

COMMENTARY

Methods for prospectively incorporating gender into health sciences research

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Abstract

Numerous studies have demonstrated that sex (a biological variable) and gender (a psychosocial construct) impact health and have discussed the mechanisms that may explain these relationships. Funding agencies have called for all health researchers to incorporate sex and gender into their studies; however, the way forward has been unclear to many, particularly due to the varied definition of gender. We argue that just as there is no standardized definition of gender, there can be no standardized measurement thereof. However, numerous measurable gender-related variables may influence individual or population-level health through various pathways. The initial question should guide the selection of specific gender-related variables based on their relevance to the study, to prospectively incorporate gender into research. We outline various methods to provide clarification on how to incorporate gender into the design of prospective clinical and epidemiological studies as well as methods for statistical analysis. © 2020 Elsevier Inc. All rights reserved.

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1. Introduction

To fully understand and improve human health, it is important to incorporate sex and gender in health sciences research. Sex is a biological variable that distinguishes individuals as male or female (or intersex) based on their genetics, anatomy, and hormones [1]. Gender, on the other hand, is a social construct. It encompasses the identities, expressions, roles, norms, behaviors, and perceptions of men, women, boys, girls, and gender-diverse people [1]. It may also include the institutionalization of these norms, and how individuals are treated by society based on their identified or perceived gender, as well as relations between individuals based on identified or perceived gender [2]. A growing body of evidence demonstrates that both sex and gender may independently influence both disease risks and outcomes [3–7] and that further investigation of the role of both is necessary [5,8]. Indeed several major funding agencies

What is new?

- Despite calls for inclusion of sex and gender into health sciences research, clear definitions and methods for doing so are often unclear to researchers.
- Methods for incorporating gender into health sciences research are outlined.

Key findings

- We outline several gender-related variables that may be collected and have proven to be important to health outcomes.
- We identify approaches for incorporating these variables into statistical analysis.

What this adds to what is known

- We clarify the definition of gender and its relevance as it pertains to health sciences research as well as methods for incorporating it into prospective research design.

What is the implication and what should change?

- Researchers should think critically about how gender may influence their outcomes or relationships of interest and incorporate it into their design accordingly.

now require the consideration of these variables into research proposals [1,9,10]. Nevertheless identifying methods for the incorporation of sex and gender remains difficult for many researchers, who often conflate these terms [11,12]. Despite increasing inclusion of female participants in clinical research and recognition of sex as an important variable, gender factors often remain neglected [13,14].

Gender, distinct from sex, has proven elusive from both a collection/measurement perspective as well as the relatively low frequency of its incorporation into health sciences research, despite long-standing recognition of its importance in the social sciences. The definition of gender changes with time and varies across cultures, disciplines, and among public health organizations and often includes imprecise, vague language [1], making the identification of appropriate scientific methods for measurement and analysis unclear. Because of these difficulties, few clinical researchers have attempted to quantify “gender” as a psychosocial construct and measure its impacts on health [4].

The objective of this study is to provide clarification on how to incorporate gender into the design of prospective clinical and epidemiological studies as well as methods for statistical analysis.

2. The integration of sex and gender into the research question

There are several ways in which sex and gender may influence the outcomes and/or the relationships of interest in human health studies. For example, although sex may influence an individual’s biological susceptibility to an infectious disease or likelihood of developing a chronic condition, gender may influence an individual’s likelihood of exposure to the disease or developing the condition through differences in social roles, responsibilities, occupation, and/or risk-taking behaviors. Similarly, sex may influence an individual’s biological reaction to a medication or intervention, but gender may impact an individual’s abilities and willingness to adhere to an intervention plan or a healthy lifestyle, which in turn alters the progression or outcome of a disease.

When developing a research question, it is imperative to account for psychosocial and behavioral factors that may explain and/or modify the scientific relationship of interest. Therefore, the research question and hypothesis should guide the consideration of which variables may be relevant to the study design, based on substantive knowledge and the resulting conceptual framework. Ideally, a literature search that includes validated instruments measuring specific gender-related variables would be included in the planning process for data collection.

3. Identifying gender-related variables

The Canadian Women’s Health Research Network identifies four domains that encompass gender: gender identity, gender roles, gender relations, and institutionalized gender [2]. Gender identity refers to the way an individual self-identifies, which may impact their behaviors and expression of gender, as well as how others treat them. Gender roles refer to the norms and behaviors typically associated with gender. Gender relations refer to the way in which people may interact with each other based on gender. Institutionalized gender reflects the distribution of power, resources, and opportunities among genders. We outline below a list of potential gender-related variables that could be collected for each of these domains, depending on a researcher’s study objectives and hypotheses (Table 1). This list is by no means exhaustive, nor is it intended as a checklist of variables for every clinical study. Researchers may choose to collect many variables that fall under all described domains, one variable from each domain, or focus primarily on one domain, depending on the objectives of their study. We recognize that some of the variables listed may be considered sensitive information, and as with any study involving human participants, informed consent must be provided, and patient confidentiality and anonymity must be ensured. We strongly recommend a patient partner be involved in the development of the questionnaire to ensure patient sensitivities and standards of practice for clinical research are respected. Participants may be most

Table 1. Examples of gender-related variables and the domains they have been used to measure

Gender dimension	Example gender-related variables
Gender identity	Gender identity (asked distinctly from sex at birth), offering options for man, woman, transgender, and other
Gender roles	Occupation
	Household responsibilities
	Caregiver responsibility
	Employment status
Gender relations	Primary earner status
	Marital status
	ENRICHED Social Support Index
Institutionalized gender	Gender-based violence
	UN Gender-Inequality Index/EIGE Equality Index
	Wage gap
	Gendered policies or laws (such as family leave, access to reproductive care, property ownership)
	Institutional policies that impact career progression

Note that this list is not exhaustive, many others may be considered depending on the study question.

comfortable filling out a paper or electronic form rather than answering in-person questions; thus, we recommend these methods for the most complete/accurate answers [15].

3.1. Gender identity

A multitude of gender identities exist on a spectrum, rather than a simple man/woman dichotomy. Again, the research question may guide which are most relevant to the study, but it is important that the choices for this question be inclusive and comprehensive, and distinct from

recording only participants' sex. We suggest that in addition to asking participants their sex at birth with the options "male," "female" or "intersex," asking "which of the following best describes your gender identity?" with at a minimum options for "woman," "man," "non-binary" [16] and "other" in which the participant can include further clarification [16,17].

If one also believes that personality traits may impact the outcomes of their study, they can include a personality questionnaire such as the Bem Sex-Role Inventory [18], Big-5 [19], or Myers-Briggs [20].

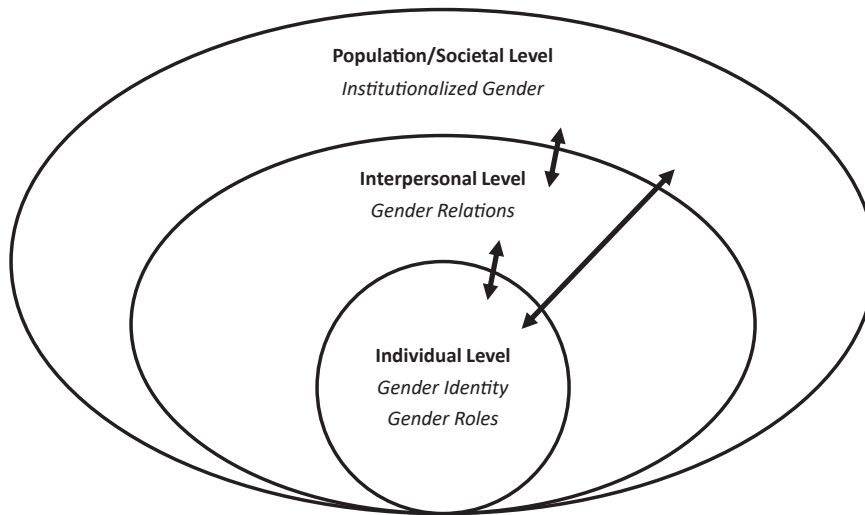


Fig. 1. The conceptual model of the dimensions of gender and on which scale they exist. Gender identity refers to the way an individual identifies, and gender roles refer to an individual's behavior and activities they fulfill. Gender relations refer to gendered interactions between individuals. Institutionalized gender refers to societal-level gendered distribution of power, resources, and opportunities. Note that these scales all interact. For example, an individual's gender identity and/or roles they occupy may influence their interpersonal relations; Institutionalized policies or norms may shape roles for individuals, whereas individual-level identities and roles in aggregate determine institutional-level variables, as well as how individuals relate to each other. Together, all these scales may directly or indirectly influence and individual's health or population health.

3.2. Gender roles

Several variables relating to traditional gender roles typically assigned to men or women can be collected based on either a literature review or a priori assessment of gendered roles identified in the social sciences. Some of these include primary earner status, primary responsibility for housework, number of hours per week spent doing housework, level of responsibility in caring for children or other family members, and level of responsibility disciplining children, as well as employment status, occupation, and several job quality–related variables [21].

3.3. Gender relations

Gender relations refer to the interactions and relationships among individuals based on their gender. The ENRICHED Social Support Instrument has been identified as a useful tool to measure gender relations as social support may vary with gender or impact individuals differently based on gender [22,23]. Researchers may also choose to simply use marital status as an indicator of gender relations, as this variable has also been demonstrated to relate to health outcomes [24]. Sexual orientation can also influence relationships between the individual and others [25]. It may also be relevant to collect information about an individual's experience with domestic or sexual violence, which directly pertains to gendered relations and impacts an individual's physical and mental health [26,27]. Additional questions regarding relationships and social support in the workplace or with peers could also be pertinent.

3.4. Institutionalized gender

Institutionalized gender reflects the way a society or culture distributes power, resources, and opportunities based on gender. Although the three aforementioned domains of gender consist of variables that can be measured at the individual or interpersonal level, this domain, which impacts individuals in terms of their socioeconomic status and their relationships, requires institutional-level variables (Figure 1). Consideration of this variable is especially important in multicenter international studies, as gender equity may vary widely among countries or regions, but it may also be considered in smaller-scale studies, such as within career fields or departments within an institution.

An example of a measurement of institutionalized gender at the country level is the Gender Inequality Index (GII) developed by the UN Development Project [28]. The GII measures gender inequality in each country, based on their distribution of parliamentary seats between men and women, proportions of men and women employed, proportions of men and women with secondary education and reproductive health (maternal mortality rate and teen birthrate) [28]. It is also possible to calculate a similar index at a state/provincial/regional level using publicly available census data and the UN's publicly available method

for calculating the GII [28]. Another similar example for only European countries is the European Institute for Gender Equality's Gender Equality Index, which includes additional details about equality based on eight domains: health, violence against women, intersecting inequalities, work, money, knowledge, time, and power [29].

Alternatively, researchers may be interested in more local institutional variables, such as a gender pay gap or sex ratio of employees in a particular field or department, or other gender-based institutionalized variables (e.g., legal rights for men, women, and gender-diverse people in a state/province or country) such as specific policies regarding enfranchisement, paid sick and family leave, and protections against discrimination or harassment. Such variables could also be important at the scale of a university or workplace, such as gender gaps in career progression in academia, particularly in science, technology, engineering, and medicine fields [30,31]. Depending on the scale of the study, it may not be possible to incorporate this domain. However, it is recommended that researchers consider institutional-level variables that may be relevant to their study to account for the distribution of power, resources, and opportunities for all genders included in their study.

4. Methods for incorporating gender-related variables into statistical analysis

4.1. Gender as an explanatory variable: individual vs. composite measure

If collecting many variables, researchers may investigate them in univariate and multivariate analyses or they may wish to reduce or consolidate them into a composite score of all gender domains or a score that reflects the individual gender domains they have investigated. This step would reduce the number of variables necessary to include in statistical models by creating one or a few metrics for gender rather than many intercorrelated gender-related variables [21,32,33]. Specifically, a factor analysis could be used to quantify the latent variable(s) of “gender” or gender-related domains that would reflect joint contributions of several directly measurable variables related to the same underlying concept or “factor” [34]. The original variables could then be replaced by aggregate factor of each emerging latent variable to create composite scores. Alternatively, researchers may wish to construct their own simple additive scores to represent each domain of gender, for example, summing various binary or Likert variables related to gender roles. Similarly, in the case of different numerical scales or units for continuous variables, original variables may be first converted into z-scores and then the summary measure can be calculated as the mean or the sum of the resulting z-scores. Such an aggregate measure may allow the comparison of the overall effects of “gender” to those of other variables in a study such as sex or clinical

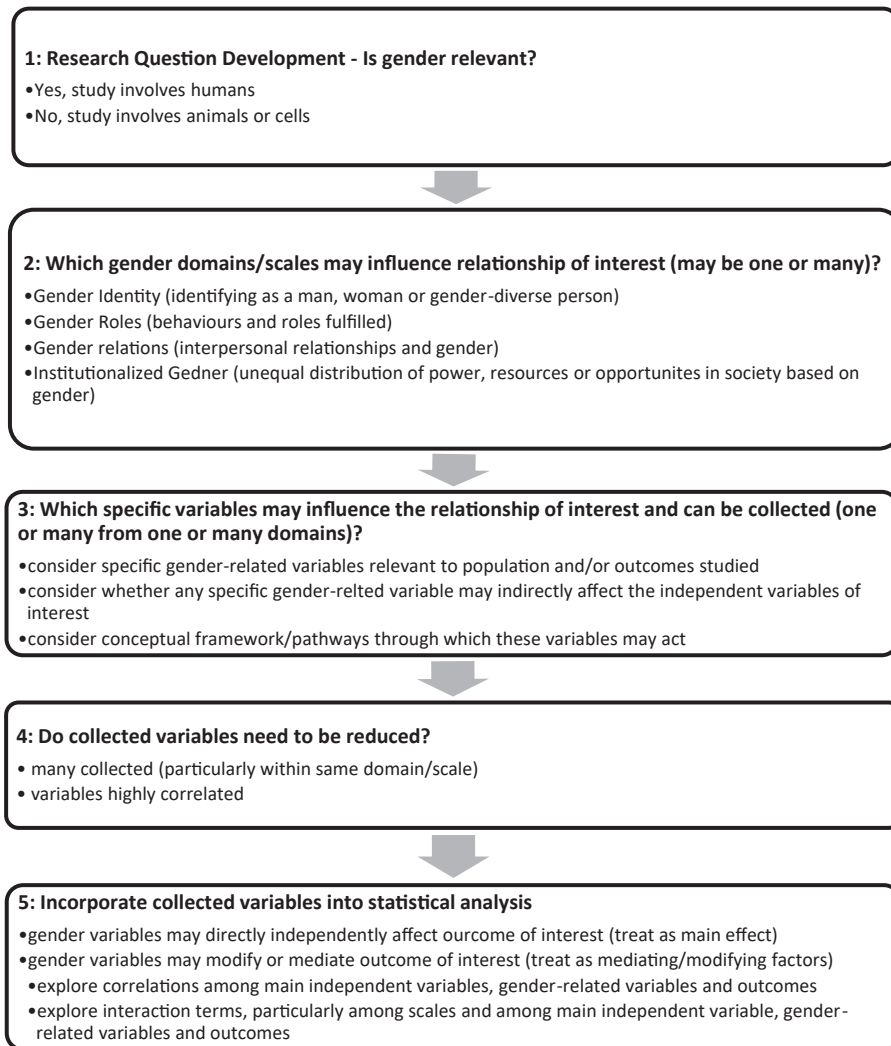


Fig. 2. Flowchart for considering and incorporating gender into prospective study design and analysis.

interventions. If interested in more precise relationships between specific gender-related variables and the outcome, treating each variable separately would be more appropriate.

4.2. Gender as a main effect, interaction term or mediating effect

The study design and the gender-related variables collected will guide the statistical analysis. It is possible that a gender-related variable may impact a health outcome directly (for example, occupation in a physical labor sector may directly increase risk of injury or poor social support may increase risk of depression or anxiety), or indirectly (for example, poor social standing or inequity may increase psychosocial stress which increases traditional risk factors for cardiovascular disease). If it is believed that gender may have an independent effect on the outcome of interest unrelated to the other independent variables in the study, an

overall measurement of gender or the separate gender-related variables collected can be considered as main effects in multivariate models alongside the exposure of primary interest to the study and relevant confounders. If it is believed that gender-related variables may indirectly impact outcome of interest, then a mediation analysis should be explored [35]. A mediating factor is one which may explain the observed relationship of interest through a causal pathway between the independent variable of interest, the mediator, and the outcome of interest. For example, sex may be associated with the likelihood of developing a chronic condition, and gender roles may partially explain this relationship. In this case, one must explore the associations between the main independent variable and the mediating variable, the mediating variable and the outcome, and the main independent variable and outcome and determine whether the mediator fully or partially mediates the relationship of interest and whether these effects are significant [36].

It is also possible that gender may modify, rather than mediate, the relationship of interest (i.e., change the direction or strength of the relationship between the independent variables and outcomes). To address this issue, interaction terms of interest should be explored. For example, interactions between gender-related variables and sex could be used to determine whether ascribing to traditional gender norms impacts men and women differently. Interactions between sex and the independent variables of interest would determine if the study treatment affects the sexes differently. Interaction terms between gendered variables/measurements and independent variables of interest could determine if the primary exposure differentially impacts gender/the measured psychosocial variables. Finally, interactions between sex and/or gender identity and a measure of institutionalized gender could determine if living in a society/environment with unequal distributions of resources, power, and opportunity differentially impacts men and women or men, women, and gender-diverse people. If there are statistically significant interaction(s) of sex/gender and the exposures or treatment/interventions of the primary interest, subgroup analysis would be essential [37]. If the sample size was not large enough to ensure adequate statistical power to detect an interaction between sex or gender and the main exposures in the study, we recommend still exploring these relationships via subgroup analysis (sex and/or gender identity) to examine how sex, gender, and the environment may affect the relationships of interest to the study but short of statistically testing for an interaction; such analyses would only be descriptive/hypothesis generating.

5. Discussion

Although numerous researchers and funding agencies have required the consideration of sex and gender in research designs, many researchers are struggling with how to operationalize the collection of these factors, particularly given that there is no standardized definition or measurement for gender. This commentary provides concrete examples of variables that can be collected to incorporate gender into prospective study design as well as strategies for analysis, while providing flexibility to researchers based on the objectives, relevance, and feasibility for their projects. We outline different aspects of gender based on common definitions as per several health research agencies and list examples of variables that fall under each of those categories, allowing for many or few variables to be collected. We then suggest multiple options for incorporating these variables into statistical models, depending on their number, the size of the cohort, and the conceptual framework (Figure 2).

The incorporation of gender into health sciences research is young, and the term itself is nebulous and evolving; therefore, a standardized or universal all-encompassing measurement is not likely to be possible or useful for researchers. We

recommend that researchers reflect on their main research questions and hypotheses and how gender-related variables may influence the variables or relationships of interest to their study. We have outlined here a set of specific, gender-related variables that may have important implications for research outcomes and can be treated as main, mediating or interacting variables in analysis, but encourage researchers to think through which gender-related variables and pathways may be relevant to their study design and hypothesis. We aim to provide a jumping-off point for the types of variables that may be considered when incorporating gender into research, which may allow researchers to elucidate specific, psychosocial determinants of health. There are many ways to incorporate gender into health research, and we hope that the strategies outlined previously will further guide researchers in their efforts to do so. This provides clarity for researchers on how to meet requirements for granting opportunities and improve health equity between sexes and among genders by incorporating gender perspectives into clinical research. It is important to note that gender is not the only social construct relevant to health, and future investigations should use an intersectional approach to explore the interaction of gender with other important social variables such as race or ethnicity, immigration status, and socioeconomic status. Such efforts would provide a fuller picture of the complex ways in which the social environment influences health and therefore highlight the steps necessary to improve health equity for all.

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