Editorial

Sex and gender bias in medical research: A barrier to equitable patient care

Samantha Fisher, BSc (Hons)[1]

1. Faculty of Medicine, Memorial University, St. John's, NL, Canada

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Sex and gender influence nearly every aspect of life. Yet many systems, standards, and everyday experiences are designed with the biological male as the default. Standard office temperatures are set to male metabolic rates, crash test dummies are modelled on male physiques, and even language often treats the masculine as the universal norm.[1] These examples illustrate the 'masculine default' – a cultural bias that centers male experiences as the norm, rendering women and gender-diverse individuals invisible or secondary.[2] Unfortunately, medicine, a field that fundamentally impacts human health and well-being, is no exception. From its historical roots to modern day, medical research has been grounded in a male-centric framework,[3] leaving critical gaps in our understanding of women's health. This paper explores how sex and gender bias persist in medical research and examines the downstream effects on patient care and health outcomes.

Before further discussion, I would like to acknowledge that sex and gender are distinct concepts: sex refers to an individual's biological characteristics, such as chromosomes, hormones, and reproductive anatomy, whereas gender is a societal construct that relates to one's identity and expression, which can vary widely across individuals and cultures. Both sex and gender play important roles in medical research and patient care. While not all individuals assigned female at birth identify as women, the literature cited here uses "female" and "women," and this editorial aligns with that terminology.

Historically, females were excluded from medical research. Clinical studies were conducted predominantly on male subjects, with findings generalized to the entire population without accounting for sex-specific physiology.[4] Several factors have been proposed to explain this disparity, including the perceived complexity of accounting for hormonal fluctuations,[5–7] concerns over fertility or pregnancy risks,[8] and systemic bias in male-dominated research and funding bodies.[9,10] The assumption that the male body represented the human "norm" further reinforced this exclusion.[7,11]

Assuming that male-derived data can be universally applied to women poses serious implications for patient care. Firstly, many diseases have sex-based presentations, with cardiovascular disease being a prime example. Women experiencing acute coronary syndrome are more likely to present with symptoms often labelled as "atypical" – including nausea, vomiting, and shortness of breath – rather than the "classic" chest pain described in men, leading to misdiagnosis and delays in treatment.[12,13] Medication efficacy also differs by sex. The Physicians' Health Study, conducted exclusively in men, found that aspirin significantly reduced myocardial infarction (MI) risk,[14] shaping its widespread use for primary and secondary prevention. However, the Women's Health Study revealed a different benefit profile: aspirin had no significant effect on MI primary prevention in women but significantly reduced the risk of stroke and ischemic stroke,[15] a benefit not observed in men.[16] These findings underscore that sex-specific medication responses can be substantial, and failing to recognize these differences risks suboptimal care for women with cardiovascular disease. Finally, drug metabolism and clearance also differ by sex. Women often have higher blood drug concentrations and slower elimination times when given standard doses, increasing the risk of adverse drug reactions.[17] For example, systemic clearance of the anticoagulant lepirudin is 25% lower in women,[18] remaining detectable in circulation for up to 48 hours in women compared to 2 hours in men, greatly increasing bleeding.[19] These findings suggest that current dosing practices may routinely overmedicate women, placing them at unnecessary and preventable risk.

While the inclusion of female participants in medical research has improved,[20–23] underrepresentation persists.[24] Even when women are included, sex-specific analysis is often lacking.[11,17,25] Zucker et al. found that fewer than half of the studies including both sexes accounted for sex in study design or data analysis.[17] Similarly, Welch et al. reported that in a review of randomized controlled trials in Canada, none accounted for the influence of sex, and only 6% performed sex-specific analyses.[26] This lack of sex-based analysis is deeply problematic, as it risks overlooking sex differences that could significantly affect health outcomes for women.

These sex disparities extend to clinical practice guidelines. A 2017 Canadian systematic review found only 35% of guidelines reported screening, diagnosis, or management considerations specific to sex or gender.[27] Even when sex differences were noted, clinical implications were often absent.[27] For example, Canadian Diabetes Association guidelines reported sex differences in response to type 2 diabetes medication in children and adolescents but did not recommend distinct treatments.[28] Guidelines translate research into clinical practice,[27] and omitting sex differences risks one-size-fits-all recommendations that fail to serve all patients.

To address sex and gender disparities in medicine, integrating sex- and gender-based medicine (SGBM) into the medical curriculum is essential. SGBM acknowledges differences in disease diagnosis, treatment, and prognosis between men and women.[29] Educating future physicians on these differences allows them to personalize treatment and reduce disparities in care. Teaching SGBM is therefore fundamental – not only to improve clinical decision-making but to foster equitable, evidence-based therapies that respect the distinct physiology and pathophysiology of all patients.[30,31]

Despite this, SGBM remains poorly represented in medical education. A survey of Canadian and U.S. medical schools found that 70% had no formal sex- or gender-specific content integrated into their curricula.[32] At Yale School of Medicine, only 8% of pre-clerkship lectures and workshops discussed the influence of sex and gender on human physiology and pathophysiology.[33] This lack of integration is not unique to North America. A study in Switzerland found medical students perceived inadequate SGBM integration into lectures and exams and expressed a desire for more.[34] Similarly, a survey of physicians in Israel reported low-to-moderate exposure during training and strong support for greater integration.[35] As Mattioli et al. said, "Teaching gender and sex differences is fundamental in medical classes because it has a strong impact in reducing disparity in treatment, in defining effective and personalized therapies that respect the different physiology and pathophysiology of women."[36] Without formal education, future physicians remain ill-equipped to identify sex- and gender- specific differences, perpetuating inequities in medical care.

In conclusion, progress has been made, but significant gaps remain. Canada has taken meaningful steps towards the integration of sex and gender into health research, as demonstrated by the Canadian Institutes of Health Research (CIHR)'s 2021 Sex and Gender-Based Analysis Plan (SGBA), which mandates sex and gender considerations in study design and practice for funded research.[37] However, enforcement remains inconsistent, leaving significant gaps in achieving equity in research and patient care. To close these gaps, action must be taken. Physicians should critically evaluate the origins of clinical guidelines, assess their applicability to specific patient populations, integrate sex-based analysis into research study designs, and advocate for the inclusion of women and underserved populations in medical research. Achieving a more equitable healthcare system will depend on the next generation of physicians taking responsibility for driving this change.

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