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Attention to Prevention—Can We Stop Perinatal Depression Before It Starts?

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The perinatal period incurs elevated rates of psychiatric illness and associated risks for maternal and infant morbidity and mortality—a staggering public health burden. Suicide accounts for 20% of deaths in postpartum women and is the second leading cause of mortality in the first year after birth.[1] The adverse impact of high maternal stress levels has been demonstrated during fetal life and results in a cascade of negative health influences that continues through the lifespan of the offspring. The rising maternal mortality rates along with the sensitivity of the fetal period to programming of long-term health and disease has intensified pursuit of interventions to promote maternal mental health. The US Preventive Services Task Force (USPSTF) B recommendation "that clinicians provide or refer pregnant and postpartum persons who are at increased risk of perinatal depression to counseling interventions"[2] acknowledges the enormous opportunity to improve the well-being of mothers and of our next generation, along with the USPSTF evidence report and systematic review.[3]

The recommendation is a prevention strategy focused on identifying women at risk for, but prior to the development of, major depressive disorder. The target population is pregnant and postpartum women (less than 1 year after birth). Increased risk is broadly defined by clinical and socioenvironmental factors, such as personal or family history of depression, physical or sexual abuse, unplanned pregnancy, and pregnancy complications. Stressful life events and

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lack of social resources also increase the likelihood of perinatal depression. The most potent clinical predictor is a previous depressive episode lasting longer than 5 years, which nearly triples the risk for depression during pregnancy, while 4 or more episodes increase the risk by 3.6 fold.[4] These risk factors are remarkably (and unfortunately) common with 55% of women of reproductive age living in poverty[5] and about 1 in 5 women experiencing childhood sexual abuse. The collective frequency of this set of risk factors in women of reproductive age compels consideration of whether all pregnant women should have the opportunity to engage in counseling as standard of practice in maternity care.

We are optimistic that investigations currently being conducted will address several areas of research need identified by the USPSTF. Improved accuracy in the identification of women at risk for perinatal depression will be enhanced by discovery of disease biomarkers. Investigators are pursuing genetic, endocrine, biochemical, immunologic, and brain magnetic resonance imaging biomarkers of perinatal depression.[6] For example, Osborne et al[7] postulated that perinatal depression is mediated by differential gene expression and epigenetic sensitivity to pregnancy hormones. Accurate prediction of postpartum depression was achieved in 2 independent replications with a biomarker model in both a high-risk and general population sample and implicated genes *HP1BP3* and *TTC9B*, which are involved in mediating synaptic plasticity, in the etiology.[7] Preventive efficacy with biomarker-based identification of risk holds great promise to reduce disease expression through accurate targeting of at-risk women with individualized interventions.

Health system delivery approaches using counseling methods are prime candidates for innovation and implementation research to prevent perinatal depression. The ROSE (Reach Out, Stay Strong, Essentials for mothers of newborns) program is an interpersonal psychotherapy-derived program that significantly reduces the emergence of postpartum depression among low-income and racially diverse women.[8] A sequential multiple assignment randomized clinical trial of the effectiveness and cost effectiveness of a stepwise approach to sustainment of ROSE in 90 outpatient clinics providing prenatal care to pregnant women on public assistance is in progress.

Home visiting programs, such as Healthy Families America and the Nurse-Family Partnership, provide services to large numbers of perinatal women and are logical settings for delivering mental health services. A comparative effectiveness trial of Mothers and Babies,[9] a 6-session group intervention with content derived from cognitive behavioral therapy and attachment theory, is being conducted across 36 home visitation programs in 7 states. This study will determine whether this group intervention, led by paraprofessional home visitors, is more efficacious than usual care and not inferior to care delivered by mental health professionals. Such studies will facilitate the scaling of established efficacious interventions in settings that serve large numbers of pregnant and postpartum women.

Two other health systems approaches, collaborative care and statewide provider support programs, are being evaluated for treatment of perinatal depression and will serve as a scaffold for future prevention studies. Collaborative care leverages a care manager as the lynchpin of a system that delivers patient-centered, evidence-driven care with measurement-based treatment outcomes for a specific patient population. Advantages over traditional

models include improved depression outcomes, enhanced quality of life, and greater patient satisfaction compared with usual care. While research on collaborative care in the perinatal setting remains in its infancy, small randomized clinical trials have demonstrated efficacy.[10] Classically applied to depression treatment, the core principles of collaborative care could be leveraged to implement evidence-based prevention opportunities and ensure that stepped care is delivered across a broad at-risk patient population. Other programs that serve as models to optimize effective linkage to depression prevention services include statewide programs such as MCPAP for Moms in Massachusetts, which assists front-line health care professionals to identify and address the mental health and substance use concerns of their pregnant and postpartum patients.

We agree with the USPSTF that research is needed to optimize the use of antidepressant medications during pregnancy, particularly for women for whom maintenance pharmacotherapy is required. Data to inform dose requirements to sustain efficacy across gestation are lacking, and modern pharmacogenomics tools have rarely been applied. In addition to the large interindividual variability in drug response in non-gravid patients, pregnancy induces alterations in the activity of several cytochrome (CYP) 450 isoenzymes. CYP3A4, CYP2D6, and CYP2C9 are increased, and doses of drugs predominantly metabolized by these CYPs may need to be increased to avoid loss of efficacy. In contrast, CYP2C19 activity decreases and dose reductions are needed to minimize toxicity. Currently under way is the National Institute of Child and Health Development–supported Optimizing Medication Management for Mothers with Depression (OPTI-MOM) study, which was designed to define optimal dosing to prevent recurrence through the childbearing period.

Beyond individually focused interventions to prevent depression, we must also advocate for policy-level changes that support perinatal mental health. The United States is the only industrialized nation without a federal paid parental leave law, although several states have adopted such mandates. Maternity leave is a critical factor in promoting maternal-infant attachment, improving health and behavioral outcomes for mother and infant, and supporting breastfeeding. Paid leave and longer duration of paid leave (more than 12 weeks) alleviates the negative effect of early return to work after childbirth and is associated with improved mental health outcomes, especially among mothers returning to full-time work.[11]

Financial coverage for preventive interventions must be part of this conversation. Despite modest momentum to fund preventive interventions across disease conditions[9] and increased billing for postpartum depression screening and treatment through Medicaid’s Early Periodic Screening Diagnosis and Treatment provision, we have yet to realize widespread payment for postpartum depression preventive interventions. Future policy efforts must unite Medicaid and private insurers to define best practices for reimbursement for interventions with proven efficacy in preventing perinatal depression. This USPSTF recommendation serves as a platform for iterative improvement in our tools to implement preventive approaches that reduce the burden that childbearing women, their families, and society bear.

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