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**The conceptual complexity of gender and its relevance to pain**

Accepted (PAIN)

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### **What is gender, how is it different from sex, and why does it matter for understanding pain?**

One of the greatest challenges with research that attempts to clarify the contributions of sex and gender in health is the confusion surrounding how the terms “sex” and “gender” are defined; therefore, one cannot proceed in a discussion about gender without first applying a definition. For the purposes of the present review, we will use the definition of gender put forward by the Canadian Institutes of Health Research Institute of Gender and Health: “*Gender refers to the socially constructed roles, behaviours, expressions and identities of girls, women, boys, men, and gender diverse people. It influences how people perceive themselves and each other, how they act and interact, and the distribution of power and resources in society. Gender is usually conceptualized as a binary (girl/woman and boy/man) yet there is considerable diversity in how individuals and groups understand, experience, and express it.*” [11]. This definition highlights the complex multidimensional nature of gender, which ranges from adherence to and construction of social roles and norms, to observable behaviours and interactions, which may represent means of expressing and understanding one’s self-identity. Gender has been demonstrated to have significant impacts on multiple domains of health, including the socially situated experience and expression of physical symptoms, beliefs and attitudes towards health, engagement in health behaviours, and interactions with the health care system. Sex, on the other hand, refers to inborn biological differences more directly related to either chromosomal complement (XX vs. XY) and/or organizational or activational effects of gonadal hormones. Both sex and gender are well-established as key determinants of health [9,52]. There is, of course, some overlap between sex and gender in humans (see below); most experts believe that animals do not have genders.

Sex and gender influences are of wide interest to the pain research community: for this topical review, we examined all research papers published in *PAIN* in 2017 and found that 56% made reference to “sex”, and 16% of the papers made reference to “gender”<sup>1</sup>. The term “sex” was generally used to refer to male-female differences. However, more than three-quarters of those articles using the term “gender” used it to refer to sex differences or to categorize

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<sup>1</sup> Of note, the majority of papers reviewed where neither the term “sex” nor “gender” was present were generally studies where the sample was comprised of exclusively one sex (e.g., only male rats). This is an issue in and of itself, but is beyond the scope of the present review – see the following references for further discussion: [23,39,41].

## GENDER AND PAIN TOPICAL REVIEW

participants as male or female, and nearly a third used the terms “sex” and “gender” interchangeably. This demonstrates that the long-standing confusions surrounding the definition of “gender”, and the mis-conceptualization of sex and gender as being interchangeable, continues to perpetuate today despite numerous attempts to provide clarification [17,23,24]. Contributing to the confusion is the alternate (and in some contexts, slightly taboo) definition of the word “sex”, and the fact that many languages do not have separate terms for the two concepts.

Differences between males and females on the basis of their biologically determined and assigned sex have been widely studied in pain [40]. In basic science research on rodents, surprisingly robust and often qualitative sex differences in pain processing have been documented, including the differential involvement in males and females of individual genes [42–44,46], opioid receptor density/function/circuitry [35,36], neurotransmitters/receptors [45], and even cell types [56]. Evidence exists for the impact on pain of sex chromosome complement [20,21], estrogen [15], progesterone and its metabolites [14], and testosterone [56]. In some cases, similar qualitative sex differences have been demonstrated in humans [16,44,46].

Increased recognition of the importance of sex in biomedical research has prompted efforts to encourage researchers to consider sex in their research designs [12]. However, gender has been largely overlooked in these initiatives. Differences within the sexes are often greater than those between, and consideration of gender may provide a means of explaining some of this variance. Male-female differences are a product of more than just biology, and although sex is generally conceptualized as anatomy and physiology while gender is conceptualized as the interactive, socially constructed and regulated ways by which males and females present themselves, the reality is that there is significant bidirectional influence and interaction between these constructs [2,38,47].

Gender as a social construct is often given cursory consideration in pain research, but is rarely studied directly. Gender is often mentioned in the discussion section of published papers as an “area for future research”, or as a hypothesized factor in explaining an observed difference. There are numerous challenges faced by researchers attempting to measure, study, and understand gender, which will be discussed in the following section. The research that has been conducted to date suggests that masculinity and femininity play important roles in understanding the pain experience, for example differences in experimental pain, health-care seeking, and constructions of meaning regarding pain [1,31]. However, gender is much more than masculinity

and femininity, and we are only beginning to scratch the surface of understanding the impact of gender on pain [9,19]. Additionally, while there are important developmental considerations in understanding the impact of gender on pain (e.g., gender identity development throughout adolescence [57]), this research is significantly lacking in pediatric populations compared to the adult literature [8].

### **Why is studying gender so challenging?**

Historically, in health research the lack of conceptual clarity in measuring gender has affected the few attempts at integrating this construct into research. The measurement of gender has typically involved examining which personality traits tend to cluster together within each sex, and the conceptualization of “gender” is often not clearly defined [10]. The field has struggled with a lack of useful tools, but also lack of shared definitions about how gender is being conceptualized, understood, and measured [18,19,29]. Due to the challenges and confusion with both the definitions and measurement of gender, this confusion extends to interpreting the conclusions of this research.

Related to this, definitions and understanding of gender have changed over time, but measurement development has not always kept pace with theoretical advances and changing social landscapes (e.g., the *Bem Sex Role Inventory* [4], which was developed in the 1970’s and continues to be widely used), or are culturally specific. For example, older measures may reflect more “traditional” gender norms, such as the concept that being the primary household income earner is a masculine behaviour, which may not be as relevant for younger populations in Western society. This is highly problematic for conducting rigorous, scientifically valid research. Some of the authors of this review have twice tried exploring gender issues in child/parent pain and in both cases ended up only publishing the sex difference data, largely due to challenges with interpreting data collected using out-dated measures of gender. It is likely that other teams are struggling with this issue as well. It is important for researchers to consider factors such as culture and age cohort/generation when attempting to conceptualize gender and its impact on pain, as well as when choosing measures of gender for use in research.

It can be overwhelming for researchers to consider the different definitions of gender, dimensions of gender, and ways of measuring gender. Table 1 illustrates some of the many ways that gender can impact the pain experience; please also see review by Bernardes and colleagues

## GENDER AND PAIN TOPICAL REVIEW

[6]. It is important to remember that gender does not need to be considered a singular overarching construct that is applied to every aspect of an individual's life. Rather, gender-related influences could be specific to given contexts, which can be a more manageable approach to take within a specific field of research like pain, but requires that researchers acknowledge what specific social influence and contextual factors they are considering. For example, one might be gendered in a traditionally male dominated work place but differently so in their personal relationships. The implication for pain research is that the influence of gender on pain could be specific and require tailored measurement (e.g., the *Gender Role Expectations of Pain* questionnaire by Robinson and colleagues [53]). Indeed, a meta-analysis demonstrated that pain-specific gender measures were more strongly associated with females' and males' responses to experimentally-induced pain than were general scales of gender role [1].

### **How to move forward: Implications for research, clinical practice, and policy**

Firstly, all researchers regardless of area of study should consider the implications of sex and gender in their research, and ensure their research is in line with current best practices in this area (see Sex and Gender Equity in Research guidelines [27]). An important starting point for research is to increase awareness of the number of ways the term "gender" can be used, and when designing and reporting on a research study, thinking carefully about the definition and measurement selected. This will increase the level of specificity in the use of the term, which may open up a range of different research and clinical possibilities. See Table 1 for examples.

We recommend that researchers develop novel ways of measuring gender that reflect contemporary understandings of this construct. The development of new measures of gender will allow researchers to include gender as a measured variable in research, which we recommend particularly when investigating sex differences. This approach would address the well-documented contributions of psychosocial influences to sex differences in pain, which will more fully explain findings by considering both psychosocial and biological influences and, importantly, their interactions. Adopting this approach will require clearly defining how gender is being conceptualized and measured. This may involve conceptualizing gender as a more fluid construct that can shift with changes in hormones, abilities, roles, socially imposed expectations (i.e., thinking about gender from a state, rather than trait, perspective). This is an important area

## GENDER AND PAIN TOPICAL REVIEW

for patient engagement, and holds potential for collaborations with our colleagues in fields such as gender studies, sociology, and anthropology.

There are a number of potentially important impacts that would result from taking a broader perspective to understanding gender. For example, a biopsychosocial perspective would move beyond the current focus, which is primarily on individual psychological factors. There is a clear need to examine the sociocultural context in which this construct is being examined. Society and culture can have an active role in determining how individuals construct and understand their own identity. In addition to understanding the social context in which gender occurs and is socially regulated, there is a need to also understand how this interacts with biological/physiological variables such as sex hormones and brain function [22,48]. Additionally, an intersectional approach that considers the juncture of gender with other key determinants of health (e.g., sex, age/developmental stage, race, ethnicity, socioeconomic status, family and living arrangement, Indigenous status, rural/urban location, psychiatric diagnoses, employment, housing, social support, access to healthcare) in research designs would place gender within a richer context of multiple other influencing factors, rather than measuring such constructs separately and assuming additive effects. Other areas of health research have been drawing on intersectionality (as proposed by Crenshaw and others), which involves understanding the social structures that impact an individual's identity, but also how society classes and interacts with each individual: situating gender within these social hierarchies [3,25,26]. For example, the impact of masculinity on the pain of a Black trans man of low socioeconomic status is likely very different than how masculinity is understood and impacts the pain of a White cisgendered man of high socioeconomic status. Finally, wherever possible, we suggest that researchers should ensure published research includes gender-non-conforming population data. This could involve drawing from other fields (e.g., discursive psychology, medical sociology) to understand how to explore the experiences of these individuals when one cannot get appropriate sample sizes for big trials.

With regard to recommendations for policy and practice in pain, it is important for administrators and clinicians to consider the impact of documented systemic gender-bias issues in care (e.g., masculinity as a barrier to accessing care, provider bias in prescribing analgesics, more frequent attributions of pain to psychological issues in female patients). Faculty should ensure that academic training of health professionals includes curriculum content on systemic

## GENDER AND PAIN TOPICAL REVIEW

gender bias in healthcare, and on providing inclusive, competent care for gender-non-conforming patients. Finally, we suggest that clinicians and administrators use the research on gender-non-conforming populations to develop policies on health care and related treatment that consider the needs of these patients within healthcare settings (e.g., inquiring about and using preferred name and pronouns when interacting with patients, providing an “other” option in addition to M/F options on intake forms or asking about sex assigned at birth, lived gender expression), while continuing to collect sufficient information to examine large-scale questions about sex and gender (e.g., in large electronic health records). Existing policies in place to address issues related to gender may help in guiding this effort (e.g., American Medical Association policies on promoting inclusive gender, sex, and sexual orientation options on medical documentation, as well as policies on gender discrimination in medicine; resources available from the National LGBT Health Education Centre as part of the Fenway Institute).

Without a doubt, the integration of gender in pain research is a challenging issue to address. Rather than shying away from the issue, our hope is that this review inspires others to embrace the challenge, and collaborate with other fields that have already made significant advances in gender-related research, policy, and practice. This issue cannot be ignored, especially as we begin to understand the significant impact of gender on health outcomes, the intersection of gender and sex with other biological and psychosocial determinants of health, and the health care needs of gender diverse populations. We have well-established (and growing) data on sex differences in pain, and incorporating a gender perspective will add richness to our understanding of the psychosocial factors that underlie sex differences and gendered approaches to pain, as well as being more inclusive.



## GENDER AND PAIN TOPICAL REVIEW

**Table 1.**

Dimensions of gender, definition, measurement, and relevance to pain research, practice, and policy.

	<b>Definition</b>	<b>Measurement</b>	<b>Relevance to pain</b>
Gender identity	An individual's internal experience of one's own gender; the label one applies to oneself and one's self-concept [27].	Asking individuals what gender they identify with/how they think of themselves, and providing options beyond male and female (e.g., trans, non-binary, agender, genderqueer, gender-fluid).	An individual's self-perception and experience of their own gender would likely contribute to the extent to which they internalize and engage in gendered pain behaviours. Research has demonstrated that identifying more strongly with a particular gender group social norm is associated with gendered pain behaviours [51]. Unfortunately, there is very little literature to date examining the impact of gender identity on the pain experience, particularly not with gender-non-conforming populations. Additionally, research is needed on the impact of experiencing chronic pain on an individual's gender identity.
Gender expression	The external or behavioural expression of one's gender, which may or may not be in line with one's internal perception or experience of their gender [32].	Self-report of engagement in specific behaviours, appearance, use of pronouns, etc. A two-item measure has been developed to inquire socially assigned gender expression in adolescents and young adults [62]. Measures have also been developed for specific target populations (e.g., <i>Gender Expression Measure among Sexual Minority Women</i> [32])	There is very little research available on the impact of gender expression on pain. Expression of "dispositional masculinity" has been found to be associated with lower pain sensitivity [60]. Research is needed to examine the intersection between gender expression and gender bias in health care, the impact of the expression of gender-non-conforming traits on pain and access to treatment, and the interaction of gender expression and nonverbal pain communication [30].
Gender role orientation	The extent to which an	The questions on the <i>Gender Role Expectations</i>	Numerous studies have described the impact of

GENDER AND PAIN TOPICAL REVIEW

	individual demonstrates characteristics, attitudes, attributes, or behaviours considered to be typically associated with a specific gender within a specific cultural context (not to be confused with sexual orientation) [50].	<i>of Pain Questionnaire</i> [53] asking how individuals perceive their pain responses compared to the typical man and woman may be considered to be a measure of gender role orientation as it relates to pain.	masculinity/femininity on the pain experience, finding that increased masculinity is associated with decreased pain sensitivity [1], and both femininity [49] and masculinity [31] have been associated with certain health risk factors. This has implications for participant recruitment and interpretation of results in pain research as well: endorsing more stereotypically masculine characteristics is associated with increased willingness to participate in pain research among men, but not women [37].
Gender ideology	Cognitions (e.g., beliefs, attitudes, expectations) that are organized in line with expectations for specific genders, often internalized based on societal influences and pressures [59].	Measured with questionnaires examining the extent to which participants endorse cognitions about how males or females should/typically behave. Examples of non-pain-specific measures include the Male Role Norms Inventory and the Femininity Ideology Scale [33,34] (for a review of masculine ideology measures, see [59]). The questions on the <i>Gender Role Expectations of Pain Questionnaire</i> [53] asking about perceptions of how the typical man compares to the typical woman with respect to pain responses may be considered to be a measure of gender ideology related specifically to pain.	Both men and women have reported expecting the typical man to be less willing to report pain, have higher pain endurance, and lower pain intensity than the typical woman [53,61], and endorsement of such beliefs have been associated with pain outcomes such as temporal summation [54].
Gender bias	Differential treatment on the basis of an	Examining differential behaviours by individuals towards males vs. females	Systemic gender bias in clinical pain treatment has been documented (see [17,28])

## GENDER AND PAIN TOPICAL REVIEW

	individual's gender, often informed by gendered cognitions [55].	(e.g., experimentally manipulating the gender of a patient in a case study while holding all other information constant and examining differences in health professional decisions/responses regarding the case).	for a review, and [5,7] for examples of bias based on patient and provider gender). Bias based on gender has been documented in adult ratings of child pain as well [13].
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*Note.* Many of the above terms have been defined and measured in multiple ways; the definition and measurement examples presented here provides one illustration of how they may be conceptualized and applied to pain research. Additionally, there are many other aspects of gender (e.g., gender representation, gender role preference) not discussed above. Tannenbaum and colleagues [58] provide a similar table specific to implementation research, which may also be of interest to pain researchers.

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## GENDER AND PAIN TOPICAL REVIEW

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## GENDER AND PAIN TOPICAL REVIEW

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