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The Prevalence of Anxiety Disorders During Pregnancy and the Postpartum Period:

A Multivariate Bayesian Meta-Analysis

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ABSTRACT

Objective: To estimate the prevalence of anxiety disorders in pregnant and postpartum women and identify predictors accounting for variability across estimates.

Data Sources: An electronic search of PsycINFO and PubMed was conducted from inception until July 2016, without date or language restrictions, and supplemented by articles referenced in the obtained sources. A Boolean search phrase utilized a combination of keywords related to pregnancy, postpartum, prevalence, and specific anxiety disorders.

Study Selection: Articles reporting the prevalence of 1 or more of 8 common anxiety disorders in pregnant or postpartum women were included. A total of 2,613 records were retrieved, with 26 studies ultimately included.

Data Extraction: Anxiety disorder prevalence and potential predictor variables (eg, parity) were extracted from each study. A Bayesian multivariate modeling approach estimated the prevalence and between-study heterogeneity of each disorder and the prevalence of having 1 or more anxiety disorder.

Results: Individual disorder prevalence estimates ranged from 1.1% for posttraumatic stress disorder to 4.8% for specific phobia, with the prevalence of having at least 1 or more anxiety disorder estimated to be 20.7% (95% highest density interval [16.7% to 25.4%]). Substantial between-study heterogeneity was observed, suggesting that "true" prevalence varies broadly across samples. There was evidence of a small (3.1%) tendency for pregnant women to be more susceptible to anxiety disorders than postpartum women.

Conclusions: Peripartum anxiety disorders are more prevalent than previously thought, with 1 in 5 women in a typical sample meeting diagnostic criteria for at least 1 disorder. These findings highlight the need for anxiety screening, education, and referral in obstetrics and gynecology settings.

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Approximately 30% of adults suffer from an anxiety disorder (AD) at some point in their lives,[1] with evidence suggesting these disorders are 2 to 3 times more common than mood, impulse-control, or substance abuse disorders over a 12-month period.[2] This represents a major public health concern because anxiety leads to significant impairments in social, emotional, and physical functioning,[3] causing a high level of health care service utilization.[4–7] In addition to direct public health costs, ADs are associated with substantial indirect costs related to functional impairment (eg, diminished work capacity, unemployment).[8,9] Women are at particular risk as they are significantly more likely (1.2 to 6.8 times) to suffer from an AD than are men.[1,10]

Maternal Anxiety and Fetal/Infant Development

Screening and treatment of peripartum ADs are especially important given the potential short- and long-term effects of anxiety on offspring. Maternal prenatal anxiety has been associated with adverse pregnancy outcomes such as miscarriage, pre-eclampsia, preterm delivery, and low birth weight,[11–17] with particularly strong evidence for increased risk of preterm birth and low birth weight.[18] Prenatally anxious women have been found to interact less skillfully and communicate less with their infants.[19] Maternal anxiety has also been associated with impaired adaptability including negative behavioral responses to novelty, negative mood, and soothing difficulty in offspring.[20,21] Finally, mothers with ADs are more likely to have children who are behaviorally inhibited and insecurely attached.[22]

Longitudinal studies of mother-child pairs demonstrate a higher rate of ADs in children of mothers with an AD compared to children of mothers without an AD.[23] Children of mothers in the top 15% for symptoms of antenatal anxiety have been shown to have twice the risk for attention-deficit/hyperactivity disorder at ages 4 and 7 years.[24,25] Finally, adolescents of mothers with high levels of anxiety during pregnancy have also shown deficits in cognitive control linked to the orbitofrontal cortex.[26]

Prenatal anxiety has also been identified as a very strong predictor of postpartum depression, even when controlling for prenatal depression levels.[27–29] Antenatal depression has also been significantly associated with preterm birth and low birth weight, with higher risk among women from lower socioeconomic status and developing

Clinical Points

- This is the first meta-analysis to correctly estimate the probability of having at least 1 of 8 common anxiety disorders across pregnancy and the postpartum period, with previous research combining prevalence estimates that were incompatible due to differences in the number of individual anxiety disorders assessed.
- Anxiety disorders in pregnancy and the postpartum period are more prevalent than previously thought, with about 1 in 5 (20.7%) women meeting diagnostic criteria for at least 1 anxiety disorder and 1 in 20 (5.5%) meeting criteria for at least 2 anxiety disorders.
- Given the attention to screening for depression during pregnancy and the postpartum period over the last decade, it is now time to spotlight the pressing need for routine perinatal anxiety disorder screening.

countries.[30] Risk factors identified for both perinatal mood and anxiety disorders include ethnic minority status, low socioeconomic status, poor educational attainment, poor-quality partner relationships, history of poor mental health, adverse circumstances around the pregnancy and birth, history of abuse/domestic violence, adverse life events, high perceived stress, being single, and unplanned or unwanted pregnancy.[31–34] Given the above, knowing the prevalence of perinatal ADs is important in helping to determine the scope of the problem and supporting the recommendation for routine perinatal anxiety screening, education, and referral to treatment in health care settings.[35]

Prior to the publication of the Fifth Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*),[36] the core ADs were obsessive-compulsive disorder (OCD), panic disorder, agoraphobia, generalized anxiety disorder (GAD), social phobia, specific phobia, posttraumatic stress disorder (PTSD), and acute stress disorder.[37] In *DSM-5*, OCD, PTSD, and acute stress disorder have been moved into their own sections (Obsessive-Compulsive and Related Disorders and Trauma- and Stressor-Related Disorders, respectively),[36] despite widespread agreement that anxiety is a core feature of these problems (eg, shared pathology and treatment response).[38] Since the *DSM-5* changes are quite recent, there are very few prevalence studies based on *DSM-5* criteria. To remain in line with the bulk of the published literature, we have operationalized total AD prevalence as meaning the probability of having 1 or more of the common *DSM-IV* ADs.

Although not included in the *DSM*, it is important to note that pregnancy anxiety or pregnancy-related anxiety has been identified in the literature as a distinct clinical phenomenon, in that worries are tied directly to pregnancy, childbirth, and the maternal role.[39–41] Similar to *DSM*-defined anxiety disorders, there is a correlation with adverse obstetric and child development outcomes that persists after controlling for medical and obstetric risk factors.[42] Factor analysis of pregnancy-related anxiety reveals 2 distinct factors: concerns about the child's health and concerns about the birth.[41] Concerns about the child's health predicted infant birth weight independently of GAD, with both factors showing only modest associations with clinical measures of generalized anxiety (Structured Clinical Interview for *DSM-IV* [SCID]).[41] Thus, it is possible that pregnancy-specific worries contribute to a portion of the symptoms experienced by women diagnosed with *DSM*-defined disorders.

Prevalence of Anxiety Disorders During the Perinatal Period

With an established emphasis on screening and treatment of perinatal depression, it is only recently that research has shined a spotlight on perinatal anxiety disorders and their frequency.[43] Several reliable prevalence estimates from well-designed studies of maternal perinatal AD now exist as a result of utilizing (*a*) gold standard assessment procedures (ie, diagnostic interviews by trained interviewers) and (*b*) representative or unselected samples. Studies that use selected samples of pregnant or postpartum women (eg, women experiencing a medically high-risk pregnancy or whose infant was stillborn) fail to provide accurate estimates of perinatal anxiety. Similarly, questionnaire-based assessments of mental health conditions significantly overestimate prevalence and incidence rates.[44]

Unfortunately, studies using representative samples with gold standard assessment procedures still vary considerably in their reported prevalence estimates. For instance, studies in which 4 or more *DSM-IV* ADs were assessed have reported estimates ranging from 5.1%[45] to 37.5%.[46] Recent meta-analyses have themselves produced estimates ranging from 8.5%[47] to 15.2%[48] prenatally and 9.9% postnatally,[48] although they have been based on 10 or fewer studies in each case. Importantly, current meta-analyses on this topic have aggregated prevalence estimates that were incompatible due to variation in (*a*) the number of disorders assessed and (*b*) the subset of ADs included. For example, Austin et al[49] defined the probability of having an AD as being diagnosed with GAD, social phobia, panic disorder, or agoraphobia, whereas Navarro et al[50] defined this same quantity as being diagnosed with GAD, panic disorder with or without agoraphobia, agoraphobia, social phobia, OCD, PTSD, or nonspecified anxiety. Nonetheless, these estimates were pooled together.[47] Statistical simulations suggest that estimating the prevalence of a disorder category—such as ADs—by combining studies that differ with respect to the disorders measured requires special consideration to avoid catastrophically underestimating the true prevalence.[51]

We address this concern by modeling the individual ADs using a modern Bayesian multivariate approach. Specifically, the current analysis estimates the probability of having 1 or more AD by combining individual disorder prevalences and simulating data from a large, typical sample to estimate the probability of having 1 or more of those disorders. We also estimate comorbidities across disorders using individual patient data, where available. This modeling approach has been shown to outperform other means of estimating the prevalence of a disorder category and permits us to make probabilistic statements about other facets of the data (eg,

comorbidity) not possible using traditional approaches (for details and code, see Fawcett et al[51]). Furthermore, the current approach is not limited to studies that include multiple AD prevalences, allowing for additional studies to be included measuring only 1 AD. Anticipating heterogeneity, we also explore potential moderators. Given the potential for ADs to have serious negative consequences for both mother and child, ascertaining the prevalence of ADs among pregnant and postpartum women may help to raise awareness of this important issue.

METHODS

Literature Search

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.[52] We conducted a search of the online resources PsycINFO and PubMed, using the following Boolean search phrase: *((“perinatal” OR “prenatal” OR “antenatal” OR “pregnancy” OR “pregnant” OR “postnatal” OR “postpartum” OR “childbirth” OR “birth”) AND (“prevalence” OR “epidemiology” OR “incidence”) AND (“anxiety disorder” OR “anxiety disorders” OR “Panic Disorder” OR “Agoraphobia” OR “Obsessive Compulsive Disorder” OR “Obsessive-Compulsive Disorder” OR “Generalized Anxiety Disorder” OR “Social Phobia” OR “Social Anxiety Disorder” OR “Specific Phobia” OR “Phobic Disorder” OR “Posttraumatic Stress Disorder” OR “Post-traumatic Stress Disorder” OR “Anxiety Not Otherwise Specified” OR “Anxiety NOS”))*. The search was conducted until July 2016 without date or language restrictions and was supplemented by articles referenced in the obtained sources. Additional articles were identified using references from review articles and meta-analyses, as well as correspondence with experts in the field.

Study Inclusion Criteria

Articles that reported the prevalence of 1 or more of 8 common ADs (panic disorder, agoraphobia, OCD, GAD, social phobia, specific phobia, PTSD, and anxiety not otherwise specified [NOS]) in pregnant or postpartum women (up to 12 months) were included. Substance-induced anxiety disorder, anxiety disorder due to a general medical condition, and acute stress disorder were not examined in the present study due to the fact that estimates of these disorders are rarely included in anxiety prevalence studies. Inclusion in the current meta-analysis also required the use of a structured diagnostic interview to diagnose ADs prospectively according to *DSM or ICD* criteria, a minimum age requirement of 16 years, and the use of a sample representative of the greater pregnant and postpartum population at large. Studies were not considered representative of the population at large if they focused on subpopulations of pregnant or postpartum women (eg, stillbirth/infant loss, women with specific medical problems, infertility, substance abuse).

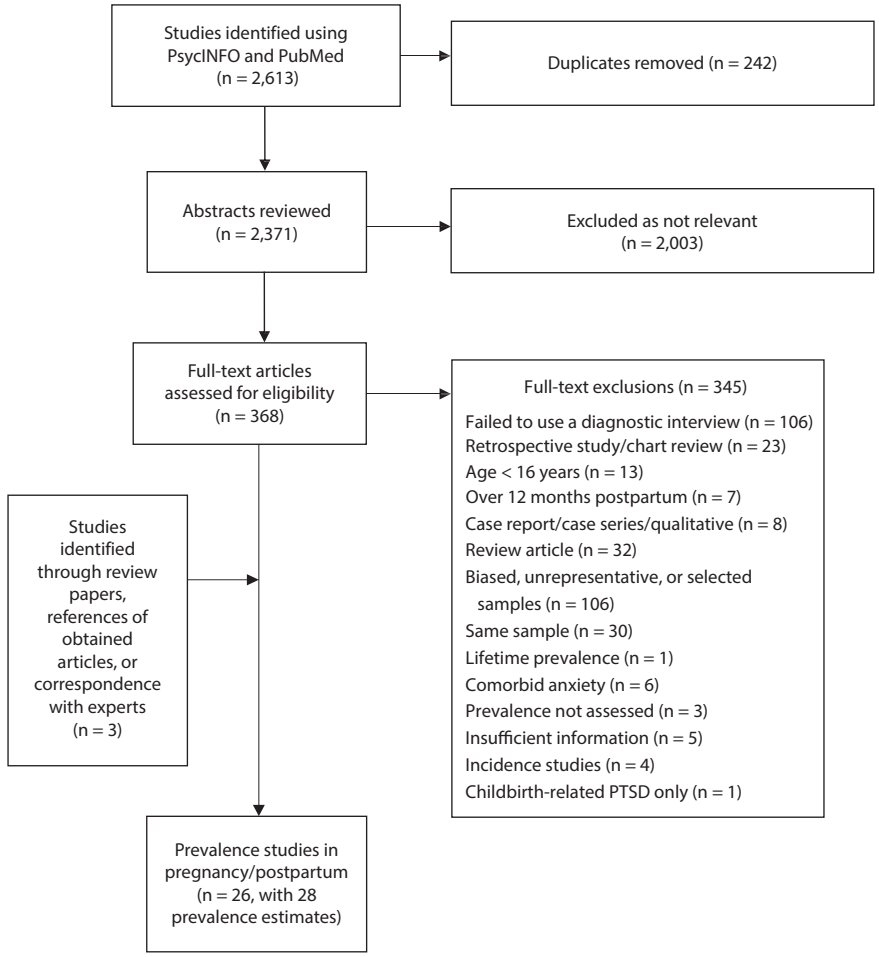
Studies were excluded for the following reasons: (1) failure to use a diagnostic interview or full diagnostic criteria not assessed, (2) retrospective studies or chart reviews, (3) falling below the minimum age requirement, (4) postpartum studies beyond the first year, (5) qualitative studies/case report/case series, (6) review articles only, (7) non-representative samples (including subpopulations, intervention studies, women who were excluded on the basis of receiving treatment for a mental health condition [eg, antidepressants], and studies that oversampled for high-risk women [eg, women experiencing intimate partner violence]), (8) the same sample and measures reported in another source, (9) lifetime only rather than current prevalence assessed, (10) comorbid anxiety reported in a sample of women with diagnosed depression or who scored above a cutoff score for depression according to a self-report questionnaire, (11) prevalence was not assessed, (12) insufficient information was presented to compute prevalence estimates, (13) only incidence reported, and (14) only childbirth-related PTSD reported.

The current modeling approach required prevalence estimates for each individual disorder measured (see Data Analysis Approach). Therefore, studies that reported only the total prevalence of multiple ADs without the individual prevalence estimates were excluded, but only in instances when this information could not be obtained through correspondence with the authors. Studies that included samples of both pregnant and postpartum women[53,54] were included if the samples were independent of one another. Specifically, for longitudinal studies in which the same sample of women was prospectively followed from pregnancy to postpartum, the samples were not independent and therefore only 1 estimate was used from either pregnancy or postpartum. For the few studies that reported prevalence estimates across both pregnancy and postpartum in the same sample,[55,56] we used the postpartum estimate as there were fewer postpartum studies compared to pregnancy studies. There were also a small number of studies in which women were assessed at multiple time points throughout the postpartum period.[56,57] As only 1 time point could be used, we used data from the first diagnostic interview in the postpartum period, as this represented the time point that was closest to the median for the other postpartum studies (12 weeks).

Data Extraction

The first author screened each article by title and abstract, retrieving articles that met inclusion criteria. The third author independently screened one third of the articles from the electronic search. Disagreements over study inclusion were resolved through discussion between the first and second author. The first author extracted the following data from each article: author name, year of publication, sample size, group (pregnant, postpartum), total AD prevalence, the number of ADs assessed, the individual prevalence of each AD measured, structured diagnostic interview used (eg, Mini-International Neuropsychiatric Interview, SCID, Diagnostic Interview Schedule), diagnostic criteria used (*ICD-10*, *DSM-IV*), country/region in which the study was conducted, average gestational week or average postpartum week, average age, proportion married or cohabitating, proportion primiparous, average education of the sample, and medically based exclusion criteria (eg, severe medical

Figure 1. Meta-Analysis Inclusion Flowchart



Abbreviation: PTSD = posttraumatic stress disorder.

problems in the mother, fetal malformation, pregnancy complications). The second and third author extracted the time frame of the diagnostic assessment (in weeks), including corresponding with authors to ascertain this information when needed. Finally, the World Bank Classifications for Income were used to classify each study country into low, lower-middle, upper-middle, and high-income categories.

Quality Ratings

To assess the quality of studies included in the current meta-analysis, the first author scored each study using a 10-point scale that was created based on key methodological criteria outlined in the literature.[58–61] Key factors assessed included description of the study setting, eligibility criteria, sampling method, response rate, demographic characteristics, information on completers vs noncompleters, time frame of the assessment, qualifications of diagnostic interviewers, reporting of AD prevalence estimates, and discussion of study limitations/potential biases. Quality ratings were then reported categorically for each study, corresponding to low (0–3), moderate (4–6), or high (7–10) quality scores. The exact questions and scoring information can be viewed in Supplementary Appendix 1.

Data Analysis Approach

Past meta-analyses in this area applied a univariate approach to prevalence estimates reflecting different combinations of disorders. This risks underestimating the prevalence of having an AD. For this reason, our analyses employed a Bayesian multivariate model, discussed in detail elsewhere,[51] to describe the data actually reported. This approach models the prevalence of each individual disorder, estimates the correlations among the disorders, uses the resulting information to produce an unbiased estimate of the probability of having 1 or more disorder in a typical sample, and also produces prediction intervals reflecting variation in the "true" underlying prevalence estimates across the distribution of included samples. To accomplish this, the correlations between the individual anxiety disorders (representing comorbidity) were estimated using all available individual patient data.[45,46,55,62–65] By estimating the correlations among disorders, we were also able to provide a meta-analytic summary of the comorbidities between disorders. Finally, study-level prognostic factors were explored by allowing the prevalence of each disorder to depend on 1 predictor variable at a time.

Table 1. Study Characteristics

First Author	Year	Group	Measure	Criteria	Average Weeks Gestation/ Postpartum	Country	N	No. of Anxiety Disorders Assessed	Quality Rating
Zar[65]	2002	Preg	ADIS-R	*DSM-IV*	32	Sweden	453	7[a]	Moderate
Andersson[67]	2003	Preg	PRIME-MD	*DSM-IV*	16	Sweden	1,556	5	Moderate
Sutter-Dallay[29]	2004	Preg	MINI	*DSM-IV*	32	France	497	6	Moderate
Felice[68]	2007	Preg	CIS-R	*ICD-10*	18.6	Malta	229	5	High
Rogal[69]	2007	Preg	MINI	*DSM-IV*	…	US	1,100	1	Moderate
Uguz[70]	2007	Preg	SCID	*DSM-IV*	35.08	Turkey	434	1	High
Borri[71]	2008	Preg	SCID-I	*DSM-IV*	13.5	Italy	1,066	8[b]	Moderate
Guler[72]	2008	Preg	SCID	*DSM-IV*	35.3	Turkey	512	1	High
Mota[54]	2008	Preg	AUDADIS-IV	*DSM-IV*	…	US	451	4	Moderate
Seng[73]	2009	Preg	NWS-PTSD	*DSM-IV*	4	US	1,581	1	Moderate
Chaudron[46]	2010	Preg	SCID	*DSM-IV*	32.63	US	24	5	Moderate
Fisher[53]	2010	Preg	SCID	*DSM-IV*	28+	Vietnam	199	2	Moderate
Uguz[74]	2010	Preg	SCID-I	*DSM-IV*	23.26	Turkey	309	6	Moderate
Matthey[64,c]	2011	Preg	MINI	*DSM-IV*	13.4	Australia	171	6	Moderate
Giardinelli[75]	2012	Preg	SCID-I	*DSM-IV*	30	Italy	590	7	Moderate
Fadzil[62,c]	2013	Preg	MINI	*DSM-IV*	26.82	Malaysia	175	6	Moderate
Kim[76]	2014	Preg	SCID	*DSM-IV*	…	US	745	1	High
Marchesi[77]	2014	Preg	PRIME-MD	*DSM-IV*	…	Italy	299	2	High
Usuda[45,c]	2016	Preg	MINI	*DSM-IV*	17.26	Japan	177	6	High
Wenzel[78]	2003	Post	SCID	*DSM-IV*[d]	8	US	68	1	Moderate
Wenzel[79]	2005	Post	SCID-NP	*DSM-IV*[d]	8.7	US	147	5[e]	High
Mota[54]	2008	Post	AUDADIS-IV	*DSM-IV*	…	US	1,061	4	Moderate
Kersting[57]	2009	Post	SCID	*DSM-IV*	2	Germany	65	4	Moderate
Fisher[53]	2010	Post	SCID	*DSM-IV*	4–8	Vietnam	165	2	Moderate
Fisher[63,c]	2010	Post	CIDI	*DSM-IV*[d]	27.6	Australia	196	5	Moderate
Martini[56]	2013	Post	CIDI	*DSM-IV*	8	Germany	281	7[f]	Moderate
Prenoveau[80]	2013	Post	SCID	*DSM-IV*	12	UK	2,202	1	Moderate
Fairbrother[55,c]	2016	Post	SCID	*DSM-IV*[d]	13	Canada	310	8	High

[a]Eight disorders were assessed in this study, but extreme fear of childbirth was not included.
[b]Ten disorders were assessed in this study, but substance-induced anxiety disorder and anxiety disorder due to a general medical condition were excluded.
[c]These authors provided us with raw data. Prevalence estimates from Matthey and Ross-Hamid[64] were calculated from raw data inclusive of 8 additional subjects beyond those reported in their article.
[d]The 6-month duration criterion for generalized anxiety disorder was waived.
[e]Six disorders were assessed in this study, but PTSD was excluded as it was only childbirth-related PTSD.
[f]Eight disorders were assessed, but phobia not otherwise specified was excluded.
Abbreviations: ADIS-R = Anxiety Disorder Interview Schedule-Revised; AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM-IV* version; CIDI = Composite International Diagnostic Interview; CIS-R = Clinical Interview Schedule-Revised; DIS = Diagnostic Interview Schedule; *ICD-10* = *International Classification of Diseases*, Tenth Revision; MINI = Mini-International Neuropsychiatric Interview; NWS-PTSD = National Women's Study PTSD Module; post = postpartum; preg = pregnant; PRIME-MD = Primary Care Evaluation of Mental Disorders; PTSD = posttraumatic stress disorder; SCID-I = the Structured Clinical Interview for *DSM-IV*; SCID-NP = Nonpatient SCID; UK = United Kingdom; US = United States.
Symbol: … = not listed or reported in the article.

Our modeling approach follows the procedure laid out in Fawcett et al,[51] including our model specification and priors. Parameters are reported as the posterior median along with a 95% highest density interval (HDI)[66] within which we are 95% certain the true parameter value lies after accounting for our model assumptions and prior knowledge. Predictors were examined individually, each in its own model; although it would be preferable to analyze all predictors concurrently, in a single model, this was not possible due to variation in the information reported across studies.

RESULTS

Description of Studies

Of the 2,613 studies initially identified, 26 studies were included (see Figure 1), including a total of 28 prevalence estimates. The prevalence studies resulted in 19 estimates during pregnancy and 9 estimates during the postpartum period. Study characteristics are summarized in Table 1.

Quality Ratings

Overall quality ratings ranged from 4 to 9 (mean = 6.3, SD = 1.04). Of the 26 included studies, 18 (69.2%) were classified as moderate quality (scores between 4 and 6) and 8 (30.8%) were classified as high quality (scores between 7 and 10; see Table 1). There was no difference in mean quality ratings between pregnant (mean = 6.42, SD = 0.69) and postpartum (mean = 5.89, SD = 1.45) samples ($t_{26} = 1.33$, $P = .20$). Furthermore, there was no statistically significant difference in prevalence rates between studies classified as moderate versus high quality for studies reporting a total "any anxiety disorder" prevalence ($t_{18} = 0.95$, $P = .35$).

Of the 10 methodological criteria that were scored for each study, the following 4 were the least likely to be met overall: sampling method, confidence intervals, nonresponders, and response rate. Specifically, of the 26 studies included, only 11.5% (3 studies) used random samples, 19.2% (5 studies) reported confidence intervals or standard errors with anxiety prevalence estimates, 30.8% (8 studies) reported information about people who completed the study versus those who

refused, and 50.0% (13 studies) reported an adequate response rate for their study (70% or higher). The biggest differences between moderate- and high-quality studies were in regard to nonresponders, confidence intervals, and setting of the study. Whereas information on nonresponders was reported by 62.5% (5/8) of the high-quality studies, it was reported in only 16.6% (3/18) of the moderate-quality studies. Confidence intervals were reported by 37.5% (3/8) of high-quality versus 11.1% (2/18) of moderate-quality studies, and the setting of the study was clearly described by 100% (8/8) of the high-quality studies versus 77.8% (14/18) of the moderate-quality studies.

Individual Disorder Estimates

The individual prevalence estimates and prediction intervals for each disorder are presented in Figures 2 and 3; further details pertaining to the model parameters are available from the authors upon request. Estimates range from 1.1% for PTSD to 4.8% for specific phobia, with the remaining estimates falling between 1.9% and 2.4%. Figures 2 and 3 also show that prevalence varies widely across studies—so estimates must be interpreted cautiously. This heterogeneity is captured by the prediction intervals, which represent the credible range of "true" prevalence estimates one might expect within a "new" population similar to those included in this analysis.

Overall Prevalence Estimate

The prevalence of having at least 1 AD during pregnancy or the postpartum period is estimated to be 20.7% ($HDI_{95\%}$ [16.7% to 25.4%]), with a trend toward greater prevalence in pregnancy versus the postpartum period (see Predictors). We attribute these estimates being higher than previous meta-analytic estimates to the fact that the present model correctly accounts for the number of disorders reported by each of the included studies whereas past studies have combined estimates based on varying combinations of disorders (for supporting simulations, see Fawcett et al[51]).[a] In addition, about 1 in 20 women (5.5%) met criteria for at least 2 ADs. See Supplementary Table 1 (in Supplementary Appendix 1) for the probability of having 1+, 2+, 3+, or 4+ anxiety disorders and associated prediction intervals.

Predictors

Having established the presence of substantial heterogeneity in our prevalence estimates, we next sought to explore potential sources of that variability through predictors. Prior to analysis, several variables were found to be unsuitable as predictors due to minimal variation across studies (percent of the sample that was married or cohabitating, diagnostic criteria, country income) and were excluded from further consideration; we return to this issue in the discussion. Of the included predictors, the comparison between pregnant and postpartum samples was of particular theoretical interest and constituted our primary predictor analysis. Although there was a trend toward pregnant women being at greater risk (21.1%, $HDI_{95\%}$ [16.7% to 25.8%]) than postpartum women (18.0%, $HDI_{95\%}$ [13.1% to 24.3%]), the difference was small and failed to exclude 0 as a credible value (3.1%, $HDI_{95\%}$ [−2.6% to 8.5%]). Even so, current evidence suggests that we are 86% certain that this difference is positive, providing preliminary—if tentative—support for the conclusion that pregnant women are at greater risk.[b]

Of the remaining predictors, region was the only other finding of note. Due to the sparsity of the disorders measured across different locations, our analysis of region compared North America to all other regions. There was a trend in this analysis suggesting a higher prevalence estimate for North American samples (26.9%, $HDI_{95\%}$ [18.1% to 37.5%]) compared to other samples (18.5%, $HDI_{95\%}$ [14.6% to 23.1%]), resulting in a difference of 8.4% ($HDI_{95\%}$ [−0.7% to 18.8%]). This effect was driven by differences in the prevalence of OCD (3.2%, $HDI_{95\%}$ [−0.3% to 8.6%]), social phobia (1.5%, $HDI_{95\%}$ [−0.8% to 4.5%]), and PTSD (2.4%, $HDI_{95\%}$ [0.2% to 4.9%]) between North America and elsewhere. Statistics pertaining to other predictors are available from the first author upon request, but none credibly predicted overall prevalence.

Comorbidity Analyses

Finally, we also estimated a comorbidity matrix reflecting the probability of having 1 anxiety disorder assuming a diagnosis of another anxiety disorder. These results are presented in Table 2. Rows reflect diagnoses that a given patient is assumed to have received, with the columns

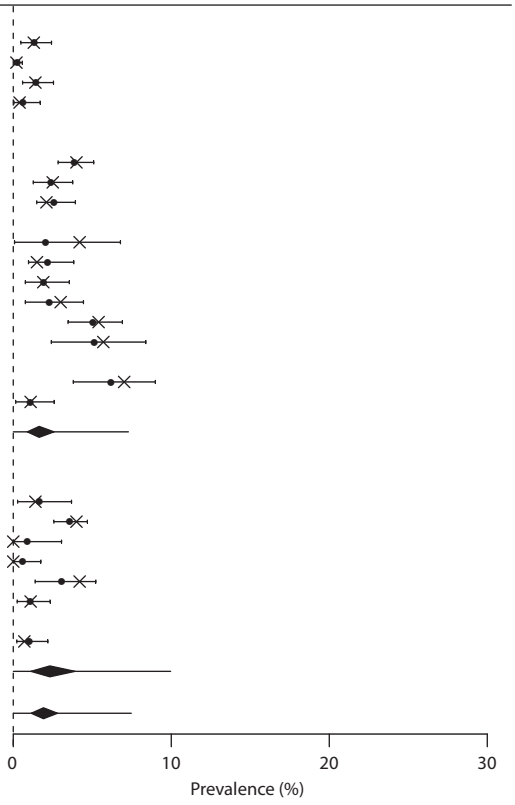
[a]In support of this assertion, a supplementary meta-analysis was conducted using the univariate approach described by Goodman et al[47] or Dennis et al[48] applied to the any disorder prevalence estimates reported by the available samples. This model produced an estimate of 9.9% (95% CI, 7.3%–13.4%). While more comparable to the prevalence estimate reported by those authors, it is our view that this underestimates the true prevalence of peripartum ADs. To further support this claim, we conducted the same analysis again including only the samples for which at least 4 disorders were measured. If we are correct that aggregating studies that differ in respect to the disorders measured underestimates the true prevalence, this new model should produce a higher estimate. Supporting our hypothesis, this model produced an estimate of 14.1% (95% CI, 10.8%–18.2%), reflecting the fact that studies measuring more disorders tend to produce higher estimates. Finally, we refit the model to the original sample of estimates, including the number of disorders measured as a moderator—and predicting the prevalence of a hypothetical study in which all 8 disorders were measured. This produced an estimate of 20.6% (95% CI, 14.1%–29.0%), which is closer to our own—only with broader confidence intervals. Simulations conducted by Fawcett et al[51] predict precisely this pattern of results. They further demonstrated that of these univariate models only the moderator approach produces an unbiased estimate, and, even then, the estimate produced by that model is more variable and less efficient than the one reported in text. Overall, these models support the notion that previous meta-analyses have underestimated the prevalence of peripartum ADs.

[b]Prevalence estimates for individual disorders broken down by peripartum group are provided in Figures 2 and 3. No single disorder prevalence varied credibly between groups with differences of −0.7% ($HDI_{95\%}$ [−2.0% to 0.4%]), 2.1% ($HDI_{95\%}$ [−0.5% to 4.9%]), 0.6% ($HDI_{95\%}$ [−2.4% to 3.1%]), −0.5% ($HDI_{95\%}$ [−1.9% to 0.6%]), 0.1% ($HDI_{95\%}$ [−1.3% to 1.3%]), −0.3% ($HDI_{95\%}$ [−2.2% to 1.5%]), 1.0% ($HDI_{95\%}$ [−0.6% to 2.4%]), and 1.6% ($HDI_{95\%}$ [−2.7% to 5.1%]) for panic disorder, agoraphobia, OCD, GAD, social phobia, specific phobia, PTSD, and anxiety NOS, respectively. As detailed by these figures, there was a trend toward greater disorder prevalence in pregnant than postpartum populations across 5 of the 8 disorders, contributing to the apparent difference reported.

Figure 2. Prevalence of Panic Disorder, Agoraphobia, Obsessive-Compulsive Disorder, and Generalized Anxiety Disorder[a]

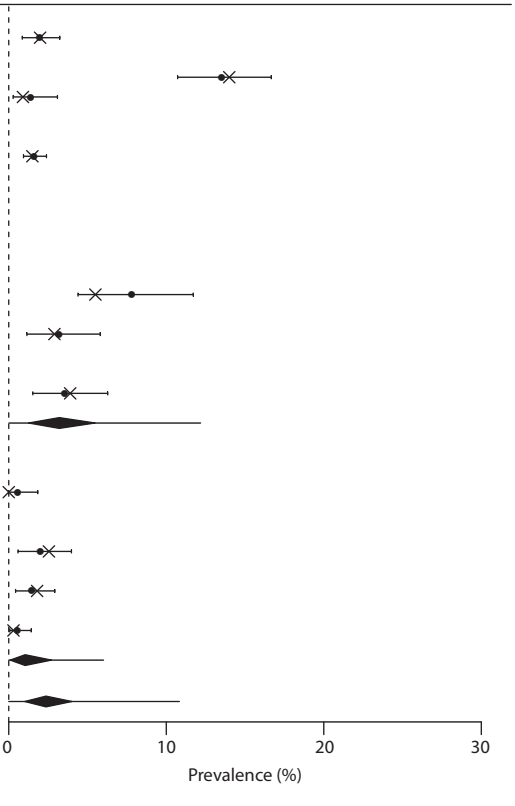
A. Panic Disorder

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	1.4 [0.5 to 2.4]
Andersson et al, 2003[67]	1,556	0.3 [0.1 to 0.6]
Sutter-Dallay et al, 2004[29]	497	1.5 [0.6 to 2.5]
Felice et al, 2007[68]	229	0.6 [0.0 to 1.7]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	3.9 [2.8 to 5.1]
Guler et al, 2008[72]	512	2.4 [1.3 to 3.8]
Mota et al, 2008[54]	451	2.6 [1.5 to 3.9]
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]	24	2.1 [0.1 to 6.8]
Fisher et al, 2010[53]	199	2.2 [1.0 to 3.8]
Uguz et al, 2010[74]	309	1.9 [0.8 to 3.5]
Matthey and Ross-Hamid, 2011[64]	171	2.3 [0.8 to 4.4]
Giardinelli et al, 2012[75]	590	5.1 [3.5 to 6.9]
Fadzil et al, 2013[62]	175	5.2 [2.4 to 8.4]
Kim et al, 2014[76]		
Marchesi et al, 2014[77]	299	6.2 [3.8 to 9.0]
Usuda et al, 2016[45]	177	1.1 [0.2 to 2.6]
RE Model	6,708	1.6 [0.9 to 2.6]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]	147	1.7 [0.3 to 3.7]
Mota et al, 2008[54]	1,061	3.6 [2.6 to 4.7]
Kersting et al, 2009[57]	65	0.9 [0.0 to 3.1]
Fisher et al, 2010[63]	196	0.6 [0.0 to 1.8]
Fisher et al, 2010[53]	165	3.1 [1.4 to 5.2]
Martini et al, 2013[56]	281	1.1 [0.2 to 2.3]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	1.0 [0.2 to 2.2]
RE Model	2,225	2.3 [1.1 to 3.9]
Overall	**8,933**	**1.9 [1.1 to 2.8]**



B. Agoraphobia

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	2.0 [0.9 to 3.2]
Andersson et al, 2003[67]		
Sutter-Dallay et al, 2004[29]	497	13.5 [10.7 to 16.7]
Felice et al, 2007[68]	229	1.4 [0.3 to 3.1]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	1.6 [0.9 to 2.4]
Guler et al, 2008[72]		
Mota et al, 2008[54]		
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]		
Fisher et al, 2010[53]		
Uguz et al, 2010[74]		
Matthey and Ross-Hamid, 2011[64]	171	7.8 [4.4 to 11.7]
Giardinelli et al, 2012[75]		
Fadzil et al, 2013[62]	175	3.2 [1.2 to 5.8]
Kim et al, 2014[76]		
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]	177	3.6 [1.5 to 6.3]
RE Model	2,768	3.2 [1.3 to 5.5]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]	147	0.6 [0.0 to 1.8]
Mota et al, 2008[54]		
Kersting et al, 2009[57]		
Fisher et al, 2010[63]	196	2.0 [0.6 to 4.0]
Fisher et al, 2010[53]		
Martini et al, 2013[56]	281	1.5 [0.4 to 2.9]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	0.6 [0.1 to 1.4]
RE Model	934	1.0 [0.1 to 2.7]
Overall	**3,702**	**2.4 [1.0 to 4.0]**

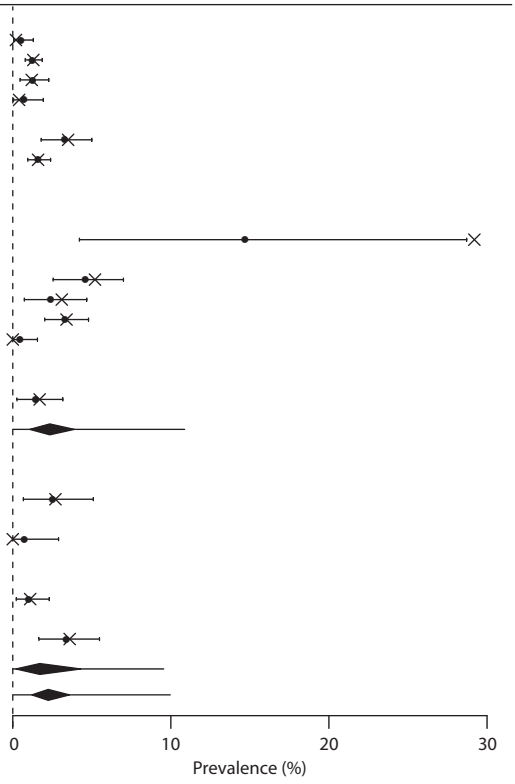


(continued)

Figure 2 (continued).

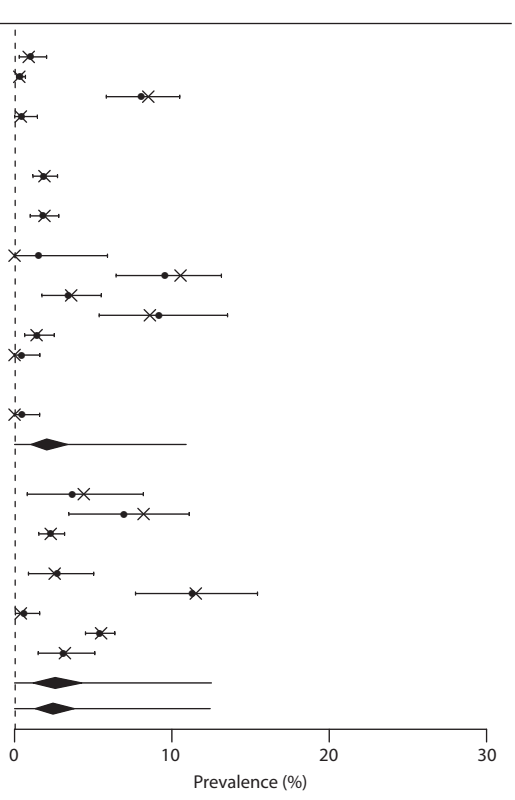
C. Obsessive-Compulsive Disorder

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	0.5 [0.1 to 1.3]
Andersson et al, 2003[67]	1,556	1.3 [0.8 to 1.9]
Sutter-Dallay et al, 2004[29]	497	1.3 [0.5 to 2.3]
Felice et al, 2007[68]	229	0.7 [0.0 to 1.9]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]	434	3.3 [1.8 to 5.0]
Borri et al, 2008[71]	1,066	1.6 [1.0 to 2.4]
Guler et al, 2008[72]		
Mota et al, 2008[54]		
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]	24	14.7 [4.2 to 28.7]
Fisher et al, 2010[53]		
Uguz et al, 2010[74]	309	4.6 [2.6 to 7.0]
Matthey and Ross-Hamid, 2011[64]	171	2.4 [0.7 to 4.7]
Giardinelli et al, 2012[75]	590	3.3 [2.0 to 4.8]
Fadzil et al, 2013[62]	175	0.5 [0.0 to 1.6]
Kim et al, 2014[76]		
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]	177	1.5 [0.3 to 3.2]
RE Model	5,681	2.3 [1.1 to 3.9]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]	147	2.5 [0.7 to 5.1]
Mota et al, 2008[54]		
Kersting et al, 2009[57]	65	0.8 [0.0 to 2.9]
Fisher et al, 2010[63]		
Fisher et al, 2010[53]		
Martini et al, 2013[56]	281	1.0 [0.2 to 2.3]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	3.4 [1.7 to 5.5]
RE Model	803	1.7 [0.2 to 4.3]
Overall	**6,484**	**2.2 [1.2 to 3.6]**



D. Generalized Anxiety Disorder

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	1.0 [0.3 to 2.0]
Andersson et al, 2003[67]	1,556	0.4 [0.1 to 0.7]
Sutter-Dallay et al, 2004[29]	497	8.1 [5.8 to 10.5]
Felice et al, 2007[68]	229	0.5 [0.0 to 1.4]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	1.9 [1.2 to 2.7]
Guler et al, 2008[72]		
Mota et al, 2008[54]	451	1.8 [1.0 to 2.8]
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]	24	1.6 [0.0 to 5.9]
Fisher et al, 2010[53]	199	9.6 [6.5 to 13.1]
Uguz et al, 2010[74]	309	3.4 [1.7 to 5.5]
Matthey and Ross-Hamid, 2011[64]	171	9.2 [5.4 to 13.5]
Giardinelli et al, 2012[75]	590	1.5 [0.6 to 2.5]
Fadzil et al, 2013[62]	175	0.5 [0.0 to 1.6]
Kim et al, 2014[76]		
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]	177	0.5 [0.0 to 1.6]
RE Model	5,897	2.0 [1.1 to 3.4]
Postpartum		
Wenzel et al, 2003[78]	68	3.7 [0.8 to 8.2]
Wenzel et al, 2005[79]	147	7.0 [3.5 to 11.1]
Mota et al, 2008[54]	1,061	2.3 [1.5 to 3.2]
Kersting et al, 2009[57]		
Fisher et al, 2010[63]	196	2.7 [0.9 to 5.0]
Fisher et al, 2010[53]	165	11.3 [7.7 to 15.4]
Martini et al, 2013[56]	281	0.6 [0.1 to 1.6]
Prenoveau et al, 2013[80]	2,202	5.4 [4.5 to 6.4]
Fairbrother et al, 2016[55]	310	3.1 [1.5 to 5.1]
RE Model	4,430	2.6 [1.2 to 4.3]
Overall	**10,327**	**2.4 [1.3 to 3.8]**

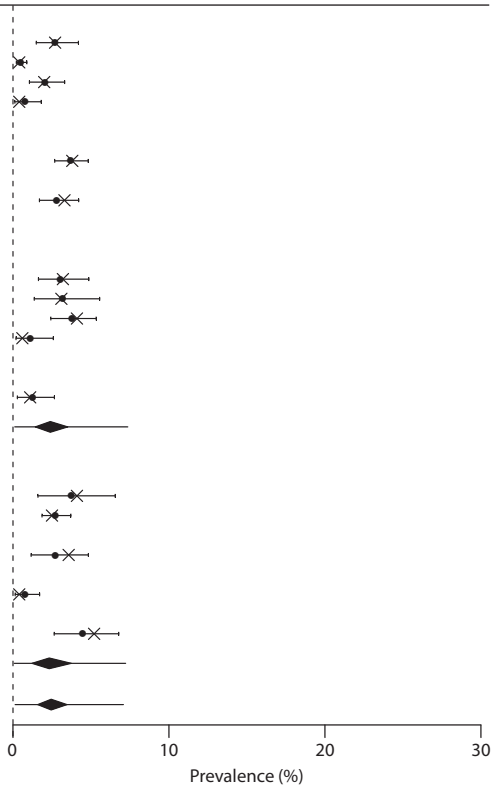


[a]Xs represent the observed prevalence estimate reported by the corresponding study. Circles and numerical prevalence values represent the shrunken estimates (with 95% highest density interval) for each study as estimated from the model including group (pregnant, postpartum) as a predictor; entries without a circle or numerical prevalence value reflect studies for which that disorder was not measured. Diamonds depict the aggregate estimate for each group and overall. Error bars surrounding each diamond represent the 95% prediction interval.

Figure 3. Prevalence of Social Phobia, Specific Phobia, Posttraumatic Stress Disorder, and Anxiety Not Otherwise Specified[a]

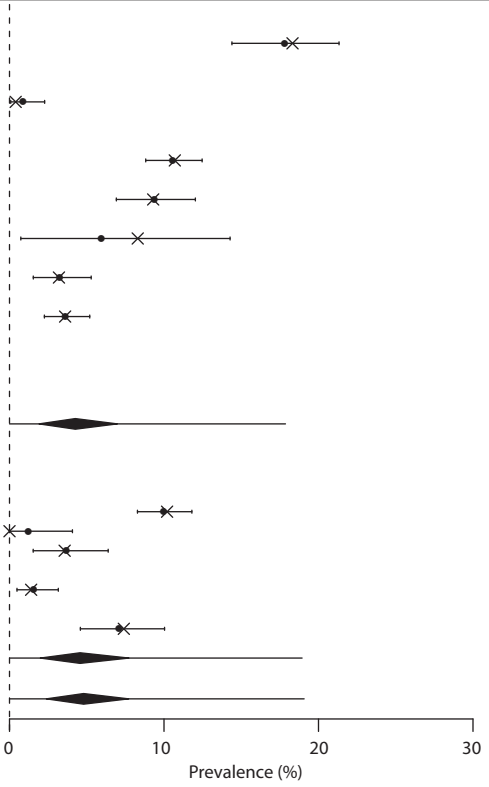
A. Social Phobia

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	2.7 [1.5 to 4.2]
Andersson et al, 2003[67]	1,556	0.5 [0.2 to 0.9]
Sutter-Dallay et al, 2004[29]	497	2.1 [1.1 to 3.3]
Felice et al, 2007[68]	229	0.8 [0.1 to 1.8]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	3.7 [2.7 to 4.8]
Guler et al, 2008[72]		
Mota et al, 2008[54]	451	2.8 [1.7 to 4.2]
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]		
Fisher et al, 2010[53]		
Uguz et al, 2010[74]	309	3.1 [1.6 to 4.9]
Matthey and Ross-Hamid, 2011[64]	171	3.2 [1.4 to 5.6]
Giardinelli et al, 2012[75]	590	3.8 [2.4 to 5.3]
Fadzil et al, 2013[62]	175	1.1 [0.2 to 2.6]
Kim et al, 2014[76]		
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]	177	1.3 [0.3 to 2.7]
RE Model	5,674	2.4 [1.4 to 3.5]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]	147	3.8 [1.6 to 6.5]
Mota et al, 2008[54]	1,061	2.7 [1.9 to 3.7]
Kersting et al, 2009[57]		
Fisher et al, 2010[63]	196	2.7 [1.2 to 4.8]
Fisher et al, 2010[53]		
Martini et al, 2013[56]	281	0.8 [0.1 to 1.7]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	4.5 [2.6 to 6.8]
RE Model	1,995	2.3 [1.2 to 3.7]
Overall	**7,669**	**2.4 [1.6 to 3.5]**



B. Specific Phobia

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	17.8 [14.4 to 21.3]
Andersson et al, 2003[67]		
Sutter-Dallay et al, 2004[29]		
Felice et al, 2007[68]	229	0.9 [0.1 to 2.3]
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	10.6 [8.8 to 12.5]
Guler et al, 2008[72]		
Mota et al, 2008[54]	451	9.4 [6.9 to 12.0]
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]	24	6.0 [0.7 to 14.3]
Fisher et al, 2010[53]		
Uguz et al, 2010[74]	309	3.3 [1.5 to 5.3]
Matthey and Ross-Hamid, 2011[64]		
Giardinelli et al, 2012[75]	590	3.6 [2.3 to 5.2]
Fadzil et al, 2013[62]		
Kim et al, 2014[76]		
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]		
RE Model	3,122	4.3 [1.9 to 7.0]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]		
Mota et al, 2008[54]	1,061	10.0 [8.3 to 11.8]
Kersting et al, 2009[57]	65	1.2 [0.0 to 4.1]
Fisher et al, 2010[63]	196	3.7 [1.5 to 6.4]
Fisher et al, 2010[53]		
Martini et al, 2013[56]	281	1.6 [0.5 to 3.2]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	7.1 [4.6 to 10.0]
RE Model	1,913	4.6 [2.0 to 7.7]
Overall	**5,035**	**4.8 [2.4 to 7.7]**

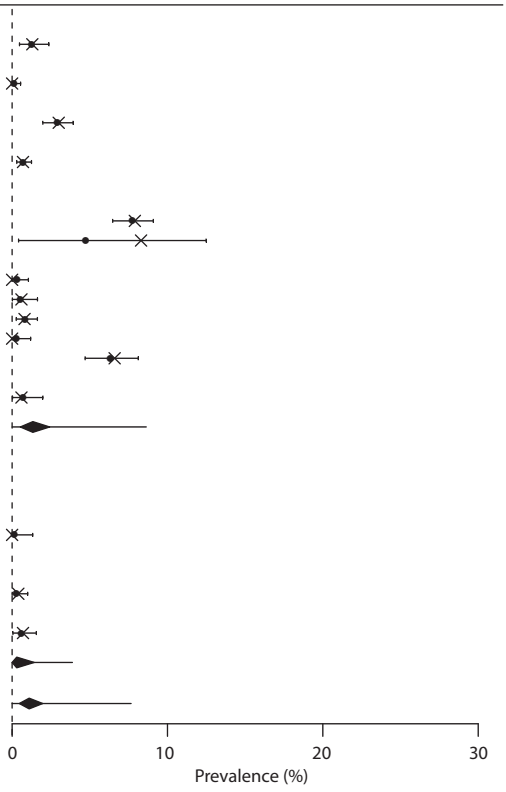


(continued)

Figure 3 (continued).

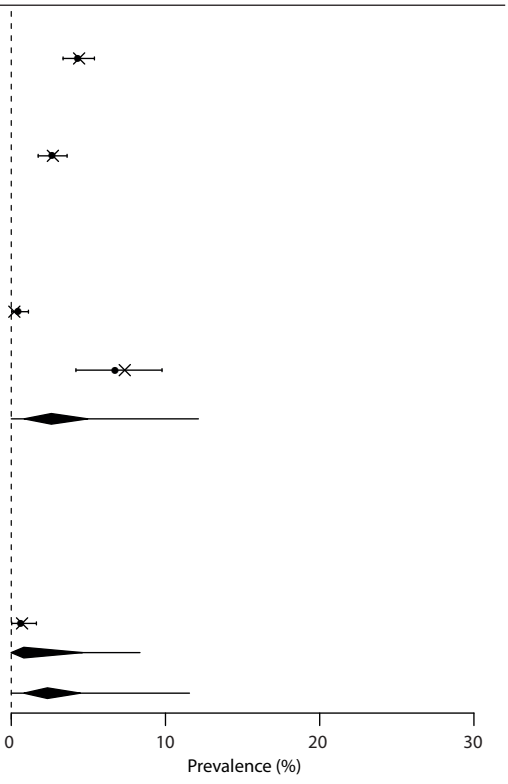
C. Posttraumatic Stress Disorder

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]	453	1.3 [0.5 to 2.4]
Andersson et al, 2003[67]		
Sutter-Dallay et al, 2004[29]	497	0.1 [0.0 to 0.5]
Felice et al, 2007[68]		
Rogal et al, 2007[69]	1,100	2.9 [2.0 to 3.9]
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	0.7 [0.3 to 1.2]
Guler et al, 2008[72]		
Mota et al, 2008[54]		
Seng et al, 2009[73]	1,581	7.8 [6.5 to 9.1]
Chaudron and Nirodi, 2010[46]	24	4.7 [0.4 to 12.5]
Fisher et al, 2010[53]		
Uguz et al, 2010[74]	309	0.3 [0.0 to 1.0]
Matthey and Ross-Hamid, 2011[64]	171	0.5 [0.0 to 1.6]
Giardinelli et al, 2012[75]	590	0.9 [0.3 to 1.6]
Fadzil et al, 2013[62]	175	0.3 [0.0 to 1.2]
Kim et al, 2014[76]	745	6.3 [4.7 to 8.1]
Marchesi et al, 2014[77]		
Usuda et al, 2016[45]	177	0.7 [0.0 to 2.0]
RE Model	6,888	1.3 [0.5 to 2.4]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]		
Mota et al, 2008[54]		
Kersting et al, 2009[57]	65	0.2 [0.0 to 1.3]
Fisher et al, 2010[63]		
Fisher et al, 2010[53]		
Martini et al, 2013[56]	281	0.3 [0.0 to 1.0]
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	0.6 [0.1 to 1.6]
RE Model	656	0.3 [0.0 to 1.4]
Overall	**7,544**	**1.1 [0.5 to 2.0]**



D. Anxiety Not Otherwise Specified

Article	N	Prevalence [%]
Pregnant		
Zar et al, 2002[65]		
Andersson et al, 2003[67]	1,556	4.3 [3.4 to 5.4]
Sutter-Dallay et al, 2004[29]		
Felice et al, 2007[68]		
Rogal et al, 2007[69]		
Uguz et al, 2007[70]		
Borri et al, 2008[71]	1,066	2.7 [1.7 to 3.6]
Guler et al, 2008[72]		
Mota et al, 2008[54]		
Seng et al, 2009[73]		
Chaudron and Nirodi, 2010[46]		
Fisher et al, 2010[53]		
Uguz et al, 2010[74]		
Matthey and Ross-Hamid, 2011[64]		
Giardinelli et al, 2012[75]	590	0.5 [0.0 to 1.1]
Fadzil et al, 2013[62]		
Kim et al, 2014[76]		
Marchesi et al, 2014[77]	299	6.8 [4.2 to 9.8]
Usuda et al, 2016[45]		
RE Model	3,511	2.6 [0.8 to 5.0]
Postpartum		
Wenzel et al, 2003[78]		
Wenzel et al, 2005[79]		
Mota et al, 2008[54]		
Kersting et al, 2009[57]		
Fisher et al, 2010[63]		
Fisher et al, 2010[53]		
Martini et al, 2013[56]		
Prenoveau et al, 2013[80]		
Fairbrother et al, 2016[55]	310	0.6 [0.0 to 1.6]
RE Model	310	0.8 [0.0 to 4.6]
Overall	**3,821**	**2.3 [0.8 to 4.5]**



[a]Xs represent the observed prevalence estimate reported by the corresponding study. Circles and numerical prevalence values represent the shrunken estimates (with 95% highest density interval) for each study as estimated from the model including group (pregnant, postpartum) as a predictor; entries without a circle or numerical prevalence value reflect studies for which that disorder was not measured. Diamonds depict the aggregate estimate for each group and overall. Error bars surrounding each diamond represent the 95% prediction interval.

Table 2. Estimated Comorbidity (%) Among Disorders[a]

	Potential Disorder							
Diagnosis	Panic Disorder	Agoraphobia	OCD	GAD	Social Phobia	Specific Phobia	PTSD	Anxiety NOS
Panic disorder	60.7 (43.2 to 76.1) [34.6 to 95.3]	22.4 (9.6 to 38.3) [0.7 to 63.9]	15.2 (4.3 to 29.7) [0.0 to 48.5]	15.9 (5.1 to 29.8) [0.0 to 50.9]	10.6 (3.0 to 21.4) [0.3 to 28.8]	24.1 (8.6 to 42.9) [0.0 to 60.5]	6.5 (0.7 to 15.8) [0.0 to 29.1]	3.2 (0.0 to 18.1) [0.0 to 25.1]
Agoraphobia	16.9 (8.2 to 28.1) [0.7 to 53.4]	51.5 (36.9 to 66.4) [27.9 to 93.4]	12.5 (3.6 to 24.0) [0.0 to 46.6]	14.6 (5.7 to 26.0) [0.0 to 43.6]	14.8 (6.3 to 25.1) [1.4 to 46.4]	10.9 (2.7 to 22.6) [0.0 to 37.1]	6.2 (1.0 to 14.6) [0.0 to 34.5]	5.1 (0.0 to 21.2) [0.0 to 29.4]
OCD	12.5 (4.1 to 24.3) [0.2 to 41.6]	13.5 (3.6 to 27.2) [0.0 to 49.4]	50.3 (34.7 to 66.0) [25.2 to 87.2]	15.7 (5.1 to 28.6) [0.0 to 46.3]	11.6 (3.4 to 22.1) [0.6 to 30.7]	15.7 (4.6 to 29.9) [0.0 to 48.9]	7.2 (0.8 to 16.6) [0.0 to 27.3]	3.0 (0.0 to 15.1) [0.0 to 24.6]
GAD	10.9 (3.1 to 20.7) [0.0 to 39.1]	13.3 (4.4 to 24.7) [0.0 to 41.2]	13.3 (4.1 to 25.4) [0.0 to 42.4]	54.5 (39.6 to 69.5) [30.8 to 90.6]	14.6 (6.5 to 24.8) [1.9 to 35.7]	23.4 (9.7 to 40.4) [0.4 to 64.0]	5.6 (0.6 to 14.0) [0.0 to 28.1]	3.5 (0.0 to 15.1) [0.0 to 22.7]
Social phobia	9.4 (2.5 to 19.0) [0.0 to 25.9]	17.3 (7.2 to 30.5) [0.1 to 51.4]	12.8 (3.7 to 24.5) [0.0 to 34.2]	18.9 (8.4 to 31.4) [0.0 to 43.8]	56.9 (42.4 to 71.2) [30.6 to 87.7]	18.2 (8.1 to 30.9) [0.0 to 42.1]	5.5 (0.5 to 13.8) [0.0 to 22.3]	9.0 (0.3 to 25.4) [0.0 to 41.1]
Specific phobia	9.6 (3.3 to 17.1) [0.1 to 29.6]	5.7 (1.3 to 12.2) [0.0 to 22.1]	7.6 (2.4 to 15.3) [0.0 to 27.2]	13.5 (6.3 to 22.8) [0.0 to 44.1]	8.2 (3.7 to 13.8) [0.7 to 19.0]	38.7 (27.7 to 50.8) [15.6 to 74.0]	8.9 (2.9 to 16.8) [0.0 to 34.7]	2.8 (0.0 to 11.2) [0.0 to 15.4]
PTSD	8.4 (0.9 to 20.5) [0.0 to 36.9]	10.6 (1.5 to 25.4) [0.0 to 51.9]	11.4 (1.3 to 26.4) [0.0 to 40.1]	10.6 (1.2 to 24.7) [0.0 to 46.6]	7.9 (0.9 to 19.8) [0.0 to 29.7]	29.0 (10.7 to 51.0) [0.9 to 76.1]	53.9 (33.6 to 74.4) [27.9 to 96.1]	3.1 (0.0 to 17.5) [0.0 to 26.6]
Anxiety NOS	2.4 (0.0 to 13.0) [0.0 to 19.5]	5.1 (0.0 to 20.4) [0.0 to 29.2]	2.8 (0.0 to 13.6) [0.0 to 22.0]	3.8 (0.0 to 15.2) [0.0 to 24.0]	7.5 (0.1 to 20.9) [0.0 to 35.8]	5.2 (0.0 to 20.0) [0.0 to 27.8]	1.8 (0.0 to 10.1) [0.0 to 15.2]	25.5 (5.9 to 50.3) [1.4 to 66.2]

[a]Off-diagonal values reflect the probability of having the disorder listed in the column given the diagnosis in the row (eg, if a patient has panic disorder the probability of also having OCD is 15.2%). Diagonal values (shaded) reflect instead the probability of having any other disorder given the diagnosis in the row (eg, if a patient has panic disorder the probability of having at least 1 other disorder is 60.7%). 95% highest density intervals are provided in parentheses, and 95% prediction intervals are provided in brackets.

Abbreviations: GAD = generalized anxiety disorder, NOS = not otherwise specified, OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder.

reflecting the probability of also having additional diagnoses. For example, someone with a diagnosis of panic disorder has a 1 in 6 chance of also having GAD in a typical sample. Diagonal values reflect the probability of having any other disorder. The highest comorbidity was found for panic disorder (60.7% chance of having another diagnosis), and the lowest comorbidity was found for anxiety NOS (25.5% chance of having another diagnosis). Overall, the probability of having an additional AD given an initial diagnosis was quite high, at approximately 50% in most cases.

DISCUSSION

The current study is the first meta-analysis to estimate the probability of having at least 1 of 8 common ADs across pregnancy and the postpartum period while correctly accounting for variation in the disorders reported by the individual estimates. Results suggest that ADs are more prevalent in these populations than previously thought, with approximately 1 in 5 (20.7%) women meeting diagnostic criteria for at least 1 AD and 1 in 20 women (5.5%) meeting criteria for at least 2 ADs. These estimates are based on studies that employed structured diagnostic interviews and are representative of community samples. Although the overall prevalence rate was 20.7% for at least 1 AD, the prediction interval ranged from 7.5% to 38.8%—reflecting a high degree of variation across populations. One major goal moving forward in this area should be identifying sources of heterogeneity.

The current prevalence estimate for having at least 1 AD during pregnancy or the postpartum period (20.7%) is 1.5 to 2.5 times larger than similar meta-analytic estimates for pregnant or postpartum women.[47,48] The prevalence rate found in the current study is consistent with 12-month prevalence rates found for ADs in national samples (18.1%)[2] or moderator based univariate meta-analytic estimates[51] but is considerably higher than Goodman and colleagues'[47] estimate of 8.5% in postpartum samples or Dennis and colleagues'[48] estimates of 15.2% and 9.9% in pregnant and postpartum samples, respectively. The "any anxiety disorder" estimates from previous meta-analyses were based on 6 postpartum estimates[47] or 9 prenatal and 9 postnatal assessments,[48] whereas 28 prevalence estimates across pregnancy and the postpartum period contributed to the current prevalence estimate.

Our study also contributes significantly to the estimation of the prevalence of individual ADs. Whereas Dennis et al[48] only report the prevalence rate for 1 individual disorder (GAD), the prevalence rates for some of the disorders in the Goodman et al[47] study were based on the availability of only 2 estimates (eg, agoraphobia, specific phobia, and anxiety disorder NOS). Thus, the current study includes significantly more individual AD estimates, ranging from 5 estimates (anxiety NOS) to 22 estimates (panic disorder). Knowing which individual ADs are most prevalent also informs clinicians and researchers where help is most needed. In the only other meta-analysis to provide prevalence estimates for the individual ADs, Goodman et al[47] found that the most

common disorders in the postpartum period were GAD, OCD, and panic disorder. In comparison, the current study found specific phobia, GAD, and social phobia to be the most prevalent perinatal disorders.

When potential predictors of anxiety disorder prevalence were examined, tentative support was found for the conclusion that pregnant women are at greater risk than postpartum women. Although this is consistent with a previous meta-analysis,[48] the current estimate shows a smaller disparity between the 2 prevalence rates (3.1% vs 5.3%), meaning that postpartum rates may be higher than previously expected. Of the remaining predictors we examined, a trend was found for region, suggesting higher anxiety prevalence for North American samples versus elsewhere. This is consistent with a systematic review and meta-regression of the global prevalence of anxiety disorders,[81] in which the risk for anxiety was found to be 20%–50% lower in all cultures compared with Euro/Anglo cultures. The fact that no other predictors were credible is perhaps unsurprising given the fact that our prevalence estimate was derived from individual disorder estimates based—at times—on few studies and within which we observed considerable heterogeneity. Further data are required before strong conclusions may be drawn concerning predictors in this literature.

Strengths and Limitations

One strength of the current analysis is that our overall prevalence estimates account for variation among the individual ADs. Previous attempts have simply combined studies reporting total AD estimates, despite variation in the ADs composing these estimates. However, the current modeling approach is therefore dependent on individual AD estimates, which are not always reported in the context of the same published sample (eg, due to practical, financial, or other considerations). For instance, only 2 of the studies included in the meta-analysis reported all 8 ADs.[55,71] Whereas panic disorder was measured most consistently across studies, agoraphobia and anxiety NOS were the 2 disorders measured most infrequently. Perhaps part of the reason that anxiety NOS is measured infrequently is the variability in how it is defined across studies. Future studies can help reduce heterogeneity by clearly defining the diagnostic categories and measuring as many disorders as possible.

Our study was also limited by its need for individual patient data. Although few studies currently report individual patient data, several authors include tables describing each patient and their assigned diagnoses, which is sufficient to recreate the data.[46,65] As a note to the field, if more researchers presented data tables such as those highlighted above, it would allow for more complex statistical models and, as a result, more meaningful conclusions.

The ability of our statistical approach to estimate comorbidity across disorders is also a unique strength. To our knowledge, this is the first study to meta-analytically aggregate comorbidity across ADs in pregnancy and the postpartum period. Our estimates suggest that if a pregnant or postpartum woman is diagnosed with an AD, there is an approximately 50% chance she will be diagnosed with an additional AD. Our estimate is consistent with the literature outside of the perinatal period, including an adolescent community sample in which 41% of participants had more than 1 AD[82] or a clinical sample in which 43% of patients had at least 1 additional AD diagnosis.[83] Furthermore, our model allows clinicians to identify which disorders are most comorbid. For instance, our findings from Table 2 predict that the highest comorbidities among disorders are between PTSD, panic disorder, and GAD with specific phobia. Consistent with these findings, Brown et al[83] found that the diagnoses associated with the highest risk of comorbid ADs were GAD and panic disorder with agoraphobia. Given the estimate that 5.5% of pregnant or postpartum women meet criteria for more than 1 AD, screening for multiple disorders and differential diagnosis is essential.

Several factors impeded our ability to identify sources of heterogeneity across AD prevalence studies in pregnancy and the postpartum period. For one, we suspect our predictor analyses were underpowered because many studies did not report the information necessary to permit inclusion in a given model. Standardized reporting of basic demographic information such as age, parity, income, and education would increase the power of such analyses and allow researchers to identify factors that explain substantial variability in prevalence estimates. When studies do report such information, it is often done so inconsistently. For instance, variation in how education level was reported across studies made it difficult to merge these categories. Similarly, ethnicity was not coded as a predictor because ethnic composition was rarely reported, with only 3 studies (11.5%) reporting the percentage of the sample that identified as African-American. One solution is for researchers to include additional demographic and study design information in an appendix or online supplement, or to be more responsive through e-mail to requests for additional study details. Full reporting of demographic variables would allow future meta-analyses the power to better examine demographic risk factors.

Clinical Implications

Given the attention to screening for depression during pregnancy and the postpartum period over the last decade, it is important that screening for anxiety disorders also take place, which is intuitive based on the well-established comorbidity of the 2 types of disorders as well as the data presented in this systematic review. Depression and anxiety are thought to share a common diathesis, and when lifetime diagnoses are considered, comorbidity rates are as high as 76%.[84] With the high prevalence for ADs in our model, and the prediction interval extending as high as 39%, our data corroborate the strong need and call for routine prenatal and postnatal anxiety screening in health care settings.[35] Although women are increasingly screened for postpartum depression using measures such as the Edinburgh Postnatal Depression Scale (EPDS),[85] ADs receive significantly less

clinical focus and media attention. However, research suggests that anxiety is likely more prevalent than depression during pregnancy and the postpartum period.[79] For example, Lee and colleagues[86] found that anxiety was more prevalent than depression in antenatal assessments (54% vs 37%, respectively). Likewise, Reck et al[87] used *DSM-IV* criteria to examine over 1,000 postpartum women across a 3-month period and found that ADs were more common than depressive disorders (11.1% vs 6.1%, respectively).

In line with these observations, the American College of Obstetricians and Gynecologists recommends that clinicians screen patients for both depression and anxiety symptoms at least once during the perinatal period with a standardized, validated tool.[88] Although there are few anxiety screening measures validated within perinatal populations, the Perinatal Anxiety Screening Scale[89] was recently developed and uses a cutoff score to identify women at risk for problematic anxiety, and the 3-item Anxiety Subscale of the EPDS (known as the EPDS-3A) is also validated for anxiety screening in this population.[90] Research measuring the prevalence of pregnancy-related anxiety is also becoming more common, including a recent revision of the Pregnancy Related Anxieties Questionnaire.[91]

Before perinatal anxiety screening programs can be implemented universally, proper mental health education and training are required for health care professionals. The unique features of anxiety and related disorders when they present during pregnancy and the postpartum are not well known and may prevent accurate and timely diagnosis. Health care providers who work with pregnant and postpartum women would benefit from education regarding the special features of perinatal anxiety disorders (eg, obsessions of infant-related harm in OCD and women's motivation to conceal the occurrence of this ideation),[92] as well as the symptom overlap with normal postpartum experiences (eg, fatigue, difficulty sleeping). Further, the fact that these conditions are more common than depression and may not be disclosed by women unless they are asked should also be taught to health care professionals who care for this vulnerable population. Staff who administer screening measures should have specific training on how to use these tools and identify women at risk (eg, through use of validated cutoff scores). The development of a consistent response protocol is needed to facilitate appropriate consultation and treatment referrals when needed, including emergency referrals due to psychosis and suicidal or homicidal ideation.[35,93] Maternal health education is also a requirement of an effective mental health program. For instance, it is important that mothers are provided with sufficient and effective education about the meaning of screening results, including understanding the difference between normal levels of anxiety, being "at risk" for an anxiety disorder, and receiving a formal psychiatric diagnosis from a licensed professional.[35,93]

Given the significant role that ADs play in women's perinatal mental health and the potential for adverse outcomes for both mothers and infants, evidence-based treatment for perinatal anxiety disorders is essential. However, research evaluating potential evidence-based treatments for perinatal anxiety is limited, with systematic reviews identifying a reliance on case reports and case series (83%),[94] with only 5 studies identified in which psychological interventions in the perinatal period are evaluated.[95] Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), the medications most commonly used to treat anxiety disorders,[96] are also the classes of medication that appear to be safest in pregnancy and the postpartum.[97,98] That said, there are a number of safety concerns related to their use in pregnant and breastfeeding women.[98–100] For instance, Furu and colleagues[101] found a 30% increase in the prevalence of cardiovascular defects after maternal exposure to paroxetine or fluoxetine. According to a recent systematic review, sertraline and paroxetine showed the best neonatal safety profile of all SSRIs/SNRIs examined during breastfeeding and are recommended as the first-line choice for antidepressants in nursing women,[102] whereas fluoxetine shows greater transfer into human milk.[103] Aside from the safety concerns, and the fact that some women may be unable or prefer not to take medications during pregnancy or breastfeeding (and hence require an alternative to pharmacotherapy), perinatal women have been found to largely prefer nonpharmacologic approaches to the treatment of AD.[104]

In a recent systematic review, cognitive-behavioral therapy (CBT) is recommended as a first-line treatment for pregnant and breastfeeding women with anxiety disorders,[94] with no known contraindications of CBT in pregnancy.[105,106] Outside of the perinatal period, CBT has also been shown to be the first-line psychological treatment for anxiety disorders.[107–109] Further, randomized controlled trials comparing pharmacologic and psychological interventions for ADs indicate that CBT is both safe and generally equal or superior to pharmacologic approaches.[105–109] Because CBT is time-consuming and expensive, it has not been broadly publicly funded. Yet, access to CBT is critical for pregnant and postpartum women due to the potential negative effects of AD medication on the developing fetus and nursing infant.[101,103] CBT is increasingly being offered in online settings and is therefore becoming more readily available to both remote and low-income populations. Self-administered, online CBT delivered with therapist support (as little as 15 minutes of therapist support a week) has been shown to be equally as effective as face-to-face treatment.[110] Now that impact can be maximized via these more accessible options, the value of providing effective and accurate perinatal AD screening dramatically increases.

Future Research

Future research should examine whether ADs are more common in pregnant and postpartum women compared to the general population. For instance, pregnant and postpartum women were found to be 1.5 to 2 times more likely to experience OCD compared to the general population,[111] suggesting that pregnancy and the postpartum period may

be an especially vulnerable period for the development of OCD. Intrusive thoughts surrounding accidental or intentional harm to the fetus or infant are common in the clinical presentation of perinatal OCD[92] but should be distinguished from postpartum psychosis. For instance, a case study[112] describes a woman who avoided bathing and being alone with her son due to obsessive thoughts and images of drowning him. In perinatal OCD, aggressive thoughts are ego-dystonic and are perceived as extremely distressing by the mother. Whereas women with OCD are not at increased risk of harming their infants, immediate intervention is critical for women with postpartum psychosis as judgment and reality testing are impaired.[113] In one sample of women with postpartum psychosis, 35% were admitted to hospital with safety concerns related to severe behavioral disturbance, acting on delusions, or incorrect handling of the infant.[114] Although postpartum psychosis is rare, women with a personal or family history of bipolar disorder are at increased risk as it often is conceptualized as an episode of bipolar disorder with psychotic features.[115]

Outside of the research on OCD, there is currently no other AD for which there is evidence of an increased risk of onset and/or exacerbation in the perinatal period. Large scale studies including both a sample of pregnant and/or postpartum women and a matched comparison group of women in the general population are severely lacking and would help to more fully determine whether the period surrounding childbirth is a risk factor for the development or exacerbation of ADs.

The majority of studies included in the current meta-analysis were classified as moderate quality. Several recommendations are shared in the hopes of encouraging higher quality studies with perinatal populations. For instance, research in this area would benefit from less reliance on convenience or consecutive sampling and greater use of random sampling. Confidence intervals or standard errors should be presented with anxiety prevalence estimates in order to measure precision of the estimate, as an imprecise point prevalence estimate is not a good representation of the true prevalence value. Researchers should also try to include information about participants who completed the study versus noncompleters and explore whether they differ in any meaningful way. Finally, with only half of the current studies reporting an adequate response rate (70% or higher), this should be a target for increasing study quality in perinatal samples. With these considerations in mind, future meta-analyses will be better poised to use a standardized quality rating system (eg, the Newcastle-Ottawa Scale),[116] which can be challenging without uniformity in research designs.

In conclusion, the current meta-analysis finds that ADs in pregnancy and the postpartum period are more prevalent than previously thought (1 in 5 women). There was substantial between-study heterogeneity suggesting that the "true" prevalence rate varies broadly across samples. Large-scale longitudinal studies are needed, including the following: multiple AD measurement, sufficient detail reported to recreate the data, and enough demographic and methodological information to readily access potential moderating variables. Further work is needed to determine which variables are contributing heterogeneity to the AD estimates. Given the personal and economic burden of both full and subthreshold ADs, as well as potential short and long-term consequences for child development, proper screening and treatment of antenatal and postnatal ADs is crucial. It is time that perinatal distress no longer be synonymous only with depression.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene P. Freeman, MD, at mfreeman@psychiatrist.com.

See supplementary material and full references for this article at PSYCHIATRIST.COM.

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Supplementary Material

Article Title: The Prevalence of Anxiety Disorders During Pregnancy and the Postpartum Period: A Multivariate Bayesian Meta-Analysis

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List of Supplementary Material for the article

1. Appendix 1 — Quality Ratings: Questions and Scoring Information
2. Table 1 — Estimated Probability (%) of Having 1+, 2+, etc, Anxiety Disorders and Corresponding Prediction Intervals

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Appendix 1

Quality Ratings- Questions and Scoring Information:

1. Was the setting of the study clearly described? (e.g., location and relevant dates or length of recruitment/data collection; both reported = 1, only 1 reported/not reported= 0)
2. Were the eligibility criteria clearly specified? (inclusion or exclusion criteria clearly specified = 1, neither specified = 0)
3. What was the sampling method used? (0 = convenience/consecutive/not reported, 1 = random)
4. Was the response rate adequate? (e.g., below 70%/not reported = 0, 70% or higher = 1)
5. Were demographic characteristics of the study population given? (e.g., age, ethnicity, education, marital status, employment, parity; not reported/only one of the above listed = 0, two or more of the above = 1)
6. Was information included about people who completed the study versus those who refused? (e.g., did they differ on any demographic variables? No/not reported = 0, yes =1)
7. Was the time frame of assessment reported or ascertainable? (e.g., past 2 weeks, past month; no = 0, yes = 1).
8. Who administered the diagnostic interview? (trained lay person/not reported = 0, trained clinician/researcher/mental health worker = 1)
9. Were confidence intervals or standard errors presented with the anxiety prevalence estimates? (not reported = 0, reported = 1)
10. Was there a discussion of limitations of the study/potential biases? (0 = no, 1 = yes)

Supplementary Table 1.

Estimated probability (%) of having 1+, 2+, etc. anxiety disorders and corresponding prediction intervals (in percentages); the probability of having 5+ diagnoses is negligible and therefore these estimates are excluded. Highest density intervals (HDI) are provided in brackets. The lower bound for some prediction intervals are equal to 0 due to rounding but this simply indicates that in some populations any given disorder could be quite rare (< 0.1%).

	Number of Diagnoses			
Disorder	*1+*	*2+*	*3+*	*4+*
Prevalence	20.7 [16.7 to 25.4]	5.5 [4.0 to 7.3]	1.6 [1.0 to 2.4]	0.5 [0.2 to 0.8]
Prediction Interval	[7.5 to 38.8]	[0.8 to 12.4]	[0.1 to 4.2]	[0.0 to 1.4]