





















RESEARCH LETTER

Who Are We Missing? Reporting of Transgender and Gender-Expansive Populations in Clinical Trials

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Transgender and gender-expansive individuals are a growing segment of the population and have elevated risks of certain cardiac conditions, such as myocardial infarction and venous thromboembolism.¹ However, few large cardiovascular clinical trials have studied or reported clinical outcome data explicitly regarding this patient population. In this research letter, we characterized the reporting and language used for transgender and gender-expansive populations in cardiovascular randomized clinical trials.

We did a systematic review of randomized clinical trials across 4 cardiovascular areas (coronary artery disease, hypertension, atrial fibrillation, and diabetes) using [ClinicalTrials.gov](https://clinicaltrials.gov), which included 79 recently completed (2018–2022) interventional studies in the United States with published results for each area. Our research was exempted from the Stanford University Institutional Review Board approval, and no informed consent was required.

A total of 451 807 participants were included ([Table](#)). We collected reporting of populations for sex and gender descriptions, as well as the inclusion and exclusion criteria. Almost all studies reported sex or gender as a single outcome variable. We inferred this to denote sex

unless it was specified otherwise. All studies reported sex, with women representing 42% of all participants. Women represented the minority of study participants in coronary artery disease (30%), atrial fibrillation (42%), and diabetes (48%) clinical trials, but the majority of participants in hypertension trials (67%). Gender identity, including the option *other*, was reported in only 1 trial (<1%). No studies reported data regarding transgender or gender-expansive identification. Several trials included *pregnant women* and *lactating women* as exclusion criteria, as well as *man* and *woman* as inclusion criteria. Our complete findings are available from the corresponding author upon request.

Our findings confirm that there is a lack of commitment in current cardiovascular randomized clinical trials to the Sex and Gender Equity in Research guidelines,² and the Measuring Sex, Gender Identity, and Sexual Orientation Report.³ These guidelines and report describe how to record and report sex and gender identification systematically within clinical research.

Furthermore, the National Institutes of Health has defined the difference between sex, “the biological differences between females and males, including chromosomes, sex organs, and endogenous hormonal

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Table. Gender Diversity by Clinical Trial Subtype

	Atrial fibrillation	Coronary artery disease	Hypertension	Diabetes	Total
Trials, n	20	20	20	19	79
Trials reporting sex, n (%)	20 (100)	20 (100)	20 (100)	19 (100)	79 (100)
Total participants, n	424 923*	11 934	2736	12 214	451 807*
Men, n (%)	242 207 (57)	8312 (70)	904 (33)	6410 (52)	257 833 (57)
Women, n (%)	179 206 (42)	3622 (30)	1832 (67)	5804 (48)	190 464 (42)
Reporting gender, n (%)	1 (5)	0	0	0	1 (1)

*N=3510 are included *other and nonreport* category.

profiles, and is typically assigned at birth,” and gender, “socially constructed and enacted roles and behaviors which occur in a historical and cultural context and vary across societies and over time.¹⁴ We found that the distinction between sex and gender was almost nonexistent when it came to reporting participants within these randomized clinical trials, with many studies misreporting sex as gender. We emphasize Sex and Gender Equity in Research’s recommendation that “authors should avoid confusing sex with gender and reducing complex or interactionist explanations to overly simple ones.” We encourage modification of the National Institutes of Health reporting guidelines to similarly require both gender and sex in reporting for human subject research.

Even when studies are not powered to detect statistical differences for gender-diverse populations, researchers and authors should consider the implication of how they summarize all populations, as clinical recommendations and guidelines are frequently extrapolated incorrectly toward minoritized groups. Additionally, we strongly recommend welcoming transgender and gender-expansive individuals into trials by replacing the category *other* with *transgender woman/transfeminine, transgender man/transmasculine, non-binary person, and prefer to self-describe* or another option that invites individuals to participate, instead of immediately *othering* them.⁵

In summary, transgender and gender-expansive individuals are not currently reported in almost all current cardiovascular clinical trials, despite being vulnerable populations with additional cardiovascular risk. Without careful collection of gender identity data, we will never fully understand the depth and breadth of disparities in this population. Recent national guidelines have called for full reporting of gender and appropriate usage of

gender-inclusive language in randomized clinical trials. Future cardiology trials should abide by the Sex and Gender Equity in Research guidelines and other expert recommendations to better represent and care for these populations.

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