

# Safety, Efficacy, and Clinical Implications of Brexanolone for Postpartum Depression: A Systematic Review of Literature

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## Background

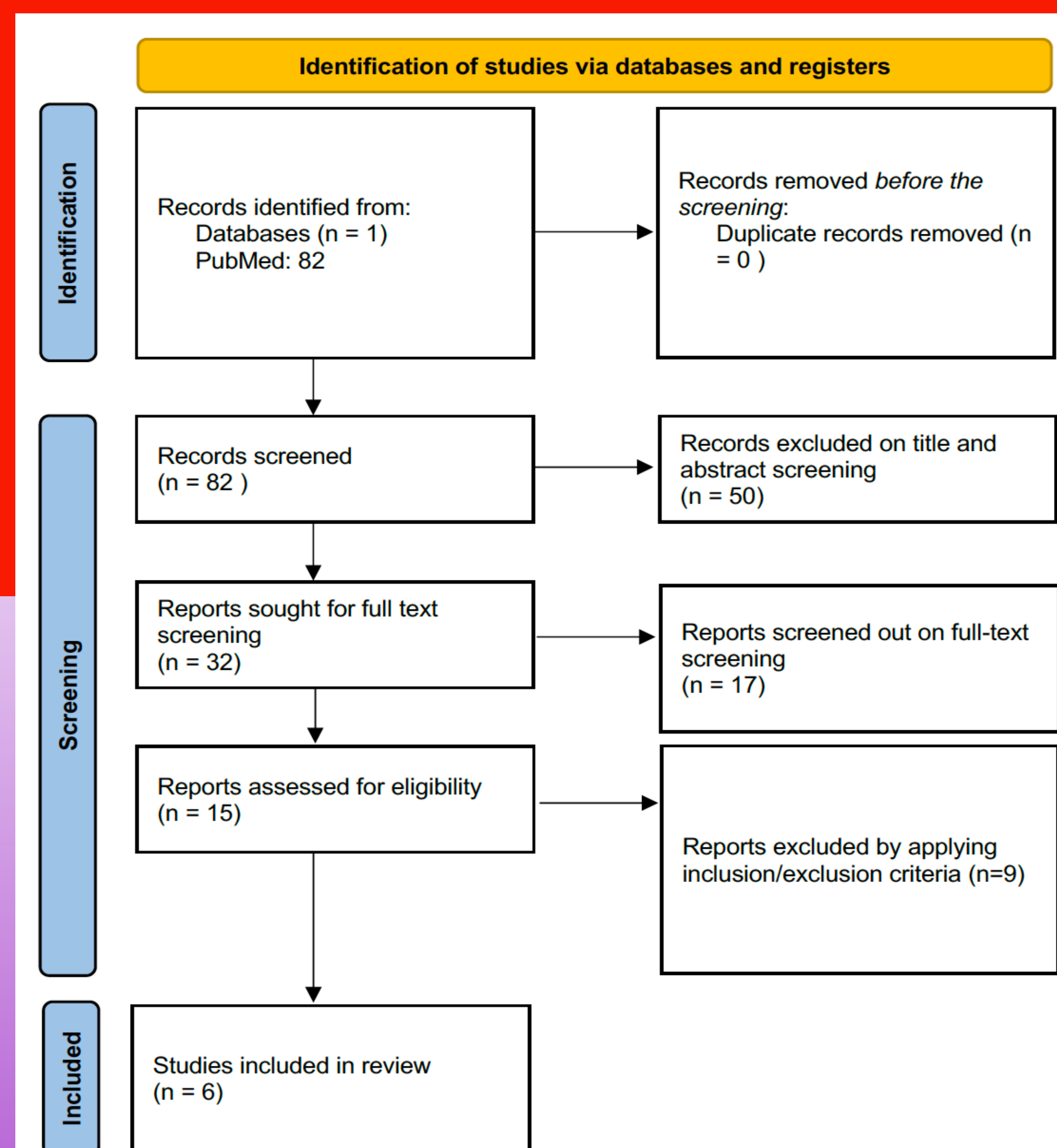
- Postpartum depression (PPD) is a prevalent condition, impacting at least 12-20% of mothers, and plays a significant role in the well-being of both infants and mothers.
- PPD often goes unreported in clinical literature due to insufficient screening and the pervasive stigma attached to diagnosing depression.
- Accepted explanations for its origins include biological, psychosocial, and integrative models.
- The severity of symptoms, prevalence, and overall impact of PPD vary worldwide and are influenced by factors like socioeconomic status and concurrent psychiatric and obstetric conditions.
- Additionally, a woman's ability to comprehend and respond to psychological stressors, known as her "sense of coherence" (SOC), has been associated with PPD.
- A high SOC serves as a protective factor against PPD.
- This, in turn, is influenced by educational attainment, demographics, employment status, marital status, and access to medical care.
- In addition to psychosocial factors, there is growing evidence indicating that endocrine and genetic factors also play a role in the biological aspects of PPD's pathophysiology.

## Method

- We performed a systematic review per PRISMA guidelines.
- The literature search was done on the database PubMed/Medline, using the keywords "brexanolone" AND "postpartum depression" from January 01, 2017, to March 30, 2023.
- The filters used to narrow our search results were
  - a) Species as Humans,
  - b) Language as English, and
  - c) Age group as Adults: 19+ years.
- We included original articles only, and animal studies, studies not published in English, reviews, and metanalysis were excluded.
- We report qualitative data for age groups, clinical efficacy, and safety of brexanolone in PPD.

## Results

- Our initial search yielded a total of 82 articles.
- Six articles were included in the analysis after the records were screened per PRISMA guidelines.
- We include 514 females aged between 18-45 years old diagnosed with PPD administered brexanolone via intravenous infusion.
- Our qualitative review for efficacy showed that brexanolone is effective in treating PPD, with significant reductions in HAM-D total scores, persistence up to day 30, and more significant reduction at the end of the 60-hour infusion compared to placebo.
- Studies also showed a significant decrease in EPDS, GAD-7, and PHQ-9 scores at all assessment times, with an 81% decrease from baseline at Hour 84. The safety of brexanolone in treating PPD was good across multiple studies.



## Discussion

- Although the precise cause of postpartum depression (PPD) is not fully understood, it is associated with fluctuations in allopregnanolone levels, a neuroactive progesterone derivative, during pregnancy and postpartum.
- Allopregnanolone levels peak in the third trimester and rapidly decline after childbirth, affecting GABA A receptors linked to anxiety and depression.
- Brexanolone, a  $\beta$ -cyclodextrin-based allopregnanolone formulation, stabilizes these fluctuations by enhancing GABA transmission, reducing anxiety, and improving depression symptoms.
- Brexanolone is a buffered isotonic solution that contains 5mg/mL of allopregnanolone and 250mg/mL of sulfobutylether- $\beta$ -cyclodextrin, which is administered over 60 hours typically started at a dose of 30 mcg/kg/hour and titrated up to a maximum dose of 90 mcg/kg/hour based on the patient's response and tolerability.
- Its therapeutic benefits can be attributed to its ability to inhibit the production of inflammatory mediators and suppress inflammatory responses to TLR4 and TLR7 activators, suggesting that inflammation plays a significant role in PPD.
- Multiple studies have shown its efficacy over placebo, though it may have tolerability issues such as headache, dizziness, and sedation. Limited data is available regarding its safety during breastfeeding. Research on Brexanolone's potential use for anxiety and insomnia requires further analysis.

## Conclusions

Brexanolone has a rapid onset of action and long-lasting effects, making it highly effective in treating PPD. Enhancing our understanding of the safety and efficacy of brexanolone could accelerate the development of more efficient treatments that prioritize patient care, reduce hospitalization, and minimize treatment expenses.

### References:

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