



Gender Differences in Chronic Pain Conditions

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There are well-established gender-based differences in the prevalence of many pain conditions that are seen across different populations. In summary, painful conditions, and chronic pain in general, tend to be more common in women than men across the lifecourse (for example, temporomandibular pain, osteoarthritis, fibromyalgia)⁽¹⁾.²⁾ However, the prevalence of many pain conditions in men is often still substantial in absolute terms. Painful conditions with a higher prevalence in men are less common (for example, cluster headaches)⁽³⁾.

These findings have to be considered with the understanding that research on gender differences in chronic pain conditions has, until very recently, been based on binary comparisons between men and women, or males and females. As such, this research has not reflected the full spectrum of gender identities, their dynamic status over time, or been explicit about the relationship of gender identity to sexual orientation and also to other social identities (for example ethnicity). In addition, few studies have explicitly explored the joint and separate contributions of gender and sex to the exploration of gender differences in pain⁽⁴⁾.

In this Fact Sheet we focus on three areas where there are, in global contexts, strong gender equity factors amplified by a current lack of research evidence and research effort. Specifically, we focus on: chronic overlapping pain syndromes; the exacerbating impact of gender-related poverty and violence in low and middle income countries and settings; and the experience of pain in transgender and gender diverse populations. In doing this, we expand on some of the areas touched on in Fact Sheet 4: Intersectionality and pain across the life course.

Chronic Overlapping Pain Conditions

The 2011 Institute of Medicine report on 'Relieving Pain in America' highlighted the significant impact of chronic pain in the USA⁽⁵⁾. Notably, the report emphasized the increasing recognition that some prevalent chronic pain conditions seem to coexist in the same individual and that these coexisting conditions tend to be more common in women as compared to men. They include, but should not be limited to:

- Vulvodynia
- Temporomandibular Disorders
- Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
- Irritable Bowel Syndrome
- Interstitial Cystitis/Painful Bladder Syndrome
- Fibromyalgia
- Endometriosis
- Chronic Tension-Type Headache
- Chronic Migraine Headache
- Chronic Low Back Pain

The concept of these coexisting pain conditions has been recognized by the US National Institutes of Health and the United States Congress and the term Chronic Overlapping Pain Conditions (COPCs) has been coined to refer to these disorders that often coaggregate^(6,7). A significantly higher pain burden has been reported in women with COPCs, worse physical, psychological, and social functioning and significantly greater healthcare utiliza-

tion⁽⁸⁻¹¹⁾. The COPCs in women result in significant paid time lost from work, decreased work productivity, and negatively impact life course potential including education and career progression⁽¹²⁻¹⁴⁾. In the USA, studies conducted by the [Chronic Pain Research Alliance](#) have provided the following estimates of the annual U.S. economic impact of COPCs: Vulvodynia (\$31-72 billion), Temporomandibular Disorders (\$32 billion), Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (\$32 billion), Irritable Bowel Syndrome (\$380 billion), Interstitial Cystitis / Painful Bladder Syndrome (\$22 billion), Fibromyalgia (\$20 billion), Endometriosis (\$22 billion), Migraine (\$17 billion), Chronic Tension-Type Headache (unknown), Chronic Low Back Pain (\$100 billion).

Recognizing the concept of the COPCs has important consequences for clinical trial design and for clinical practice. The clinical presentations of the COPCs are diverse and the etiologies are multifactorial. Central and peripheral pain mechanisms result in widespread hyperalgesia and genetic variations have been postulated to influence pain amplification and psychosocial variability^(15,16). In clinical trial design little attention has been paid to the COPCs, that affect mainly women. When recruiting for clinical trials, potential participants who have other pain conditions in addition to the index pain condition for which the trial has been designed, are typically excluded. This is of concern, since many, if not most, patients enrolled in clinical studies are actually not representative of the wider chronic pain population and the results of the clinical trials assessing analgesic interventions might not be applicable to the majority of women with COPCs⁽⁶⁾.

In clinical practice patients with COPCs are typically seen by several different specialists for each of the different pain conditions, but there is often no concerted effort to address the overlapping aspects of the different pain complaints. Importantly, clinical observational studies have shown that COPCs may exacerbate each other, and treatment of one pain syndrome may result in improvement of another COPC as well^(17,18). These results highlight the importance of investigating and treating these COPCs collectively in clinical practice.

The Compounding Effect of Poverty and Violence on Gender-Related Differences in Chronic Pain Syndromes

In low-income countries and settings, gender differences in chronic pain syndromes are compounded by poverty. It is clear that the risk of developing chronic pain as an adult is increased when people have suffered adverse childhood experiences or childhood trauma. In low-income settings, the rates of childhood trauma are 1.5 times greater than in high-income settings with girls being at greater risk than boys⁽¹⁹⁾. Experiencing trauma as an adult also increases the risk of developing a chronic pain

condition, therefore the increased rates of PTSD in women in low-income settings also increases the risk of chronic pain⁽²⁰⁾. In low-income settings, intimate partner violence, and sexual violence against women is also 1.5 times higher than in high income settings⁽²¹⁾. Low levels of education and low socioeconomic status are risk factors for suffering intimate partner violence as adult.

The increased risk for developing a chronic pain condition in resource-poor settings applies for all who identify as women. In many low-income settings, people identifying as transgender (TG; a person whose sex at birth is different than the gender identity traditionally associated with it) and gender diverse (GD; i.e., non-binary, gender fluid) women are additionally vulnerable to develop chronic pain conditions due to ongoing trauma (see also following section). For example, the hate crime of corrective rape, which involves the rape of someone who does not conform to cisgender norms is more prevalent in these settings⁽²²⁾. Hence, the compounding effect of poverty on gender differences in pain is clear as girls are more likely to suffer childhood trauma, and less likely to receive education, while women are likely to have lower levels of education, fewer socioeconomic opportunities and are at greater risk of suffering ongoing intimate-partner and gender-based violence.

Transgender and Gender Diverse Populations

Biomedical and clinical research has historically taken a binary approach to sex and gender differences in chronic pain. As previously described, the affirmation of one's gender identity is flexible across the lifespan, and is a different concept than one's sex assigned at birth. Pain burden and experience in cisgender individuals (i.e., men and women) is well-documented. Exploring differences in chronic pain prevalence, incidence and mechanisms in TG and GD individuals is relatively new, and this field remains largely unresearched. There are clear gaps in researchers' understanding of TG and GD individuals and their pain experience, which is the result of underrepresentation in scientific studies, as well as a lack of clear definitions and useful instruments to assess gender identity and related experiences⁽²³⁾. Cumulatively, this has led to inconsistent or absent reporting of gender identities of study participants, limiting the relevance and translatability to these populations.

Though limited, there is some evidence suggesting differences in the pain experience across diverse gender identities. It is hypothesized that both TG and GD populations have an increased risk of developing a chronic pain condition due to stress associated with stigma, prejudice and discrimination^(24,25), as well as experiencing higher rates of depression and anxiety⁽²⁶⁻³³⁾. Moreover,

TG individuals are more likely to experience experimental pain much like their cis-gendered counterparts (i.e., cis-women & trans-women) compared to those of the same natal sex (i.e., trans-woman and cis-man)⁽³⁴⁾. It is unclear if gender differences in pain perception and experience are due to hormones, sex assigned at birth, gender identity, or combinations of these factors across different domains. Too little is also known about the effects of gender affirming hormone therapy on pain, though one study suggests estrogen supplementation may increase pain prevalence in trans-women and that taking testosterone may decrease pain prevalence in trans-men⁽³⁵⁾. Moreover, the unparalleled violence experienced by these individuals, as described in the preceding section, can contribute to poor pain outcomes, as experiencing violence has been shown to be associated with increased pain prevalence and severity⁽³⁶⁻³⁸⁾.

To improve our understanding of pain in TG and GD populations, it will be important to create suitable and acceptable measures that consider alternative or additional response options that characterize TG and GD individuals⁽²³⁾. Most importantly, it is absolutely imperative to gain the trust of these communities in order to work together and include them on the quest to understand the pain experiences of these uniquely vulnerable populations.

Conclusion

The well-known patterning of chronic pain conditions by gender sometimes obscures important equity considerations across diverse areas – for example, unequal pain burden, the compounding disadvantages of poverty, violence and minority status, and barriers to improving the research evidence base needed to drive change. The current challenge for clinicians is to translate and apply research evidence which often either excludes the typical patient, for example with COPC, or does not reflect the diversity and challenges faced by the person with pain, to the person living with complex pain presenting in the clinic.

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