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The relationship between preterm birth and postpartum anxiety: A first-in-field systematic review

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ABSTRACT

Introduction: Preterm birth poses substantial risks to infant health and maternal mental health, particularly anxiety. The evidence base for associations between gestational age and postpartum anxiety has yet to be synthesised as a whole. This first-in-field systematic review aimed to investigate the relationship between gestational age at delivery and postpartum anxiety, and explore the experiences of mothers of premature infants with postpartum anxiety.

Materials and methods: Searches were conducted across 10 psychological, clinical, and allied health databases from inception to 6th October 2024 (PROSPERO CRD: CRD42023369647). There were no restrictions on language or study design. Only studies that assessed the relationship between gestational age at delivery, or preterm birth, and maternal anxiety assessed during the first postpartum year were eligible for inclusion in this review. Initial searches were conducted by one author. Identification and data extraction of studies were performed by two different authors independently.

Results: Twenty-three studies were eligible for inclusion in the review. All studies were quantitative; no qualitative studies were eligible for inclusion. Data were synthesised via narrative synthesis. Taken together, the results indicate an inverse association between gestational age at delivery (preterm birth) and anxiety.

Conclusions: Variable timing of assessment and tool(s) used to measure postpartum anxiety, alongside limited consideration of categories of gestational age (i.e., extremely, very, moderate-to-late preterm) limit the ability to make firm conclusions about the extent of this relationship.

1. Introduction

Preterm birth remains a worldwide public health concern, with profound and sustained impacts on infants and their families. Recent global estimates suggest approximately 9.9% of all births are premature, of which approximately 4.2% and 10.4% are considered extremely premature (<28 weeks' gestation) and very premature (28-<32 weeks' gestation), respectively [1], requiring increased neonatal care [2]. Preterm birth is associated with numerous short- and long-term adverse physical and psychological health difficulties [3]. The severity of outcomes may be worsened in infants born extremely or very premature, decreasing in babies considered moderate-to-late premature (32-<37 weeks' gestation; [4]).

Consideration of the psychological impact of preterm birth has recently received more attention, despite historically being under-prioritised and under-funded. Risk factors for preterm birth have previously been synthesised [5], and these are particularly pertinent, given rates of preterm birth globally are, at best, remaining static [6]. The potential for the development of postpartum anxiety may be exacerbated in the context of preterm birth, perhaps due to the unexpected nature of the birth if the labour was spontaneous [7] and concerns over infant health, particularly in the case of extreme prematurity [8]. Anxiety symptoms can persist well into the first postpartum year, particularly if infants are admitted to neonatal intensive care units (NICU) [9].

Despite growing recognition of the impact of preterm birth on women's mental health, no systematic synthesis of evidence for the relationship between preterm birth and postpartum anxiety has been undertaken. Through this review, we therefore aimed to answer:

[1] Joint senior authors.

Abbreviations

NICU – Neonatal Intensive Care Unit
PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses
CASP – Critical Appraisal Skills Programme
VLBW – Very Low Birthweight
OCD – Obsessive Compulsive Disorder
PTSD – Post-traumatic Stress Disorder
GAD – Generalised Anxiety Disorder
PASS – Perinatal Anxiety Screening Scale
PSAS – Postpartum Specific Anxiety Scale
PSAS-RSF – Postpartum Specific Anxiety Scale - Research Short Form
STAI – State Trait Anxiety Inventory
GAD-7 – Generalised Anxiety Disorder Scale - 7-item
SAS – Zung Self-Rating Anxiety Scale
HAM-A – Hamilton Anxiety Scale
SCID-I – Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
WHO – World Health Organization

1) What is the relationship between gestational age and postpartum anxiety?
2) What are the experiences of mothers of premature infants with postpartum anxiety?

2. Material and methods

2.1. Registration

This systematic review was registered prospectively on the PROSPERO international prospective register of systematic reviews in February 2023 (CRD: CRD42023369647; [10]) and is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [11].

2.2. Eligibility criteria

Studies were eligible for inclusion if they included a sample of mothers of premature infants aged from birth to 12 months (corrected age, if reported) – a term sample may have been included in these studies as a comparator, but mothers who had given birth prematurely were the main focus of the review. Anxiety could have been measured at any time during the first postpartum year (birth to 12 months). We did not include specific anxiety disorders other than generalised anxiety disorder, for example obsessive compulsive disorder [OCD] or post-traumatic stress disorder [PTSD], in the search strategy as they have previously been reported as having distinct clinical features, which can obfuscate symptoms of anxiety [12,13]. Furthermore, they do not feature in the same axes as anxiety in the Diagnostic and Statistical Manual of Mental Disorders 5. Generalised Anxiety Disorder [GAD] was included in the searches as it is commonly used as a diagnosis in perinatal populations [14]. Studies which only considered the prevalence of anxiety disorders were excluded as they did not directly assess the relationship between gestational age and anxiety; rather just reported prevalence in this population. We followed the PCC framework for systematic reviews, whereby P (population) is women of reproductive age, C (concept) is anxiety as described above, and C (context) is mothers of premature infants aged between birth and 12 months). Eligibility criteria can be found in Table S1.

2.3. Information sources

We searched both empirical and grey literature, as well as theses/dissertations. All databases were searched on 6 October 2024 from inception to present, and included a range of psychological, clinical, and allied health databases. For full details of the search strategy and databases, see Table S2.

2.4. Selection process

All database searches were conducted by one member of the authorship team [SW]. Outputs were imported to Rayaan online software for systematic review screening [15,16]. All outputs were screened at title and abstract stage by two authors [SW, TD], independently of one another. Records deemed potentially eligible were then screened for inclusion at full-text stage, twice, independently by two of the following authors [SW, SAS, VA, SD, AM, ECB, VV, VF, IP, SP, ACF, RA, AMDV, RSC, CI, GC, OW, LJ, LP, SC, BVGB, DF, BFB, TD, LH, CD, GM-K, OP, MA, BG, EM, RCK, MM, MMa, FdM, CR, AB, EP, NCR, LAM, PvD, MEAG, LB, MB, HM, ML, KMSTDA, PD, LDP, REF, SP]. All included articles were double extracted and double assessed for risk of bias into an Excel spreadsheet

by one of the following authors [SD, ECB, IP, CI, GC, BVGB, RC, LJ, ACF, OW, GM-K, RCK, NCR, MM, MMa, PD, REF, MEAG, LDP, LB, CR, HM, EM, AA, GH, LCN, MMu, ZE-D, HM, TDi, DM, LKS, AF, SZ, PH]. Discrepancies between reviewer judgements were sent to a third reviewer for arbitration [SAS].

2.5. Data management and handling

Data extraction was facilitated by a Microsoft Excel spreadsheet, with columns for the study aim, details of the sample and sampling methods, how anxiety was measured, as well as the study findings. A full list can be found in Table S3.

2.6. Synthesis methods

Data were synthesised via narrative synthesis [17]. This was considered the most appropriate method over a meta-analysis due to heterogeneity between studies, variation in study designs (e.g., case control, cohort, descriptive, cross-sectional etc.), sampling

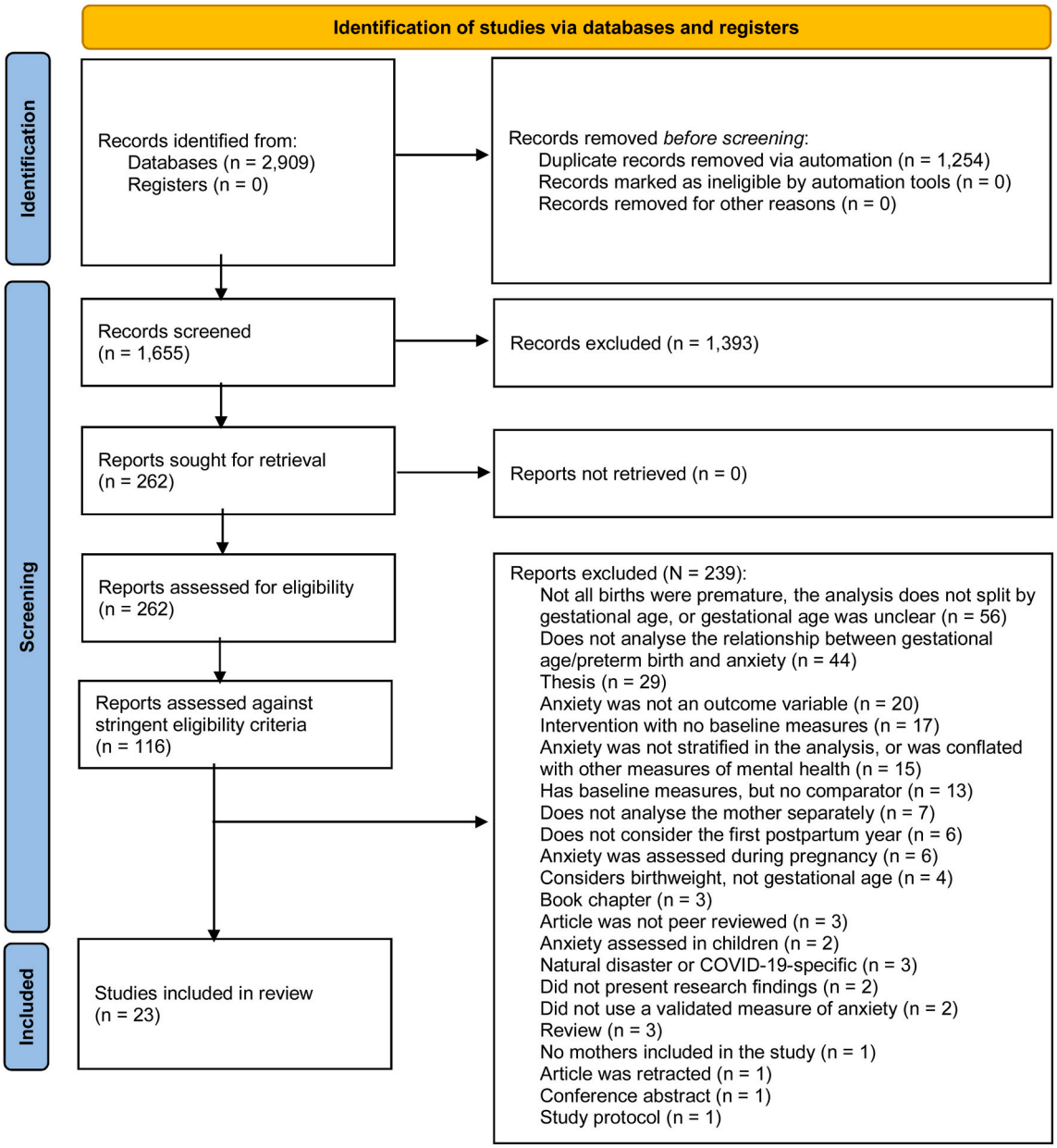

Fig. 1. PRISMA 2020 flow diagram.

methods, and follow-up periods (which would result in high I^2 value), making meaningful interpretation challenging. Furthermore, data were synthesised by the measure of anxiety used, given the increased calls for attention regarding the measurement of perinatal-specific mood disorders, particularly anxiety [18].

2.7. Risk of bias assessment

Risk of bias assessment was conducted using the relevant Critical Appraisal Skills Checklist (CASP; [19]) for the study design. Each checklist is rated via a 'yes', 'no', 'can't tell' system, with the opportunity for authors to provide further comments, where necessary. Whilst the CASP checklists do not routinely score the risk of bias assessment, it is common practice to award responses to checklist items as follows: Yes = 2; Can't Tell = 1, and No = 0; as well as providing associated comments. No studies were excluded from the review based on risk of bias since, as a first in field review, we sought to synthesise all available evidence. Instead, we used risk of bias judgements to aid interpretation of the evidence.

2.8. Study selection

Initial database searches identified 2,909 titles. Duplicates automatically detected by Rayaan were checked manually by one author [SW] before being removed, leaving 1,655 titles to be screened at title and abstract level. A total of 262 publications were screened at full-text stage. Full-text screening yielded 116 publications to be data extracted and risk of bias assessed. Upon data extraction, 12 records were identified as ineligible for inclusion, leaving 104 publications. Two articles were translated by an author fluent in Russian [SZ] and Portuguese [GM-K] respectively. When the lead author [SW] or independent third party (where SW was an author on the article) performed the independent, second data extraction and risk of bias assessment, it became apparent that inclusion criteria had been interpreted more broadly than intended. Whilst we present data extraction and quality assessment for all 104 articles, ultimately only 23 articles were eligible for inclusion in the synthesis, adhering strictly to the protocol (see Table S4 for data extraction and quality assessment of the remaining 81 studies not synthesised in this review).

Although the initial protocol planned to include theses and/or dissertations, after consultation with other authors [SW, PC, AK, VF, SAS], it was deemed appropriate to exclude them in favour of a focus on peer-reviewed literature. Secondly, we also deemed it appropriate to exclude studies specific to the pandemic or natural disasters due to potential confounding factors that may independently exacerbate anxiety. See Fig. 1 for PRISMA 2020 flow diagram. Due to the lack of qualitative studies eligible for inclusion in the review, only the first research question could be addressed.

3. Results

3.1. Study characteristics

The 23 studies included in this systematic review were published between 1986 and 2024, with sample sizes ranging from 29 to 1,227 (N = 4,522). Study designs were cohort (n = 11; [20–30]), case-control (n = 3; [31–33]) or descriptive or cross-sectional (n = 9; [8,34]; 35–41). Studies were conducted in Asia (n = 7; [21,26,31,36,41] [30,33]), Europe (n = 7; [[22,23,25,27,32,35,38]), South America (n = 2; [20,37]), or North America (n = 2; [24,29]), although the study location was unclear or unreported for some (n = 3; [28,39,40]) and recruitment was international for others, with more than one country site (n = 2; [8,34]).

The checklist for case control studies has twelve items (n = 3; two scoring 15 [31,33]; one scoring 17 [32]). For cohort studies the CASP checklist has fourteen items (n = 11; with three scoring ≤20 [20,26,30]; six scoring between 22 and 25 [21,22,24,25,27,28]; and two scoring ≥27 [23,29]). The cross-sectional or descriptive study CASP checklist has eleven items (n = 9; with four scoring ≤18 [8] [36,37,41]; one scoring 19 [35]; and four scoring 20 [34,38–40].

We synthesised included studies narratively according to the psychometric measure of anxiety used: postpartum-specific measures, clinical measures, and generalised measures, to enhance the practical and clinical relevance of our findings. Finally, the term of birth was sometimes defined as a continuous variable expressed in weeks or sometimes defined as a categorical variable (preterm or term) so both gestational age and preterm birth are used throughout the synthesis. Whilst all articles – significant, partially significant, or non-significant comprise the review, we present below only the synthesis of significant results, with the synthesis of those reporting non-significant and/or partially significant results removed to Table S8. The exception to this is the inclusion of a partially significant relationship reported by the only article which utilised a clinical measure [35]. This exception was made on the basis of clinical measurement being the gold standard in mental health practice, compared to generalised or specific non-clinical measures. See Table S3 for characteristics of included studies and Tables S5–S7 for risk of bias assessment of included studies.

3.2. Postpartum specific measures

Four studies [8,30,33,34] used postpartum-specific measures of anxiety. Generally, they were of medium-to-high quality, scoring between 15 and <20 on the CASP. Of these, two [30,33] used the Perinatal Anxiety Screening Scale (PASS; [42]), one study [34] used the Postpartum Specific Anxiety Scale (PSAS; [43]) and another [8] used its short-form derivative (PSAS-RSF; [44]). Three studies [8, 34,30] identified an inverse relationship between gestational age/preterm birth and postpartum anxiety, with one identifying a partial relationship (i.e., significant in one analysis but not another [33].

3.2.1. Perinatal Anxiety Screening Scale

When considering mothers of late premature infants alone, mean PASS [42] scores were significantly higher 12-14 weeks after birth compared to 4-10 days after birth ($p = \cdot003$), in a small sample ($N = 35$; [30]).

3.2.2. Postpartum Specific Anxiety Scale

Women of premature infants (classified as >28 weeks - <37 weeks), had higher scores for anxiety about infant care than the term group ($p < .001$). However, women with extremely premature infants (<28 weeks) had higher scores for anxiety about infant safety on the PSAS [43] than women in the term group ($p = \cdot021$; [34]). However, when comparing between categories of prematurity using the PSAS-RSF [44], both infant care related, and safety and welfare-focused anxiety were higher in mothers of extremely premature ($p<\cdot001$) and late premature ($p = \cdot019$) infants than in mothers of term infants [8].

3.3. Generalised measures

Generalised measures of anxiety were reported by 19 studies 20–29,31,32,35–41. Overall, these were of medium-to-high quality, with scores ranging between <18 and >27 on the CASP. Of these, 11 identified an inverse relationship between gestational age/-preterm birth and anxiety [20,21,23,26,27,29,31,32,35,38,41]; five studies identified some significant results but not in all analyses or measures [22,25,28,37,39] and three studies did not find a relationship between preterm birth and postpartum anxiety [28,36,40].

3.3.1. State Trait Anxiety Inventory

Of the 13 studies utilising the STAI [45], nine studies found a significant inverse relationship between gestational age/preterm birth and anxiety [20,23,26,27,29,31,32,35,38], and five found some significant associations but not in all analyses [22,25,28,37,39].

One study reported a significant negative relationship between state anxiety and gestational age ($r = -.34$, $p = .04$; [20]), in that higher levels of anxiety were associated with lower gestational age.

Similarly, when considering women with very low birthweight preterm infants, there were significantly higher state anxiety scores than among women whose infants were born at term (no p-value provided). Furthermore, these women had a 7.1-times higher risk of anxiety symptoms, and when predicting anxiety using the STAI, preterm VLBW/term in the model was significant ($\beta = 5.1$, 95%CI = 1.86 - 8.41, $p < .05$; [35]).

Other studies also considering state and trait anxiety found that higher maternal trait anxiety was associated with an increased incidence of preterm birth. Mothers of preterm infants had significantly higher levels of anxiety symptoms compared to women whose infants were born at term (state anxiety for mothers of preterm infants = M = 41.56 (SD = 13.41); mothers of term infants M = 33.62, (SD = 9.89); $p = .000$; trait anxiety for mothers of preterm infants = M = 39.0 (SD = 11.48); mothers of term infants M = 33.62 (SD = 9.89); $p = .000$; [38]).

When considering infants born at less than 33 weeks' gestation [27], there was a statistically significant effect of time following birth on state anxiety scores, with mothers' state anxiety significantly increasing from within two weeks postpartum to just after NICU discharge, rising from a mean of 21.5 (SD = 2.8) to 23.8 ($p = .001$).

Similarly, after adjusting for confounders, trait anxiety levels of mothers with late preterm infants were significantly higher than those of women with full-term infants (45.8 ± 10.1 vs. 39.0 ± 6.1, $p = .002$) as were state anxiety levels (49.5 ± 9 vs. 42.6 ± 5.3, $p = .0005$; [32]).

However, another cohort study [23] demonstrated a significant reduction in the levels of anxiety symptoms over time (after birth, one month after birth, before NICU discharge, three months corrected age): $F(2, 62) = 21.27$, $p < .001$, with symptoms significantly associated with gestational age at birth (Spearman's $p = .33$, $p = .004$, $n = 74$).

Up to four months postpartum, it was found that mothers of late-preterm infants were significantly more likely than mothers of infants born at term to report excessive anxiety (score of >40 on the STAI) (OR = 2.07, 95 %CI = 1.08,3.98), even after controlling for confounders [29].

In another study 24-72 h after birth, the mean state anxiety score in the preterm birth group (M(SD) = 43.07(8.91)) was significantly higher than among women in term group (M(SD) = 35.57(7.79); $t = 7.747$; $p < .001$) [31].

Similarly, one day after birth, the anxiety scores of the mothers of premature infants were higher than among women in the general population in China ($t = 2.779$, $p = .007$; [26]), although the comparison group was not described in any further detail.

3.3.2. Generalised Anxiety Disorder Scale – 7-item

One study [41] used the Generalised Anxiety Disorder 7-item scale (GAD-7; [46]). It was found that mothers of preterm infants admitted to NICU had a significantly higher likelihood of anxiety symptoms compared with women whose infants were born at term and not admitted to NICU (OR = 2·21; 95% CI 1·34–3·65, $p = \cdot002$). There was also a significant negative association between gestational age and anxiety symptoms (OR = 2·35; 95% CI 1·12-4·96) in mothers of preterm infants.

3.3.3. Zung Self-Rating Anxiety Scale

One study [21] used the Zung Self-Rating Anxiety Scale (SAS; [47]), demonstrating mothers who gave birth at term had significantly lower anxiety scores than women in the preterm group ($\chi^2 = 36.23$, $p < 0.0001$).

3.3.4. Hamilton Anxiety Scale

A final study [25], in addition to the STAI, used the Hamilton Anxiety Scale (HAM-A; [48]). After adjusting for heterogenous

variances, 14 days after delivery state anxiety scores were significantly higher in the preterm group (M(SD) = 7.78 (5.98)) compared to the control group of term mothers (M(SD) = 3.97(3.63), tadj = 3.012, p = .004). Additionally, a further six months after birth, anxiety scores were significantly higher in the preterm group (M (SD) = 5.41 (4.54) compared to the control group (M (SD) = 2.54(2.39), t = 2.893, p = .006).

3.4. Clinical measures

3.4.1. Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM), Fourth Edition (SCID-I)

One study [35] utilised both a clinical measure and a generalised measure of anxiety, the latter of which will be discussed elsewhere, scoring highly on the CASP. Using the SCID-I [49] to assess women at 4-6 weeks postpartum, mothers of very low birthweight [VLBW] preterm infants had no increased risk of at least one anxiety disorder, compared to mothers of infants born at term. However, mothers of preterm infants had a three times higher risk of prior anxiety disorder than women whose babies were born at term. It is, however, worth noting this assessment was only taken at a singular timepoint, 4-6 weeks postpartum.

4. Discussion

This systematic review aimed to investigate the relationship between gestational age at delivery (preterm birth) and postpartum anxiety, alongside women's experiences of postpartum anxiety following preterm birth. Due to the lack of qualitative studies identified, our results focused exclusively on our first aim.

4.1. Measurement of anxiety

Contrary to recent research, policy, and practice suggestions, clinician-administered measures of anxiety were rarely employed by studies eligible for inclusion in this systematic review. The single study which used a clinical measure of anxiety [35] only found a partial association between preterm birth and anxiety disorders, assessed at a single timepoint. The lack of evidence base on clinician-administered measurement is concerning, given that a systematic review [50] found clinical levels of anxiety are common and occur in approximately 8.5% of women. Acknowledging that anxiety may be exacerbated in women who have given birth prematurely is essential, given the adverse, and anxiety inducing, experiences involved. Whilst self-report tools were widely used by included studies, they lack the precision required to distinguish diagnosable anxiety disorders from adaptive anxieties usually experienced by many women postpartum, which do not cause functional impairment [51]. As such, estimating the true prevalence of postpartum anxiety disorders among women following preterm birth is impeded by the absence of clinical assessment in the literature and may result in underestimation of prevalence or mischaracterisation of adaptive experiences during transient timepoints for this specific population.

Despite consistent calls discouraging the use of general anxiety measures to study perinatal populations [52], their use persists. Although the PASS [42] has good psychometric properties, foci of anxiety during pregnancy are distinct from those which arise postpartum [53], and so may not fully capture the nature or severity of anxiety, which a postpartum-specific measure may.

4.2. Timing of assessment

We identified wide variation in the timing of included studies' assessments of postpartum anxiety, from as early as 24 hours postpartum and the initial days after birth [31,32,39,41], the first three months [22,23,26,28,30,35,38], the first six months [25,27,29,36,40], and throughout the first postpartum year [8,34,20]. However, four studies did not clearly report the timing of measurement [21,24,33,37], whilst seven studies also used longitudinal designs or repeated measures [20,23,25,27,28,32,36].

Most studies that reported the timing of assessment found higher anxiety symptoms soon after birth, compared to later in the postnatal period. One-off measurements may not capture the long-term trajectories of immediate postnatal anxiety across the first postpartum year. Longitudinal studies are essential to consider the trajectory of anxiety symptoms over time.

4.2.1. Categories of prematurity

Eight studies [22,24,25,27–30,32] enrolled women with very preterm or moderate-to-late preterm infants, whereas only two studies [8,34] considered all three categories of prematurity defined by the World Health Organization [54]. Thirteen studies did not categorise participants by degree of prematurity [20,21,23,26,31,33,35–40]. As a result, the experiences of women whose babies were born extremely preterm (<28 weeks' gestation) may have been neglected in existing literature, perhaps because infants born at this degree of prematurity are comparatively rare compared to other degrees of prematurity. Given the potential for more severe anxiety symptoms following more severe prematurity [55], it is surprising that few studies focused on this population. Lack of attention to the timing and nature of preterm birth (for example, planned early delivery for medical reasons versus spontaneous early labour) and the timing of anxiety assessment also makes it difficult to disentangle symptoms arising from early labour itself, from those linked to the NICU experience. Future research on the mental health impacts of preterm labour should report gestational age at delivery and categories of prematurity when conducting research into women's experiences of this time.

4.2.2. Clinical implications

Despite advances in global understanding of perinatal mental health, validated, specific postnatal anxiety measurement scales,

screening tools, and interventions for women with premature infants across the first postpartum year remain limited [56]. Although recognition of postpartum anxiety disorders among women who experience preterm labour is encouraging, there is no specific mental health guidance for professionals supporting women and families who have experienced preterm birth. Whilst specialist practitioners may provide psychological support to mothers with babies admitted to NICU, provision of specialist postpartum care and support varies across countries, and even within national healthcare systems, especially following hospital discharge [57]. This is particularly problematic for marginalised and minoritised groups, who may find healthcare harder to access and navigate [58] than other groups. These populations face disproportionate social adversity and health inequities [59], compounded by racial and cultural discrimination in healthcare settings [60]. Some women do not report mental health symptoms for cultural or religious reasons, or fear of anticipated consequences [61,62]. There are currently no perinatal-specific tools to measure anxiety specific to preterm birth or NICU admission and none of the tools utilised by included studies captured the unique experience of having a premature baby. General anxiety scales are unlikely to capture symptoms specific to the experience of prematurity. Furthermore, the striking lack of qualitative evidence means that diverse women's experiences of this time have not been explored in depth.

5. Conclusion

Most included studies reported an inverse relationship between gestational age at birth (preterm birth) and postpartum anxiety in mothers, but heterogeneity of measurement and inconsistent adjustment for confounding variables, timing of assessments, and measurement scales impacted the strength of evidence. No qualitative studies were eligible for inclusion; future studies are essential to explore women's experiences of anxiety symptoms following preterm birth. Longitudinal, prospective measurement, careful consideration of the timing of assessments, sub-analysis by categories of prematurity, and measurement tool selection, are essential to enhance the field and strengthen the evidence base.

CRediT authorship contribution statement

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Practice points

- Despite advances in global understanding of perinatal mental health, validated, specific postnatal anxiety measurement scales, screening tools, and interventions for women across the first postpartum year remain limited.
- Although recognition of postpartum anxiety disorders among women who experience preterm labour is encouraging, there is no specific mental health guidance for professionals supporting women and families who have experienced preterm birth.
- There are currently no validated perinatal-specific tools to measure anxiety specific to preterm birth or NICU admission and none of the tools utilised by included studies captured the unique experience of having a premature baby.

Research agenda

- Longitudinal, prospective measurement, careful consideration of the timing of assessments, sub-analysis by categories of prematurity, and measurement tool selection, are essential to enhance the field and strengthen the evidence base.

Ethics statement

Not applicable.

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Declaration of competing interest

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Appendix A. Supplementary data

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