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David A. Kalmbach
Henry Ford Health, DKalmba1@hfhs.org

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Editorial

EDITORIAL

The emerging role of prenatal insomnia therapy in the prevention of perinatal depression and anxiety

David A Kalmbach[1,2,*]

[1]Thomas Roth Sleep Disorders and Research Center, Henry Ford Health System, Detroit, MI 48202, USA and [2]Department of Pulmonary and Critical Care and Sleep Medicine, Wayne State University School of Medicine, Detroit, MI 48201, USA

*Corresponding author. David A. Kalmbach, 39450 W 12 Mile Rd, Novi, MI 48377, USA. Email: dkalmba1@hfhs.org.

Historically, providers and researchers alike have downplayed sleep problems during pregnancy and postpartum as inevitable and inconsequential. Even when pregnant women report experiencing insomnia, these complaints are often dismissed as a normative feature of peripartum without need for intervention. Thankfully, scientific investigation of perinatal insomnia has increased substantially since the early 2000s, really proliferating over the past 10 years. Major findings include estimates that about half of women endorse insomnia symptoms during pregnancy and postpartum [1-4], women with insomnia disorder and perinatal sleep disruption deserve clinical attention [5], insomnia symptoms increase across pregnancy [2], and untreated prenatal insomnia increases risk for perinatal depression [6, 7], adverse pregnancy outcomes such as preterm birth[8] and gestational hypertension [9], and a chronic course of insomnia that often persists for years after childbirth [2]. Troublingly, epidemiological studies estimate that 26%–41% of women complain of insomnia symptoms 2 years after childbirth [3, 5]. Important to emphasize is that women who meet diagnostic criteria for insomnia disorder and those who endorse insomnia symptoms (but do not fully meet criteria) both report elevated mental health symptoms and warrant clinical attention [5]. Despite the significant morbidity and chronicity of perinatal insomnia, only recently have treatment options been empirically supported for pregnant women.

In 2017, Tomfohr-Madsen and colleagues provided the first preliminary data from an open label trial supporting cognitive-behavioral therapy for insomnia (CBTI)—the gold standard and first-line recommended treatment for insomnia in the general population [10]—to improve sleep and mood in pregnant women with insomnia. In 2019, Manber and colleagues published data from their seminal randomized controlled trial (RCT) showing that clinician-led CBTI is efficacious for insomnia during pregnancy [11]. Not only did CBTI reduce prenatal insomnia symptoms, but CBTI also alleviated comorbid depression. Given that 20%–50% of pregnant women with insomnia have comorbid major or minor depression [4, 6, 12], the antidepressant effects of CBTI were very encouraging and supported the notion that insomnia therapeutics could play a role in managing perinatal depression. The following year, two additional RCTs replicated efficacy findings using CBTI delivered via an automated digital program [13, 14], which has immense potential to maximize access to this specialty care for pregnant women. Although CBTI is efficacious in this population, patient feedback and identification of factors associated with poor treatment response may guide adaptation to better address sleep problems in pregnancy [15, 16].

All of this leads to the present issue of *SLEEP*, which includes the next seminal research report on the treatment of insomnia in pregnancy. Felder and colleagues conducted an RCT examining the long-term therapeutic effects of digital CBTI in 208 pregnant women with insomnia [17] (this is a follow-up to their 2020 report on acute effects) [13]. Although support for acute CBTI effects in pregnancy has been strong [11, 13, 14, 18], the potential long-term benefits for sleep and mood into postpartum has remained unclear. CBTI in the general population is touted for its long-term durability [19], yet the postnatal period poses several unique challenges to maternal sleep and mood (e.g., nocturnal infant caregiving and parenting stress) that could impact the durability of insomnia therapy gains.

Felder and colleagues' findings offer encouraging results regarding the durability of CBTI effects after childbirth [17]. Despite its prenatal administration, CBTI produced significantly higher insomnia remission rates six months after childbirth (remission

rates were 1.5 times higher in CBTI group relative to control). Interestingly, data from this trial and a previous RCT [14] did not reveal robust insomnia effects in the first 2 to 3 postnatal months. Taken together, it is possible that the long-term effects of prenatal CBTI on postnatal sleep are most apparent after the newborn period when maternal sleep and infant sleep begin to decouple.

Moreover, Felder et al. showed that CBTI produced long-term antidepressant and anxiolytic effects that were observed 3 to 6 months after childbirth [17]. Really let that sink in: By improving sleep *during pregnancy*, women still benefited from improved mood and decreased anxiety for months after childbirth, despite myriad postnatal changes to nightly sleep, daily routines, and the overall adjustment to caring for a newborn. It is worth emphasizing that the long-term antidepressant and anxiolytic effects were observed 3 months earlier than the long-term insomnia effects, thereby suggesting that CBTI exerts durable influences on affective symptoms that are not completely attributable to sleep effects. These results are promising and should be replicated in pregnant women presenting with insomnia and comorbid mental illness, which would offer greater insight into clinical value of CBTI for comorbid perinatal depression and anxiety.

The most novel and exciting results pertain to the prevention of perinatal mental illness [17]. Prevention, as opposed to treatment, has potential to be more impactful in reducing perinatal depression burden. Indeed, the United States Preventive Services Task Force (USPSTF) recommends prevention to be the prevailing health strategy for perinatal depression. In Felder et al.'s RCT: Among the 143 non-depressed pregnant women with insomnia before treatment, 0% of CBTI patients developed major depression 3 months after childbirth compared with 18% of untreated women. This depression prevention effect was also observed 6 months after childbirth (0% vs 10%). Similarly, among the 158 non-anxious patients at baseline, CBTI reduced risk for incident anxiety 3 months after childbirth (1% vs 15%).

Prevention efforts are most effective when directed at at-risk individuals rather than when deployed universally, the latter of which is cost-ineffective and difficult to implement [20]. Therefore, to best prevent perinatal depression, the USPSTF recommends that *pregnant women at risk for perinatal depression* be referred to therapy interventions. In a recent editorial, Drs. Dietch and Manber proposed delivering insomnia therapy to pregnant women with insomnia as a promising strategy to reduce risk for perinatal depression [16]. I will not retread their fantastic piece here, which I encourage you to read as it covers specific therapy targets and potential enhancements to current therapies. Rather, I want to highlight that the results of Felder and colleagues' RCT strongly support Dietch and Manber's proposal to direct therapy services to pregnant women with insomnia to reduce risk for perinatal depression efficiently and effectively.

In addition to the main study findings, certain methodological aspects of Felder et al.'s RCT should be emphasized [17]. First, CBTI was delivered digitally, which yields smaller treatment effects than clinician-led CBTI in pregnant and non-pregnant samples [15, 21]. Nevertheless, Felder's team observed durable sleep and mood effects. This further supports the deployment of widely accessible and convenient digital CBTI to pregnant women with insomnia. Even so, future research is needed to examine the long-term effects of clinician-led CBTI (or enhanced CBTI-based interventions as proposed by Dietch and Manber [16] and our team [15]), which may provide greater long-term benefits for pregnant women than a digital program.

Second, Felder et al.'s study included few exclusion criteria, benefiting the generalizability of their results [17]. I believe it is especially worth emphasizing that women were eligible whether their insomnia symptoms developed before or during pregnancy, thereby assailing notion that therapy may not be appropriate for women whose insomnia complaints may be related to pregnancy-related sleep disturbances. Along these lines, a recent report recommended that both pregnant women with insomnia disorder and those with subclinical symptoms are likely to benefit from insomnia treatment to improve sleep and mental health [5]. Quite importantly, Felder's team treated both nulliparous and multiparous women in their RCT, thereby supporting CBTI and its long-term effects for both first-time moms and those with other children at home. Third, it is perhaps worth noting that this RCT was not designed nor powered to detect prevention effects. This detail makes the detection of prevention all the more impressive. Fully powered prevention trials with longer follow-up assessments are needed to better determine prevention effects of insomnia therapeutics for perinatal depression.

In just 5 years, the field has gone from having zero empirically supported treatment options for pregnant women with insomnia to now having empirical evidence showing that insomnia therapy (whether clinician-led or digital) improves sleep and mood in pregnancy, has long-lasting benefits after childbirth, and reduces risk for developing perinatal depression and anxiety. I am excited to see how the conceptualization, assessment, and treatment of perinatal insomnia evolve over the next 5 years and beyond.

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