

Getting to the heart of it: sex and gender considerations in the management of cardiovascular disease



Nabilah Gulamhusein^{a,b} and Sofia B. Ahmed^{a,c,d,*}

^aCumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

^bLibin Cardiovascular Institute, University of Calgary, Calgary, Alberta, Canada

^cFaculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

^dWomen and Children's Health Research Institute, University of Alberta, Edmonton, Alberta, Canada



How important are sex and gender factors in studies informing management of cardiovascular disease, the leading global cause of death? Overall, rates of cardiovascular disease are decreasing, suggesting research informing current treatment practices is serving populations with and at risk of cardiovascular disease well. However, mounting evidence has highlighted the widening disparities in cardiovascular morbidity and mortality between groups who are represented in study populations and those who are not. For example, acute myocardial infarction hospitalisations increased in individuals under 55 years of age relative to older persons, and this increase was most pronounced among young women.¹ Similarly, individuals of minoritised gender identity and sexual orientation experience disproportionate cardiovascular burden compared to their cis-gender and heterosexual peers.² Other gender factors, including caregiving obligations and primary responsibility for household domestic duties, are associated with cardiovascular risk.³ Amidst the growing awareness that sex and gender considerations impact the etiology, prevalence, manifestation, and treatment of cardiovascular disease, how well are sex and gender incorporated into contemporary clinical cardiovascular guidelines?

In this issue of *The Lancet Regional Health—Europe*, Bastian-Pétrél⁴ and colleagues aimed to analyse publications cited in the 2019 European Society of Cardiology (ESC) guideline recommendations on chronic coronary syndromes for sex- and gender-related biases. They found that among the twenty ESC recommendations, none were gender-specific and only one in five contained sex-related statements. Of the 108 articles published between 1991 and 2019 informing these recommendations, only three considered sex and none considered gender in the study design or analysis, and the term “gender” was exclusively and erroneously used to denote “sex”. Women represented just over a quarter of study participants; interestingly, higher numbers of

women study participants were observed in publications where the first or senior authors were women.

This work by Bastian-Pétrél and colleagues adds to the abundance of data for the urgent need to shift away from the “one size fits all approach” in the diagnosis and management of cardiovascular disease. In alignment with their observations, a recent report highlighted that anti-hypertensive medication literature informing international hypertension guidelines rarely incorporated sex and gender-based reporting and analysis.⁵ Others have described that inadequate enrollment and reporting by sex or gender impeded the implementation of sex- or gender-specific guideline recommendations on the management of ST-segment-elevation myocardial infarction.⁶

The observation of a lack of women representation in study populations informing guideline recommendations, and the positive association between having a woman as first or senior author and higher women enrollment deserves further mention. Others have reported similar findings from preclinical to population health research,⁷ and frameworks have been developed to diversify cardiovascular research collaborations and outputs.⁸ As outlined by the authors, ensuring an appropriate population to prevalence ratio in cardiovascular trials is warranted; we also suggest that simply adding more women to the study population may not be sufficient. Female sex-specific (e.g., reproductive, pregnancy, menopausal) and female sex-predominant (e.g., depression, autoimmune disease, breast cancer therapies) factors impact cardiovascular health⁹ and should be considered in recruitment, data collection, analysis, and reporting of results.¹⁰ Similarly, accounting for important gender factors such as identity, roles, relations, and institutionalised gender in research would ultimately allow for greater precision in recommendations around cardiovascular care, resulting in optimisation of health outcomes for all.

Going forward, intentional use of appropriate sex and gender terminology to foster rigour and reproducibility in cardiovascular (and all) health research is critical. As reported in the present study, sex and gender terms are commonly conflated, leading to uncertainty as to the generalisability of results. Sex refers to biological attributes, while gender refers to social constructs. The implementation of mandates to incorporate sex and gender considerations into research from funders, governments, and journals, coupled with the Sex and

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*Corresponding author. 11-135 Clinical Sciences Building, 11220 83 Ave NW Edmonton, Alberta, T6G 2B7, Canada.

E-mail address: sofia.ahmed@albertahealthservices.ca (S.B. Ahmed).

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Gender Equity in Research guidelines should facilitate this work, and it is time for the research community to fully adopt this framework to ultimately reduce the overall burden of cardiovascular disease.

And so, in response to our initial question—how important are sex and gender factors in cardiovascular disease research informing guideline recommendations?—the answer is obvious. However, the more pressing question is: *are* sex and gender factors considered in the management of cardiovascular disease? Bastian-Pétre and colleagues provide us with yet another example of how much work remains to be done. There is copious evidence for the urgent need to move away from our current uniform approach in the diagnosis and management of cardiovascular disease. Let us get to the heart of it: it is time for a change.

Contributors

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Declaration of interests

No authors declare any conflicts of interest related to the submitted work.

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