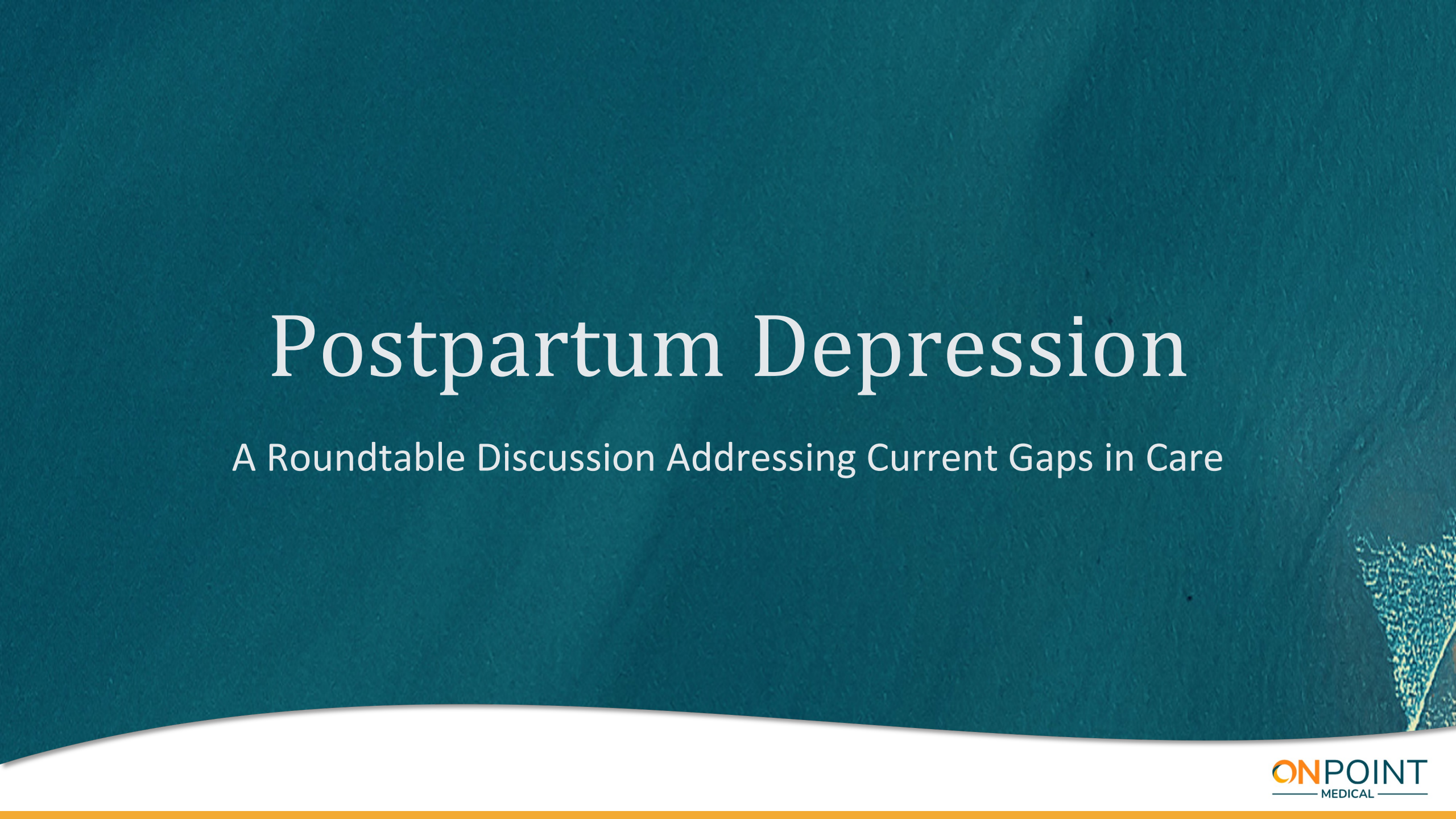
Postpartum Depression

A Roundtable Discussion Addressing Current Gaps in Care



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Learning objectives

- Understand the pathophysiology, symptoms, risk factors, screening methods, and current treatment strategies associated with postpartum depression (PPD)
- Differentiate between PPD and postpartum “baby blues” by identifying key distinguishing characteristics
- Recognize existing gaps in PPD screening, diagnosis, and treatment, especially factors that impact proper care
- Devise strategies to address current needs and improve policies on PPD management

PPD is one of the most common complications of childbirth[1]

- PPD is a depressive mood disorder that occurs during pregnancy or in the first 12 months after delivery[2]
- PPD is diagnosed if at least 5 of the listed symptoms are present for a minimum of 2 weeks, and at least one of the symptoms is either depressed mood or anhedonia[2]

1 in 8

women are affected by PPD[3]

SYMPTOMS[2]
Feelings of sadness or depression
Anhedonia (inability to feel pleasure)
Feelings of worthlessness or guilt
Unrealistic worries about or disinterest in the baby
Significant weight changes or loss of appetite
Suicidal ideation
Insomnia or hypersomnia

1. Liu X, Wang S, Wang G. Prevalence and risk factors of postpartum depression in women: A systematic review and meta-analysis. *J Clin Nurs*. 2022;31(19-20):2665-2677 **2.** ACOG committee opinion no. 757: Screening for perinatal depression. *Obstet Gynecol*. 2018;132(5):e208-e212 **3.** Bauman BL, Ko JY, Cox S, et al. Vital signs: postpartum depressive symptoms and provider discussions about perinatal depression — United States, 2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(19):575-581.

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The exact etiology of PPD is unknown, but multiple hormonal stressors may play a role[1]

- PPD is thought to arise from a complex interplay of genetic, biological, and psychosocial factors[1]
- In particular, depressive disorders often involve HPA axis dysfunction characterized by dramatic changes in the following hormones[1]:
  - Estrogen
  - Progesterone
  - Corticotropin-releasing hormone
  - Oxytocin
  - Serotonin

RISK FACTORS[2]
Personal history of depression or PPD
Family history of depression
Significant life stressors
History of sexual abuse
Lack of social support
History of smoking during pregnancy
Lack of proper sleep and exercise
Preterm labor, prior miscarriage, or history of other poor obstetric outcomes
Problems with breastfeeding

HPA, hypothalamic-pituitary-adrenal

1. Rupanagunta GP, Nandave M, Rawat D, Upadhyay J, Rashid S, Ansari MN. Postpartum depression: aetiology, pathogenesis and the role of nutrients and dietary supplements in prevention and management. *Saudi Pharm J*. 2023;31(7):1274-1293. doi:10.1016/j.jsps.2023.05.008 **2.** Simas M. *Summary of Perinatal Mental Health Conditions Baby Blues Unipolar or Major Depression Bipolar Disorder*. Accessed March 5, 2024. https://www.acog.org/-/media/project/acog/acogorg/files/forms/perinatal-mental-health-toolkit/summary-of-perinatal-mental-health-conditions.pdf.

Despite recommendations by various medical societies, PPD screening methods are not universal

The US Preventive Services Task Force recommends screening only when effective treatment and follow-up options are available[1]

The Canadian Task Force on Preventive Health Care recommends against instrument-based depression screening during the perinatal period[2]

The American College of Obstetricians and Gynecologists (ACOG) recommends using a validated screening tool at least once during the perinatal period*[3]

The American Academy of Pediatrics recommends screening for perinatal depression at all infant well visits until 6 months of age[4]

*Validated screening tools include Edinburgh Postnatal Depression Scale (EPDS), Patient Health Questionnaire-9 (PHQ-9), and Postpartum Depression Screening Scale (PDSS)

1. Siu AL, US Preventive Services Task Force (USPSTF), Bibbins-Domingo K, et al. Screening for depression in adults: US Preventive Services Task Force recommendation statement: US preventive services task force recommendation statement. *JAMA*. 2016;315(4):380-387. doi:10.1001/jama.2015.18392 **2.** Lang E, Colquhoun H, LeBlanc JC, et al. Recommendation on instrument-based screening for depression during pregnancy and the postpartum period. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2022;194(28):E981-E989. doi:https://doi.org/10.1503/cmaj.220290 **3.** ACOG committee opinion no. 757: Screening for perinatal depression. *Obstet Gynecol*. 2018;132(5):e208-e212 **4.** Earls MF. Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. *Pediatrics*. 2010;126(5):1032-1039. doi:https://doi.org/10.1542/peds.2010-2348.

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PPD is different from the “baby blues”[1]

Baby Blues	PPD
Usually starts 2-3 days after childbirth	Usually starts 1-3 weeks after childbirth
Typically presents as a mild form of depression	Interferes with ability to do daily life activities
May include feelings of worry, unhappiness & fatigue	May include anhedonia
Lasts up to 2 weeks postpartum	Lasts for months or longer
Usually gets better on its own	Usually requires treatment

- Following delivery, there is a drop in reproductive hormones, which can lead to what is commonly known as the “baby blues”[1]
- While the “baby blues” generally resolve within two weeks postpartum, PPD persists longer than 2 weeks and can be disabling, significantly impacting daily activities[1]

1. Perinatal Depression. National Institute of Mental Health. Revised 2023. Accessed February 27, 2024.

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Case study: Overview

S, a 28-year-old African American woman, presented at the Department of Psychiatry at the Detroit Medical Center with symptoms of depression, lack of energy, concentration difficulties, sleep disturbances, and loss of appetite 2 months after giving birth to her first child. She also experienced detachment from her newborn, leading to feelings of guilt. After struggling with unsuccessful breastfeeding attempts for 3 weeks, she eventually gave up, further intensifying her sense of guilt. Unable to provide adequate care for her baby, she relies on her husband and immediate family for support.

During her visit, she shares that, despite expressing concerns about her mental health during her 6-week wellness appointment, her OB dismissed them as postpartum "baby blues," advising her to "try to get sleep when your baby sleeps."

Case study: Question 1

What factors differentiate postpartum “baby blues” from PPD in this case?

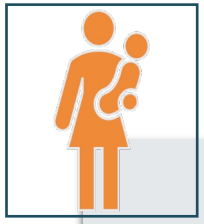
A. Unresolved depressive symptoms at 6 weeks

B. Inability to provide adequate care for the baby

C. Negative impact on quality of life (i.e., sleep and appetite issues)

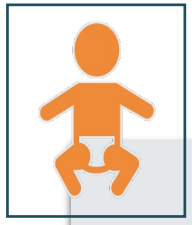
D. All of the above

PPD creates an environment that can be potentially detrimental to both maternal and infant health[1]



Maternal Health

- Increased anxiety
- Increased depression
- Increased weight retention
- Deterioration of social and partner relationships
- Increased likelihood of engaging in addictive behaviors
- Suicidal ideation
- Shorter breastfeeding duration



Infant Health

- Decreased weight gain
- Stunted growth
- Decreased development
  - Cognitive
  - Language
  - Emotional
  - Social
  - Behavioral
- Deterioration of overall health

1. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Women's Health (Lond Engl)*. 2019;15:1745506519844044.

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PPD treatment options are limited

Psychotherapy[1]

- Options include CBT and IPT
- While psychotherapy may be more effective than medications in cases of mild to moderate PPD, it is often time-consuming and costly

Pharmacotherapy[1-3]

- Options include drugs used to treat MDD, such as SSRIs and SNRIs, and drugs specifically approved by FDA for PPD: Brexanolone (IV) and Zuranolone (PO)
- In general, antidepressants may offer convenience, but concerns about their presence in breast milk and other potential adverse effects should be considered

Recommended Treatment Options Based on PPD Severity[1]

Mild to moderate PPD
Psychotherapy

Moderate to severe PPD
Psychotherapy + pharmacotherapy

CBT, cognitive behavioral therapy; IPT, interpersonal therapy; MDD, major depressive disorder

1. Treatment and management of mental health conditions during pregnancy and postpartum. Clinical Practice Guideline No. 5. American College of Obstetricians and Gynecologists. Obstet Gynecol 2023;141:1262-88. **2.** ZULRESSO. Prescribing Information. Sage Therapeutics; 2019 **3.** ZURZUVAE. Prescribing Information. Biogen; 2023.

Zulresso (brexanolone) and Zurzuvae (zuranolone) are the only drugs specifically approved for PPD[1,2]

	Zulresso IV[1] (brexanolone)	Zurzuvae PO[2] (zuranolone)
Indication	Treatment of PPD in adult women	
Mechanism of Action	Allosteric modulator of gamma-aminobutyric acid (GABA) receptor	
Dosage	Continuous IV infusion over 2.5 days, titration to 90 mcg/kg/hr	50 mg PO once daily in the evening for 14 days
Warnings/AE	Suicidal thoughts, sedation, loss of consciousness, dry mouth, and flushing	CNS depression, suicidal thoughts, diarrhea, nasopharyngitis, and urinary tract infection
Cost	$34,000 (available through REMS)	$15,900 (available through REMS)

1. ZULRESSO. Prescribing Information. Sage Therapeutics; 2019 **2.** ZURZUVAE. Prescribing Information. Biogen; 2023.

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Zulresso may offer rapid reduction of depressive symptoms over the course of 2.5 days[1]

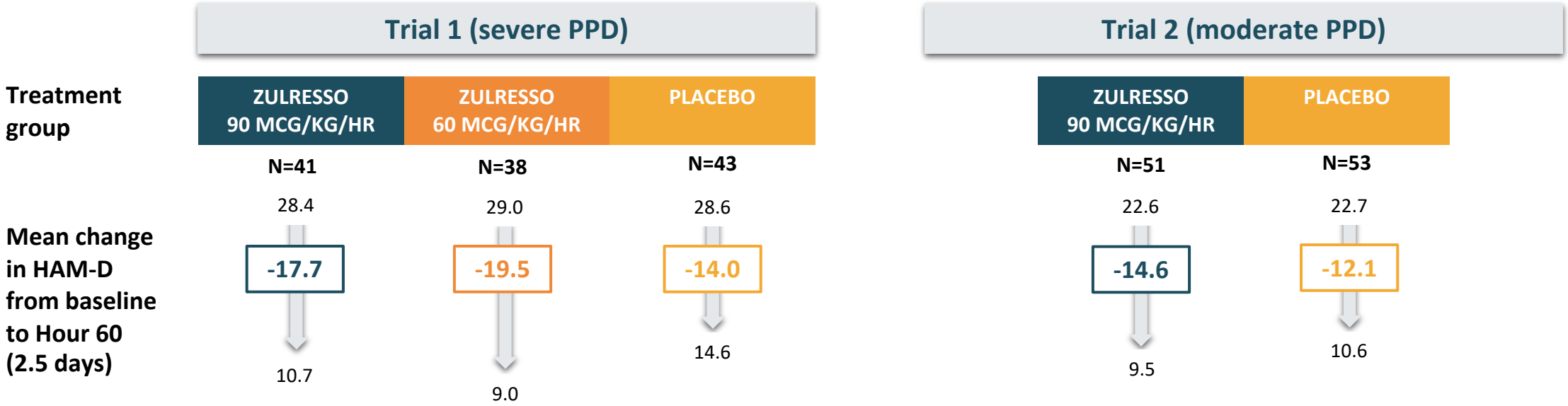
Two Phase 3, Randomized, Double-Blinded, Placebo-Controlled Clinical Trials

Inclusion Criteria

Women (18 to 45 years) with PPD who met the DSM-IV criteria for a major depressive episode starting in the 3rd trimester or within 4 weeks of delivery

Primary Endpoint

Improvement in HAM-D scores



HAM-D, Hamilton Rating Scale for Depression

1. ZULRESSO. Prescribing Information. Sage Therapeutics; 2019.

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Zurzuvae (PO) also offers relief of depressive symptoms by Day 3 of treatment[1]

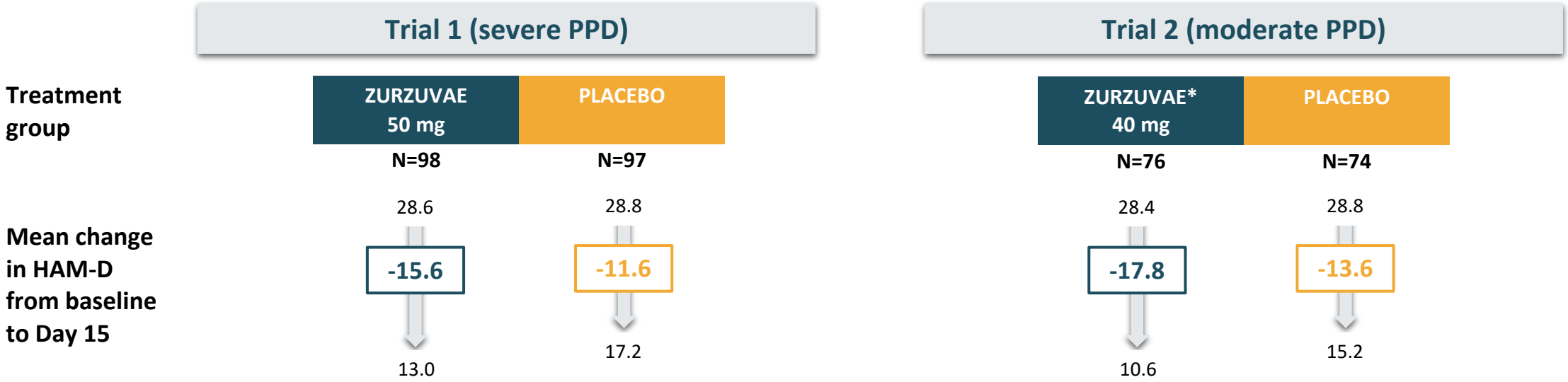
Two Phase 3, Randomized, Double-Blinded, Placebo-Controlled Clinical Trials

Inclusion Criteria

Women (18 to 44 years) with PPD who met the DSM-V criteria for a major depressive episode starting in the 3rd trimester or within 4 weeks of delivery

Primary Endpoint

Improvement in HAMD-17 scores



*In Trial 2, patients received the generic zuranolone formulation, which is approximately equivalent to 40 mg of Zurzuvae.

HAMD-17, Hamilton Rating Scale for Depression

1. ZURZUVAE. Prescribing Information. Biogen; 2023.

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Case study: Question 2

After taking a detailed past medical and social history, the psychiatrist performs a screening assessment using the EPDS screening tool, confirming that S has severe postpartum depression. What is the most appropriate course of action at this point?

(Note: S does not have history of suicidal ideation but has frequent thoughts of harming her baby).

What is the most appropriate initial course of action at this point?

A. Refer to a psychotherapist for CBT

B. Prescribe sertraline only

C. Refer to a psychotherapist for CBT and prescribe Zuranolone

D. Prescribe Zulresso only

EPDS, Edinburg Postnatal Depression Scale

With limited treatment options and high prevalence of PPD, HCPs should prioritize early intervention

However, recent findings report:

20%
of women are not asked about depression during prenatal visit[1]

60%
of PPD cases go undiagnosed[2]

50%
of women with PPD are not treated[2]

- Consequently, women with PPD contribute to significantly higher delivery costs, further emphasizing the increased need for preventing PPD[3]

Increased annual cost of hospitalization in the US:

$102 million
among deliveries to women with mental health disorders[3]

1. Bauman BL, Ko JY, Cox S, et al. Vital signs*:* postpartum depressive symptoms and provider discussions about perinatal depression — United States, 2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(19):575-581 **2.** Ko JY, Farr SL, Dietz PM, Robbins CL. Depression and treatment among U.S. pregnant and nonpregnant women of reproductive age, 2005–2009. *J Womens Health (Larchmt)* 2012;21:830–6 **3.** Brown CC, Adams CE, George KE, Moore JE. Mental health conditions increase severe maternal morbidity by 50 percent and cost $102 million yearly in the United States. *Health Aff (Millwood)*. 2021;40(10):1575-1584.

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HCPs, patients, and families deserve better: what are we missing?

Limited treatment options tailored to PPD[1]

- Only 1 oral drug for the treatment of PPD; IV formulation requiring 60-hour infusion may be inconvenient for patients
- Pharmacological treatment options are not preferred in breastfeeding women

No consistent definition of PPD across guidelines

- ACOG: PPD includes major and minor depressive episodes that occur during pregnancy or within 12 months of delivery[1]
- DSM-5: PPD is a major depressive episode that occurs during pregnancy or within 4 weeks of delivery[2]
- This wide range of definitions may leave HCPs confused about screening and diagnostic guidelines

Maternal care and early intervention is lacking

- Due to a lack of early screening for PPD, HCPs are missing out on timely intervention opportunities—a key part of diagnosing and managing PPD
- Postpartum care is lacking: ACOG guidelines only recommend check-ups at 2 and 6 weeks after birth[1]
- Support for mothers with PPD is lacking, with up to 50% of affected women not receiving the necessary treatment[3]

1. Treatment and management of mental health conditions during pregnancy and postpartum. Clinical Practice Guideline No. 5. American College of Obstetricians and Gynecologists. Obstet Gynecol 2023;141:1262-88. **2.** DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition **3.** Ko JY, Farr SL, Dietz PM, Robbins CL. Depression and treatment among U.S. pregnant and nonpregnant women of reproductive age, 2005–2009. *J Womens Health (Larchmt)* 2012;21:830–6.

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Case study: Question 3

In supporting S's journey toward improved mental health, what additional strategies can the psychiatrist employ?

A. Schedule regular follow-up visits to monitor treatment efficacy and safety

B. Offer an educational handout that de-stigmatizes PPD and highlights the importance of open communication

C. Solely handle S's care plan for relapse prevention to avoid overburdening her other providers

D. A and B only

Key takeaways

- “Baby blues,” characterized by milder and transient depressive symptoms, typically resolve within the first two weeks after delivery, distinguishing it from the more persistent and disabling nature of PPD
- Antidepressants commonly used for MDD may not be as effective for PPD
    - Limited tailored options exist, with only one oral drug receiving approval for PPD to date
- Critical gaps in postpartum mental health care exist, including the lack of timely screening, absence of universal diagnostic methods, limited treatment choices, and insufficient community support
- It is imperative to prioritize early interventions to mitigate the profound developmental and health consequences for both the mother and the infant

Strategies for better care

Collaborative care models[1]

- PCP, mental health specialist, and care manager involvement
- Systemic follow-up and monitoring

Family-focused interventions[1,2]

- Emotional and parenting support
- In-home support, nurse visits, internet communities, peer support, educational classes

Evidence-based guidelines[3]

- Routine screening practices and treatment initiatives
- Appropriate behavioral and/or pharmacological interventions

1. Wells T. Postpartum depression. *Prim Care*. 2023;50(1):127-142. doi:10.1016/j.pop.2022.10.011 **2.** Earls MF, Yogman MW, Mattson G, et al. Incorporating recognition and management of perinatal depression into pediatric practice. *Pediatrics*. 2019;143(1):e20183259. doi:10.1542/peds.2018-3259 **3.** McKinney J, Keyser L, Clinton S, Pagliano C. ACOG committee opinion no. 736: Optimizing postpartum care: Optimizing postpartum care. *Obstet Gynecol*. 2018;132(3):784-785. doi:10.1097/AOG.0000000000002849.

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