# Treating Insomnia During Pregnancy

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# Accreditation Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of The American Academy of Sleep Medicine and the Michigan Academy of Sleep Medicine. The American Academy of Sleep Medicine is accredited by the ACCME to provide continuing medical education for physicians.

# Conflict of Interest Disclosures for Speakers

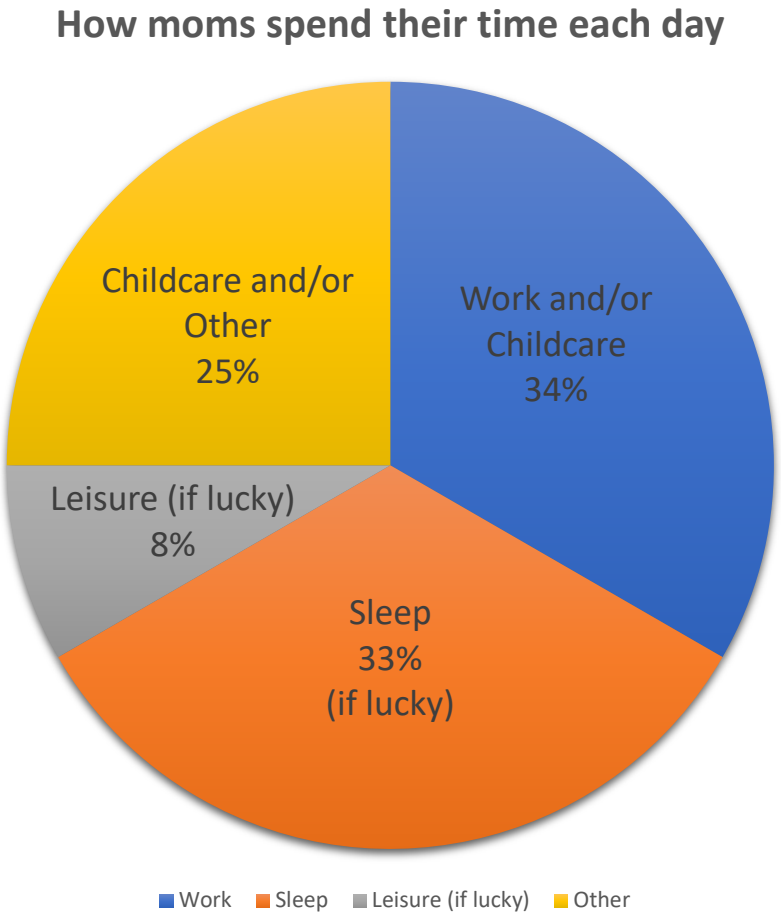
**David A Kalmbach PhD has no relevant financial relationships with ineligible companies to disclose.**

# Learning Objectives

- Upon completion of this course, attendees should be able to…
  1. Know the prevalence of insomnia in pregnancy and the associated perinatal complications.
  2. Understand the different treatment options for pregnant women with insomnia.
  3. Have awareness of the many barriers to accessing sleep care for pregnant women.

# Why care about sleep during pregnancy?

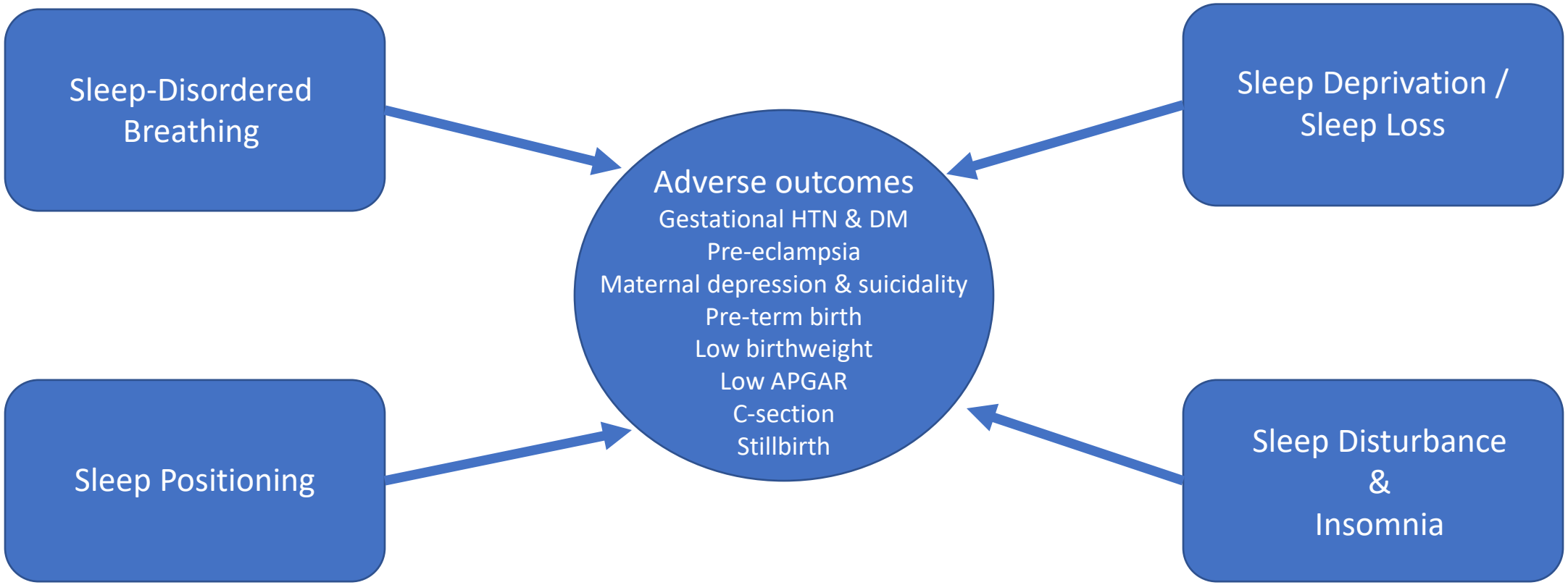
If moms spend about 1/3 of the day sleeping, then that's about 3 months of pregnancy that is spent asleep.



# Sleep changes in pregnancy

- Increased sleep disturbances
  - Discomfort, nocturia, heartburn, nausea, restless legs, PUPPP rash, stress, etc.
- Sleep loss or sleep deprivation
  - Can be related to sleep disturbances or perinatal complications
  - Pregnancy makes it difficult to cope with pre-existing sleep deprivation
- Sleep-breathing issues
  - Weight gain, exacerbates pre-existing risk factors
- Sleep positioning
  - Supine can be most comfortable
  - Supine can be most dangerous
- Some changes are normal (even if unpleasant), but some are not.

# Effects of poor sleep on pregnancy.




Chen et al., 2021 in AJOG; Facco et al., 2017 in Obstetrics & Gynecology; Felder et al., 2017 in Obstetrics & Gynecology; Gordon et al., 2015 in Obestrics & Gynecology; Heazell et al., 2017 in BJOG; Kalmbach, Cheng, & Drake, 2021 in SLEEP; Okun & O'Brien, 2018 in Sleep Medicine; Sedov & Tomfohr-Madsen, 2021 in BSM; Palagini et al., 2014 in Sleep Medicine; Warland et al., 2018 in Sleep Medicine Reviews

# Sleep disturbances & insomnia

# Are sleep disruptions normal change during pregnancy?

- Normal changes
  - Frequent nighttime awakenings
    - Nocturia, change positions, etc.
  - Increased fatigue and sleepiness
- Abnormal changes, but not insomnia
  - Due to some pregnancy-related medical issue
    - Uncontrolled heartburn, nausea, PUPPP rash, pain
  - Due to an occult sleep disorder
    - RLS ($1^{st}$: 8%, $2^{nd}$: 16%, $3^{rd}$: 22%, Postpartum: 4%).
    - Obstructive Sleep Apnea (affects 25-30% by $3^{rd}$ trimester)
    - But these can be comorbid with insomnia

PUPPP = Pruritic urticarial papules and plaques of pregnancy

# Is it insomnia?

- Half of women endorse insomnia by the end of pregnancy.
  - 20-25% endorse diagnostic criteria for DSM-5 insomnia disorder
- Perinatal sleep disturbance vs Insomnia
  - Rule out medical reasons
  - Normal change in sleep?
  - Trouble falling asleep or returning to sleep?
    - Frequent awakenings <u>without</u> prolonged wakefulness = perinatal sleep disturbance
- Are the sleep problems really about sleep?
  - Why do patients seek insomnia treatment?
  - 4-13% of women who endorse insomnia symptoms have MINIMAL wakefulness throughout the night.

See Quinn et al., 2022 in SLEEP (Differentiating perinatal insomnia disorder and sleep disruption); Kalmbach et al., 2022 in Sleep Advances (DSM-5 insomnia disorder in pregnancy)

# OK it’s insomnia.


- Perinatal sleep disruptions are often considered normal (even if unpleasant).
  - <5% of pregnant women are diagnosed with insomnia.
- Half of pregnant women with insomnia discuss sleep with their providers.
  - Provider factors
  - Patient factors
  - System factors

Felder, Hartman, Epel, & Prather, 2020 in BSM: Pregnant patient perspectives of provider detection and treatment of insomnia. Kalmbach et al., 2019 in Nature and Science of Sleep: Insomnia, short sleep, and snoring in mid-to-late pregnancy.

# Why should we care about insomnia?

- Consequences of untreated insomnia vs no insomnia
  - Chronicity
    - 50% of moms sleep poorly 2 years after delivery
    - Impaired postpartum bonding
  - Perinatal Depression: 53% vs 11%
  - Suicidal ideation: 21% vs 3%
  - Excessive sleepiness: 68% vs 16%
  - Gestational hypertension
  - Preterm birth
  - C-section

Felder et al., 2017 in OB&GYN; Kalmbach et al., 2021 in BSM; Kalmbach et al., 2022 in Sleep Advances; Okun & O'Brien, 2018 in Sleep Medicine; Zhang et al., 2017 in J of Maternal-Fetal & Neonatal Medicine

# How can we help?

- No real standard of care
- Sleep hygiene – not an insomnia treatment.
- Prescription medications
  - Category C (Risk cannot be ruled out)
    - Z dugs (zolpidem, zopiclone, eszopiclone)
    - antidepressants (trazodone, mirtazapine, amitryptyline)
  - Dual orexin receptor antagonists (DORAs) unknown (too new)

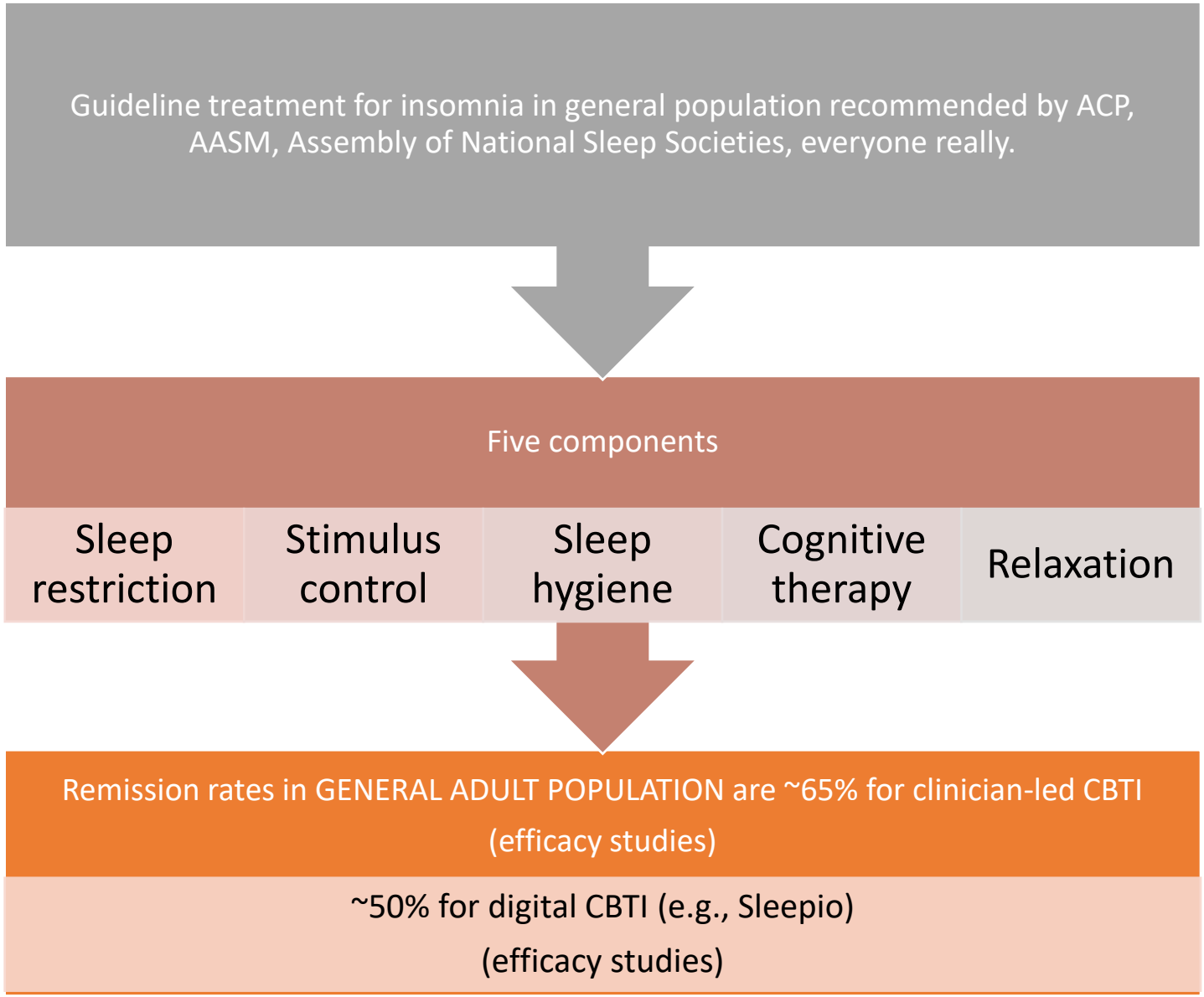
Okun et al., 2014 in AJOG: A review of sleep-promoting medications used in pregnancy. Felder et al., 2022 in BSM: Examining Experiences of Poor Sleep During Pregnancy: A Qualitative Study to Inform the Development of a Prenatal Sleep Intervention.

# How can we help?

- Over-the-counter (OTC) sleep aids
  - Category A (no risk in human studies)
    - Doxylamine, used to treat morning sickness (combined with pyridoxine [B-6])
  - Category B (no known risks in animal studies, but unsure in humans)
    - Diphenhydramine, used to treat allergic reactions
  - Widespread use
  - But not recommended for prenatal insomnia
- Melatonin
  - Safe during pregnancy?
    - Not recommended due to lack of safety data, but we know melatonin crosses placenta.
  - AASM does NOT suggest melatonin for insomnia in general adult population.
  - Recommended by OBs and many pregnant women take it…

Okun et al., 2014 in AJOG: A review of sleep-promoting medications used in pregnancy. Felder et al., 2022 in BSM: Examining Experiences of Poor Sleep During Pregnancy: A Qualitative Study to Inform the Development of a Prenatal Sleep Intervention.

# Cognitive behavioral therapy for insomnia



# CBTI in pregnancy: How effective?

- Clinician-led CBTI
  - Insomnia remission rates
    - In-person CBTI: 64%
    - Telemedicine CBTI: 65%
  - Mixed antidepressant effects (small or non-sig)
- Digital CBTI
  - Insomnia remission rate: 35%
  - Mixed antidepressant effects (small or non-sig)
- CBTI (clinician-led and digital) confer postpartum sleep benefits
  - Mom and infant sleep must decouple.
- Overall, CBTI is a good option for prenatal insomnia.

Manber et al., 2019 in Obstetrics & Gynecology: Cognitive behavioral therapy for prenatal insomnia; Manber et al., 2023 in JCSM: Randomized controlled trial of cognitive behavioral therapy for perinatal insomnia: postpartum outcomes; Felder et al., 2020 in JAMA Psychiatry: Efficacy of digital cognitive behavioral therapy for the treatment of insomnia symptoms among pregnant women; Felder et al., 2020 in SLEEP: Randomized controlled trial of digital cognitive behavior therapy for prenatal insomnia symptoms: effects on postpartum insomnia and mental health; Kalmbach et al., 2020 in Sleep Medicine: A randomized controlled trial of digital cognitive behavioral therapy for insomnia in pregnant women.

# Who doesn't respond to CBTI in pregnancy?

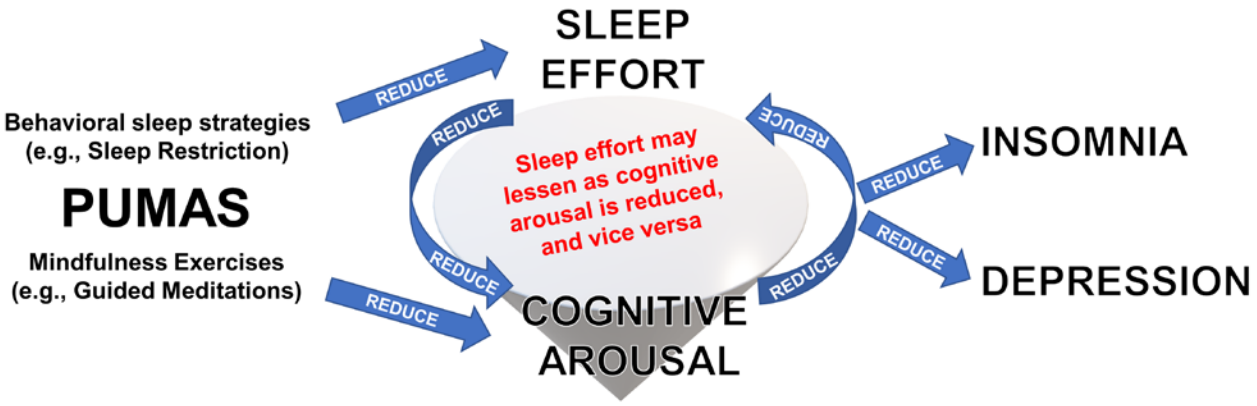
- Refractory cognitive arousal
  - Heightened cognitive activity, e.g., worry, rumination, "planning," etc. at night
  - Before CBTI, most patients have high cognitive arousal at night.
    - But half of pregnant women still have high arousal after CBTI
      - Remission is 4x's more likely when cognitive arousal decreases with therapy.
      - Important to sleep and depression gains.
  - Per data from general insomnia population, this issue is not unique to pregnancy.
    - But there is opportunity for tailoring intervention because pregnant women have a shared stressor.

- Racial disparities in digital insomnia therapy engagement & outcomes
  - Some evidence suggests Black pregnant women benefit less from CBTI.
    - Disparities in digital CBTI.

Felder & Gutierrez, 2023: Letter to the editor on racial disparities in engagement with digital CBT-I among pregnant women; Kalmbach et al., 2022 in BSM: Examining patient feedback and the role of cognitive arousal in treatment non-response to digital cognitive-behavioral therapy for insomnia during pregnancy; Kalmbach et al., 2022 in Sleep Health: Racial disparities in treatment engagement and outcomes in digital cognitive behavioral therapy for insomnia among pregnant women.

# Enhancing patient outcomes: Cognitive arousal

- **Perinatal Understanding of Mindful Awareness for Sleep (PUMAS)**
  - Developed at HFH
  - CBTI may be insufficient for some patients
  - Combining behavioral sleep strategies with mindfulness
  - How does it work?
  - Proof-of-concept trial: PUMAS produced 83% remission
  - 3-arm RCT remission rates
    - PUMAS: 82%
    - CBTI: 65%
    - Control: 15%
  - PUMAS produces large effects on depression, nocturnal cognitive arousal, and sleep effort.




- How does reducing cognitive arousal enhance outcomes?
  - Reducing cognitive arousal mediates the effects of PUMAS on insomnia (26%) and depression (41%)
  - Combining mindfulness and behavioral sleep strategies may dually target cognitive arousal and sleep effort by fostering a calm mindset at night when sleep pressure is behaviorally maximized.

Kalmbach et al., 2023 in Sleep Medicine: Perinatal Understanding of Mindful Awareness for Sleep (PUMAS): A single-arm proof-of-concept trial of a mindfulness-based intervention for DSM-5 insomnia disorder during pregnancy; Kalmbach et al., 2023 in Sleep Advances: Reducing cognitive arousal and sleep effort alleviates insomnia and depression in pregnant women with DSM-5 insomnia disorder treated with a mindfulness sleep program; Kalmbach et al., 2023 in Journal of Sleep Research: Preliminary evidence of psychological improvements and increased maternal-fetal attachment associated with a mindfulness sleep programme.

# Enhancing patient outcomes: Addressing racial disparities

- Why the difference in pregnancy?
  - Minority pregnant women have poor engagement and outcomes in mental health treatment.
    - Lower utilization of prenatal care and mental health treatment during pregnancy
  - Social determinants of health
    - Neighborhood noise, crowded living environments, working multiple jobs, community stress
  - Black Women's Health Study: Culturally tailoring digital CBTI
    - SHUTi-BWHS: Stakeholder-informed, tailored version of SHUTi for Black women
      - Black men and women in all visual content
      - How to implement stimulus control in crowded living environment
      - Addressing neighborhood noise
    - More patient engagement with SHUTi-BWHS vs SHUTi
      - 78% vs 65% completion rate

Zhou et al., 2022 in JAMA Psychiatry: Effect of culturally tailored, internet-delivered CBTI in black women.

# Learning Objective 1

- Know the prevalence of insomnia in pregnancy and the associated perinatal complications.
  - About half of women will develop insomnia by the end of pregnancy, which often becomes chronic for months or years after childbirth.
  - Prenatal insomnia can increase risk for…
    - Maternal depression, anxiety, and suicidal ideation
    - Poor maternal-fetal attachment and postpartum bonding
    - Pre-term birth, gestational hypertension, other complications

# Learning Objective 2

- Understand the different treatment options for pregnant women with insomnia.
  - **Not recommended, not widely used.**
    - Prescription sleep aids: Not considered safe, uncommonly used in this population.
  - **Widespread use despite lack of evidence for efficacy.**
    - OTC sleep aids: Widespread use, but safety and effectiveness are not supported.
      - Commonly recommended by OBGYN providers.
    - Melatonin: Widespread use, but safety and effectiveness are not supported.
  - **Efficacy is supported, but very limited implementation in real-world clinics.**
    - CBTI: Highly effective for sleep, but limited support for depression and cognitive arousal. Access to care is limited.
      - Clinician-led CBTI (in-person or telemedicine) produces better outcomes than digital CBTI.
      - Digital CBTI should be used to address lack of access.
    - PUMAS: Highly effective for sleep, depression, and cognitive arousal. Access is severely limited.
      - Delivered in individual format (similar to CBTI)
      - But may be delivered in group formats (similar to other MBIs)

# Learning Objective 3

- Have awareness of the barriers to accessing sleep care for pregnant women.
  - Provider factors
    - Lack of awareness of…
      - Insomnia as a problem during pregnancy and its harmful effects.
      - Effective treatment options.
  - Patient factors
    - Lack of awareness of…
      - Insomnia as a problem during pregnancy and its harmful effects.
      - That insomnia is a health condition that warrants treatment.
      - Effective treatment options, rather relying on OTC sleep aids, supplements, other unsupported approaches.

# Learning Objective 3 continued

- Have awareness of the barriers to accessing sleep care for pregnant women.
  - System factors
    - Limited time for sleep assessment in prenatal care appointments.
    - Limited or no access to insomnia therapy services in general: Provider shortage.
      - Even less access to those who specialize in perinatal sleep health
      - Long wait times for insomnia therapy, which complicates care for pregnant women.
  - Other factors
    - Lack of access
      - Rural patients, who are at elevated risk
      - Low socioeconomic position, who are at elevated risk
    - Maternity leave.
    - Balancing several medical appointments for routine prenatal care already
      - More if there are already complications.

# Any questions?