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May 11, 2021

Jennifer Bright, MPA
Executive Director
Innovation and Value Initiative
917 Prince Street
Alexandria, VA 22314

Rick Chapman, PhD
Chief Scientific Officer
Innovation and Value Initiative
917 Prince Street
Alexandria, VA 22314

Re: Innovation and Value Initiative
Major Depressive Disorder Value Model Scope, Public
Comment Period

Submitted electronically via
public.comment@thevalueinitiative.org

Dear Ms. Bright and Dr. Chapman,

On behalf of the Society for Women's Health Research (SWHR), I am writing to provide comments on the Innovation and Value Initiative (IVI) Major Depressive Disorder (MDD) Value Model Scope.

SWHR is dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. For over 30 years, SWHR has brought attention to diseases and conditions that disproportionately or differently impact women.

MDD is nearly twice as likely in women than men, with lifetime prevalence rates of 21% and 12%, respectively.¹ This increased prevalence for women emerges around puberty and continues throughout the lifespan.² While it is unclear exactly why the gender gap in MDD exists, hormonal changes, inherited traits, and stressful

¹ Sloan, DM, & Sandt, AR (2006). Gender differences in depression. *Women's Health*, 2(3), 425-434.

² Albert, PR (2015). Why is depression more prevalent in women? *Journal of Psychiatry & Neuroscience*, 40(4), 219-221. doi: 10.1503/jpn.150205

personal life circumstances and experiences are all associated with a higher risk of depression in women.

In October 2019, SWHR launched our first-ever set of value assessment principles,³ conceived to help ensure value frameworks and value assessments 1) account for patient population diversity, including sex and gender, and 2) have the infrastructure and analytic capability to evaluate data that matter to women. Grounded in these principles, SWHR is pleased to provide the following information and guidance to inform IVI's model scope on MDD:

Target Population

SWHR recommends the model population simulate gender differences observed in real-world populations, i.e., designed to capture the observed higher rates of depression in women versus men. Gender disparities in MDD prevalence may be related to reproductive differences (such as those associated with the menstrual cycle, pregnancy, or menopause), prevalence of stressful life events (which women report occurring more frequently, on average), and behavioral genetics (e.g., the diathesis-stress model).⁴

In considering how reproductive changes may contribute to differing experiences of MDD, we recommend careful consideration of how pregnancy affects the definition of depression. SWHR suggests IVI explicitly and operationally define postpartum depression within the list of exclusion criteria. There remains a great deal of debate as to whether a depressive episode occurring during the postpartum period is sufficiently different than MDD episodes that occur outside of this life stage. Evidence as to the clarity and certainty of this distinction is mixed, and largely depends on how the postpartum period is classified (e.g., depression occurring early in the postpartum period — up to eight weeks postpartum — may be distinct from depression with onset during the later postpartum period, with the latter more similar to typical MDD episodes).⁵ Therefore, it will be important to carefully examine the evidence base when creating criteria for inclusion and exclusion in the model.

We additionally encourage IVI to take into account the impact of gender identity and notably higher rates of depression in transgender individuals. For example, lifetime prevalence of MDD is up to 62% among transgender women, compared to almost 17% in the population at large.⁶

Finally, SWHR recommends using gender to define subgroups for further examination. It is well-known that symptom presentation varies by gender. For example, women with

³ Society for Women's Health Research. Health Care Value Assessment Principles. Retrieved from: https://swhr.org/swhr_resource/swhrs-health-care-value-assessment-principles/

⁴ Sloan, DM, & Sandt, AR (2006). Gender differences in depression. *Women's Health*, 2(3), 425-434.

⁵ Batt, MM, et al. (2020). Is postpartum depression different from depression occurring outside of the perinatal period? A review of the evidence. *Focus*. doi: 10.1176/appi.focus.20190045

⁶ Hoffman, B. (2014). An overview of depression among transgender women. *Depression Research and Treatment*, 2014. doi: <https://doi.org/10.1155/2014/394283>

MDD are more likely to report prototypical symptoms of depression, including depressed mood, feelings of worthlessness, anxiety, psychomotor retardation, somatic concerns, and increases in appetite and weight gain. Men with MDD are more likely to report symptoms more commonly associated with anger, such as loss of appetite, weight loss, insomnia, and irritability. They are also more likely to engage in alcohol and substance abuse than depressed women.⁷

The clear differences in prevalence, presentation, and coping are important to consider in determining value of treatments. There exists some evidence that certain treatments may be more effective depending on an individual's biological sex — for example, selective serotonin reuptake inhibitors (SSRIs) may be more effective in the presence of estrogen.⁸ Therefore, we strongly recommend IVI work to consider the influence of sex and gender throughout its MDD value model, in addition to subgroups already identified (age, race/ethnicity, socioeconomic status, etc.).

Time Horizon

SWHR appreciates IVI's understanding that time horizon is important to consider and that long-term outcomes may be equally relevant as short-term. Across the board, SWHR recommends value assessments take into consideration both short- and long-term benefits to ensure models account for the full value of a therapy or intervention, especially considering that the benefits of some therapies may continue to accumulate over time. This is particularly important to consider when attempting to understand the effects of emotional or behavioral interventions, such as those reviewed in the scoping document.

Patient Input & Experience

As outlined in SWHR's value assessment principles,⁹ women are frequently primary caregivers for their family members. Nearly 70% of caregivers are women.¹⁰ Women serve multiple roles while caregiving: Hands-on caregiver, case manager, companion, decision-maker, and advocate.

Caregivers may tend to those suffering from mental health conditions, and they may also experience their own episodes of MDD. Reports suggest that up to 20% of family caregivers suffer from depression — a rate approximately twice that of the general population. In general, women who provide care for family members experience higher rates of depression than men.¹¹ SWHR strongly recommends the needs and input of caregivers be considered when evaluating patient needs and experience. We are

⁷ Ibid.

⁸ Gorman, JM. (2006). Gender differences in depression and response to psychotropic medication. *Gender Medicine*, 3(2), 93-109. doi: 10.1016/s1550-8579(06)80199-3.

⁹ Society for Women's Health Research. Health Care Value Assessment Principles. Retrieved from: https://swhr.org/swhr_resource/swhrs-health-care-value-assessment-principles/

¹⁰ Family Caregiver Alliance. Who Are Family Caregivers? <https://www.apa.org/pi/about/publications/caregivers/faq/statistics>.

¹¹ Family Caregiver Alliance. Caregiver depression: A silent health crisis. <https://www.caregiver.org/resource/caregiver-depression-silent-health-crisis/>



pleased to see IVI's attention to this within the model scope, and we recommend this continue to be a priority.

SWHR appreciates the opportunity to comment on this important model scope. If you have any questions, please do not hesitate to reach out to me at kathryn@swhr.org.

Sincerely,

A handwritten signature in black ink that reads "Kathryn G. Schubert". The signature is written in a cursive, flowing style.

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