Female Authorship in Preclinical Cardiovascular Research
Temporal Trends and Influence on Experimental Design

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HIGHLIGHTS
- In this analysis of 3,396 preclinical studies published in 5 leading cardiovascular journals over a 10-year period, women accounted for 24 ± 17% of authors per manuscript.
- Female authorship is increasing in preclinical cardiovascular science, but the proportions of articles with first and senior authors of different sex have remained unchanged, which suggests that segregation by sex in mentorship relationships exists and persists.
- In preclinical studies that reported the sex of the animals used, female authorship was positively associated with studying female animals, using animals of both sexes, and reporting sex-specific results, which are findings that persisted in adjusted and sensitivity analyses.
- Author sex was not associated with other measures of methodological rigor or with 60-month citation counts.

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In this analysis of 3,396 preclinical cardiovascular studies, women were first, senior, and both first and senior authors in 41.3%, 20.7%, and 11.0% of the studies, respectively. Female authorship increased over a 10-year period. However, the proportion of studies with first and senior authors of differing sex was low and stable, suggesting that segregation by sex in mentorship relationships exists and persists. Female authors were more likely to consider sex as a biological variable, but author sex was not associated with other measures of experimental rigor or research impact, indicating that women’s underrepresentation was not due to differences in research capacity or impact. (J Am Coll Cardiol Basic Trans Science 2019;4:471–7) © 2019 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

**METHODS**

As described (10), all preclinical studies published between July 2006 and June 2016 in *Circulation; Circulation Research; Hypertension; Stroke; and Arteriosclerosis, Thrombosis, and Vascular Biology* were reviewed. Studies were included if they reported original data from in vivo experiments using nonhuman mammals and proposed therapeutic applications or implications to specific human disorders. Pre-specified variables collected included the disease studied, the animal model(s) used and their sex, and whether any study result was reported by sex. Because of the possibility that differences in female animal inclusion or sex-specific analyses might be attributable to broader differences in experimental design, we also analyzed whether animals were randomized, whether blinding was used (concealed allocation or...
blinded outcome assessment), and whether sample size and/or power estimations were performed.

Study author names were extracted from Scopus. Author sex was determined using the online database genderize.io, which included >216,000 first names across 79 countries and 89 languages when queried. The database determines the sex of a name with an associated certainty factor. First authors are generally considered to have executed most of the published work, whereas senior authors are usually the study supervisors or principal investigators, and are generally considered to have contributed most to study planning and design (11,12); therefore, these were selected as our primary analyses. Female authorship as a proportion of all authors per manuscript was examined as a secondary analysis (per 10% increase and dichotomized as ≥33% of authors). Scopus was also queried to determine citation counts at 60 months for articles published between July 2006 and June 2011, as described (10). Post hoc analyses of mentorship relationships by sex were performed, with senior authors designated as mentors and first authors as mentees. A certainty factor of ≥70% was used to assign author sex for all analyses, otherwise sex was considered unknown. Articles with authors of unknown sex were excluded in primary analyses but were included in secondary and post hoc analyses to minimize missing data. Sensitivity analyses using a certainty factor of ≥90% for author sex and of sex-specific reporting restricted to studies in which animals of both sexes were used were performed.

Categorical variables are reported as number (percentage) and were compared using chi-square tests. Continuous variables are reported as mean ± SD or median with interquartile range (25th to 75th percentiles) (IQR) and were compared using Student’s t-tests or Mann-Whitney U tests, respectively. Temporal trends were assessed using Cochran-Armitage tests or Spearman’s rank-order correlation (r) using 12-month intervals. The associations of author sex with factoring sex of the animals studied in the reporting, design, and analysis of experiments and with the implementation of other study design elements were examined using chi-square tests (reported as absolute percent differences in study characteristics) and via simple and multivariable logistic regression (reported as odds ratios [ORs] with 95% confidence intervals [CIs]). Citation count comparisons were performed via stratification and multivariable linear regression. All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina) using a 2-tailed z level of 0.05 (corrected using the Bonferroni method to account for multiple comparisons when specified).

RESULTS

Of 28,636 articles screened, 3,396 met the study inclusion criteria (Figure 1). Women accounted for 24 ± 17% of authors per manuscript, with 542 articles (16.0%) not including any female authors and none being authored solely by women. After excluding articles with authors of unknown sex, women were identified as first authors of 1,016 of 2,458 articles, senior authors of 569 of 2,749 articles, and both first and senior authors of 235 of 2,135 preclinical studies (41.3%, 20.7%, and 11.0%, respectively). The distribution of observed mentorship relationships differed from the expected distribution, with disproportionately high numbers of same-sex mentorships identified (p < 0.001), including a relative 50% greater than expected frequency of male to male mentorships. No difference was observed in the number of coauthors of articles with female versus male first or senior authors (9.6 vs. 9.6; p = 0.864; and 9.2 vs. 9.5; p = 0.075; respectively). Five-year citation counts were comparable between female and male authors (21 [interquartile range (IQR): 13 to 31] vs. 20 [IQR: 12 to 33]; p = 0.509 for first authors; 18 [IQR: 12 to 30] vs. 20 [IQR: 13 to 31]; p = 0.170 for senior authors). Author sex was similarly not predictive of citation counts in multivariable models that adjusted for cardiovascular disease studied, publication date, and journal.

Temporal analyses over 10 years indicate that the proportions of female first and senior authors each increased, with women accounting for between 32.3% and 46.3% of first authors and between 11.8% and 26.1% of senior authors (Figure 2A). There was a corresponding temporal increase in the proportion of manuscripts with women as both first and senior authors (full range: 5.5% to 14.9%; P_trend = 0.001). The proportions of articles with first and senior authors of differing sex did not change (full range: 28.5% to 34.3%; P_trend = 0.663 for female first and male senior authorship; full range: 5.5% to 14.9%; P_trend = 0.184 for male first and female senior authorship). Per article, the mean proportion of female authors slightly increased (full range: 21.4% to 26.8%; p < 0.001) (Figure 2B).

Female and male authors were equally likely to report the sex of animals used in preclinical experiments (815 of 1,016 [80.2%] vs. 1,150 of 1,442 [79.8%]; p = 0.776 for first authors; 455 of 569 [80.0%] vs. 1,767 of 2,180 [81.1%]; p = 0.556 for senior authors). However, when the sex of the animals was reported, women were more likely to have used female animals in their experiments (292 of 815 [35.8%] vs. 313 of 1,150 [27.2%], p < 0.001 for first authors; 181 of 455 [39.8%] vs. 492 of 1,767 [27.8%], p < 0.001 for senior authors).
authors), to have used animals of both sexes (156 of 815 [19.1%] vs. 179 of 1,150 [15.6%]; p = 0.038 for first authors; 98 of 455 [21.5%] vs. 262 of 1,767 [14.8%]; p < 0.001 for senior authors), and to have reported sex-specific results (326 of 815 [40.0%] vs. 380 of 1,150 [33.0%]; p = 0.002 for first authors; 199 of 455 [43.7%] vs. 597 of 1,767 [33.8%]; p < 0.001 for senior authors). Similar findings were observed when female authorship was examined as a proportion of all authors per manuscript. In contrast, female authorship was not associated with randomization, blinding, or sample size estimation after correcting for multiple

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**FIGURE 1** Literature Search

- 28,636 articles screened
- 9,579 articles screened in *Circulation*
- 3,875 articles screened in *Circ Res*
- 4,407 articles screened in *Hypertension*
- 6,949 articles screened in *Stroke*
- 3,826 articles screened in *ATVB*
- 672 studies included from *Circulation*
- 486 studies included from *Circ Res*
- 860 studies included from *Hypertension*
- 501 studies included from *Stroke*
- 877 studies included from *ATVB*
- 3,396 studies analyzed

Literature search, ATVB = Arteriosclerosis, Thrombosis and Vascular Biology; Circ Res = Circulation Research. Modified from Ramirez et al. (10).

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**FIGURE 2** Female Authorship in Preclinical Cardiovascular Research

(A) Proportion of women as first and senior authors. (B) Mean proportion of women as authors per study. Error bars depict SD.
comparisons (Figure 3). The preceding differences persisted when female authorship was examined on an interval scale (per 10% increase) and after adjusting for pre-specified potential confounders (Table 1). All findings were also comparable in sensitivity analyses using a minimum certainty factor of 90% for author sex. When restricted to studies that included both male and female animals (N = 335 to 421), female senior authorship (but not first or cumulative authorship) remained associated with reporting sex-specific results after adjusting for pre-specified potential confounders (OR: 2.2; 95% CI: 1.1 to 4.4; p = 0.036).

**DISCUSSION**

Sex differences in innate scientific ability have long ago been refuted (13); however, career trajectories and personal and professional experiences often differ between male and female academics (8,13), which may influence researchers’ priorities and practices. Although there are clear societal benefits to promoting sex inclusivity in research, its impact on the quality and impact of research remains unexplored (9). Our analysis of preclinical cardiovascular research demonstrates that: 1) approximately 41% of first authors and 21% of senior authors over a recent 10-year period were women; 2) although female authorship is increasing, segregation by sex in mentorship relationships exists and persists; and 3) when women influence experimental design and reporting or are a larger proportion of the research team, studies are more likely to include female animals and to explore sex-based differences, but author sex is not associated with other measures of methodological rigor or research impact.

Preclinical research using animal models often precedes and informs clinical trials. However, important and remediable methodological shortcomings remain prevalent in preclinical cardiovascular research (10), including a tendency to exclude females in animal experiments and to ignore the potential influence of sex on study outcomes (1). Women’s perspectives have been suggested to uniquely promote scientific progress in general and advances in women’s health in particular, in part due to their greater tendency to explore the effects of gender and sex (5,6). Our data suggest that women are indeed more attuned to considering sex as a biological variable in preclinical experiments, but that male and female researchers are more alike than they are different when broader measures of scientific rigor and research impact are considered.

A corollary to the previously described findings is that the persistent underrepresentation of women in preclinical cardiovascular research is highly unlikely to be attributable to differences in research capacity or potential impact. Rather, systemic factors are probably influential. For instance, although modern scientific endeavors are increasingly reliant on research teams and networks—settings in which a diversity of viewpoints and experiences are sought...
and valued (6)—our analysis highlights a persistent predominance of same-sex mentorships. Because of the relative paucity of available female mentors, this practice has the potential to perpetuate women’s underrepresentation in the field and to hinder efforts to improve the status quo (7).

**STUDY LIMITATIONS.** The journals examined were selected based on their prominence in cardiovascular research, their collective focus on a wide range of cardiovascular disorders, and their endorsement of NIH guidelines on rigor and reproducibility (10). However, they might not be representative of all preclinical cardiovascular journals. Author sex was determined using an arbitrary certainty factor, which might have resulted in misclassification in a minority of cases. However, our results were comparable in sensitivity analyses using a more stringent criterion. Our analysis did not capture instances of multiple first or corresponding authors (equally contributing authors) and used author position as a proxy for mentor–mentee relationships. Presumed author sex might not reflect author gender, which might be a relevant distinction in our analysis. Our analysis also focused on experimental and reporting standards proposed by the NIH, which were not exhaustive.

**CONCLUSIONS**

Women’s involvement in preclinical cardiovascular research is positively associated with considering sex as a biological variable, which is a practice that is expected to inform and promote advances in women’s health. Researcher sex is not associated with other measures of experimental rigor or research impact. Limited mentorship opportunities may be contributing to women’s underrepresentation in this field.

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**TABLE 1** Association Between Female Authorship and Experimental Design Characteristics in Preclinical Cardiovascular Studies

|                                | N  | Crude OR (95% CI) | Adjusted OR (95% CI) | p Value† |
|--------------------------------|----|-------------------|----------------------|---------|
| **Female first author**        |    |                   |                      |         |
| Reporting sex of animals       | 2,458 | 1.03 (0.84-1.26) | 0.96 (0.77-1.19)     | 0.698   |
| Inclusion of female animals‡   | 1,965 | 1.49 (1.23-1.81) | 1.60 (1.30-1.96)     | <0.001  |
| Inclusion of animals of both sexes‡ | 1,965 | 1.28 (1.01-1.63) | 1.29 (1.01-1.66)     | 0.046   |
| Sex-specific reporting of results‡ | 1,965 | 1.35 (1.12-1.63) | 1.33 (1.10-1.62)     | 0.004   |
| Randomization                  | 2,458 | 0.95 (0.78-1.16) | 1.03 (0.83-1.28)     | 0.776   |
| Blinding                       | 2,458 | 0.91 (0.76-1.08) | 0.95 (0.79-1.15)     | 0.608   |
| Sample size estimation         | 2,458 | 0.70 (0.41-1.20) | NR                   |         |
| **Female senior author**       |    |                   |                      |         |
| Reporting sex of animals       | 2,749 | 0.93 (0.74-1.18) | 0.83 (0.65-1.07)     | 0.153   |
| Inclusion of female animals‡   | 2,222 | 1.71 (1.38-2.12) | 1.81 (1.43-2.28)     | <0.001  |
| Inclusion of animals of both sexes‡ | 2,222 | 1.58 (1.22-2.04) | 1.58 (1.20-2.08)     | 0.001   |
| Sex-specific reporting of results‡ | 2,222 | 1.52 (1.24-1.88) | 1.44 (1.16-1.79)     | 0.001   |
| Randomization                  | 2,749 | 0.90 (0.71-1.12) | 0.88 (0.68-1.13)     | 0.308   |
| Blinding                       | 2,749 | 1.02 (0.84-1.23) | 1.14 (0.92-1.42)     | 0.219   |
| Sample size estimation         | 2,749 | 0.32 (0.13-0.80) | NR                   |         |
| **Female authorship (per 10% increase)** |                   |                      |         |
| Reporting sex of animals       | 3,396 | 1.04 (0.98-1.09) | 1.02 (0.97-1.09)     | 0.435   |
| Inclusion of female animals‡   | 2,718 | 1.20 (1.14-1.26) | 1.20 (1.13-1.26)     | <0.001  |
| Inclusion of animals of both sexes‡ | 2,718 | 1.13 (1.07-1.21) | 1.12 (1.05-1.20)     | <0.001  |
| Sex-specific reporting of results‡ | 2,718 | 1.13 (1.08-1.19) | 1.11 (1.05-1.17)     | <0.001  |
| Randomization                  | 3,396 | 0.95 (0.90-1.00) | 1.00 (0.94-1.06)     | 0.949   |
| Blinding                       | 3,396 | 0.99 (0.94-1.03) | 1.04 (0.99-1.09)     | 0.173   |
| Sample size estimation         | 3,396 | 1.08 (0.94-1.24) | NR                   |         |

*Refers to the total number of studies included in analyses. †Adjusted for disease studied, animal model(s) used, journal of publication, date of publication, and number of co-authors. ‡Analysis restricted to studies in which the sex of animals used was reported. Bonferroni corrected a level of 0.007 used to define statistical significance (α = 0.05 divided by 7). CI = confidence interval; NR = not reported due to small number of events per predictor variable; OR = odds ratio.
PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In this analysis of 3,396 preclinical studies in 5 leading cardiovascular journals, female authorship was positively associated with considering sex as a biological variable, but not with other measures of methodological rigor or 60-month citation counts. Over a 10-year period, the proportion of studies with first and senior authors of differing sex was low and stable, suggesting that segregation by sex in mentorship relationships exists and persists. These data indicate that women’s underrepresentation in preclinical cardiovascular research is not due to differences in research capacity or impact. Limited mentorship opportunities for women in preclinical cardiovascular research may be an important contributor.

TRANSLATIONAL OUTLOOK: Further study to identify and understand barriers to women’s involvement in preclinical cardiovascular research is warranted. Enhancing mentorship opportunities for women should be explored as a potential strategy to improve the status quo.

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