

Research aims to shape more precise treatments for depression in women

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Credit: University of California, San Francisco

Among women in the United States, depression is at epidemic levels: Approximately 12 million women in the U.S. experience clinical depression each year, and more than 12 percent of women can expect to experience depression in their lifetime. Moreover, many experts believe the numbers are likely higher, given the degree of under-reporting about the condition, the fact that depression in women is often misdiagnosed and the fact that fewer than half of women who experience clinical depression will ever seek care.

The public health implications are undeniable. Beyond the condition's isolated impact, [depression](#) can have lasting physical and mental health effects that ripple through an individual's lifetime, with research also indicating that a mother's depression can affect the mental and physical development of her child.

In response to these concerns, Interim Dean Sandra Weiss of the UC San Francisco School of Nursing is leading three major studies aimed at shedding important light on some of the most pressing issues facing American women with depression and the clinicians who treat them.

National Study Characterizes Symptoms

The first study takes a systematic look at the etiology, triggers, symptoms, comorbidities and treatment of women who experience depression in the hope that a more comprehensive and detailed understanding of the disorder can improve screening in primary care settings and lead to more precisely targeted treatments. Weiss is co-principal investigator of this nationwide, multisite study that involves nine leading universities. Funded by the National Network of Depression Centers and its participating sites, the study enrolls women ranging from adolescence through old age – primarily women who are not already undergoing treatment with a mental health professional.

"This is not the typical group of women in most depression studies," says Weiss. "Instead, we are trying to understand symptom presentation for depression and comorbid anxiety by screening women at nonpsychiatric settings, such as ob-gyn, primary care or pediatric settings where the women's children receive care."

Some of the questions the study explores are: How many of these women meet the criteria for depression and, of those, how many actually make it to treatment? What types of treatment are most common, and how is

treatment linked to the severity and nature of their symptoms? If the study can offer some definitive answers to these questions, it could modify screening and referral guidelines and, perhaps, make the case for more integrated behavioral and [mental health resources](#) in primary and specialty care settings. Some studies have shown that integrating behavioral health in [primary care](#) can be successful in catching [mental health problems](#) before they become more severe and, therefore, more difficult to treat.

In addition, Weiss hopes she and her fellow researchers will be able to add to emerging knowledge about how best to target treatment options to a particular set of symptoms, at a particular time in life – a form of precision medicine for women's depression. The study is using standardized, validated tools to determine, for example, whether there are different symptom clusters that may reflect different subtypes of women's depression, and how symptoms might differ at different times in a woman's life. The findings that emerge could help create more evidence-based clinical guidelines than current treatment approaches, which tend to rely on the same guidelines for both men and women or an individual provider's clinical wisdom.

She adds that the study could also help clinicians understand potential red flags for depression. "One of the interesting things to me is that it's widely believed that people get more depressed as they get older, but so far we've found that older women are less depressed," says Weiss. "We also found the importance of a key social determinant: When women are unemployed, they have over twice the odds of experiencing depression. Although there has been evidence of this effect for men, it has often been assumed that employment per se is not particularly salient for women's mental health."

While the study, which began in 2014, will take place over an extended period of time, an initial paper, based on the first wave of participants,

has been accepted for publication in the *Journal of Women's Health*. The paper demonstrates the feasibility of creating a large-scale, multisite infrastructure and managing a complex registry of data from diverse professionals and clinical sites.

"It's very exciting to be creating a pooled data set in collaboration with the country's top experts in depression," says Weiss. "We already have 1,500 participants and plan to increase the number substantially, as well as follow the cohort over time."

Transmitting Psychological Distress from Mother to Child

The importance of this larger study grows when one considers two other studies for which Weiss is principal investigator, both funded by the National Institutes of Health (NIH). The first examines how exposure of a fetus to stress-related hormones may affect development of brain areas that shape an infant's response to stress after birth – with lasting consequences for later mental and physical health.

Based on her previous research, Weiss hypothesizes that stress-related hormones during pregnancy – either from corticosteroids prescribed as part of treatment or from a mother's own hormonal production – may program development of the stress-response system in preterm babies.

"Prescribed corticosteroids help promote fetal lung development and reduce the risk of death in premature infants, but our initial data suggests that babies whose mothers receive corticosteroids have difficulty mounting a normal response to stressors, as shown in suppressed cortisol levels and dampened heart rate variability," says Weiss. "This difficulty wasn't found among babies whose mothers didn't receive corticosteroids, causing us to be concerned that exposure to these hormones could

modify development of the infant's stress-response system, known as the HPA [hypothalamic-pituitary-adrenal] axis."

She adds that stress hormones that a mother secretes in response to her own psychological distress can also affect development of the infant's HPA axis. Because stress can modify a number of important biological systems, Weiss' team is also studying its effects on the infant's microbiome and telomere length. Telomeres – caps at the ends of each strand of DNA – protect the chromosomes and affect how cells age.

"There is growing evidence from animal research," Weiss notes, "that stress is linked to higher levels of pathogenic bacteria in the microbiome, which, in turn, have a detrimental effect on health. But almost no data is available to explain how fetal exposure to stress and its related hormones may affect early development of the microbiome in human infants." Weiss is examining the effect of maternal stress on diminished cellular integrity by measuring telomere length.

To assess how hormonal exposure in the womb will affect all of these important aspects of development over time, Weiss' team is following infants through their first year of life. She is hopeful that the results of this study will help clinicians identify who may be at greatest risk from any adverse effects of corticosteroids and, therefore, help clinicians better weigh the risks and benefits of these treatments. "We can also tailor interventions for those mothers who are most vulnerable in light of their stress and depression profiles," she says.

Effects of Depression on Mother-Infant Interaction

In her second NIH-funded study, Weiss is looking at the impact of maternal depression on a mother's interaction with her infant.

"Parenting involves some of the most complex skills and abilities of any

role in life," says Weiss. "It can be very difficult for women who are struggling with their own emotional challenges to provide care that is sensitive to the child's needs, assures effective cognitive and other stimulation, expresses positive regard and reduces their child's distress in optimal ways."

With investigators from two other American universities, Weiss is studying how adversities such as poverty and trauma, a mother's other [mental health](#) problems and her infant's unique characteristics may influence whether a mother's depression has a negative impact on the way she relates to her child. By understanding the effect of these moderating factors, clinicians will be better able to identify mothers at particular risk for parenting problems. Preventive interventions can then be tailored to target the most vulnerable families as well as the specific parenting qualities that need attention.

"I have great expectations for the research we are doing," says Weiss. "I believe that the findings from our studies can ultimately make a real difference in helping [women](#) who experience depression and stress, and in preventing adverse sequelae for their children. This is what it's all about for me; it's why I derive such purpose and fulfillment as a scientist."

Provided by University of California, San Francisco

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