Words Matter Sex and Gender as Unique Variables in Research



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Sex and gender are not equivalent concepts, even though these 2 variables are often used interchangeably by researchers. The precise use of variables is critical to ensure that research and theoretical work is of the highest quality. This article defines sex and gender and the importance of recognizing both of these variables as being unique and then demonstrates the benefit of measuring both of these variables using the cardiovascular disease literature as an exemplar. Additionally, recommendations for scholars regarding the use of sex and gender in the research and theoretical literature are provided. **Key words:** *cardiovascular diseases, female, gender, male, nursing research, nursing theory, research design, sex, transgender, variables*

T O ACHIEVE high levels of credibility, dependability, transferability, validity, and reliability in research, it is important that researchers pay close attention to the variables and phenomena that they are exploring or measuring.¹ Researchers must operationalize or measure these variables and phenomena accurately. After all, one of the most fundamental steps of designing a research study is developing a research question or hypotheses and then making clear what variables will be considered within the study.² If researchers do not accurately define and apply variables or concepts within a study, the conclusions

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drawn may be flawed. Moreover, as scholars build and refine theories, they must carefully define concepts included within these theories, in order to ensure that the theories will accurately function to describe, explain, or predict phenomena.³ The purpose of this article is twofold: (*a*) to define sex and gender and the general importance of recognizing both of these variables as being unique and (b) to provide recommendations to scholars regarding the use of sex and gender in the research and theoretical literature. The cardiovascular disease literature is used as an exemplar to demonstrate the benefit of considering both sex and gender.

Two variables that are often confused and used incorrectly in the research and theoretical literature are sex and gender. It is not uncommon for researchers to substitute the term gender for the term sex.⁴ Moreover, researchers tend to use sex and gender as proxies for each another.⁵ However, sex and gender are not equivalent concepts.⁶ Researchers may feel that the term gender is "softer" and less taboo than the term sex.

While scholars may use the term gender in a given article, many times they are actually operationalizing this variable more like sex and are ignoring the sociocultural dimensions central to the construct of gender.⁷

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Statements of Significance

What is known or assumed to be true, about this topic:

It is imperative that scholars use variables and concepts correctly when conducting research or developing theory. While the terms are not interchangeable, sex and gender are often used incorrectly in the research and theoretical literature. Some confusion exists as to the differences between sex and gender and how scholars should use and interpret these terms.

What this article adds:

This article defines sex and gender and then explores why it is important to recognize both sex and gender as unique variables, in the context of the cardiovascular research literature. Additionally, recommendations for scholars to integrate the variables sex and gender precisely are provided to help facilitate highquality research and theory development.

Additionally, researchers do not often make clear their rationale for using the variables sex or gender in a study.^{7,8} In fact, at the turn of the century, the Institute of Medicine (IOM)⁶ called attention to the misuse of the variables sex and gender in the research literature and noted that it is important that researchers use these variables appropriately and understand their rationale for incorporating sex, gender, or both into a study.

DEFINING SEX AND GENDER ACCURATELY

Every human being has both a sex and a self-identified gender. However, investigators only occasionally acknowledge both sex and gender in studies, making it difficult to tease out sex-based and gender-based differences.⁷ According to the IOM, sex is "the classification of living things, generally as male or female, according to their reproductive organs and functions assigned by the chro-

mosomal complement."^{6(p1)} The terms male and female are often associated with sex. It is estimated that 1% to 2% of the population is born with chromosomal configurations that do not match a strictly female or male form, known as intersex.^{9,10} Thus, even though sex is often thought of in a binary way,¹¹ sex is not dichotomous, and a binary system seems to create more problems than solutions.⁹

The IOM defines gender as "a person's selfrepresentation as male or female, or how that person is responded to by social institutions on the basis of the individual's gender presentation."6(p1) The World Health Organization¹² similarly defines gender, noting that from one society to another, gender is socially constructed and that gender roles and norms may vary. Though "male," "female," and "intersex" are terms often reserved for discussing sex, terms more often used to describe gender include "man," "woman," and "transgender." While sex is determined by genetic composition (ie, the 23rd chromosome), gender is a broader construct influenced not only by biologic makeup but also by societal norms, preferences, and behaviors.¹² Gender is often thought of in terms of a continuum from masculine to feminine, and individuals may not feel that their gender matches their biologic sex.^{4,13} As many as 1 in 250 US adults identify as transgender.¹⁴ While concepts such as genetics, molecules, cells, and physiology may be related to biologic sex, concepts like sociocultural and environmental influences may be more integral to gender.¹⁵

Indeed, gender is complex and involves multiple dimensions. Tannenbaum et al¹⁶ have suggested that there are 4 major dimensions of gender important for researchers to address, including gender roles, gender identity, gender relations, and institutionalized gender issues. Gender roles are represented by the "behavioral norms applied to men and women in society, which influence individuals' everyday actions," and gender identity "describes how we see ourselves, and are seen by others, as female or male."^{16(p3)} Gender relations is more broad and "refers to how we interact with or are treated by people in the world" because of gender, and institutionalized gender "reflects the distribution of power between men and women in the political, educational, and social institutions in society."^{16(p3)} Both sex and gender-based stereotypes exist, directly affecting an individual's health.¹¹ Table 1 includes other important terms used in relation to sex and gender. While they are unique variables, sex and gender are not often measured in a precise and explicit way.^{17,18} For example, while systematic reviews have the ability to synthesize large amounts of information and assist researchers in drawing conclusions about the effectiveness of interventions, in many cases, a lack of gender- and sex-specific reporting in studies makes it difficult to design systematic

Term	Definition
Androgynous	Identifying and/or presenting as neither distinguishably masculine or feminine. ^b
Cisgender	A term used to describe a person whose gender identity aligns with those typically associated with the sex assigned to them at birth. ^b
Gender	A person's self-representation ^c ; socially constructed characteristics of women and men—such as norms, roles, and relationships of and between groups of women and men. It varies from society to society and can be changed. ^d
Gender dysphoria	Clinically significant distress caused when a person's assigned birth gender is not the same as the one with which they identify ^b
Gender expansive	Conveys a wider, more flexible range of gender identity and/or expression than typically associated with the binary gender system ^b
Gender	External appearance of one's gender identity, usually expressed through
expression	behavior, clothing, haircut, or voice, and which may or may not conform to socially defined behaviors and characteristics typically associated with being either masculine or feminine ^b
Gender fluid	A person who does not identify with a single fixed gender ^b
Gender nonconforming	A broad term referring to people who do not behave in a way that conforms to the traditional expectations of their gender, or whose gender expression does not fit nearly into a attemptive.
Intersex	An umbrella term used to describe a wide range of natural body variations. In some cases, these traits are visible at birth, and in others, they are not apparent until puberty. Some chromosomal variations of this type may not be physically apparent at all. ^b
Nonbinary	An adjective describing a person who does not identify exclusively as a man or a woman. ^b
Sex (or biologic sex)	The classification of living things, generally as male or female, according to their reproductive organs and functions assigned by the chromosomal complement. ^c
Sex assigned at birth	The sex (male or female) given to a child at birth, most often based on the child's external anatomy. ^b
Transgender	An umbrella term for people whose gender identity and/or expression is different from cultural expectations based on the sex they were assigned at birth. Being transgender does not imply any specific sexual orientation. ^b

Table. Important Sex and Gender Vocabulary^a

^aImportant sex and gender vocabulary that may be used in research and theory.

^bHuman Rights Campaign.⁸⁵

^cInstitute of Medicine.⁶

^dWorld Health Organization.¹²

reviews in such a way that would elicit any gender- or sex-based differences.^{5,8} Even though researchers may enroll individuals with various genders and sexes, they do not often publish gender- and sex-based analyses in manuscripts, and results are reported in the aggregate for all sexes and genders enrolled.^{19,20}

The nursing profession respects and values the rights and health of all human beings and recognizes the importance of key ethical principles such as beneficence and autonomy.²¹ There is indeed an imperative that nurses should "treat everyone the same,"^{11(p1)} regardless of sex or gender identity. However, to realize this imperative, researchers must ensure that all sexes and genders are being acknowledged in the literature. As investigators expand the scope of nursing research to encompass more individuals who identify as a gender minority or who are intersex, it is critical to accurately measure these variables.

As Eliason et al²² have noted, there is a need for emancipatory efforts, especially related to transgender issues. Within nursing, there is a lack of knowledge regarding gender and sex issues not only in the clinical setting²³ but also in the educational setting.²⁴ Clearly differentiating gender and sex as variables to improve what Eliason et al²² call "discursive power"^(p214) will further the ability to actually bring to light and discuss in the nursing literature issues that are gender- and sex-sensitive. We must talk about sex and gender differences in order to acknowledge them, but we first have to uncover those differences, through research.

THE EXEMPLAR OF CARDIOVASCULAR DISEASE

Regardless of sex or gender, more people die from cardiovascular disease than from any other cause in the United States and globally.^{25,26} While cardiovascular disease remains an important health concern, lack of knowledge and biased attitudes of both patients and health care professionals threaten improvements in cardiovascular outcomes.²⁷ Additionally, a historic lack of inclusion of women in cardiovascular clinical research has contributed to this issue.28 Cardiovascular disease has historically been considered a disease predominately affecting males, but cardiovascular disease also affects females at staggering rates.²⁸ Some populations experience cardiovascular disease in greater proportion than others do. For example, transgender individuals are at higher risk of cardiovascular disease and poorer health overall than many individuals who do not identify as transgender,^{29,30} and programs like Healthy People 2020 have called for improvements in transgender health.³¹

The cardiovascular disease literature will be used here as an exemplar to illustrate the unique contribution that both variables provide to understanding sex- and genderbased differences in cardiovascular disease. Gender and sex are distinct, and both of these variables have an effect on cardiovascular health.^{28,32,33} Many problems and disparities that exist among different populations of individuals with cardiovascular disease are multifactorial, resulting from both sex- and gender-based origins.34 Given a focus on precision medicine and tailoring health care to specific individuals, recognizing the unique impact of sex and gender on cardiovascular health is important.³² While it is impossible to summarize all sex and gender differences related to cardiovascular health within this article, an overview illustrating the significant role that these 2 variables play is provided here. These examples are not meant to be exhaustive and only provide a glimpse into the importance of both sex and gender in the research literature.

From a sex-based perspective, males and females are biologically different, and these differences affect cardiovascular disease rates. While a bit dated now, researchers engaged in the Women's Ischemia Syndrome Evaluation Study (WISE)³⁵ provided landmark information about differences between females and males in terms of heart disease. For example,

the WISE study noted significant differences in artery function, atherosclerotic plaque formation, and metabolism.³⁵ Females have smaller coronary arteries than males do, and they have different levels of sex hormones.³⁶ As compared with males, females are more likely to experience nonobstructive coronary artery disease, where the coronary artery is obstructed by smaller plaques.³⁷ However, these smaller plaques may be less stable and more prone to rupture or erode, causing a myocardial infarction (MI).38 Even though estrogen and other factors may be protective for females prior to menopause, premenopausal females with diabetes are at similar risk for heart disease as males at any age,^{39,40} and females' vascular systems are more negatively affected by diabetes than males.⁴¹ Females are also at higher risk of having coronary artery vasospasms⁴² and spontaneous coronary artery dissection, and both of these problems have the potential to cause an MI.⁴⁰ All of these aforementioned issues have a strong biologic (sex) component, but not all differences are driven by sex differences.

In addition to sex differences, gender differences are prominent and play a different role in moderating and mediating various cardiovascular phenomena. For example, several studies have explored the unique contribution of gender, in addition to sex, on health outcomes. The Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome (GENESIS-PRAXY) study, a multicenter, prospective cohort study that enrolled 1213 patients, focused specifically on the unique contributions of both sex and gender on various cardiovascular outcomes.43 One finding from this large study was that gender-as measured by specific indicators such as femininity score, social support, and housework responsibility-played a more important role than sex in predicting quality of life in patients after they had experienced acute coronary syndrome (ACS).44

Pelletier and colleagues⁴⁵ analyzed secondary data from the GENESIS-PRAXY study, including 273 women and 636 men, and explored the incidence of ACS and major adverse cardiovascular events over a period of 1 year. As a part of this study, the researchers developed a Gender Index, incorporating a number of variables to reflect the gender construct. The researchers found that feminine gender, as measured by the Gender Index, conferred a larger amount of risk over the study period than sex alone, suggesting that even biologically male individuals had a higher risk of cardiovascular events if they identified with a more feminine gender.45 Notably, Pelletier et al⁴⁵ found no sex differences between males and females in the study. Thus, if the researchers had not specifically conducted a gender-based analysis, in addition to a sex-based analysis, they may have concluded that there were no differences between men and women. Additionally, the authors found that gender is indeed a construct located along a continuum, with some males assuming a feminine gender and some females reflecting a masculine gender.45

Using data from a different registry, Norris and colleagues⁴⁶ applied a sequential linear modeling approach and explored overall health status in patients with coronary artery disease and how both sex and gender contributed to this status. Norris et al⁴⁶ used the Gender Index to measure a person's gender. Interestingly, sex only accounted for a very small difference in overall health status, while gender contributed significantly more information to the statistical model.⁴⁶ Earlier, Norris et al⁴⁷ had demonstrated that gender role, as a unique variable separate from sex, affected quality of life for patients with coronary artery disease. They used a structural equation modeling approach that uncovered the unique contribution that gender role makes on quality of life for these patients.⁴⁷

Gender may also play a role in other aspects of cardiovascular health. In their comprehensive review of studies exploring gender as a risk for cardiovascular disease, O'Neil et al³³ discovered that many health behaviors are related to gender. For example, during childhood, males may be socialized to "display stoicism and reject strong and

intimate friendships,"33(p857) which may lead to weaker social support networks. As a result, unhealthy, antisocial behaviors like drinking excessive alcohol may occur, and a lack of emotional processing may contribute to a higher cardiovascular risk for men.³³ Because of stereotypical gender roles, women may feel more responsibility for taking care of their family, increasing stressors at home, in addition to any stressors that may be present in the workplace, leading to a higher rate of cardiovascular disease.³³ In addition, those who identify as transgender are likely to experience multiple stressors, such as stigma, discrimination, and a lack of social support⁴⁸ also potentially leading to worse cardiovascular outcomes. Indeed, addressing cardiovascular disease remains a priority for the transgender population.49

Though the evidence is a bit dated and few recent studies have explored the issue, the literature has demonstrated that sex and gender play a role in the way that women's MI symptoms are addressed by health care providers and how women are treated. For example, women have reported feeling that they were not as involved in their cardiovascular care as they should have been and that secondary prevention strategies were not discussed with them in detail following cardiovascular events.50,51 Other women have noted that their MI symptoms have been ignored and discounted by some health care providers and that they have been marginalized.^{52,53} A more recent exploration of women's direct perceptions of bias during their MI triage experience revealed that women encounter barriers to prompt diagnosis and management.54 Specifically, some women have reported feeling that providers see them as being "whiny" and that if they had been a man, they would have "been taken more seriously." 54(p170) Results from the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients study also support that women are less often told by health providers that they are at risk for cardiovascular disease, even when they have risk factors present.55 Additionally, it has been shown that women treated in the emergency department for MI have a lower mortality rate when treated by female physicians, as compared with male physicians.⁵⁶ It is not clear from the research literature whether these differences in care are due to sex, gender, or both, but there may be an interplay between sex and gender. That is a person's physical appearance as a male or female (sex) may convey some importance, while gender roles and stereotypes also add to the aforementioned issues.

Additionally, while it is also unknown whether the differences are due to sex, gender, or both, women and men may present with ACS symptoms in a different way than men.^{57,58} Women are more likely than men to experience a greater number of MI symptoms, along with more nonclassic symptoms, though chest discomfort remains the most prominent acute MI symptom for men and women.^{28,59,61} Overwhelming fatigue is also a symptom experienced by the majority of women in the weeks and months leading up to an MI.⁶²

It is also important to note that genderand sex-based differences exist within not only the cardiovascular literature but also many other areas of research. The importance of recognizing both sex and gender as unique variables has been noted in many different areas, such as communication patterns and styles,⁶³ traumatic brain injury,⁶⁴ schizophrenia,⁶⁵ health care utilization and performance measurement,⁶⁶ critical care outcomes,⁶⁷ diabetes,⁴¹ and medication use and adherence.⁶⁸

RECOMMENDATIONS: A FOCUS ON METHODS

Understanding that sex and gender are unique, how can researchers best differentiate between these 2 variables and decide which to use in a study? What considerations are important when designing a study to incorporate sex and/or gender? How can editors and reviewers play a role in increasing the recognition of sex and gender as distinct and important variables? Given that there is a current, widespread lack of attention to the distinction between sex and gender in the existing published literature, how should we interpret and use these studies? This section of the article addresses these questions and provides some general recommendations.

Which to choose: Sex, gender, or both?

Care must be taken when deciding whether to use sex, gender, or both in a research study. Sex and gender should never be assumed to be the same. If a researcher jumps to a decision prematurely without much thought, a helpful exercise may be for that researcher to take a time out and to ask themselves "Do I really mean sex, or am I actually interested in gender? Or, do I need to measure both sex and gender?" This decision requires careful consideration of the phenomena or other variables under study and the potential need for sex- or gender-based subanalysis. It is good practice for researchers to reflect carefully prior to making a decision. Researchers should examine the extant literature for evidence of any sex- or gender-based differences that might require the researcher to consider one or both of these variables in a study. If there is not sufficient evidence in the literature, then the researcher may be wise to consider both gender and sex as potentially important demographic variables.¹⁶

If researchers are interested in examining differences in a target population based strictly on biologic differences, sex is most likely the most appropriate variable to select. On the other hand, if a phenomenon or intervention could be affected by environmental or sociocultural factors specifically related to norms of men and women within society, then gender would be the most appropriate variable. For a number of research questions, exploring sex and gender differences could be important. A researcher might ask, for example, "Are the differences in the experience of chest pain during a myocardial infarction due to sex, gender, or both?" Plausibly, sex-based factors, such as coronary artery size or heart muscle mass, could play a role in this symptom experience, as could genderbased factors, like gender roles and gender stereotypes. Once a researcher determines whether sex, gender, or both will be measured, it is important to make the rationale for that choice clear, especially when publishing the results of findings.⁶⁹ In addition, if certain genders or sexes are excluded from a study, a rationale should be provided.⁶⁹

Measurement and instrumentation

Once a researcher decides whether to measure sex, gender, or both within a study, the question turns to *bow* the variable(s) should be measured. No matter how the variable(s) is ultimately measured, the researcher should include a description of how it was measured, so that it is clear to readers. In general, variables can be measured at 4 levels: nominal, ordinal, interval, and ratio.⁷⁰ While nominal variables are merely categories, such as "man," "woman," or "intersex," measurement at higher levels, such as interval or ratio, involves a score like "degree of masculinity," as measured by a questionnaire. Additionally, variables are often either directly or indirectly measured. Direct measurement is easier when a variable or construct is directly observable, while indirect measurement is used when a variable or construct cannot be directly observed. Because gender is not directly observable, it is not often feasible to measure it in a direct way, and observation studies that claim to measure gender via observation may be inappropriate. While sex may usually be directly observable, as many as 1 in 50 people may have chromosomal compositions that do not strictly match a male (XY) or female (XX) genotype.¹⁰

Gender can be measured nominally by simply asking participants to list their gender. While this type of measurement is straightforward and allows the research participant to self-identify however they want, because gender is a complex construct, this sort of identification does not allow for the examination of traits underlying gender, such as degree of femininity or a gender role score. It would not be feasible to create a score based on gender, if it is only queried in a nominal way, limiting some quantitative analysis. It is also possible to list several options for gender and ask participants to select their gender. If participants are forced to choose from a list, the researcher is then challenged to be inclusive. While the terms "man," "woman," and "transgender" may be adequate for some participants, there are individuals who do not identify with any of these terms, and gender is associated with a number of other potential terms.⁷¹ Use of the term "other" as an option could also increase the feeling of "otherness"72 and marginalization on the part of the participant. That is, if a participant feels that they do not identify with any other options and must choose "other," then it is pointing out to them that they are an "other," out of the mainstream or norm of society. No matter the specific method, if individuals are asked to self-identify their gender, there is also a possibility that answers may not be fully accurate, given that there may be concern or stigma associated with being a gender minority.⁷³ Theoretically, studies that are fully anonymous may be more likely to secure responses that are accurate, given that participants would not be as likely to feel that they are "outing" themselves by taking part in the study.

When measuring gender, the researcher must recognize that gender is not unidimensional.¹⁶ As such, gender as a latent construct can most accurately be measured using a multidimensional instrument, rather than a single question. Because a number of factors affect the gender construct, several instruments have been developed to measure not only gender but also several dimensions of gender (or gender-related constructs).¹⁶ For example, the researcher could administer an instrument to participants and measure the degree to which a person falls along a masculine to feminine continuum, or the researcher could administer an instrument that measures a person's assumed gender roles.¹⁶ Because gender is not a binary¹¹ and cannot be reduced to a simple membership category, measurement that allows for determining a score, such as using an instrument that provides a gender score of some sort, is perhaps preferable to asking participants to select one gender (measured at the nominal level). However, if a research question or study hypotheses do not specifically involve any sex and/or gender differences or relationships, then nominal categories may be sufficient to summarize the sample demographics. No matter the instrument(s) used in a study, researchers are advised to consider important dimensions of each instrument carefully and to ensure that the psychometric properties of the instrument(s) are sufficient for the target population under study.

Sex could also be measured in a number of ways. While a researcher may choose to ask a person to self-report their sex on a demographic questionnaire, it is also possible to examine DNA and the 23rd chromosome to determine whether a person is "male," "female," or "intersex." Certainly, limitations of self-report exist, and it is possible for participants to report a sex different from their genetic make-up.

Just as sex and gender are confusing terms to some researchers, it is understandable that many study participants may be confused if asked about both their sex and gender on the same questionnaire. That is, they may think, "Why are these researchers asking me about my sex and my gender? I thought sex and gender were the same thing!" Researchers will need to guide participants to select the sex and gender that best represents them and may need to provide to participants an explanation regarding sex and gender. Realistically, this endeavor may be difficult. Using a gender measurement instrument that yields a gender score of some sort, rather than asking the participants to identify as one gender category (such "man," "woman," "masculine," or "feminine"), may be less confusing for participants. Participants would be able to self-select a sex and then provide answers to other questions creating a gender score, not generating the confusion between having to select both a sex and gender.

One more note about measurement and instrumentation is warranted. Existing surveys, instruments, and electronic records used not only in research but in everyday clinical practice often ask only about sex or gender, but not both,^{17,66,74,75} even though sex and gender may be independently important. It is likely that researchers may be interested in both sex and gender or that they may not be asking about the most helpful variable in a given situation. An example involves the Behavioral Risk Factor Surveillance System (BRFSS). The BRFSS is a comprehensive, nationwide survey used to determine the health of the nation and identify risk behaviors.⁷⁶ Historically, the BRFSS had not included questions directly related to gender identity, limiting analyses that could take place. Recognizing this limitation, an optional section was added to the BRFSS, and a number of states have begun adding this section to their BRFSS survey.⁷⁷ Consequently, it is now possible to obtain more information about risk factors related to gender minorities.⁷⁷ As researchers (as well as clinicians, educators, and policy makers) review existing surveys and other questionnaires, it is important to consider whether these instruments are measuring the necessary variables of sex and/or gender.

Emphasizing subanalyses

Policies at various levels play a significant role in health care research, and policy analyses may help to provide a better understanding of where existing policies both support high-quality research and fall short-and how policies might be made stronger. Perhaps the most significant policy change affecting the inclusion of all sexes in research originated with the National Institutes of Health Revitalization Act of 1993. Given the historic lack of inclusion of females and minorities in clinical research, a portion of this act was dedicated to increasing the representation of these individuals in research.⁷⁸ Through the National Institute of Health's (NIH) guideline statements in 1994⁷⁹ and 2000,⁸⁰ the agency reaffirmed that it would not fund any grants or contracts that

did not include females as participants, unless a qualifying exception existed. Additional updates to this policy have been made, with the latest major revision in 2001,⁸¹ which focused on increasing the inclusion of females specifically in phase III clinical drug trials and ensuring that study designs and analyses take into account females' differences. However, the NIH policy does not include a directive to enroll intersex or transgender individuals, nor does the NIH policy make clear that both gender and sex should be considered.

While the NIH policy has resulted in an increased number of females in research overall,⁸² additional challenges remain. After a review of NIH-funded studies, Geller and colleagues¹⁹ found that females still only accounted for about 37% of research participants, and only about 25% of the studies actually reported results by sex. That is, while the studies enrolled females, the overall analysis did not consider any differences between females and males.¹⁹ Polit and Beck⁷⁸ have noted that only about one quarter of nursing researchers have conducted sex-based subanalyses in their work, where they examined differences between males and females.

As researchers design studies, it will be important to consider the requisite sample size to be able to conduct sex-based and/or gender-based subanalyses and maintain adequate power. Typically, the more subanalyses that are planned, the larger the sample size that is needed. Even where financial or logistical constraints prevent the recruitment of a robust sample size, researchers can still clearly report gender and/or sex demographics within the article. When enrolling purposive samples of participants for qualitative or mixed-methods studies, researchers can also ensure that both sex and gender are considered as potentially important demographic characteristics of participants. Additionally, after data are collected, researchers must take the next step and actually analyze data at the level of sex and/or gender, to identify whether there are any differences. Finally, when writing manuscripts, it is important for researchers to include the findings of these sex- and gender-specific subanalyses because if these subanalyses are not reported (even if they are done), readers have no way of knowing whether any differences potentially exist.

Editorial and publishing standards

In order for most manuscripts to be published, they must first undergo peer review as well as review by an editor or editorial team. As such, reviewers and editors are important gatekeepers to high-quality research. When considering the publication of manuscripts where sex and gender are important variables, reviewers and editors alike should consider focusing on researchers' use of these variables. If the authors have not clearly explained their rationale for the use of sex and/or gender, or if subanalyses are not clear, the investigators could be asked to revise the manuscript. Gross misuse of the variables sex or gender could also result in rejection of a manuscript. It may also be wise for journal author guidelines to include a discussion of sex and gender, especially related to how these 2 variables should be operationalized and how they should be reported within manuscripts.

Aside from increasing standards, editors and reviewers can also embrace the use of the "singular they" in manuscripts. For some time, there have been calls to decrease the use of specific singular gendered pronouns, such as "he," "she," "him," and "her" and to replace these pronouns with the term "they."⁸³ For example, instead of saying, "The participant was asked if he or she had ever experienced fatigue," the sentence could be revised to read, "The participant was asked if they had ever experienced fatigue." Even though "they" is often thought of as a plural pronoun, academicians have suggested for some time that it is important to allow for the use of the singular "they," especially when no specific gender has been previously attached to the pronoun.^{83,84} Because gender is not a binary construct, writing "he or she" or "him or her" in a sentence is not inclusive of individuals who do not identify with either of these gender constructions. Thus, use of the singular "they" has the ability to allow for inclusion of all gender identities. As reviewers and editors critique manuscripts, it is important to recognize the singular "they" construction as a more inclusive form of writing—not as incorrect language usage. Indeed, it may take some time before researchers commonly use the singular "they" in scholarly work, but a starting point is the allowance of its usage within manuscripts and other forms of dissemination.

Interpreting existing research

A difficult question remains. How should scholars interpret and handle research that has already been published but that does not precisely use sex and gender? Arguably, some studies could have made important contributions to the knowledge base, but there may be some weaknesses in the ways that researchers operationalized sex and gender in these works. Unfortunately, there is little published guidance on how to handle this issue.

Previous articles dealing with sex and/or gender concepts should be carefully reevaluated by scholars to determine whether the conclusions were valid, based on the way sex and/or gender were operationalized. The rationale for using sex and/or gender should be carefully reviewed, as well as the appropriateness of use, based on the existing literature or theoretical importance. When reading the results of a published study, it is always important to consider limitations of the study and to closely critique the article's design, methods, analysis, and conclusions. The case is no different with studies that have used the variables sex and/or gender. When determining whether these variables have been appropriately addressed within a study, it is advisable to carefully consider the research question and any specific aims and objectives. How are sex and/or gender incorporated into the overall study design? Does the article rely on a careful measurement of sex and/or gender, or can the question(s) be answered without such an analysis?

Even if the authors have not explicitly made the case for measuring sex, gender, or both, or have not described explicitly how these variables were measured, it is sometimes possible for the reader to infer this information. If researchers have described their sample and other demographics well, the reader may have an easier time inferring this information. A review of other literature may also help inform the reader as to whether sex, gender, or both are important variables to consider for the topic of the manuscript under examination. It may be that sex and gender have relatively modest or no significant bearing on a particular area of research.

In studies where sex and/or gender appear to have been inappropriately (or not clearly) measured, it may be reasonable for a researcher to consider conducting a replication study, operationalizing sex and/or gender in a more precise way, to determine whether the results of the original study are supported. If the investigators have conducted some analyses stratified by sex or gender but have incorrectly used these variables, the reader should take caution in interpreting the findings of these specific subanalyses. While we may not fully "throw the baby out with the bathwater," as conscientious consumers of research, we must limit the conclusions we draw from the study results. While other analyses, not based

on sex or gender, may be valid, those relying on sex or gender should be interpreted with more restraint.

CONCLUSION

Sex and gender are different variables, and they cannot be used interchangeably. While some researchers may view sex and gender from a rather sterile viewpoint, treating them as any other run-of-the-mill demographic variables, these variables are of critical importance to individuals. Indeed, precisely operationalizing and measuring these variables honors individuality and more accurately represents participants' unique identities.

While sex is biologically determined, gender is a much broader construct, affected by a number of social, cultural, and personal values and norms. Indeed, a person's sex and gender may not be congruent. When designing studies and reading research reports, it is important for scholars to carefully operationalize these variables, and it may well be appropriate to measure both sex and gender within the same study. The careful use of these variables will lead to a clearer picture of various phenomena, given that sex and gender often confer unique variability and information.

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