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Supporting Information for

Biomedical Research Funding by Gender: A Survival Analysis

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Supporting Information Text

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Survival Definition Sensitivity. We considered investigators to have left the NIH funding pool if their last awards were followed by 3 or more years without NIH funding. We used a 3-year cutoff in order to strike a balance between including recent investigators in our analysis and allowing investigators sufficient time to have definitively exited the funding pool. Additionally, NIH renewal policy restricts amended application submissions to 3 years if an application is not funded. However, to understand the tradeoffs that that are incurred as we shift the cutoff times, we considered the results of the survival analysis given cutoffs of 1, 3, 5, and 7 years without funding.

The full survival curve (considering all investigators) demonstrated significant gender differences using all cutoffs (tests: Mantel-Haenszel [MH] and Gehan-Wilcoxon [GW]), suggesting robustness of the overall finding:

1-year gap - MH $\chi^2(1) = 25.5$, $p < 0.001$; GW $\chi^2(1) = 16.7$, $p < 0.001$
3-year gap - MH $\chi^2(1) = 15.5$, $p < 0.001$; GW $\chi^2(1) = 10.2$, $p < 0.01$
5-year gap - MH $\chi^2(1) = 9.1$, $p < 0.01$; GW $\chi^2(1) = 5.8$, $p = 0.02$
7-year gap - MH $\chi^2(1) = 6.1$, $p = 0.01$; GW $\chi^2(1) = 4.0$, $p = 0.05$

However, we did find that the 1991-1995 and 1996-2000 cohorts exhibited significant gender differences with a 3-year cutoff which were not observed when using a 5-year cutoff:

1991-1995 Cohort:
3-year gap - MH $\chi^2(1) = 6.6$, $p = 0.01$; GW $\chi^2(1) = 3.9$, $p = 0.05$
5-year gap - MH $\chi^2(1) = 4.3$, $p = 0.04$; GW $\chi^2(1) = 2.9$, $p = 0.09$

1996-2000 Cohort:
3-year gap - MH $\chi^2(1) =4.6$, $p = 0.03$; GW $\chi^2(1) = 4.0$, $p = 0.05$
5-year gap - MH $\chi^2(1) = 3.3$, $p = 0.07$; GW $\chi^2(1) = 3.1$, $p = 0.08$

Investigator Characteristics Analysis. Gender distributions of investigator characteristics potentially influencing the overall survival curves were calculated prior to performing a survival analysis that accounted for these covariates. The variables studied included age of investigator at first award, degree held by investigator (PhD, MD/PhD, or MD), type of RPG received as first award, year first funded (cohort), NIH funding rank of investigator's institution at first award, and Carnegie classification of investigator's institution at first award. NIH funding rank, divided into quintiles, was determined based off the amount of NIH support an institution received relative to all other institutions receiving NIH support for the fiscal year in which the investigator received his or her first award. Distributions of these covariates by gender, with the results of Wilcoxon Rank-Sum (numeric) or Chi-Squared (categorical) statistical tests for significance, can be found in Table S1.

Matched Survival Analyses. Using the MatchIt (1) package in R to perform propensity score nearest neighbor matching, we selected a subset of male investigators that best matched female investigators on the covariates mentioned above: age, degree, first RPG type, year first funded (cohort), institutional NIH funding rank, and institutional Carnegie classification. Here we excluded investigators without reported dates of birth, and investigators with degrees reported as "Other." Matching on these characteristics resulted in a sample of 10,212 women and 10,212 matched men. After matching, all *p*-values were greater than 0.42 and all standardized mean differences were less than 0.03. We also note that adding a caliper was not necessary: a caliper as small as 0.01 only resulted in 97 unmatched women.

A survival analysis comparing women and matched men revealed no difference in survival (MH: $\chi2(1) = 0.2$, $p = 0.63$; GW: $\chi2(1) = 0.1$, $p = 0.82$; Figure S3a). Comparing funding and review characteristics across women and matched men, we also found that gender differences previously observed in funding per year no longer existed (Women: $317,641; Men: $315,904; Wilcoxon Rank-Sum Score: 51,598,949; $p = 0.20$; Table S2). To account for the randomness in breaking ties when matching, we reran the analysis 10 times with different random seeds and found consistent results across all 10 runs.

Based on the importance of renewal submission rate, as identified in the Random Survival Forest analysis, we repeated this matching process for renewal submission rates and first funded year (to avoid right-censoring incongruities on matched pairs). Specifically, we selected a subset of male investigators that best matched female investigators on renewal submission rate and first funded year. This resulted in a sample of 9,395 women and 9,395 matched men. After matching, both *p*-values were greater than 0.98, and both standardized mean differences were less than 0.001. We also note that adding a caliper was not necessary: a caliper as small as 0.01 resulted in 0 unmatched women.

A survival analysis comparing women and matched men revealed no difference in survival (MH: $\chi2(1) = 0.3$, $p = 0.60$; GW: $\chi2(1) = 1.6$, $p = 0.20$; Figure S3b). Comparing funding and review characteristics across women and matched men, we also found that gender differences previously observed in funding per year no longer existed (Women: $316,671; Men: $328,029; Wilcoxon Rank-Sum Score: 44,709,337; $p = 0.12$; Table S2). To account for the randomness in breaking ties when matching, we reran the analysis 10 times with different random seeds and found consistent results across all 10 runs.

Career Timelines. To better understand our investigators' career paths, we calculated investigator age at first award and time from degree to first award. For age at first RPG (98.82% of birth dates reported), we found that on average, men (N = 23,838) obtained their first RPGs at age 41.86—less than five months earlier (W = 120,411,713, $p < 0.001$) than women (N = 10,517; mean age: 42.22). Within cohorts, this difference was only significant for the 1991-1995 group (Women: 40.29, Men: 39.85; N Women = 2,179, N Men = 5,527; W = 5,650,730, $p < 0.001$). We also considered the number of years that investigators took to earn a first major RPG after completing their terminal degrees (86.30% of degree years reported). On average, women (N = 9,260) earned their first major RPG 11.04 years after completing their terminal degrees, less than a year earlier than men (N = 20,745), who took 11.71 years (W = 99,800,836, $p < 0.001$). This difference was significant for all but the 2006-2010 cohort (all *p*-values < 0.002). Finally, to supplement these data, we explored literature on the amount of time postdoctoral researchers tended to spend in postdoctoral positions historically, when our group of investigators would have (roughly) been in these positions. This averaged 4-5 years (2).

References

1. Ho DE, Imai K, King G, & Stuart EA (2011) MatchIt: Nonparametric preprocessing for parametric causal inference. *J Stat Softw* 42(8).
2. Kahn S & Ginther DK (2017) The impact of postdoctoral training on early careers in biomedicine. *Nat Biotechnol* 35(1):90-94.

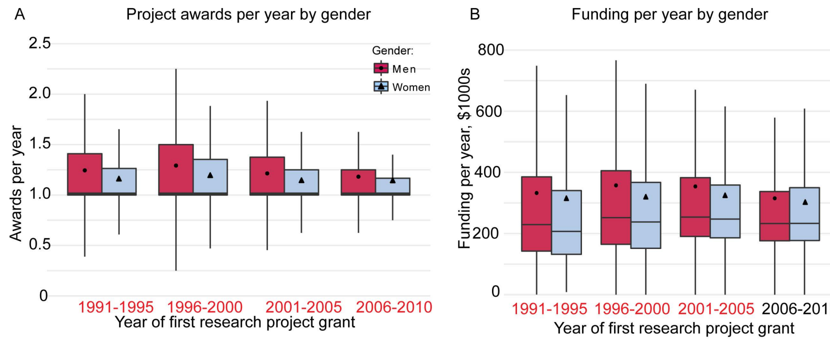

Fig. S1. Boxplots of project awards and funding per year, by gender and cohort. Markers indicate means; bars indicate medians. Red cohort labels indicate statistically significant gender differences ($p \leq 0.05$; Wilcoxon Rank Sum test, two-tailed). Outliers not shown. (A) Men held more projects per year than women, overall and across cohorts (1991-1995: N Women = 2,192, N Men = 5,539; W = 6,538,011, $p < 0.001$; 1996-2000: N Women = 2,436, N Men = 5,876; W = 7,727,149, $p < 0.001$; 2001-2005: N Women = 2,690, N Men = 6,068; W = 8,716,580, $p < 0.001$; 2006-2010: N Women = 3,342, N Men = 6,627; W = 1,1426,566, $p = 0.004$). (B) Men held more funding per year than women, overall and across the first three cohorts (1991-1995: W = 6,506,441, $p < 0.001$; 1996-2000: W = 7,550,885, $p < 0.001$; 2001-2005: 8,501,697, $p = 0.002$). Y-axis limited to $800,000 for clarity.

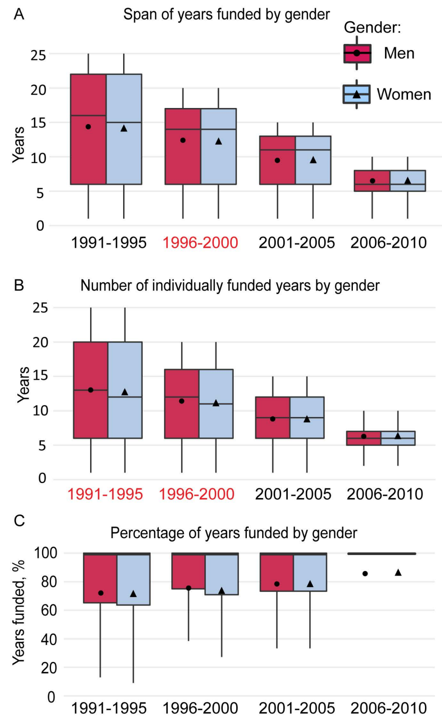

Fig. S2. Boxplots of years of funding, by gender and cohort. Markers indicate means; bars indicate medians. Red cohort labels indicate statistically significant gender differences ($p \leq 0.05$; Wilcoxon Rank Sum test, two-tailed). Outliers not shown. (A) Women held RPG funding for shorter spans of time than men, though by cohort, this difference was only significant for the 1996-2000 cohort (N Women = 2,436, N Men = 5,876; W = 7,387,058, $p = 0.02$). (B) Women held funding for fewer total years compared to men, a difference significant for the 1991-1995 (N Women = 2,192, N Men = 5,539; W = 6,256,887, $p = 0.04$) and 1996-2000 (N Women = 2,436, N Men = 5,876; W = 7,478,524, $p = 0.001$) cohorts. (C) For percentage of years funded, women and men did not differ significantly overall, or by cohort (1996-2000: N Women = 2,436, N Men = 5,876; W = 7,310,585, $p = 0.06$; all other p-values > 0.57).

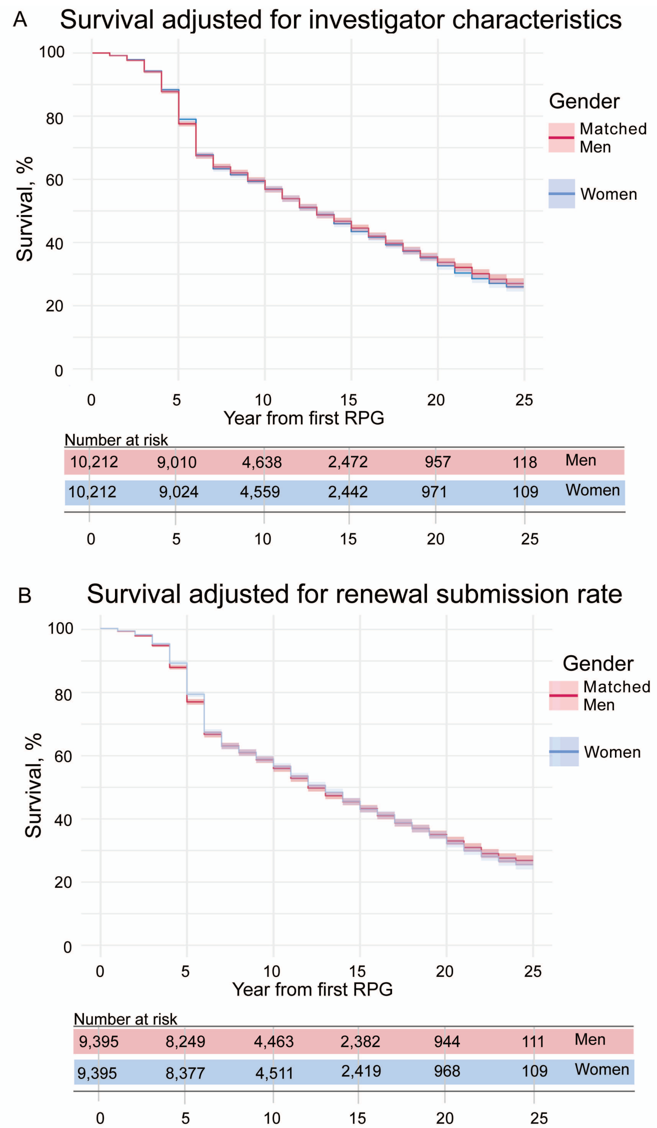

Fig. S3. Kaplan-Meier survival plot of investigators' sustained NIH RPG funding for matched women and men. Number of individuals at risk listed below plot. 95% confidence intervals pictured (Greenwood's formula). (A) Propensity score nearest neighbor matching was used to select a sample of women (N=10,212) and matching men (N=10,212) on age, degree, first RPG type, first year funded (cohort), institutional NIH funding rank, and institutional Carnegie classification. Matched men and women stayed in the funding pool at similar rates (Mantel-Haenszel [MH] test: $\chi2(1) = 0.2$, $p = 0.63$; Gehan-Wilcoxon [GW] test: $\chi2(1) = 0.1$, $p = 0.82$). (B) Propensity score nearest neighbor matching was used to select a sample of women (N=9,395) and matching men (N=9,395) on renewal submission rate and first funded year. A survival analysis comparing women and matched men revealed no difference in survival (MH: $\chi2(1) = 0.3$, $p = 0.60$; GW: $\chi2(1) = 1.6$, $p = 0.20$).

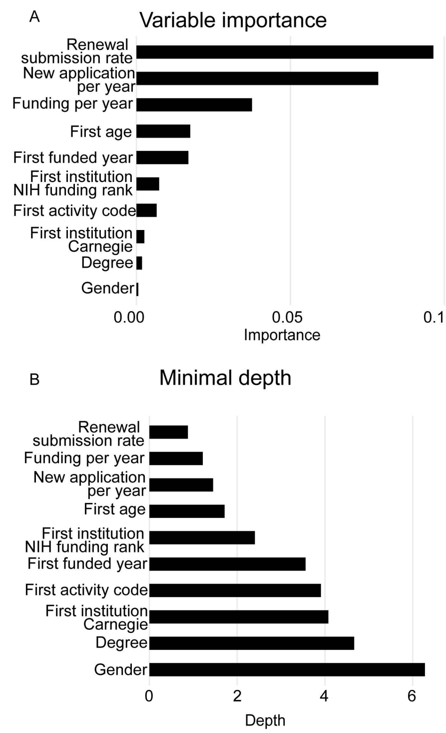

Fig. S4. Random Survival Forest algorithm used to produce a predictive, non-parametric model of survival time. Covariates: gender, degree, age at first year of funding (first age), year of first award (first funded year), first RPG type (first activity code), first institution's NIH funding rank, first institution's Carnegie classification, new project applications per year (new application per year), renewal submission rate, and funding per year. Using a model with 1000 trees resulted in a Harrell's concordance index above 0.82 (N = 31,987). (A) Variable importance (VIMP), which is a measure of how much the accuracy of the model is reduced by the removal of a variable, indicates that gender has almost no effect on accuracy (VIMP < 0.001). (B) Minimal depth (MD), which is a measure of how far on down the trees one has to go on average before a variable is used to split the data, also indicates that gender is the least useful variable in predicting survival time (MD = 6.28). The most predictive variables were renewal submission rate (VIMP = 0.10, MD = 0.88), new applications per year (VIMP = 0.08, MD = 1.45), and funding per year (VIMP = 0.04, MD = 1.22).

Table S1. Investigator characteristics by gender. Continuous variables (age) tested for significance using Wilcoxon Rank-Sum test, two-tailed. Categorical variables tested using Chi-squared test. Associated *p*-values and standardized mean difference (SMD) listed. RPG = Research Project Grant.

Covariate	Women	Men	P-Value	SMD
Cohort			<0.001	0.094
1991-1995	20.6%	23.0%		
1996-2000	22.9%	24.4%		
2001-2005	25.2%	25.2%		
2006-2010	31.4%	27.5%		
Age (mean)	42.2	41.9	<0.001	0.051
Degree			<0.001	0.264
PhD	73.7%	63.6%		
MD	14.3%	19.2%		
MDPhD	9.1%	15.4%		
All Other Degrees	3.0%	1.8%		
First RPG Mechanism			<0.001	0.049
R01	79.9%	79.7%		
R29	13.5%	12.5%		
Other	6.6%	7.7%		
First Award Institution Characteristics				
Funding Quintile			0.43	0.019
1	85.2%	84.6%		
2	9.1%	9.2%		
3-5	5.7%	6.2%		
Carnegie Classification			<0.001	0.033
Highest Research	55.9%	55.4%		
Medical Schools and Centers	12.2%	11.6%		
All Others	10.4%	10.3%		
Not in Carnegie	21.5%	22.7%		

Table S2. Gender differences in funding measures and application outcomes for full sample and matched samples. Full set includes all investigators in original analysis (N Women = 10,660; N Men = 24,110). Match 1 includes 10,212 women and 10,212 men matched on age, degree, first grant type, cohort, Carnegie classification of first institution, and NIH funding rank for first institution. Match 2 includes 9,395 women and 9,395 men matched on project renewal submission rate and first funded year. Wilcoxon Rank Sum test statistic (W) and *p*-value (two-tailed) displayed for each measure.

	Full Set				Match 1				Match 2			
Measure	**Men**	**Women**	**W**	***p***	**Men**	**Women**	**W**	***p***	**Men**	**Women**	**W**	***p***
Project awards per year	1.24	1.17	136,646,273	<0.001	1.22	1.17	54,091,121	<0.001	1.21	1.18	45,614,864	<0.001
Funding per year	$343,496	$316,628	133,016,978	<0.001	$315,904	$317,641	51,598,949	0.20	$328,029	$316,671	44,709,337	0.12
Funding per project	$282,337	$269,527	128,055,744	0.60	$264,897	$269,555	49,630,455	<0.001	$274,386	$266,761	43,706,560	0.25
Span of years funded	10.56	10.08	133,563,024	<0.001	10.26	10.23	52,305,808	0.70	10.45	10.59	43,408,985	0.05
Number of individually funded years	9.77	9.28	134,003,822	<0.001	9.49	9.40	52,511,823	0.38	9.60	9.72	43,373,768	0.04
Percentage of years funded	94.62%	94.45%	128,264,309	0.72	94.66%	94.37%	52,501,672	0.27	94.23%	94.17%	44,203,098	0.81
New project applications per year	0.45	0.38	137,514,629	<0.001	0.45	0.38	54,991,950	<0.001	0.44	0.38	46,422,131	<0.001
New project funding rate	24.67%	24.67%	67,687,328	0.19	23.76%	24.61%	27,068,346	0.13	24.51%	25.06%	23,563,138	0.23
New project score percentile	26.00	25.77	23,671,657	0.37	25.90	25.76	9,684,980	0.70	25.98	25.74	8,287,974	0.50
Renewal project submission rate	45.44%	42.45%	114,500,128	<0.001	45.80%	43.12%	46,352,691	<0.001	43.14%	43.12%	44,136,300	0.99
Renewal project funding rate	39.28%	35.98%	34,579,705	<0.001	37.86%	36.20%	13,755,797	0.01	37.91%	36.20%	12,667,565	0.01
Renewal project score percentile	23.00	23.76	8,520,363	0.01	23.05	23.77	3,556,214	0.03	23.22	23.77	3,167,903	0.09