

Letter to the editor

Pregnancy: A Final Frontier in Mental Health Research

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14 This spring, The Food and Drug Administration (FDA) in the United States made further allowances for the
15 participation of pregnant women in research. Up until recently, pregnant women were in a special protected class for
16 human research subjects because they were considered “vulnerable to coercion”. Leaving pregnancy out of research
17 is not limited to drug trials, however. Even at the funding level, women’s health during this critical stage of a
18 woman’s life is an overlooked area of research: 2017 is the earliest year listed for The National Institutes of Health
19 (NIH) classification of funding dedicated to pregnancy or maternal health categories.

21 The awareness of these research oversights and the implications of them are reaching mainstream media. A recent
22 piece in the Washington Post brought public attention to what many of us already recognized as a key issue in the
23 field of women’s health—the lack of basic and clinical research when it comes to pregnancy (Johnson 2019). In the
24 article, the author makes the case that the limited research on pregnancy affects everything from innovation and
25 emerging companies to clinical decisions on prescriptions to understanding the basic physiological shifts that come
26 with pregnancy, parturition, and postpartum. This was a fair analysis and, if anything, it wasn’t critical enough of
27 how science fails pregnant women.

29 Peripartum mental health likely suffers the most neglect as a field of research—with large gaps in knowledge that
30 are slow to fill. This especially rings true for antepartum mental illnesses and their treatment. Take, for example,
31 peripartum mood and anxiety disorders (PMAD), disease states that are beginning to show very unique
32 neurobiological profiles which likely warrant unique treatments (Pawluski et al, 2017). Unfortunately, we know very
33 little about how the brain changes during a healthy pregnancy, let alone in a diseased state (Barba-Müller et al.
34 2018)(Pawluski et al. 2017).

36 Not surprisingly, we have yet to have a specific medication, which is considered risk-free and effective, to treat
37 affective disorders in *pregnant* women. In fact, we are using medications, such as selective serotonin reuptake
38 inhibitors, that can be very effective in many women, without knowing how the serotonergic system of the maternal
39 brain is altered (Lonstein 2019). Zulresso (Sage Therapeutics) is the *first* unique treatment approved by the FDA for
40 postpartum depression (Meltzer-Brody et al. 2018); granted there are inherit criticisms of this medication. The point
41 here is that there is only one unique pharmacotherapy treatment for disorders of the peripartum period. Disorders

that affect up to 20% of peripartum women. This is an ever present reminder that peripartum mental health research needs more support to benefit women during pregnancy, parturition, *and* postpartum.

There are many reasons why research on peripartum mental health lags behind other fields. At its most basic level, pregnancy and postpartum are hard to study. The body changes, physiological processes shift, hormones rise and fall to levels that do not naturally occur at any other time of life, model systems in the lab are imperfect models for human pregnancy. Studying pregnancy also carries an added complication—the health and development of the fetus. And, unfortunately, we must consider that we live in a society that doesn't prioritize women's health. Research and funding tends to focus on the infant when it comes to mother-infant dyad; a mother's mental illness becomes a *risk factor* for the developing child, rather than a focal point. This is a false choice, of course; a mother's health should carry equal weight and equal importance to the health of the child.

The issues with lack of data on mental health and pregnancy extend beyond scientific knowledge gaps. Treatment and innovation for peripartum mental illnesses also suffers. We are a data driven, evidence-based society. Data opens doors. Clinical decisions and changes in care are limited to the depth and breadth of the available evidence, not lack thereof. Investing money and time in emerging technologies to improve peripartum health is dependent on clear data presenting the need for and viability of the solution. More data means more innovation, more solutions, and better outcomes. The ability to increase the opportunity of including pregnant women in research is promising and is a great first step to gain much needed data to improve outcomes for mother and child.

As health care providers, scientists, and members of the general population, we need to continue to advocate for change; for research dollars devoted to studies on peripartum mental health, implementation of findings, and elevated standards of peripartum mental healthcare worldwide.

Compliance with Ethical Standards and conflicts of interest

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