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June 16, 2020

Celeste Philip, MD, MPH
Deputy Director, Non-Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA 30329

Submitted electronically to: https://www.regulations.gov

Re: Docket No. CDC-2020-0029 Management of Acute and Chronic Pain: Request for Comment

Dear Dr. Philip:

The Society for Women's Health Research (SWHR) appreciates the opportunity to provide comments on the Centers for Disease Control and Prevention (CDC) Docket No. CDC-2020-0029, Management of Acute and Chronic Pain. Pain is an enormous public health issue with profound individual and societal consequences. SWHR commends the CDC for seeking input from diverse stakeholders to inform its understanding of values and preferences related to pain and pain management options.

SWHR is a 30-year-old national nonprofit dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. Because of SWHR's advocacy efforts, women are now routinely included in most major medical research studies, and scientists funded by the National Institutes of Health (NIH) are required to consider sex as a biological variable (SABV) in their research.

It is well-known that biological sex differences exist at all levels — cellular, molecular, and systems — and that these differences affect health outcomes and response to treatment for a variety of drugs and biologics. SWHR is committed to ensuring that researchers consider the role of biological sex and the unique needs of women across all areas of health care.

Evidence for sex differences in pain is wide ranging, and we urge the CDC to consider these differences when approaching pain management. Women suffer from chronic pain and disability at increased rates in comparison to men. Women generally report experiencing more recurrent pain,

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more severe pain, and longer lasting pain than men. Basic science, epidemiology, and clinical research show differences in how women and men process and respond to pain.[1] For example, research suggests women have lower pain thresholds and tolerance to pain stimuli compared to men. Women also experience lower pain reduction responses to opioids than men.[2] Because women may experience pain differently than men, the resulting pain management options may be different for women or men, which may inform clinicians' and patients' decision-making.

Sex differences exist in the prevalence rates for many painful conditions:

- Three of four people with migraine are women.[3]
- Fibromyalgia is twice as common in women as men.[4]
- More women report orofacial pain than men.[5]
- Women are more likely to develop knee and hand osteoarthritis.[6] Among the older Medicare population, women are 79% more likely to develop osteoporotic fractures than men.[7]

Women face unique challenges with pain across the lifespan. Women's circumstances, preferences, risks, and overall health goals related to pain and pain management vary at different stages of life. For example, pain is common in pregnancy. An estimated quarter to more than half of pregnant women suffer some lumbopelvic or peripartum pelvic pain; of those, about 8% become severely disabled and need hospitalization.[8] As women get older, their risk of chronic pain increases and nearly doubles with the onset of menopause symptoms. When estrogen levels are fluctuating during perimenopause or post-menopause, the risk for common conditions that cause or exacerbate pain is highest.[9]

Psychological and sociocultural influences play a large role in women's pain management decision-making. A 2011 study by the Institute of Medicine (IOM) of the National Academies of Sciences, Engineering, and Medicine found that not only did women appear to suffer from more pain than men, but women's reports of pain were more likely to be dismissed.[10] For example, women with endometriosis — an inflammatory disease with a pain symptomology spectrum including chronic pelvic pain, painful periods, painful sex, and back pain — may experience their health care providers trivialize pain symptoms or be quick to dismiss them as "normal," leading to a provider-related delay in diagnosis.[11]

In addition, Black patients are at increased risk of having their pain dismissed, and some health care providers are documented as falsely believing that Black patients experience less pain than white patients[12,13] and that endometriosis does not occur in Black women.[14] At the intersection of sex and ethnicity, Black women are especially likely to have their pain dismissed: Black women with endometriosis are misdiagnosed more than white women and face increased risks of being viewed as narcotic seeking.[15,16] As a consequence, women's pain continues to be improperly treated and managed.

To improve pain care, our nation must address gaps in research, innovation, and provider and patient education, as well as barriers to accessing care. A report developed by the U.S. Department of Health and Human Services (HHS) Pain Management Best Practices Inter-agency Task Force, an advisory group mandated by Congress through the Comprehensive Addiction and Recovery Act of 2016, provides a blueprint for change and insight into experiences managing pain. SWHR strongly endorses the report's best practices

and recommendations (several of which are outlined below) that aim to employ an integrated, comprehensive treatment approach for addressing both the complex and individualized nature of pain.

Last March, SWHR provided comments to HHS in response to the task force's draft report. Importantly, the task force highlighted the need for increased research on sex differences in pain responses and mechanism-based therapies. As discussed in a 2019 *Biology of Sex Differences* article, consideration of sex and gender differences is essential to the development of a successful response to the opioid crisis.[17]

SWHR calls on the CDC to incorporate the HHS Pain Management Best Practices Inter-agency Task Force's recommendations into its own updated pain management guidance and education materials. Specifically, we urge the CDC to:

- Expand on basic, translational, and clinical research examining sex differences in chronic and acute pain.
- Leverage existing interagency resources, information, and best practices to inform the CDC research agenda and approach.
    - For example, the NIH Office of Research on Women's Health and the Office of Women's Health at the Food and Drug Administration (FDA) have expertise in the inclusion of SABV in clinical and preclinical studies and in the creation and implementation of SABV policies for intramural and extramural researchers.
    - Additionally, the FDA has protocols to examine sex differences in data on safety and effectiveness, post-marketing monitoring and safety alerts, and sex analysis in clinical trials.[18]
- Increase inclusion of complex patient populations at high risk for pain in ongoing research, including pregnant and lactating women and women in menopausal transition and post-menopause.
- Prioritize multidisciplinary treatment research as well as studies involving non-opioid options (e.g., medication; interventional procedures including evidence-based device interventions, alternative therapies) for managing pain symptoms.
- Conduct and publish sex- and gender-based analyses in order to best understand potential differences in response to treatment.
- Coordinate with CMS to address reimbursement and access issues for non-opioid treatment options for both chronic and acute pain.
- Capture the patient voice when updating CDC pain management guidance to reflect the diversity of patient experiences and perspectives with pain.
    - Patient input is especially critical now, as changes to health care delivery and access due to COVID-19 may impede or alter routine care for patients dealing with pain.
- Develop and disseminate public, patient, and provider education materials about pain conditions that are more prevalent in women and their full range of treatment options, with a particular focus on addressing complex and poorly understood pain conditions, such as endometriosis and fibromyalgia, and eliminating stigma related to these conditions.

Thank you for the opportunity to provide a response to your request for comment and for allowing us to provide perspective on patient experiences of pain. We look forward to serving as

a resource on this important topic. If you have any questions, please feel free to contact Sarah Wells Kocsis, our Vice President of Public Policy and SWHR CDC lead, at swellskocsis@swhr.org or 202-496-5003.

Sincerely,

Kathryn G. Schubert, MPP
President and Chief Executive Officer
Society for Women's Health Research

Cc: Shannon Lee, Centers for Disease Control and Prevention

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