical activity and reduce research effort that can reduce their incentive to apply for grants. In contrast, 46 of 49 K99 PIs in the present study hold PhDs or other research doctorates and achieved positions in the R00 phase where continued research effort and grant submissions are expected when the R00 funding ends.

Unique characteristics of the K99/R00 program may also promote positive outcomes and prevent well-trained PIs from leaving research after a small number of grant submissions. K99 applications must include an explicit plan for 1 to 2 years of mentored training followed by a transition to early independence as a tenure-track assistant professor or equivalent during the 3-year R00 phase of the grant. When this transition is initiated, it is reviewed internally by NHLBI staff to determine whether the institutional support is sufficient to launch the newly independent PI and that there is a realistic timetable to apply for future funding. K99 PIs are encouraged to transition to a new institution for the R00 phase, which may also promote the acquisition of job searching skills. Although similar plans may be proposed by other K applicants, a general timetable and milestones are not specified in their program announcements. In the present study, 57% of the K99 PIs moved from their K99 institution to pursue the R00 phase, whereas only 7% of K08 PIs and 10% of K23 PIs relocated during their K project periods. In most cases, the new hiring institution provides resources for the PI, including significant salary support, start-up funding, protected time, and advice from senior faculty about gaining tenure and future research funding. In the present study, success rates to get subsequent funding of 75% for the K99 PIs who moved to a new institution and 52% for those who did not move do not differ ( $P < 0.10$ ). Nonetheless, this trend suggests that the skills and experience in securing a

position in a new environment augment the resilience needed to obtain the next grant and avoid institutional reliance on the K99 mentor as the main source of professional and possible fallback support as the PI moves forward.

### Implications for K Award PIs and Future Applicants

We conclude that the K Award mechanisms in our analysis are similar in developing the scientific capabilities of the recipients. However, the K99 program seems superior in promoting research independence based on success in gaining subsequent research funding. A major associated factor is persistence in applying for the next grant. An appropriate goal for all K PIs is to submit an R01 or equivalent grant application before or by the start of the final 2 years of K Award support. This strategy allows a resubmission while the K Award is still active and minimizes a hiatus in funding if additional submissions are needed for success. To this end, NHLBI has been holding an annual meeting on the NIH campus for all of our K Award PIs to encourage and facilitate this approach. Our findings stress the importance of intentional and detailed planning for a transition to independent status. Training plans should hone more than scientific skills. While preparing to apply for any K Award<sup>9,10</sup> and early after its start, mentor and PI should develop and then refine a realistic plan for an independent position. When staying at the same institution, the K PI should work with the mentors and senior administration to understand what positions are available, the expectations for the trainee, and the institutional commitments beyond those from the mentor that will support the trainee's path to independence. Well-crafted milestones tailored to the candidate are especially important. In summary, newly independent investigators benefit most from K Award support when their programs include intentional and detailed planning for the future both in terms of applying for research grants and in

obtaining a truly independent research position. Persistence in grant writing is a significant factor in this process, and active institutional support beyond that from the K Award mentor enhances the prospect of success.

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### Disclosures

None.

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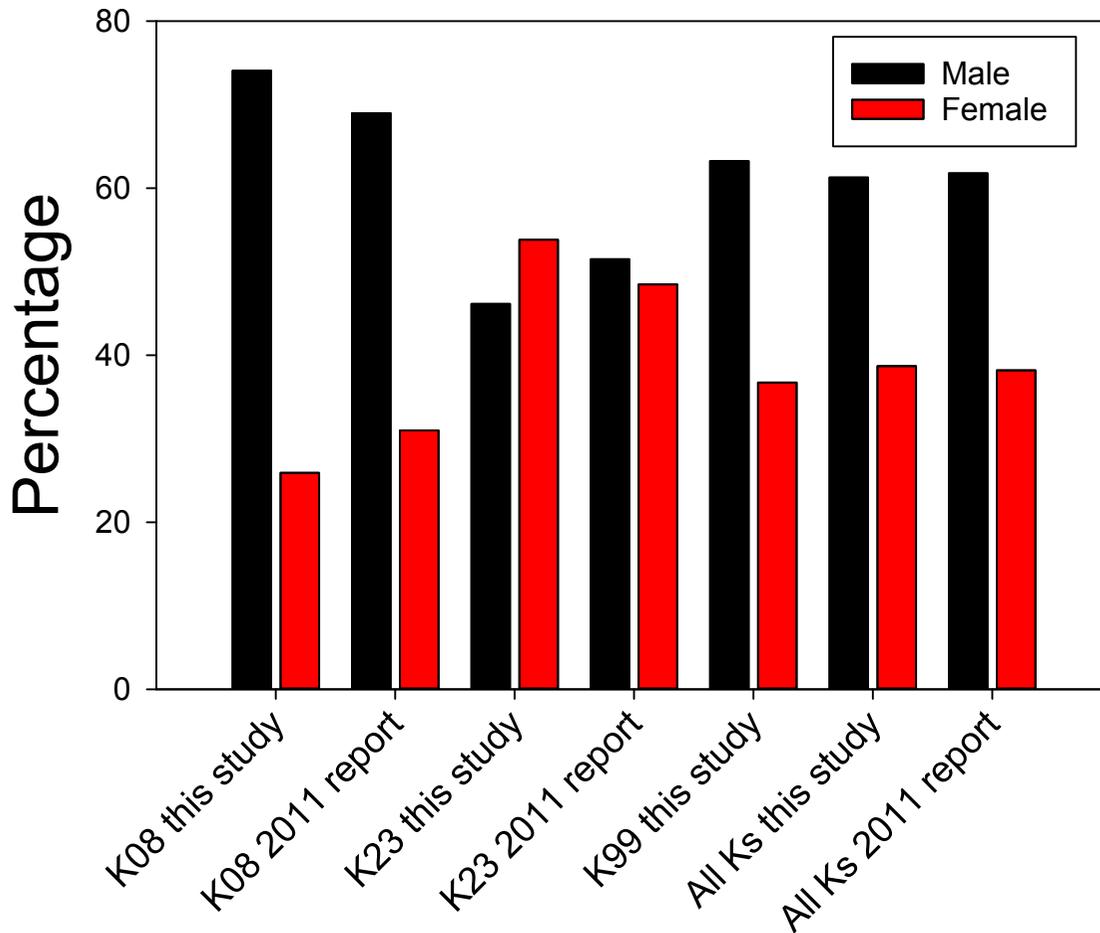
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## **Supplemental Material**

### **Detailed Methods**

The publications attributed to each funded K Award were linked to a Thomson-Reuters InCites database that includes 260,000 NHLBI-supported articles published between January 1981 and December 2013. This resource has been used by DCVS previously<sup>1,2</sup> to assess research productivity and impact. To correct for differing citation rates between scientific disciplines<sup>3</sup>, this database provides a publication percentile indicating how often an article has been cited compared with articles in the same subject category. An article with the greatest number of citations merits a percentile of 0, and one with the least citations is assigned a percentile of 100.

Statistical tests were done using the *Prism 6 for Windows* Software package from GraphPad Software, Inc., La Jolla, CA. The Chi-Square test was used to test differences between success rates in obtaining grant awards. The Kruskal-Wallis test followed by the Dunn's multiple comparisons test was used to assess the differences among multiple median values.



Online Fig. 1. Gender Distribution for all K groups in this study and for the groups reported in National Institutes of Health Individual Mentored Career Development Awards Program.

[http://grants.nih.gov/training/K\\_Awards\\_Evaluation\\_FinalReport\\_20110901.pdf](http://grants.nih.gov/training/K_Awards_Evaluation_FinalReport_20110901.pdf).

Prepared by Discovery Logic for the NIH; 2011

Online Table I. Baseline data for K Awards FY2007 - FY2009

Type of K Award	K Award Success Rate (%) for all Applicants	Percent K Award Pls that completed the entire K Project	Percent with both Clinical and Research Doctorates
K08	42.5	96.4	44.4
K23	38.0	98.1	13.5
K99	29.7	92.5	2.0
P Value	0.052	0.38	<0.01

Online Table II. Number (percent) of grants awarded by different agencies to each group of K Award PIs in the DCVS portfolio.

Funding Agency*	K08	K23	K99	All Ks
NHLBI	21 (65.6)	21 (77.8)	38 (86.4)	80 (77.7)
AHRQ		1 (3.7)		1 (1.0)
NIA	3 (9.4)			3 (2.9)
NIAAA			1 (2.3)	1 (1.0)
NIAID			1 (2.3)	1 (1.0)
NIAMS		1 (3.7)		1 (1.0)
NCATS	1 (3.1)		1 (2.3)	2 (1.9)
NICHHD	1 (3.1)			1 (1.0)
NIDA		1 (3.7)		1 (1.0)
NIDDK	3 (9.4)		1 (2.3)	4 (3.9)
NIGMS			1 (2.3)	1 (1.0)
NIMHD		1 (3.7)		1 (1.0)
NLM			1(2.3)	1 (1.0)
VA	3 (9.4)	2 (7.4)		5 (4.9)
Total	32 (100)	27 (100)	44 (100)	103 (100)

\*NHLBI, National Heart, Lung, and Blood Institute; AHRQ, Agency for Healthcare Research and Quality; NIA, National Institute on Aging; NIAAA, National Institute on Alcohol Abuse and Alcoholism; NIAID, National Institute of Allergy and Infectious Diseases; NIAMS, National Institute of Arthritis and Musculoskeletal and Skin Diseases; NCATS, National Center for Advancing Translational Sciences; NICHHD, National Institute of Child Health and Human Development; NIDA, National Institute on Drug Abuse; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; NIGMS, National Institute of General Medical Sciences; NIMHD, National Institute on Minority Health and Health Disparities; NLM, National Library of Medicine; VA, Department of Veterans Affairs.

Online Table III. Number (Number or yield per PI) of grants awarded to each group of K Award PIs. The yield per PI differed among groups for the R01 (P = 0.0056, Kruskal-Wallis test) and the Total (P = 0.027, Kruskal-Wallis test) rows.

Activity Code*	K08	K23	K99	All Ks
R01	23 (0.426)	16 (0.308)	35 (0.714)	74 (0.477)
R15			1 (0.020)	1 (0.006)
R18		1 (0.019)		1 (0.006)
R21	4 (0.074)	3 (0.058)	3 (0.061)	10 (0.065)
R34		1 (0.019)		1 (0.006)
R44		2 (0.038)	1 (0.020)	3 (0.019)
R56	1 (.019)		1 (0.020)	2 (0.013)
G13			1 (0.020)	1 (0.006)
P01		1 (0.019)	1 (0.020)	2 (0.013)
S12		1 (0.019)		1 (0.006)
UH2	1 (0.019)		1 (0.020)	2 (0.013)
I01	3 (0.056)	1 (0.019)		4 (0.026)
I21		1 (0.019)		1 (0.006)
Total	32 (0.593)	27 (0.519)	44 (0.898)	103 (0.665)

\*R01, Research Project Grant; R15, Academic Research Enhancement Award; R18, Research Demonstration and Disseminations Project; R21, Exploratory/Developmental Research Grant; R34, Planning Grant; R44, Small Business Innovation Research (SBIR) Grant; R56, High Priority, Short-Term Project Award; G13, Health Sciences Publication Support Award; P01, Research Program Project Core or Sub-Project PI; S12, Lasker Clinical Research Scholars Program; UH2, Exploratory/Developmental Cooperative Agreement Phase I; I01 and I21, Department of Veterans Affairs Grants.

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