



April 8, 2022

Docket No. CDC-2022-0024

RE: HealthyWomen's comments to inform the CDC Clinical Practice Guideline for Prescribing Opioids—United States, 2022

[HealthyWomen](#) thanks the CDC for the opportunity to provide comments on the proposed clinical practice guideline, CDC Clinical Practice Guideline for Prescribing Opioids—United States, 2022 or the clinical practice guideline. These new guidelines will go a long way towards addressing issues surrounding prescribing opioids but a number of concerns remain.

First, thank you for the opportunity to comment on the 2016 CDC Guidelines for Prescribing Opioids for Chronic Pain and providing evidence-based recommendations for clinicians including primary care physicians and clinicians involved in managing pain in the outpatient settings. Second, we want to acknowledge CDC's efforts to provide evidence and focus on certain chronic painful conditions such as lower back pain, chronic neck pain, osteoarthritis, fibromyalgia, and chronic tension headache and episodic migraine. It is well documented that painful conditions are more prevalent in women compared to men.¹ According to CDC's own recent data from 2016, 21.7 percent women have chronic pain (versus 19 percent men) and about 8.5 percent of women have high-impact chronic pain compared to 6.3 percent men.²

One of HealthyWomen's key focus areas is chronic pain in women. In July 2019, HealthyWomen convened a two day summit: [Chronic Pain in Women— Focus on Treatment, Management and Barriers](#) to focus on challenges, barriers and opportunities specific to women for treatment, management and access to care connected to chronic pain conditions. The discussions at the summit clearly identified areas of need for women living with chronic pain, and highlighted opportunities for conversations between HealthyWomen and its partners about collaborating to overcome unique barriers to care faced by women with chronic pain conditions. This summit was attended by a diverse group of stakeholders from leading academic researchers, clinicians, patient advocates, advocacy organizations and representatives from federal agencies.

Following the success of the summit, HealthyWomen established the [Chronic Pain Advisory Council](#) (CPAC) to serve as a collective authority on the issues of women and chronic pain. CPAC's vision is to empower women to make decisions to optimize pain management and improve function. The CPAC achieves this by educating stakeholders to improve pain health for women recognizing the importance of sex, gender and cultural differences in pain. It is with this goal in mind that we hope our comments will be taken into consideration to inform the CDC clinical practice guidelines for prescribing opioids as it applies to women living with chronic pain.

¹ Berkley KJ. Sex differences in pain. Behav Brain Sci. 1997 Sep;20(3):371-80; discussion 435-513. doi: 10.1017/s0140525x97221485. PMID: 10097000.

² Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016. MMWR Morb Mortal Wkly Rep. 2018 Sep 14;67(36):1001-1006. doi: 10.15585/mmwr.mm6736a2. PMID: 30212442.

In a survey of over a 1000 women conducted by HealthyWomen in 2019 to assess their concerns and attitudes towards seeking treatment, living with chronic pain and their interactions with their health care providers, we found that:

- 90% of women surveyed had multiple painful conditions and comorbidities. These include fibromyalgia, rheumatoid or osteoarthritis, autoimmune conditions, bone issues such as osteoporosis and spinal cord problems.
- Almost half surveyed were taking opioids, but also combined other modalities in managing pain.
- Women are seeking non-invasive and non-pharmacological treatment options to manage their pain. These included physiotherapy (38%), mind therapies (25%), massage therapy (30%), herbal remedies (36%), marijuana use (20%) and to a lesser extent seeking chiropractor (18%) and acupuncture (13%).
- One third of women surveyed continued to feel hopeless and unhappy with their pain management.
- 17% felt that their providers did not understand their pain suggesting a need for better communication with their physician.
- 96% of those surveyed indicated that pain impacted their quality of life and half expressed lack of sleep due to their pain.
- 65% expressed that we need more trained providers.
- 58% needed more support and resources from their health care providers.

These survey results clearly demonstrate that real-life patient experiences are important, and need to be acknowledged and taken into consideration by clinicians when discussing a treatment or a management plan with patients, especially women. This should be noted by CDC as well when guiding physicians. As was noted in the guidelines, clinician and patient communication and collaboration is key, and it is very important for clinicians to discuss clinical care and management with their patients. This communication and collaboration is particularly important for women as their concerns are very different from men and are often dismissed by primary care physicians.

Treating chronic pain in women is complicated and the guidelines have very little discussion on managing comorbidities. Women have multiple pain related and co-morbid conditions,³ are less likely to be queried about pain at medical appointments,⁴ their symptoms severity for several chronic pain conditions vary across the menstrual cycle,⁵ and they tend to show higher rates of pain intensity, greater disability and emotional distress due to higher rates of interpersonal trauma and

³ Maixner W, Fillingim RB, Williams DA, Smith SB, Slade GD. Overlapping Chronic Pain Conditions: Implications for Diagnosis and Classification. *J Pain*. 2016 Sep;17(9 Suppl):T93-T107. doi: 10.1016/j.jpain.2016.06.002. PMID: 27586833.

⁴ Samulowitz A, Gremyr I, Eriksson E, Hensing G. "Brave Men" and "Emotional Women": A Theory-Guided Literature Review on Gender Bias in Health Care and Gendered Norms towards Patients with Chronic Pain. *Pain Res Manag*. 2018 Feb 25;2018:6358624. doi: 10.1155/2018/6358624. PMID: 29682130.

⁵ Iacovides S, Avidon I, Baker FC. Does pain vary across the menstrual cycle? A review. *Eur J Pain*. 2015 Nov;19(10):1389-405. doi: 10.1002/ejp.714. Epub 2015 Apr 21. PMID: 25899177.

PTSD.⁶ Finally women show differential response to opioids and non-pharmacological approaches.⁷ Taking these factors into consideration, it is essential for clinicians to communicate and understand the specific and unique issues that affect women when treating them for chronic pain.

The U.S Department of Health and Human Services (HHS) in their Pain Management and Best Practices Inter-Agency Task Force Report: Updates, Gaps, Inconsistencies and Recommendations, pointed out that the the unique issues women face in pain management are due to the differences between women and men with respect to pain sensitivity, response to pain medication and predisposition to clinical pain conditions. These sex and gender differences are well documented in pain research literature yet these differences were not mentioned in the draft clinical practice guidelines.^{8 9 10 11}

In the draft clinical practice guidelines, CDC has acknowledged that women may be at higher risk for inadequate pain -management even though they have higher opioid prescription fill rates than men at a population level (page 8 line 148-150). In fact, according to the Department of Health and Human Services Office of Women's Health report, increases in opioid prescribing between 1999-2015 coincided with increases in opioid overdose deaths. The death rate from opioids in women increased by 471 percent compared to 218 percent among men.¹² From 1999-2017, the deaths from prescription opioids increased for every age group from 30-64 years but the greatest increase (>1000%) was among women aged 55-64 years.¹³ Therefore, there needs to be increased efforts to address the unique needs for women and have a better strategy to manage their chronic pain.

As noted above, according to HealthyWomen's 2019 survey, women are seeking non-invasive and non-pharmacological treatment options. We agree that clinicians should discuss these options with their patients and not default to using opioids as the first line of treatment. But the one-size-fits all approach does not work for women, nor likely men too . Designing a more individualized patient-centered approach including a balanced pain management is needed in treatment plans for women and should be based on the biopsychosocial model of care. Women preferred to use a

⁶ Åkerblom S, Perrin S, Rivano Fischer M, McCracken LM. The Impact of PTSD on Functioning in Patients Seeking Treatment for Chronic Pain and Validation of the Posttraumatic Diagnostic Scale. *Int J Behav Med*. 2017 Apr;24(2):249-259. doi: 10.1007/s12529-017-9641-8. PMID: 28194719.

⁷ Pieretti S, Di Giannuario A, Di Giovannandrea R, Marzoli F, Piccaro G, Minosi P, Aloisi AM. Gender differences in pain and its relief. *Ann Ist Super Sanita*. 2016 Apr-Jun;52(2):184-9. doi: 10.4415/ANN_16_02_09. PMID: 27364392.

⁸ Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL 3rd. Sex, gender, and pain: a review of recent clinical and experimental findings. *J Pain*. 2009 May;10(5):447-85. doi: 10.1016/j.jpain.2008.12.001. PMID: 19411059.

⁹ Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth*. 2013 Jul;111(1):52-8. doi: 10.1093/bja/aet127. PMID: 23794645.

¹⁰ Sorge RE, Mapplebeck JC, Rosen S, Beggs S, Taves S, Alexander JK, Martin LJ, Austin JS, Sotocinal SG, Chen D, Yang M, Shi XQ, Huang H, Pillon NJ, Bilan PJ, Tu Y, Klip A, Ji RR, Zhang J, Salter MW, Mogil JS. Different immune cells mediate mechanical pain hypersensitivity in male and female mice. *Nat Neurosci*. 2015 Aug;18(8):1081-3. doi: 10.1038/nn.4053. Epub 2015 Jun 29. PMID: 26120961.

¹¹ Samulowitz A, Gremyr I, Eriksson E, Hensing G. "Brave Men" and "Emotional Women": A Theory-Guided Literature Review on Gender Bias in Health Care and Gendered Norms towards Patients with Chronic Pain. *Pain Res Manag*. 2018 Feb 25;2018:6358624. doi: 10.1155/2018/6358624. PMID: 29682130

¹² Office on Women's Health. [Final Report: Opioid Use, Misuse, and overdose in women](#). July 19, 2017

¹³ VanHouten JP, Rudd RA, Ballesteros MF, Mack KA. Drug Overdose Deaths Among Women Aged 30–64 Years – United States, 1999–2017. *MMWR Morb Mortal Wkly Rep* 2019;68:1–5. DOI: <http://dx.doi.org/10.15585/mmwr.mm6801a1external.icon>.

combination of opioids with other modalities to best manage their pain, according to our survey. However, clinicians should screen for Opioid Use Disorder (OUD) before prescribing them even though research has shown that only a small number of patients with chronic pain develop OUD (1-8%). For example, prescribing opioids are not recommended for those with migraines.¹⁴ And, in some patients, the clinician, based on that screening, may need to combine opioids with other treatment options to effectively manage pain based on the severity of the chronic pain. Clinicians should consider how opioids might affect the quality of life and functionality in their women patients at the same time while weighing their risk for opioid use disorder.

In the draft clinical practice guidelines, we noticed that the evidence for non-invasive non-pharmacological approaches for the individual chronic pain conditions listed was mostly scored as Type 3 evidence (observational or randomized clinical trials with notable limitations) which should be considered weak. Given that women are seeking non-invasive and non-pharmacological approaches to manage their chronic pain and are vulnerable to opioid use disorder, it is important for the federal agencies work together to ensure development and availability of treatments for pain, particularly that are non-addictive and make it a priority within the agencies. To this extent, HealthyWomen has previously submitted this [sign-on letter](#) to the FDA, NIH and also CDC, endorsed by 33 organizations, urging the agencies to move forward in implementing the [SUPPORT Act](#) (Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act). The SUPPORT Act was designed to curb overuse of opioids but also strengthen the clinical guidelines and expand treatment options for people living with pain.

With regard to the proposed recommendations numbers 3, 4 and 5, the evidence presented is weak or of poor quality (evidence type 3 or 4). For these set of recommendations, it is important to consider sex differences whether starting or prescribing opioid therapy or considering initiating or increasing a particular dose. This is especially important when we know that women tend to be given opioids at higher doses over longer periods of time than men.

Recommendation 11 attempts to warn clinicians to use extreme caution when prescribing opioids with benzodiazepines. Both these medications are respiratory depressants and thus contraindicated in combination. It is important to note that women are also often prescribed opioids in combination with benzodiazepines and careful consideration should be given to women being prescribed opioids with benzodiazepines which can be fatal in some.¹⁵ Research in animal models have shown that sex hormones influence opioid receptors which may explain why women are more likely than men to overdose as a result of respiratory depression.¹⁶

One critical issue, we note that has not been mentioned in the practice guidelines is the use of telehealth to prescribe opioids. Telehealth is now seen as an important component of

¹⁴ Lipton RB, Buse DC, Friedman BW, Feder L, Adams AM, Fanning KM, Reed ML, Schwedt TJ. Characterizing opioid use in a US population with migraine: Results from the CaMEO study. *Neurology*. 2020 Aug 4;95(5):e457-e468. doi: 10.1212/WNL.0000000000009324. Epub 2020 Jun 11. PMID: 32527971.

¹⁵ Lamvu G, Soliman AM, Manthena SR, Gordon K, Knight J, Taylor HS. Patterns of Prescription Opioid Use in Women With Endometriosis: Evaluating Prolonged Use, Daily Dose, and Concomitant Use With Benzodiazepines. *Obstet Gynecol*. 2019 Jun;133(6):1120-1130. doi: 10.1097/AOG.0000000000003267. PMID: 31135725.

¹⁶ Pattinson KT. Opioids and the control of respiration. *Br J Anaesth*. 2008 Jun;100(6):747-58. doi: 10.1093/bja/aen094. Epub 2008 May 1. PMID: 18456641.

physicians/patient relations due to the COVID-19 pandemic. Usage of telehealth surged during the pandemic and the option was expanded to include the prescribing of opioids. Telehealth usage continues at a higher rate than prior to the pandemic and it is important that prescribing opioids via telehealth remain an option going forward .

Finally, depression and anxiety are prevalent in women with various chronic pain conditions.¹⁷ Since mental health conditions may alter pain perception, it is important for clinicians to evaluate the existence of mental health conditions in their patients and assess the risk for addiction before initiating opioid therapy. However, more research is needed to better understand sex and gender differences in response to opioids and the biological connections between mental health conditions and pain.

We once again thank you for the opportunity to offer input on the proposed draft CDC Clinical Practice Guideline for Prescribing Opioids. We look forward to continued collaboration with the CDC.

Sincerely,

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Founded in 1988, HealthyWomen is the leading nonprofit women's health information source with a mission of educating women ages 35 to 64 to make informed health choices. Throughout the years, we have informed consumers and healthcare providers about advances in women's health, from the latest information on diseases and conditions to various milestones pertaining to access to care. We ensure that women have accurate, balanced, evidence-based information so they can make informed decisions in partnership with their healthcare providers. We also educate our audience regarding innovations in research and science, as well as changes in policy that affect women's access to treatment and care so that women are prepared to self-advocate for better health outcomes.

¹⁷ Hooten WM. Chronic Pain and Mental Health Disorders: Shared Neural Mechanisms, Epidemiology, and Treatment. Mayo Clin Proc. 2016 Jul;91(7):955-70. doi: 10.1016/j.mayocp.2016.04.029. Epub 2016 Jun 22. PMID: 27344405.