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Association Between Maternal Perinatal Depression and Anxiety and Child and Adolescent Development
A Meta-analysis

Alana Rogers, BA(Hons); Shelley Obst, BAppSc(Hons); Samantha J. Teague, PhD; Larissa Rossen, PhD; Elizabeth A. Spry, PhD; Jacqui A. Macdonald, PhD; Matthew Sunderland, PhD; Craig A. Olsson, PhD; George Youssef, PhD; Delyse Hutchinson, PhD

IMPORTANCE There is widespread interest in associations between maternal perinatal depression and anxiety and offspring development; however, to date, there has been no systematic, meta-analytic review on the long-term developmental outcomes spanning infancy through adolescence.

OBJECTIVE To provide a comprehensive systematic review and meta-analysis of the extant literature on associations between maternal perinatal depression and anxiety and social-emotional, cognitive, language, motor, and adaptability outcomes in offspring during the first 18 years of life.

DATA SOURCES Six databases were searched (CINAHL Complete, Cochrane Library, Embase, Informit, MEDLINE Complete, and PsycInfo) for all extant studies reporting associations between perinatal maternal mental health problems and offspring development to March 1, 2020.

STUDY SELECTION Studies were included if they were published in English; had a human sample, quantitative data, a longitudinal design, and measures of perinatal depression and/or anxiety and social-emotional, cognitive, language, motor, and/or adaptability development in offspring; and investigated an association between perinatal depression or anxiety and childhood development.

DATA EXTRACTION AND SYNTHESIS Of 27 212 articles identified, 191 were eligible for meta-analysis. Data were extracted by multiple independent observers and pooled using a fixed- or a random-effects model. A series of meta-regressions were also conducted. Data were analyzed from January 1, 2019, to March 15, 2020.

MAIN OUTCOMES AND MEASURES Primary outcomes included social-emotional, cognitive, language, motor, and adaptability development in offspring during the first 18 years of life.

RESULTS After screening, 191 unique studies were eligible for meta-analysis, with a combined sample of 195 751 unique mother-child dyads. Maternal perinatal depression and anxiety were associated with poorer offspring social-emotional (antenatal period, r = 0.21 [95% CI, 0.16-0.27]; postnatal period, r = 0.24 [95% CI, 0.19-0.28]), cognitive (antenatal period, r = −0.12 [95% CI, −0.19 to −0.05]; postnatal period, r = −0.25 [95% CI, −0.39 to −0.09]), language (antenatal period, r = −0.11 [95% CI, −0.20 to 0.02]; postnatal period, r = −0.22 [95% CI, −0.40 to 0.03]), motor (antenatal period, r = −0.07 [95% CI, −0.18 to 0.03]; postnatal period, r = −0.07 [95% CI, −0.16 to 0.03]), and adaptive behavior (antenatal period, r = −0.26 [95% CI, −0.39 to −0.12]) development. Findings extended beyond infancy, into childhood and adolescence. Meta-regressions confirmed the robustness of the results.

CONCLUSIONS AND RELEVANCE Evidence suggests that perinatal depression and anxiety in mothers are adversely associated with offspring development and therefore are important targets for prevention and early intervention to support mothers transitioning into parenthood and the health and well-being of next-generation offspring.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author Delyse Hutchinson, PhD, Centre for Social and Early Emotional Development, School of Psychology, Faculty of Health, Deakin University, Burwood, Victoria, Australia 3125 (delyse.hutchinson@deakin.edu.au).

n high-income countries, approximately 5% of mothers experience clinical depression, and 13% experience clinical anxiety perinatally. In low- and middle-income countries, estimates range from 15% to 50%.[1,2] There is widespread interest in the association between maternal perinatal mental health and offspring development. A number of systematic narrative reviews of this literature have been conducted[3-12]; however, to our knowledge, no systematic review and meta-analysis to date has evaluated the longer-term associations of maternal antenatal and postnatal depression and anxiety with a range of key developmental domains from infancy through adolescence. Herein we present findings from a meta-analysis of evidence on the association of antenatal and postnatal anxiety and depression with early life development with the aim of informing perinatal preventative intervention and treatment initiatives.

The perinatal period spans conception through pregnancy (antenatal), birth, and the first year of life (postnatal).[13] Although numerous factors within and beyond the perinatal period may influence offspring development (eg, medication use, continuing maternal depression and anxiety, social factors), the perinatal period is in itself a time of unprecedented growth and sensitivity, during which intrauterine exposures and early life experiences may modify fetal, infant, and later development.[14,15] There are various possible mechanisms via which perinatal depression and anxiety may negatively affect offspring development. Antenatal depression and anxiety have each been shown to increase fetal cortisol concentration,[16] leading to changes in fetal hypothalamic-pituitary-adrenal axis activity and brain function[17] and reducing placental blood flow and oxygen and nutrients to the fetus.[18] In addition, studies suggest that antenatal depression and anxiety may lead to epigenetic dysregulation in offspring hypothalamic-pituitary-adrenal pathways and serotonin transmission, resulting in increased offspring hypothalamic-pituitary-adrenal reactivity and changes in brain serotonin levels that can influence development.[19] Furthermore, antenatal depression and anxiety may disrupt neurocognitive changes that prepare mothers to sensitively respond to their infants.[20] Postnatal depression and anxiety are also theorized to delay offspring development by reducing a mother's ability to sensitively respond to infant cues and, subsequently, the likelihood of a secure infant attachment.[21,22] Notably, postnatal depression has been associated with maternal disengagement,[23] whereas postnatal anxiety has been associated with overintrusive parenting.[24]

Given these putative mechanisms, numerous studies have examined whether perinatal depression and anxiety are associated with adverse offspring development. Across the domains of social-emotional, cognitive, language, motor, and adaptive behavior development, effect sizes range from large to negligible. Within the social-emotional domain, although not all studies found evidence of association,[3] children born to mothers with perinatal depression or anxiety have been shown to have higher rates of insecure attachment, fewer prosocial behaviors,[25,26] and more temperamental difficulties,[27] internalizing,[28] externalizing,[28] and peer-related problems.[29] Although some studies show associations between perinatal

depression and anxiety and cognitive deficits,[30,31] particularly in the domains of executive functioning,[30] memory,[30] processing speed,[31] academic achievement, and intelligence,[32,33] others demonstrate no significant effect.[34,35] In addition, numerous studies suggest perinatal depression and anxiety may delay language and motor maturation, specifically expressive and receptive communication and gross and fine motor skills[36,37]; however, others show no evidence of association.[38,39] Comparably fewer studies have examined adaptive behavior development, with some showing no association[40,41] and others finding small associations between perinatal depression and anxiety and poorer offspring adaptive behavior.[37]

The inconsistency between studies may be due to differences in type of exposure (ie, depression or anxiety), timing of exposure (ie, antenatal or postnatal), child age, and assessment method (ie, self-report or assessment), making it difficult to ascertain the magnitude of effects for each developmental domain. Various reviews have attempted to synthesize the available research.[3-5,7-12,42] However, to our knowledge, no study to date has comprehensively reviewed both the antenatal and postnatal periods and depression and anxiety across key developmental domains from infancy through adolescence, nor have they performed a meta-analysis of the available studies, making it difficult to ascertain the magnitude of the effects. The aim of this systematic review is 2-fold: (1) to provide meta-analytic estimates of the association of maternal perinatal depression and anxiety on social-emotional, cognitive, language, motor, and adaptive behavior development in offspring from infancy through adolescence; and (2) to assess whether this association is moderated by timing of exposure (ie, antenatal and postnatal exposure), type of mental illness (ie, maternal depression and anxiety), and offspring age (ie, infancy, childhood, middle childhood, and adolescence).

Methods

Search Strategy
This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting

Key Points

Question Are maternal perinatal depression and anxiety adversely associated with social-emotional, cognitive, language, motor, and adaptive behavior development in offspring during the first 18 years of life?

Findings In this systematic review and meta-analysis, maternal perinatal depression and anxiety were associated with poorer social-emotional, cognitive, language, motor, and adaptive behavior development in offspring. Developmental outcomes extended beyond infancy, into childhood and adolescence.

Meaning Evidence suggests that perinatal depression and anxiety in mothers are adversely associated with offspring development and, therefore, are important targets for prevention and early intervention to support mothers transitioning into parenthood and the health and well-being of next-generation offspring.

Inclusion Criteria

1. Available in English
2. Human sample: offspring aged 4 wk to <18 y
3. Empirical study
4. Quantitative data, analyzing an association between maternal perinatal depression and/or anxiety and childhood development
5. Prospective longitudinal design, with mental health measured before the child outcome measure[a]
6. Measure of perinatal anxiety or depression (symptoms and/or diagnosis)
7. Measure of child development
   a. Social-emotional: externalizing, internalizing, peer problems, prosocial, attachment, dysregulation, positive and negative emotionality, orienting, and difficulty
   b. Cognitive: visual spatial, verbal IQ, inhibition, quantitative and working memory, and academic achievement
   c. Language: expressive and receptive
   d. Motor: fine and gross
   e. Adaptability: ability to respond to environmental demands and manage daily needs
8. Investigated maternal antenatal depression and/or anxiety and childhood development

Exclusion Criteria

1. Sample consisted of individuals recruited because they had a medical condition or were taking medication, alcohol, or other drugs
2. Sample was involved in a perinatal maternal depression and/or anxiety therapeutic intervention

[a] Longitudinal studies were selected to ensure that the exposure occurred before the developmental outcome, in turn minimizing the risk that the exposure had a concurrent effect on the developmental outcome. Retrospective cohort studies were also excluded owing to the documented bias associated with retrospective compared to prospective reporting.[44-46]

guideline (PROSPERO registration, CRD42018098834).[43] A systematic search of extant peer-reviewed literature published to March 1, 2020, was conducted. Databases searched included CINAHL Complete, Cochrane Library, Embase, Informit, MEDLINE Complete, and PsycInfo. Search terms included the concepts of *time in pregnancy*, *mental illness*, and *longitudinal* (eTable 1 in the Supplement). Additional searches were performed for gray literature with forward and backward citations.

Selection Criteria

Eligibility criteria are described in the **Box**. Exposures of interest were perinatal combined anxiety and depression, anxiety alone, or depression alone (including symptoms and diagnosis); outcomes of interest were offspring social-emotional, cognitive, language, motor, and adaptive development, from 4 weeks to 18 years of age. Articles' titles and abstracts were first screened by 2 researchers (A.R. and S.O.), with 99% agreement on a blind double-screen of 5% of articles (S.J.T. and L.R.). Candidate articles were then reviewed in full text (A.R. and S.O.), with 100% agreement on a blind double-screen of 10% of articles (S.J.T. and L.R.).

Data Extraction and Study Quality

Data were extracted using a standardized pro forma method (A.R. and S.O.), with 10% cross-checked. Data extracted included research design, sample size, country, recruitment method, mean maternal age, time of assessments, measures, and relevant statistics. Where studies did not report correlations, effect sizes were transformed and converted to Pearson *r* correlations (eTable 2 in the Supplement).[47,48] To assess risk of bias, a quality assessment was completed using the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, designed to examine study quality according to Cochrane collaboration criteria.[49,50]

Data Synthesis

Data were analyzed from January 1, 2019, to March 15, 2020. A series of meta-analyses estimated the pooled associations between perinatal maternal depression and/or anxiety and offspring development. Studies were excluded from analyses if measurements of antenatal and postnatal periods were combined, enabling examination of the differential associations of the 2 periods and disorders. Results were stratified by psychopathology type (ie, combined depression and anxiety, depression only, or anxiety only), perinatal period (ie, antenatal or postnatal), and child age at outcome assessment (ie, all ages combined, infancy [<2 years], early childhood [2 to <5 years], middle childhood [5 to <13 years], and adolescence [13 to <18 years]). The effects of antenatal and postnatal depression and anxiety were investigated in both separate and combined models to explore the independent and combined effect of these 2 disorders. Meta-analyses were classed into 5 categories (ie, social-emotional, cognitive, language, motor, and adaptability) that map to domains used in criterion-standard assessments of child development.[51] Separate meta-analyses were performed when there were at least 2 studies providing effects for an outcome.

When a meta-analysis consisted of 1 effect per study, we used a standard random-effects meta-analysis with the metafor package, version 1.9.8,[52] in R software, version 3.5.0 (R Project for Statistical Computing). Otherwise, a robust variance meta-analysis approach was applied, using the robumeta package, version 2 (R Project for Statistical Computing), to account for multiple effects from the same sample. The I^2 statistics were reported as measures of heterogeneity.[53] We used guidelines to interpret correlational effect sizes that are meaningful, accounting for the cumulative influence of small effects over time, where 0.05 is very small, 0.10 is small, 0.20 is medium, 0.30 is large, and greater than 0.40 is very large.[54] Meta-regressions were conducted to determine whether timing of exposure (antenatal or postnatal), type of mental illness (depression or anxiety), mental health measure (self-report or assessment), child development measure (mother report or observer rated), and offspring age (infancy, early and middle childhood, and adolescence) moderate the association between maternal perinatal depression and anxiety and offspring development. Two-sided $P < .05$ indicated significance based on z tests (when using metafor), t tests (when using robumeta), or Wald tests (for moderation results, using clubSandwich package, version 0.4.2 [R Project for Statistical Computing]).

Results

Study Selection, Characteristics, and Quality

Of the 27 212 articles assessed for eligibility, we screened the full text of 783 (**Figure**). In total, 308 studies met eligibility criteria, with 191 studies quantitatively synthesized. Full study characteristics are summarized in eTable 3 in the Supplement. Sample sizes ranged from 27 to 82 383 (mean [SD], 1928 [3037]). Geographically, most studies were conducted in the United Kingdom (50 [26.18%]), United States (46 [24.08%]), the Netherlands (14 [7.33%]), and Australia, Canada, and Norway (each 10 [5.24%]).

The quality assessment suggests that most articles used a range of robust study design features (eTables 4 and 5 in the Supplement). Notably, all studies stated their research questions objectively, used valid and reliable measures, and allowed sufficient time between the assessment of exposure and outcome. Studies varied as to whether mental health was measured continuously or categorically. Although most studies had relatively large sample sizes, the most notable risk of bias related to a lack of information on statistical power to determine sample size, in addition to sample selection and attrition. Of those articles that reported a dropout rate, attrition was generally greater than 20%, suggesting a risk of selective sampling bias (eg, greater loss of participants who are disadvantaged and/or have poorer mental health); results should therefore be interpreted within the context of these limitations.

Meta-analytic Results

Developmental domains and subdomains are summarized in **Table 1**. Meta-analytic results are presented in **Table 2** and **Table 3**, with age-specific analyses and exemplar forest plots in eTables 6 to 10 and eFigures 1 to 8 in the Supplement. Data and coding for all analyses are available through Open Science Framework (https://osf.io/h4b9u/).

Maternal Mixed Depression and Anxiety

For the composite measure of social-emotional development, evidence suggested a moderately strong association with maternal depression and/or anxiety (antenatal period, $r = 0.21$ [95% CI, 0.16-0.27]; postnatal period, $r = 0.24$ [95% CI, 0.91-0.28]) and small-to-moderate associations with offspring externalizing (antenatal period, $r = 0.18$ [95% CI, 0.13-0.22]; postnatal period, $r = 0.18$ [95% CI, 0.15-0.20]) and internalizing (antenatal period, $r = 0.17$ [95% CI, 0.13-0.21]; postnatal period, $r = 0.19$ [95% CI, 0.15-0.23]) behaviors. Antenatal associations were similar at each age or stage of development from infancy through adolescence, with internalizing behaviors evident only in early childhood ($r = 0.18$ [95% CI, 0.12-0.25]). Postnatal depression and/or anxiety were associated with adverse outcomes for the composite measure ($r = 0.24$ [95% CI, 0.19-0.28]) and with externalizing and internalizing behaviors from infancy through middle childhood (externalizing, $r = 0.18$ [95% CI, 0.15-0.20]; internalizing, $r = 0.19$ [95% CI, 0.15-0.23]).

Antenatal depression and/or anxiety were also associated with poorer offspring prosocial behavior, albeit with small effect sizes (antenatal period, $r = -0.07$ [95% CI, −0.13 to −0.01]). For temperament, evidence was found of small associations between perinatal depression and/or anxiety with negative emotionality (antenatal period, $r = 0.14$ [95% CI, 0.0-0.20]; postnatal period, $r = 0.21$ [95% CI, 0.13-0.30]). These associations were evident antenatally in infancy and postnatally in infancy and early childhood. Combined depression and/or anxiety in both perinatal periods were also associated with offspring difficulty in infancy (antenatal period, $r = 0.19$ [95% CI, 0.13-0.25]; postnatal period, $r = 0.25$ [95% CI, 0.20-0.30]) and with dysregulation in early childhood (antenatal period, $r = 0.21$ [95% CI, 0.11-0.31]; postnatal period, $r = 0.31$ [95% CI, 0.19-0.42]).
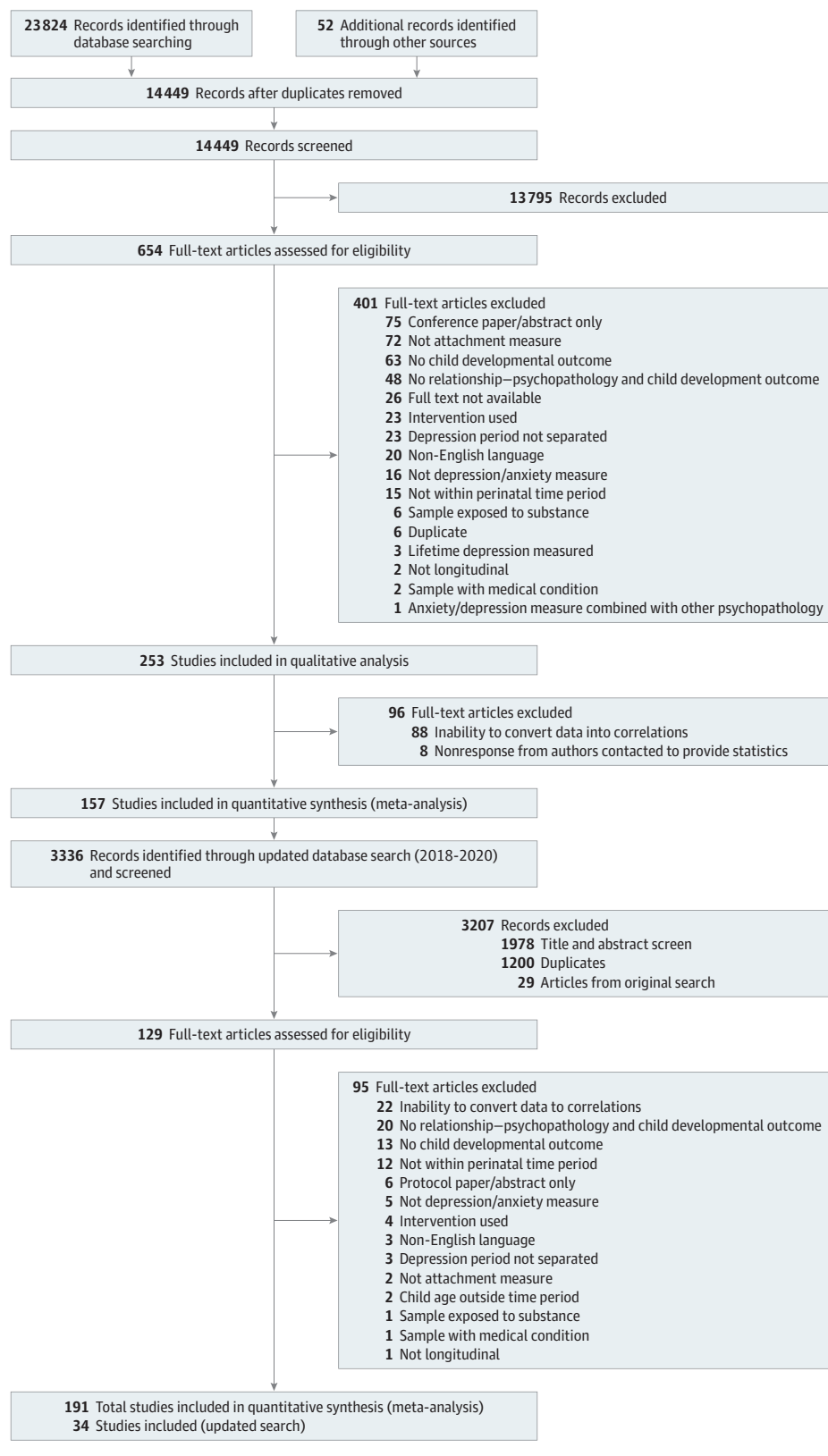
Considering other developmental domains across the antenatal period, there was evidence of small negative associations with infant cognitive (composite) ($r = -0.12$ [95% CI, −0.19 to −0.05]) and language development ($r = -0.11$ [95% CI, −0.20 to 0.02]). There was evidence of a small negative association with motor development at younger than 2 years (antenatal period, $r = -0.12$ [95% CI, −0.19 to −0.04]). Across development, depression and anxiety were associated with reduced motor development (antenatal period, $r = -0.07$ [95% CI, −0.18 to 0.03]; postnatal period, $r = -0.07$ [95% CI, −0.16 to 0.03]). There was a large negative association with infant adaptive behavior development (antenatal period, $r = -0.26$ [95% CI, −0.39 to −0.12]). Postnatal, there was evidence of medium-to-large negative associations between maternal anxiety and/or depression and offspring cognitive development (composite $r = -0.25$ [95% CI, −0.39 to −0.09]) and language development (composite $r = -0.22$ [95% CI, −0.40 to 0.03]).

Maternal Depression

Maternal depression was associated with poorer social-emotional development as evidenced by social-emotional composite (antenatal period, $r = 0.21$ [95% CI, 0.13-0.29]; postnatal period, $r = 0.24$ [95% CI, 0.20-0.29]), externalizing behaviors (antenatal period, $r = 0.20$ [95% CI, 0.13-0.27]; postnatal period, $r = 0.18$ [95% CI, 0.16-0.21]), internalizing behaviors (antenatal period, $r = 0.19$ [95% CI, 0.10-0.27]; postnatal period, $r = 0.19$ [95% CI, 0.16-0.22]), peer problems (postnatal period, $r = 0.16$ [95% CI, 0.08-0.24]), and prosocial behavior (antenatal period, $r = -0.07$ [95% CI, −0.15 to 0.01]). For attachment and dysregulation, postnatal depression was associated with infant attachment problems ($r = -0.30$ [95% CI, −0.44 to −0.14]), with little evidence of associations antenatally. There was evidence of a medium association between antenatal depression and infant dysregulation ($r = 0.22$ [95% CI, 0.12-0.24]) and a small-to-moderate association with temperamental negative emotionality ($r = 0.12$ [95% CI, 0.03-0.21]) and difficulty ($r = 0.18$ [95% CI, 0.11-0.24]). Postnatal depression was also moderately associated with temperamental negative emotionality ($r = 0.24$ [95% CI, 0.11-0.38]), orienting/regulation ($r = -0.07$ [95% CI, −0.21 to 0.08]), and difficulty in infancy ($r = 0.25$ [95% CI, 0.20-0.29]).

Regarding other domains, perinatal depression was associated with poorer cognition (antenatal period, $r = -0.14$ [95% CI, −0.21 to −0.06]; postnatal period, $r = -0.26$ [95% CI, −0.42 to −0.09]). There was evidence of a small association between postnatal depression and poorer memory ($r = -0.14$

Figure. PRISMA Diagram

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┌──────────────────────────────┐   ┌──────────────────────────────┐
│ 23824 Records identified      │   │ 52 Additional records         │
│       through database        │   │    identified through other   │
│       searching               │   │    sources                    │
└──────────────┬───────────────┘   └──────────────┬───────────────┘
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       ┌──────────────────────────────────────────┐
       │ 14449 Records after duplicates removed    │
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                      ▼
       ┌──────────────────────────────────────────┐
       │ 14449 Records screened                    │
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                      │            │ 13795 Records excluded            │
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       │ 654 Full-text articles assessed for       │
       │     eligibility                           │
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401 Full-text articles excluded
   75 Conference paper/abstract only
   72 Not attachment measure
   63 No child developmental outcome
   48 No relationship—psychopathology and child development outcome
   26 Full text not available
   23 Intervention used
   23 Depression period not separated
   20 Non-English language
   16 Not depression/anxiety measure
   15 Not within perinatal time period
    6 Sample exposed to substance
    6 Duplicate
    3 Lifetime depression measured
    2 Not longitudinal
    2 Sample with medical condition
    1 Anxiety/depression measure combined with other psychopathology

253 Studies included in qualitative analysis

96 Full-text articles excluded
   88 Inability to convert data into correlations
    8 Nonresponse from authors contacted to provide statistics

157 Studies included in quantitative synthesis (meta-analysis)

3336 Records identified through updated database search (2018-2020) and screened

3207 Records excluded
1978 Title and abstract screen
1200 Duplicates
   29 Articles from original search

129 Full-text articles assessed for eligibility

95 Full-text articles excluded
   22 Inability to convert data to correlations
   20 No relationship—psychopathology and child developmental outcome
   13 No child developmental outcome
   12 Not within perinatal time period
    6 Protocol paper/abstract only
    5 Not depression/anxiety measure
    4 Intervention used
    3 Non-English language
    3 Depression period not separated
    2 Not attachment measure
    2 Child age outside time period
    1 Sample exposed to substance
    1 Sample with medical condition
    1 Not longitudinal

191 Total studies included in quantitative synthesis (meta-analysis)
 34 Studies included (updated search)

Table 1. Summary of Developmental Domains and Subdomains in the Meta-analysis

Domain	Subdomain	No. of meta-analyses[a]
Social-emotional	11 Subdomains analyzed: social-emotional composite, externalizing behavior, internalizing behavior, peer problems, prosocial behavior, attachment, dysregulation, and temperament, including positive emotionality, negative emotionality, orienting/regulation, and difficulty	176
Cognitive	8 Subdomains analyzed: cognitive composite, verbal IQ, inhibition, performance IQ, memory, working memory, visual spatial, and academic achievement	56
Language	3 Subdomains analyzed: language composite, expressive language, and receptive language	27
Motor	3 Subdomains analyzed: Motor composite, gross motor, and fine motor	18
Adaptability	1 Subdomain analyzed: adaptability composite	3

[a] Includes all the permutations of diagnosis (combined, antenatal only, and postnatal only) by child age (infancy, early and middle childhood, and adolescence) and developmental subdomain.

[95% CI, −0.24 to −0.04]) and a large association with poorer performance IQ (r = −0.57 [95% CI, −0.79 to −0.20]) in early childhood; however, only 2 studies[55,56] were included. Postnatal depression was associated with poorer language ability (composite) in infancy and early childhood (r = −0.21 [95% CI, −0.04 to −0.01]). Further, antenatal depression was associated with poorer infant motor ability (composite: r = −0.11 [95% CI, −0.18 to −0.04]) and adaptive behavior (r = −0.20 [95% CI, −0.30 to −0.01]).

Maternal Anxiety

Perinatal anxiety was adversely associated with social-emotional development, particularly in the antenatal period for the social-emotional composite (r = 0.22 [95% CI, 0.15-0.23]), externalizing behavior (r = 0.19 [95% CI, 0.07-0.31]), internalizing behavior (r = 0.19 [95% CI, 0.06-0.32]), negative emotionality (r = 0.18 [95% CI, 0.14-0.21]), and difficulty (r = 0.25 [95% CI, 0.11-0.38]). Postnatally, anxiety was associated with poorer overall social-emotional development (r = 0.19 [95% CI, −0.06 to 0.31]), externalizing behavior (r = 0.19 [95% CI, 0.19-0.28]), internalizing behavior (r = 0.22 [95% CI, 0.05-0.39]), and temperamental negative emotionality (r = 0.18 [95% CI, 0.15-0.21]).

Few studies examined the association of maternal perinatal anxiety with offspring cognition, language, and motor development. Nevertheless, evidence suggested a small association between antenatal anxiety and lower verbal IQ (r = −0.05 [95% CI, −0.07 to −0.02]). Antenatal anxiety was associated with poorer language (composite) in early childhood (r = −0.19 [95% CI, −0.24 to −0.13]), and postnatal anxiety was associated with poorer language (composite) in infancy (r = −0.21 [95% CI, −0.38 to −0.04]). We also found evidence of a medium-to-large association between postnatal anxiety and poorer gross motor ability (r = −0.31 [95% CI, −0.54 to −0.03]), but only 2 studies[57,58] were included.

Moderation Analyses

Little systematic evidence suggested that meta-analytic effects were moderated by exposure timing, mental illness type, child development stage, or maternal/child assessment method (eMethods and eTables 11-16 in the Supplement). Notably, few moderations could be conducted because there were often fewer than 2 effects per level of each moderator. Owing to low power, results should be interpreted cautiously.

Discussion

Herein we report findings from systematic review and meta-analysis examining the association of maternal perinatal depression and anxiety with offspring social-emotional, cognitive, language, motor, and adaptive behavior development from infancy through adolescence. Results from 191 articles showed consistent evidence of small-to-moderate associations across the perinatal period for social-emotional development; small-to-moderate associations antenatally and moderate-to-large associations postnatally across facets of cognitive and language development; and small-to-moderate associations for motor abilities post partum and adaptive behavior development antenatally. The findings are of public health significance[59] and support investment in interventions aimed at prevention of perinatal maternal mental health problems.

This review highlights important differential associations related to the timing and type of symptom exposure on offspring development across infancy, childhood, and adolescence. Specifically, perinatal depression and anxiety (combined) was adversely associated with composite social-emotional development in offspring from infancy through adolescence, with no evidence of weakening associations with age. This finding extended to the subdomains of externalizing and internalizing behavior and to temperamental negative emotionality and difficulty. These results are consistent with prior qualitative reviews,[3-5,7,8,42] suggesting that the risks associated with maternal perinatal mental health problems are not limited to a single period of offspring development.

Furthermore, maternal antenatal depression and anxiety (combined) was inversely associated with offspring prosocial behaviors (r = −0.07); yet this association was not consistent across all developmental stages. Associations were also inconsistent in the domains of peer problems and temperament orienting/regulation, with evidence suggesting that adverse development is associated with postnatal, but not antenatal, mental health. Antenatally, only 2 studies[25,60] investigated dysregulated behavior in infancy, specific to depression, with results indicating a large association (r = 0.22).

Notably, only postnatal depression was associated with infant attachment difficulties. This finding supports theoretical perspectives that suggest that postnatal depression negatively affects maternal sensitivity and attachment.[22,23,61] It is also consistent with theories suggesting that the experience of maternal-infant interactions may more strongly influence attachment than intrauterine factors.[22,23,61] However, in other research, antenatal depression has been shown to contribute to the development of a mother's ability to respond sensi-

Table 2. Association Between Antenatal Depression and Anxiety and Offspring Development Across All Ages of Development[a]

Outcome	Combined anxiety and/or depression				Anxiety				Depression			
	No. of studies (No. of effects/ associations)	Correlation, r (95% CI)	P value	I² value, %	No. of studies (No. of effects/ associations)	Correlation, r (95% CI)	P value	I² value, %	No. of studies (No. of effects/ associations)	Correlation, r (95% CI)	P value	I² value, %
Social-emotional												
Composite	18 (73)	0.21 (0.16 to 0.27)	<.001	91	9 (38)	0.22 (0.15 to 0.23)	<.001	93	15 (35)	0.21 (0.13 to 0.29)	<.001	91
Externalizing	36 (147)	0.18 (0.13 to 0.22)	<.001	98	11 (69)	0.19 (0.07 to 0.31)	.007	99	18 (68)	0.20 (0.13 to 0.27)	<.001	98
Internalizing	31 (88)	0.17 (0.13 to 0.21)	<.001	97	9 (44)	0.19 (0.06 to 0.32)	.01	98	13 (40)	0.19 (0.10 to 0.27)	<.001	94
Peer problems	2 (4)	0.39 (-0.99 to 1.00)	.35	100	NA	NA	NA	NA	NA	NA	NA	NA
Prosocial	8 (18)	-0.07 (-0.13 to -0.01)	.03	74	6 (9)	- 0.05 (-0.14 to 0.04)	.23	80	7 (9)	-0.07 (-0.15 to 0.01)	.08	68
Attachment	2 (5)	-0.19 (-0.94 to 0.88)	.36	61	NA	NA	NA	NA	2 (5)	-0.19 (-0.94 to 0.88)	.36	61
Dysregulation	2 (12)	0.21 (0.11 to 0.31)	.03	54	NA	NA	NA	NA	2 (10)	0.22 (0.21 to 0.24)	.004	0
Positive emotionality	7 (84)	-0.09 (-0.19 to 0)	.06	89	5 (55)	-0.13 (-0.28 to 0.01)	.06	73	4 (29)	-0.04 (-0.13 to 0.05)	.21	23
Negative emotionality	18 (116)	0.14 (0.08 to 0.2)	<.001	94	11 (66)	0.18 (0.14 to 0.21)	<.001	75	14 (50)	0.12 (0.03 to 0.21)	.01	96
Orienting regulation	9 (46)	-0.09 (-0.18 to 0.01)	.07	90	7 (28)	-0.11 (-0.26 to 0.06)	.16	93	6 (18)	-0.06 (-0.19 to 0.08)	.35	88
Difficulty	13 (46)	0.19 (0.13 to 0.25)	<.001	98	8 (26)	0.25 (0.11 to 0.38)	.005	100	10 (20)	0.18 (0.11 to 0.24)	<.001	79
Cognition												
Composite	12 (17)	-0.12 (-0.19 to -0.05)	.004	62	4 (5)	0.04 (-0.24 to 0.31)	.68	68	10 (12)	-0.14 (-0.21 to -0.06)	.004	63
Verbal IQ	3 (8)	- 0.16 (-0.52 to 0.24)	.20	89	3 (3)	-0.05 (-0.07 to -0.02)	<.001	0	2 (5)	-0.12 (-0.73 to 0.60)	.32	92
Inhibition	2 (3)	0.23 (- 1 to 1)	.529	85	NA	NA	NA	NA	NA	NA	NA	NA
Performance IQ	2 (2)	-0.12 (-0.29 to 0.06)	.19	97	NA	NA	NA	NA	2 (2)	-0.12 (-0.29 to 0.06)	.19	97
Working memory	3 (4)	0.01 (-0.30 to 0.27)	.84	77	3 (3)	-0.01 (-0.12 to 0.12)	.96	78	NA	NA	NA	NA
Language												
Composite	5 (8)	-0.11 (-0.20 to 0.02)	.03	69	2 (2)	-0.19 (-0.24 to -0.13)	.0001	0	5 (6)	-0.08 (-0.23 to 0.08)	.22	47
Expressive	2 (3)	-0.27 (-0.99 to 0.97)	.38	98	NA	NA	NA	NA	2 (2)	-0.26 (-0.58 to 0.14)	.20	98
Receptive	2 (2)	-0.35 (-0.83 to 0.44)	.39	99	NA	NA	NA	NA	2 (2)	-0.35 (-0.83 to 0.44)	.39	99
Motor												
Composite	9 (18)	-0.07 (-0.18 to 0.03)	.16	64	4 (7)	-0.01 (-0.31 to 0.28)	.89	72	7 (11)	-0.06 (-0.20 to 0.08)	.33	70
Adaptive behavior												
Composite	3 (3)	-0.26 (-0.39 to -0.12)	<.001	54	NA	NA	NA	NA	2 (2)	-0.2 (-0.3 to -0.1)	<.001	0

Abbreviation: NA, not applicable (not enough studies to run meta-analysis).

[a] Includes 150 studies, 190 articles, and 195 751 participants.

tively to her offspring.[20] With only 2 studies[26,62] included in the meta-analysis on antenatal depression and attachment, this result requires replication.

In other developmental domains, although there was some heterogeneity in results, the direction and stability of the associations suggest that perinatal maternal depression and anxi-

Table 3. Association Between Postnatal Depression and Anxiety and Offspring Development Across All Ages of Development[a]

Outcome	Combined anxiety and/or depression				Anxiety				Depression			
	No. of studies (No. of effects/associations)	Correlation, r (95% CI)	P value	I² value, %	No. of studies (No. of effects/associations)	Correlation, r (95% CI)	P value	I² value, %	No. of studies (No. of effects/associations)	Correlation, r (95% CI)	P value	I² value, %
Social-emotional												
Composite	24 (85)	0.24 (0.19 to 0.28)	<.001	92	5 (21)	0.19 (−0.06 to 0.31)	.01	96	24 (64)	0.24 (0.20 to 0.29)	<.001	91
Externalizing	37 (88)	0.18 (0.15 to 0.20)	<.001	79	6 (8)	0.19 (0.19 to 0.28)	.005	82	35 (76)	0.18 (0.16 to 0.21)	<.001	75
Internalizing	33 (79)	0.19 (0.15 to 0.23)	<.001	84	6 (8)	0.22 (0.05 to 0.39)	.02	93	31 (70)	0.19 (0.16 to 0.22)	<.001	77
Peer problems	6 (15)	0.16 (0.08 to 0.23)	.02	5	NA	NA	NA	NA	6 (14)	0.16 (0.08 to 0.24)	.02	0
Prosocial	8 (12)	−0.10 (−0.21 to 0.01)	.05	71	NA	NA	NA	NA	8 (11)	−0.11 (−0.23 to 0.01)	.06	76
Attachment	6 (12)	−0.30 (−0.44 to −0.14)	.005	59	NA	NA	NA	NA	6 (12)	−0.30 (−0.44 to −0.14)	.005	59
Dysregulation	3 (3)	0.31 (0.19 to 0.42)	<.001	14	NA	NA	NA	NA	3 (3)	0.31 (0.19 to 0.42)	<.001	14
Positive emotionality	6 (30)	−0.07 (−0.18 to 0.04)	.14	94	2 (7)	−0.13 (−0.75 to 0.62)	.31	80	5 (23)	−0.02 (−0.11 to 0.07)	.52	57
Negative emotionality	20 (64)	0.21 (0.13 to 0.30)	<.001	93	8 (17)	0.18 (0.15 to 0.21)	<.001	32	19 (43)	0.24 (0.11 to 0.38)	.001	94
Orienting regulation	7 (16)	−0.06 (−0.17 to 0.04)	.21	94	3 (5)	0.01 (−0.35 to 0.37)	.92	88	6 (11)	−0.07 (−0.21 to 0.08)	.28	94
Difficulty	13 (22)	0.25 (0.20 to 0.30)	<.001	82	NA	NA	NA	NA	13 (21)	0.25 (0.20 to 0.29)	<.001	82
Cognition												
Composite	18 (26)	−0.25 (−0.39 to −0.09)	.004	93	2 (2)	−0.16 (−0.34 to 0.02)	.08	0	16 (23)	−0.26 (−0.26 to −0.42)	.006	94
Visual spatial IQ	3 (4)	−0.35 (−0.93 to 0.74)	.35	95	NA	NA	NA	NA	3 (4)	−0.35 (−0.93 to 0.74)	.35	95
Verbal IQ	4 (7)	−0.3 (−0.76 to 0.36)	.24	95	NA	NA	NA	NA	4 (5)	−0.31 (−0.76 to 0.35)	.24	94
Performance IQ	2 (3)	−0.84 (−0.98 to −0.07)	.04	99	NA	NA	NA	NA	3 (3)	−0.84 (−0.98 to −0.07)	.04	99
Quantitative	2 (2)	−0.15 (−0.29 to 0)	.06	0	NA	NA	NA	NA	2 (2)	−0.15 (−0.29 to 0)	.06	0
Memory	3 (3)	−0.12 (−0.21 to −0.03)	.01	0	NA	NA	NA	NA	3 (3)	−0.12 (−0.21 to −0.03)	.01	0
Working memory	3 (6)	−0.21 (−0.8 to 0.59)	.41	95	NA	NA	NA	NA	3 (5)	−0.22 (−0.80 to 0.58)	.39	95
Academic achievement	3 (13)	−0.08 (−0.19 to 0.03)	.08	75	NA	NA	NA	NA	3 (9)	−0.07 (−0.10 to −0.03)	.02	71
Language												
Composite	11 (14)	−0.22 (−0.40 to 0.03)	.03	88	3 (3)	−0.21 (−0.38 to −0.04)	.01	33	10 (11)	−0.21 (−0.40 to 0)	.050	88
Expressive	3 (4)	−0.60 (−0.98 to 0.69)	.19	99	NA	NA	NA	NA	3 (4)	−0.60 (−0.98 to 0.69)	.19	99
Receptive	3 (4)	−0.49 (−0.98 to 0.87)	.34	98	NA	NA	NA	NA	3 (4)	−0.49 (−0.98 to 0.87)	.34	98
Motor												
Composite	9 (11)	−0.07 (−0.16 to 0.03)	.14	63	NA	NA	NA	NA	9 (10)	−0.07 (−0.16 to 0.03)	.15	63
Gross	2 (3)	−0.32 (−0.97 to 0.88)	.25	75	2 (2)	−0.31 (−0.54 to −0.03)	.03	80	NA	NA	NA	NA

Abbreviation: NA, not applicable (not enough studies to run meta-analysis).

[a] Includes 150 studies, 190 articles, and 195 751 participants.

ety are broadly associated with poorer offspring cognitive, language, motor, and adaptive behavior development. Notably, negative small-to-moderate associations antenatally and moderate-to-large associations postnatally were observed for cognitive and language development. Furthermore, relatively consistent evidence suggested small-to-moderate associations post

partum for motor abilities and antenatally for adaptive behavior development.

A considerable number of the articles included focused exclusively on depression (123 articles and 100 studies). Overall, results suggest that perinatal depression influences all childhood developmental domains. Various mechanisms may

explain this association. Offspring may be adversely affected in utero through exposure to increased cortisol concentrations and reduced blood flow through the placenta.[19] Furthermore, antenatal depression may interfere with the neurocognitive changes mothers experience that prepare them to sensitively respond during maternal-infant interactions.[20] In the postnatal period, depression may also reduce maternal-infant engagement.[23]

For maternal anxiety (27 articles and 23 studies), research focused predominantly on the antenatal period, indicating adverse associations with offspring social-emotional, cognitive, and language development. Although all associations for postnatal anxiety were in the expected direction, meaningful associations did not extend to all developmental domains. One explanation may be that anxiety has a greater effect on intrauterine exposure.[16,17] Postnatally, maternal anxiety has been linked with overintrusive parenting.[24] Given the associations observed between postnatal anxiety and externalizing and negative emotionality, this parenting style may contribute to these behaviors.[63,64]

The extant literature review has several limitations. First, most studies used self-report assessment of maternal mental health (n = 159) and child development (n = 120). An overreliance on self-report measures may lead to shared method variance and bias in child development reports.[65] Furthermore, self-report measures commonly assess symptoms rather than clinical diagnoses, which may be differentially associated with development. Future research would benefit from the use of clinician-administered, criterion-standard diagnostic interviews and observational developmental assessment batteries. Second, research to date has primarily focused on early offspring development. Future research exploring later developmental stages would strengthen the evidence base. Third, many studies had samples consisting of participants only representing Western, educated, industrialized, rich, and democratic societies.[66] Future studies with more diverse samples would inform the extent to which these meta-analytic results are generalizable to other sociodemographic groups. Fourth, this review highlights the paucity of research on child adaptability (n = 3), with greater research on this domain warranted. Finally, it would be beneficial for future research to also examine the potential longer-term effects of antenatal medication use, maternal depression and anxiety beyond the perinatal period, and the role that social factors may play in offspring development.

Limitations

This meta-analysis has 3 key limitations. First, owing to the scope of literature available, a systematic qualitative review was not undertaken, possibly resulting in the omission of some important subjective information. Second, we analyzed correlational associations. Thus, the direction of causal relations is unknown, and the associations found may be explained by confounding variables. However, meta-analyzing effects adjusted for confounders was considered implausible because of extensive variability in covariates across studies, with no common set of confounders examined. We look to future meta-analytic designs that focus on pooling adjusted associations from studies that have a set of consistent covariates to address this limitation.[67] Furthermore, given the number of analyses conducted, some associations may be affected by type I error. However, we note that many of the associations had very small *P* values (<.001), which would likely withstand even very stringent corrections. Nevertheless, the results should be interpreted in light of the possibility of an increased error rate.

Conclusions

The results of this meta-analysis underscore the importance of early screening and preventative intervention for anxiety and depression in mothers during the perinatal period. This finding is consistent with an established evidence base on the efficacy of early interventions in reducing perinatal mental illness in mothers.[68,69] However, the results are less consistent in regard to associated improvements in child development as a result of maternal intervention.[70] This inconsistency may be related to study limitations, such as the delayed assessment of child development, and the influence of other factors associated with maternal perinatal mental health that affect child maturation. Nevertheless, emerging evidence suggests that maternal intervention is also associated with clinical improvements in offspring development in some (but not all) cases.[71]

Taken together, results suggest that both maternal antenatal and postnatal depression and anxiety are associated with poorer offspring social-emotional, cognitive, language, motor, and adaptive behavior development, providing compelling evidence that the perinatal window is a period of sensitivity for offspring development. Moreover, these associations are not confined to infancy and early childhood alone but extend into middle childhood and adolescence. With estimates indicating that 1 in 4 mothers experience symptoms of perinatal depression or anxiety,[72] this meta-analysis has important implications for a population-level approach to prevention, screening, and targeted intervention to support women's mental health in the transition to parenthood and consequently the health and well-being of next-generation offspring.

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