Let’s Talk About Sex…and Gender!

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In recent years, there has been an increasing emphasis on women’s cardiovascular health as evidenced by movements of the American Heart Association “Go Red for Women” campaign and other public health efforts to better prevent and treat heart disease in women. Funding agencies, such as the Canadian Institutes of Health Research and National Institutes of Health, call for incorporating sex and gender in the study and reporting of study results. Though these efforts are commendable, there is one major language hurdle that needs to be overcome. Sex and gender are not synonymous.

There seems to be great confusion about how these terms are used let alone how they are measured and understood. Most often the word gender is used to mean sex. This lack of clarity results in missed opportunities to understand and improve cardiovascular health in both men and women.

Sex is a biological construct whereby an individual is defined as being a man or woman according to anatomy (eg, reproductive/sexual anatomy), physiology (hormone levels and function), and genetics (chromosomes and gene expression). Gender, on the contrary, is a psychosocial construct and has a wider scope incorporating the effects of social norms and expectations, roles, behaviors, expressions, and identities of women, men, boys, and gender-diverse people in a given society.

There is no consensus about the terminology which should be used to differentiate sex and gender; however, applying the terms masculine and feminine to represent gender-related characteristics, rather than man/woman or male/female, help distinguish sex from gender-related factors. The Women’s Health Research Network of the Canadian Institutes of Health Research has developed a conceptual framework for understanding gender and is represented by 4 main features: gender roles (eg, child care, housework), gender identity (eg, personality traits such as being sensitive to the needs of others or having leadership abilities), gender relations (eg, social support), and institutionalized gender (eg, career opportunities, personal income, educational background).

Given that gender is a concept that is neither simple to define nor to measure, the operationalization of gender in health research has largely been neglected. Thinking around gender and the measurement of this concept has evolved over time. However, measurement of gender has often focused on personality traits and largely neglected how components of gender (eg, roles, expectations) can vary throughout time, or according to age and culture. Despite the complexity of teasing apart sex from gender, there have been several attempts to differentiate between the constructs. Although these studies represent an important first step in highlighting the differences between sex and gender, there remains the need for a more cohesive and systematic method of measuring gender. In response, Pelletier et al constructed a method to score gender in a recent prospective cohort study, Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond-Premature Acute Coronary Syndrome (GENESIS-PRAXY) of young (<55 years old) acute coronary syndrome patients. Using the framework established by the Canadian Institutes of Health Research Women’s Health Research Network and collected data on gender-related factors (eg, level of responsibility for caring for children), the authors conducted principal component analysis (to determine coefficient estimates for each gender component) followed by logistic regression with sex as the dependent variable to construct a gender index. The gender score is represented on a continuum scored from 0 to 100, where lower scores represent masculine characteristics and higher scores represent feminine characteristics.

Results from the GENESIS-PRAXY study using the gender index showed that, regardless of sex, a higher feminine gender score was associated with traditional (eg, hypertension, diabetes mellitus) and nontraditional (eg, anxiety, depression) risk factors for cardiovascular disease. A 12-month follow-up in the same cohort also showed that those who identified as feminine gender were also at increased risk of recurrent acute coronary syndrome, regardless of whether they were men or women. Thus, personality traits and gender roles typically attributed to women and recognized as feminine are positively associated with cardiovascular risk and outcomes in both men and women.

Clearly, there is a distinct impact of sex and gender on the health of both men and women. Accordingly, sex differences in health have become a necessary focus of recent research, with important topics, such as sex-specific drug response and adverse effects, as well as sex-specific risk factors, such as pregnancy complications and menopause, being addressed. However, there lacks an observed corresponding increase in research that focuses on gender, as a distinct construct from
sex, and the impact of gender on health. Highlighting the importance of this knowledge gap, the Canadian Institutes of Health Research Institute of Gender and Health provides an online training seminar\(^7\) and casebook\(^8\) for researchers to learn about sex and gender and explore how to incorporate these variables in all fields of health. The National Institutes of Health has also provided researchers with an infographic to help understand how sex and gender can affect health.\(^9\)

Thus, substantial opportunities now exist to incorporate both sex and gender in cardiovascular disease research, including clinical interventions. One critical area of inquiry is to better understand the impact of both sex and gender in determining risk of major adverse cardiovascular events and death, functional impairment (eg, activities of daily living, return to work, etc.), as well as quality of life and overall well-being. Sex and gender should also be specifically considered in diagnosis and treatment of cardiovascular disease (eg, sex-specific cut-offs), as well as in drug and device development. The inclination toward personalized medicine effectively calls for researchers to examine how women respond to medications in comparison to men. The same is true for imaging studies and nonpharmacological therapies. Of course, in terms of pathophysiology, sex-dependent mechanisms are of significant importance. However, it is equally important to understand how gender can modulate these physiological pathways.

The integration of a gender-based framework in health research is considered to be a much needed and long-awaited development.\(^4\) To ensure the inclusion of women and subgroups of women, funding agencies need to continue promoting research specifically focused on sex- and gender-related outcomes. Also, journals should require and enforce measures to ensure women are equally included in research and, where appropriate, that gender is considered. Both editors and reviewers alike should ensure proper application of the terms sex and gender as defined as biological and psychosocial concepts, respectively. These steps would help emphasize the importance of sex and gender as essential factors pertaining to cardiovascular research. Perhaps, most importantly, researchers can make strides at the outset of planning a project and make sure to talk about sex... and gender!

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