The Cost of Restricting Knowledge

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Although clinicians lack evidence-based treatments for mental illness in perinatal women, this insufficiency does not constitute "operating in a vast sea of ignorance."[1] In the relative absence of clinical studies, clinicians rely upon community-based standards of care that emerge from clinical experience, descriptive/observational studies, guidelines of professional associations, and the adaptation of scientific evidence from other populations. While these sources are less robust than the gold standard of research, randomized placebo-controlled trials (RCTs), findings from these sources still provide credible treatment rationales.

This state of affairs prompts a more substantive question: What prevents randomized, placebo-controlled trials in perinatal women? Like perinatal women, children constitute a vulnerable population requiring special protections, yet placebo-controlled trials of antidepressants among children appear in the literature today.[2] We acknowledge the dual requirement to protect the fetus and the mother, and recognize that the ethical considerations complicating perinatal research are inescapable. However, the lack of robust research with perinatal women blinds us to the unknown risks or benefits of treatment *and the lack of treatment* to both mother and child over time. Nevertheless, funding agencies and regulatory boards continue to disqualify research with perinatal women that incorporates a placebo arm. Might we be, as Alta Charo provocatively asks, "Protecting [Women] to Death"?[3]

Ethicists, investigators, and clinicians have suggested that a framework for ethical decision-making in perinatal research would give all stakeholders an important tool to address this inequity in research.[4] Such a framework has already been suggested for decision-making in the clinical setting.[5] In this risk-benefit model for the treatment of schizophrenia in perinatal women, clinician and patient together carefully consider interventions by incorporating the values of both parties about treatment alternatives and possible outcomes. Collaboratively, those involved decide upon an integrative choice of treatment that is open to revision as necessary.

However, this promising clinical model does not address the additional ethical considerations of perinatal research; therefore, we propose an equally collaborative development of a set of guidelines to aid all stakeholders in optimizing the risk-benefit ratio in the design and ethical conduct of RCTs. One approach toward the development of such guidelines is to invite investigators, decision-makers in regulatory and funding agencies, legal experts, community health providers, research participants, and patients and their partners to describe their experiences, values, and beliefs regarding perinatal mental health research. In an ongoing investigation, we have identified concerns of prominent perinatal mental health investigators in the domains of informed consent, inclusion/exclusion criteria, randomization, and therapeutic misconception. Our unpublished preliminary information identifies these domains as important targets to address in a more inclusive group

of stakeholders. Subsequently, a bioethical analysis of the issues and prospective solutions would generate guidelines and, in turn, an algorithm useful for weighing the risks and benefits as they are understood by all of the stakeholders. We recognize that excluding perinatal women and their unborn children from research disadvantages them across all medical treatments, so mental health guidelines for this population could stimulate the development of similar decision-making frameworks for other populations and conditions. We invite your comments.

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