Anxiety Disorders During Pregnancy: A Systematic Review

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ABSTRACT

Objective: To systematically evaluate the literature on anxiety disorders during pregnancy.

Data Sources: MEDLINE, PsycINFO, and CINAHL were searched through October 2013 for original research studies published in English using combinations of the terms *pregnancy, prenatal*, or *pregnancy outcomes; anxiety disorder;* and *generalized anxiety*. Reference lists of included studies were hand-searched and a PubMed search for in-process reports was conducted.

Study Selection: Relevant studies of anxiety disorders during pregnancy as determined by diagnostic interview were included if they reported on prevalence; course, onset, and/or risk factors; maternal, obstetric, or fetal/child outcomes; and/or treatment trial results.

Data Extraction: Two reviewers independently extracted relevant data and assessed methodological quality of each study.

Results: Fifty-seven reports were included. Reports provided information on panic disorder (25 reports), generalized anxiety disorder (17 reports), obsessive-compulsive disorder (OCD) (23 reports), agoraphobia (6 reports), specific phobia (10 reports), social phobia (14 reports), posttraumatic stress disorder (14 reports), and any anxiety disorder (18 reports). Twenty reports provided information on prevalence, 16 on course, 10 on risk factors, and 22 on outcomes. Only 1 treatment study was identified. High anxiety disorder prevalence in pregnancy was found; however, estimates vary considerably, and evidence is inconclusive as to whether prevalence among pregnant women differs from that of nonpregnant populations. Considerable variation in prenatal course of OCD and panic disorder was found. Substantial heterogeneity limits conclusions regarding risk factors or outcomes.

Conclusions: Additional research of higher methodological quality is required to more accurately determine prevalence, understand course, identify risk factors and outcomes, and determine effective treatments for anxiety disorders in pregnancy.

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Anxiety disorders are diagnosed nearly twice as often in women compared to men.[1–3] Approximately 30% of women will experience an anxiety disorder during their lifetime. Given their relatively early onset and often chronic course, anxiety disorders are experienced by many women during pregnancy.

High rates of anxiety symptoms have been reported among pregnant women.[4–7] Several studies suggest that the prevalence of anxiety symptoms may be higher during pregnancy than in the postpartum period[5–8] and may be more common during pregnancy than depression.[5] However, the prevalence of anxiety disorders during pregnancy remains unclear. In order to plan effective services, accurate prevalence estimates are needed. Furthermore, identifying women most at risk for anxiety disorders in pregnancy is important so targeted prevention and early intervention can be implemented. Although several meta-analyses[9–12] have summarized risk factors for postpartum depression and, more recently, a review[13a] of risk factors for depression in pregnancy appeared in the literature, there has been no systematic synthesis of the literature regarding risk factors for anxiety disorders during pregnancy. Understanding the pregnancy course of preexisting anxiety disorders also has implications for risk determination and management of anxiety disorders during pregnancy.

Research indicates a link between prenatal maternal stress and anxiety and adverse obstetric, fetal, and neonatal outcomes.[13b–19] Most of the research in this area has focused on anxiety symptoms—usually determined by self-report or rating scales—rather than on clinically diagnosed anxiety disorders. Anxiety meeting levels of clinical disorders is particularly relevant, representing the most severe, persistent anxiety, which would impact functioning and, potentially, pregnancy outcomes and fetal and child outcomes. Identification of negative consequences associated with prenatal anxiety disorders has important implications for pregnant women and those planning pregnancy with histories of anxiety disorders. Identification of safe and effective treatments for use during pregnancy is imperative to ameliorate adverse consequences for mother and child.

Ross and McLean[20] provided the first research review of perinatal anxiety disorders, covering the published literature up to early 2005, and concluded that there is a paucity of quality research evidence in this topic area. The purpose of the current review is to provide a comprehensive, systematic, and up-to-date evaluation of the literature on anxiety disorders during pregnancy.

OBJECTIVES

A systematic review of relevant published studies was conducted to answer the following questions:

1. How common are anxiety disorders during pregnancy?
2. Does pregnancy have an effect on the onset and course of anxiety disorders?
3. Are there known risk factors for anxiety disorders in pregnancy?

Clinical Points

- The prevalence of anxiety disorders is high among pregnant women.
- Identification and treatment of anxiety disorders in pregnancy are especially important because of the potential impact of untreated anxiety disorders during pregnancy on maternal, obstetric, and fetal/child outcomes.
- As recommended screening for perinatal depression becomes integrated into obstetric and other practice settings, screening for anxiety disorders should also be considered.

4. Are there known maternal, obstetrical, or child outcomes associated with anxiety disorders during pregnancy?
5. What are the evidence-based treatments for anxiety disorders during pregnancy?

DATA SOURCES

This study was conducted by using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist.[21] Anxiety disorders considered in the review included generalized anxiety disorder (GAD), panic disorder, obsessive-compulsive disorder (OCD), phobias, and posttraumatic stress disorder (PTSD).

In consultation with an experienced research librarian, relevant published research articles were identified by a systematic search of the following databases from their inception through October 2013: MEDLINE, PsycINFO, and CINAHL. The search strategy involved exploding the subject heading *anxiety disorders*, so that the search also included narrower subject headings, such as "stress disorders, post-traumatic," "panic disorder," "phobic disorders," and "obsessive- compulsive disorder." The results were then combined by using "OR" with a keyword search for "generalized anxiety disorder." In a separate search, the authors used the keywords *prenatal, antenatal, pregnancy outcomes,* OR the exploded subject heading "pregnancy." The authors then used the AND operator to combine the 2 searches and find the overlap of articles. Search limits were English language and human. Reference lists of included studies and review articles obtained through the electronic search were hand-searched. A search of PubMed was also conducted using the terms *pregnancy* and *anxiety disorder* to search for any in-process reports relevant to the review.

STUDY SELECTION

Studies were considered for inclusion if they met the following predefined criteria: a primary research study that (1) aimed to examine 1 or more anxiety disorders during pregnancy in women aged 17 years or older; (2) used diagnostic interviews to determine specific anxiety disorder diagnoses according to standard diagnostic criteria from a version of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*)[22] or the *International Statistical Classification of Diseases and Related Health Problems* (*ICD*)[23] or Research Diagnostic Criteria[24]; and (3) met 1 or more of the following criteria—the study estimated the prevalence of prenatal anxiety disorder(s); described the course, onset, and/or risk factors for anxiety disorders during pregnancy; examined specific maternal, obstetric, or fetal/child outcomes associated with anxiety disorders during pregnancy; and/or provided results of a treatment trial targeting prenatal anxiety disorders. To answer the question "Does pregnancy have an effect on the onset and course of anxiety disorders?" we also included studies in which a clinical diagnosis of an anxiety disorder was made at a psychiatric clinic using diagnostic criteria. This allowed inclusion of studies in which course of illness in women previously diagnosed with an anxiety disorder was examined.

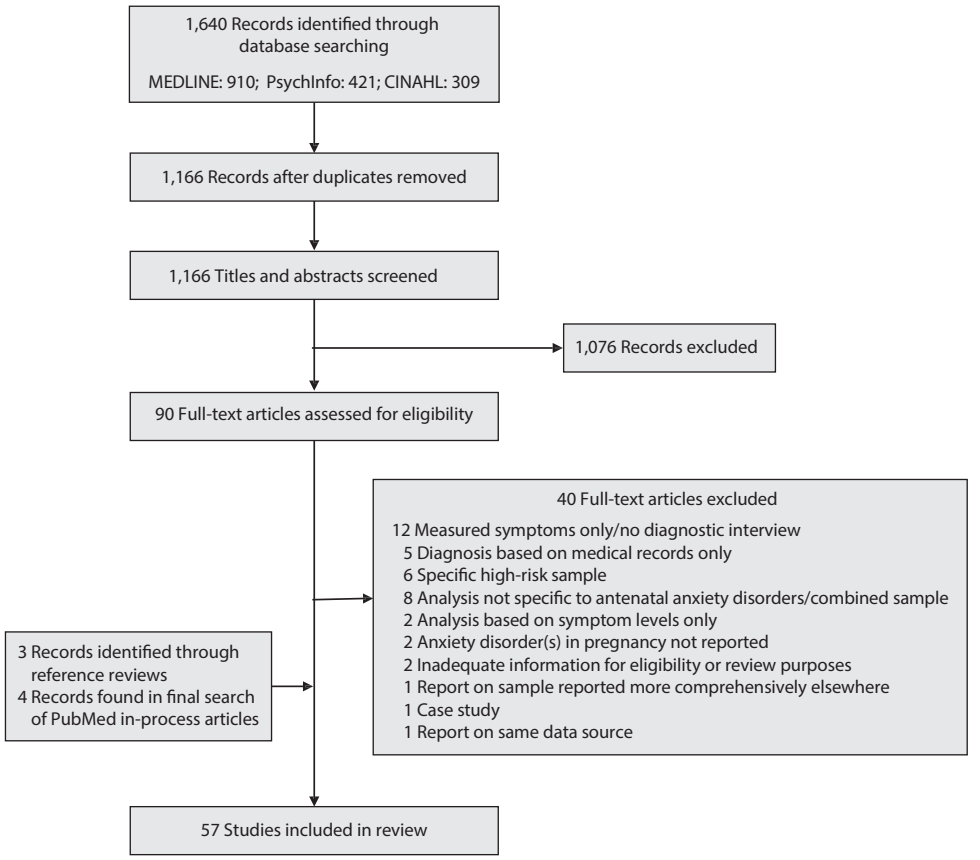
Studies were excluded that (1) measured anxiety symptom level using screening scales or self-report only; (2) were single case reports or small case series ($N < 5$) (larger case series were included); (3) were composed of a sample of a specific subpopulation of pregnant women (eg, adolescents only, disaster survivors, women with abuse histories, patients with substance abuse problems, and women with specific medical or gestational problems such as hyperemesis and previous still birth); (4) considered anxiety disorders only in conjunction with other psychiatric disorders (eg, depression), which prevents the possibility to differentiate effects or outcomes of anxiety disorders specifically; and (5) provided insufficient information to answer review questions.

We imported all articles identified by the searches into a database. After removing duplicates, 2 researchers (J.H.G. and K.L.C.) independently screened titles and abstracts to identify those meeting inclusion criteria. Articles likely to contain data on anxiety disorders in pregnancy were then retrieved and examined in full text to determine their eligibility for inclusion. Results were compared and any disagreements resolved by consensus.

DATA EXTRACTION, QUALITY ASSESSMENT, AND ANALYSIS

Two reviewers (J.H.G. and K.L.C.) independently extracted critical data using a data extraction form developed specifically for this review, which included the following for each study: study aim, setting, design, inclusion/exclusion criteria, number and characteristics of participants included, methods, process by which anxiety disorder was diagnosed (including diagnostic criteria used and interviewer expertise), anxiety and other measures used, information regarding any treatment received (medication or therapy), and details on the outcomes of interest. We assessed the methodological quality and bias risks of each study at the same time as data extraction by collecting and considering the following data regarding predefined criteria derived from the literature[25–27]: specification of the target population, sampling method, sample size, response rate, case definition, validity of measurement instruments, reporting of confidence intervals or standard errors, study limitations, and bias risks. For treatment studies, we also extracted information regarding treatment description, if and what control groups were used, and outcomes reported.

Figure 1. Flowchart of Primary Study Selection



Data from individual studies were organized according to research question(s) addressed (eg, prevalence, course, onset, risk factors, outcomes, and treatments) and by specific anxiety disorders or any anxiety disorder. Because of the heterogeneity of populations, methodologies, measures used, and specific outcomes in the various studies included in the review, it was not possible to pool data for meta-analytic analysis regarding any of the review questions. A descriptive and narrative approach was used to summarize the key findings.

RESULTS

Study Selection

Database searches yielded 1,640 citations. Initial screening of titles and abstracts yielded 90 potentially eligible studies for review. Full text review of these 90 articles identified 52 that met study eligibility criteria. Three additional studies were identified through hand searches of references of included studies and 4 through a final search of PubMed for in-process articles. Two studies[28,29] analyzed data derived from the same US 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions sample, using only slightly different inclusion criteria for age. Only the study with the more inclusive age range for eligibilty[29] was included in this review. A total of 57 studies were included in the review. A flowchart of study selection is shown in Figure 1.

Table 1 presents characteristics of included studies. The 57 included reports comprised 45 separate samples. Seven studies resulted in more than 1 article published, each addressing different research questions and using a subsample of the original primary study. A diversity of populations was represented with studies that were carried out in 16 different countries and included participants ranging in socioeconomic status (SES), educational levels, and cultural backgrounds. Samples were recruited from prenatal care settings and psychiatric clinic settings. Study designs varied and included predominantly cross-sectional, retrospective, prospective, and a few longitudinal studies. Thirty-seven studies focused on a single anxiety disorder, and the remaining examined 2 or more disorders. Sample sizes ranged from 10 to 14,549.

Most studies used diagnostic criteria from the *DSM*, 1 used *ICD-10* criteria,[35] and 1 used Research Diagnostic Criteria.[67] Only 1 study[49] specified any modifications for anxiety disorder diagnostic criteria in pregnancy. The most commonly used diagnostic interview was a version of the Structured Clinical Interview for *DSM*,[86] which was used in 22 studies, followed by the MINI-International Neuropsychiatric Interview,[87] which was used in 13 studies. Seventeen reports provided no information on the professions or qualifications of the interviewers determining diagnoses. In 24 studies, a psychiatrist, psychologist, or other mental health clinician

Table 1. Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Prevalence studies					
Adewuya et al, 2006[30] (Nigeria)	MINI for *DSM-IV* (psychiatrists)	Third trimester	Pregnant women in late pregnancy recruited from prenatal clinics in a semi-urban town in Nigeria. Comparison group of nonpregnant women matched for age, marital status, parity, and social class from general practice clinics. Excluded women who were receiving any mental health treatment. Pregnant women: age, 26.86 ± 6.76 y; 12.2% unmarried; 41.3% low SES; 10% with present medical condition.	344 Total 172 Pregnant women 172 Comparison group women	344/361 Eligible women (95%) participated. Women who refused did not differ from participants on age or marital status. Excluded women who were receiving any mental health treatment.
Andersson et al, 2003[31] (Sweden)	Screened with PRIME-MD Patient Questionnaire, then screen-positive women administered the PRIME-MD Clinician Evaluation Guide for *DSM-IV* by phone (1 research nurse, 4 obstetricians)	Second trimester (16–17 wk)	Consecutive pregnant women attending routine ultrasound screening at 2 obstetric clinics in Northern Sweden. Excluded women with fetal malformation or missed abortion by ultrasound. Age, 29.4 ± 4.6 y.	1,556	Large, population-based sample. 1,734/1,795 eligible women (96.6%) screened. 766/815 screen-positive women (94%) completed interview. Women who refused interview had higher prevalence of positive screens and were significantly older. Information regarding psychotropic or other treatment during pregnancy not reported.
Borri et al, 2008[32] (Italy)	SCID-I for *DSM-IV* (clinicians trained and certified)	12–15 wk	Recruited all pregnant women 12–15 weeks' gestation presenting for first ultrasound at clinic in Italy. Exclusions: age < 18 y, no fixed residence. Age, 32.3 ± 3.9 y; 90% with at least 13 years of education; 92% married or cohabiting; 83% employed; 91% medium SES; 33% with 1 or more children.	1,066	1,066/2,598 Eligible women (49.9%) participated. Sociodemographic information on women who declined participation not available. Information regarding psychotropic or other treatment during pregnancy not reported.
Fadzil et al, 2013[33] (Malaysia)	MINI for *DSM-IV* (interviewer not reported)	Any point during pregnancy	Pregnant women > 18 y attending prenatal clinic at tertiary hospital in Malaysia. Excluded women considering termination of pregnancy. Age, 31.02 ± 4.91 y (range, 19–46); gestational age, 26.82 ± 6.94 wk. Majority were Malays, were married, and had completed secondary education. 74% multiparas.	175	175/180 (97.2%) Participation rate. Information regarding psychotropic or other treatment during pregnancy not reported.
Farias et al, 2013[34] (Brazil)	MINI for *DSM-IV* (trained medical doctors and medical graduate students)	First trimester	Pregnant women ages 20 through 40 years, less than 13 weeks' gestation, and without any chronic disease (except obesity), recruited from prenatal clinics of public health center in Rio de Janeiro, Brazil. Exclusions: any infectious or chronic disease (except obesity), twin pregnancy, taking antidepressant medication. Age, 26.7 ± 5.4 y; education, 8.8 ± 2.9 y; 79% in stable relationship; parity, 1.0 ± 1.1; 7.1% current smoking; 19.7% current alcohol consumption. Mainly low-income sample	239	299/322 (93%) Initial participation rate; 60 additional excluded due to exclusion criteria assessed at baseline. Excluded women with antidepressant use in pregnancy.
Felice et al, 2007[35] (Malta)	Clinical Interview Schedule Revised (CIS-R) for *ICD-10* anxiety disorders (interviewer not reported)	CIS-R at first prenatal visit and at 36 weeks' gestation	Random sample of pregnant women in prenatal clinics in Malta. No exclusions. Age, 27.1 ± 5.6 y; 93% married or cohabiting; average gestation at first assessment was 18.6 wk; 47.7% primiparas.	229	229/239 (95.4%) Participation rate. Information regarding psychotropic or other treatment during pregnancy not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Giardinelli et al, 2012[36] (Italy)	SCID-I for *DSM-IV* (psychiatrists and psychologists)	Third trimester (between 28 and 32 gestational wk—7 mo)	Pregnant women aged 18 y and older between 28–32 weeks' gestation consecutively recruited from childbirth preparation course in Italy. Age, 34.0 ± 4.2 y; 85.5% primiparas; 99.5% married or cohabiting; most employed; 46% college or higher.	590	590/760 Eligible women (77.6%) participated. Did not report differences between participants and women who declined participation. Sample consisted of mostly first-time mothers, which may increase anxiety in pregnancy. Information regarding psychotropic or other treatment during pregnancy not reported.
Guler et al, 2008[37] (Turkey)	SCID-I for *DSM-IV* (psychiatrists)	Third trimester (35.30 ± 3.69 wk)	Pregnant women in third trimester consecutively recruited from 2 university-affiliated prenatal clinics in Turkey. Excluded women with medical issues. Pregnant subjects: Age, 27.41 + 5.69 y (range, 17–44); all married, 87% nonemployed housewives, 8 illiterate, 70% with primary school as highest educational level. 36% Primiparas; no. of pregnancies, 2.27 ± 1.33	512	512/663 Eligible women (77.2%) participated. Did not report differences between participants and women who declined participation. None of participants with panic disorder received medication or psychotherapy during pregnancy.
Lilliecreutz and Josefsson, 2008[38] (Sweden)	Women screened positive for blood/injection phobia were administered diagnostic interview to determine if they met *DSM-IV* criteria for blood/injection phobia (experienced psychotherapist administered by phone)	12–16 Weeks' gestation	Pregnant women consecutively recruited from women attending first visit at prenatal care clinics in Sweden. No exclusions. Age, median ± SD = 29 ± 4.91 y (range, 17–45); equal number of primiparas and multiparas.	1,529	1,529/1,606 (95.2%) Participation rate. Information regarding psychotropic or other treatment during pregnancy not reported.
Rogal et al, 2007[39] (United States)	MINI for *DSM-IV* (trained bachelor's- or master's-level research staff)	Any point during pregnancy	Pregnant women (English- or Spanish-speaking) recruited by convenience sampling from prenatal clinics. No exclusions specified. Age, 24.5 + 5.8 y (non–PTSD women), 24.3 + 5.6 y (PTSD women); 87% nonwhite.	1,110	1,339/1,511 Eligible women (88.6%) participated. Of these, only the 1,100 for which medical records were available (82% of those in original sample of 1,339) were included in study. Women who lacked birth outcome data (not included in analysis) had higher rates of PTSD and substance abuse than those with birth outcome data that may have led to a biased sample. Information regarding psychotropic or other treatment during pregnancy not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Seng et al, 2009[40] (United States)	National Women's Study (NWS) PTSD Module, Life Stressor Checklist (lifetime history of trauma exposure) (interviews conducted via phone by survey research organization by diverse women experienced in mental diagnostic phone interviews. 10% of interviews monitored for quality and accuracy)	Before 28 wk	Pregnant English-speaking women aged 18 y and older expecting their first infant consecutively recruited at first prenatal care visit at Medicaid (predominantly) and privately insured prenatal clinics in midwestern United States. Sociodemographically and racially mixed sample of women expecting their first infant. Oversampled for African American women (45%).	1,581	1,581/1, 653 Eligible women (95.6%) who were able to be contacted completed interview and were available for analysis. Not able to compare sample with those who were eligible but were missed in recruitment, those who were not reached after expressing interest, or who declined. Large, racially, economically, and geographically diverse sample. Information regarding psychotropic or other treatment during pregnancy not reported. Only women expecting first child included and therefore only focused on prepregnancy trauma exposures and may not generalize to multigravid pregnant women.
Seng et al, 2010[41] (United States)	NWS PTSD Module, Life Stressor Checklist (lifetime history of trauma exposure) (interviews conducted via phone by survey research organization by diverse women experienced in mental diagnostic phone interviews. 10% of interviews monitored for quality and accuracy)	Before 28 wk	Pregnant clinic sample (same as Seng et al[40]). Pregnant English-speaking women aged 18 y and older expecting their first infant consecutively recruited at first prenatal care visit at Medicaid (predominantly) and privately insured prenatal clinics in midwestern United States. Comparison group: subsample of women in a similar age range from the US NWS (n = 2,000).	3,148 Total 1,581 Pregnant clinic sample 2,000 Comparison sample	Compared sample from Seng et al[40] with sample of women in a similar age range from the US NWS. All women in pregnant clinic sample completed the NWS PTSD module, whether or not they disclosed a trauma exposure, whereas the NWS only assessed PTSD among trauma-exposed women. Pregnancy status in the NWS sample was not queried, nor were pregnant women excluded. Authors estimated that approximately 5% of that sample may have been pregnant. 15 Years separate diagnostic interviews for the 2 data sets. Awareness of PTSD most likely has increased, and increased reporting might follow increased awareness.
Seng et al, 2011[42] (United States)	NWS PTSD Module, Life Stressor Checklist (lifetime history of trauma exposure) (interviews conducted via phone by survey research organization by diverse women experienced in mental diagnostic phone interviews. 10% of interviews monitored for quality and accuracy)	Before 28 wk	Same sample as Seng et al,[40] minus 4 women who declined to answer racial identity items. 709 Women (45%) self-identified as African American; 868 women did not.	1,577	Subsample of Seng et al.[40]

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Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Smith et al, 2004[43] (United States)	PTSD module from the MINI for *DSM-IV* A time frame of 1 mo was used for PTSD diagnoses (bachelor's- or master's-level social workers)	Any time point in pregnancy	Consecutively recruited English- or Spanish-speaking pregnant women receiving prenatal care from either of 2 federally funded hospital-based obstetric clinics or 2 affiliated community health center obstetric programs in New Haven, Connecticut area. Average of 23.8 + 11.2 weeks' pregnant (range, 6.7–41.1). Majority African American or Hispanic and insured through Medicaid.	387	377/385 (98%) Participation rate. Information regarding psychotropic or other treatment during pregnancy not reported
Smith et al, 2006[44] (United States)	PTSD module from the MINI for *DSM-IV* supplemented by an 11-question event list from the CIDI (bachelor's- or master's-level social workers)	Any time point in pregnancy	Pregnant women consecutively recruited from 3 federally funded obstetric clinics. Duration of pregnancy, mean = 25.8 wk (SD = 9.9; range, 4–41.7); 52.7% Hispanic, 32% non-Hispanic black, and 12.9% non-Hispanic white. Comparison group: 584 nonpregnant traumatized women from the National Comorbidity Survey.	948 Pregnant women 584 Comparison women	948/1,037 (91.4%) Recruitment rate. Concern for bias due to possible case misidentification. Information regarding psychotropic or other treatment during pregnancy not reported.
Sutter-Dallay et al, 2004[45] (France)	MINI for *DSM-IV* (research psychologists)	Third trimester	Consecutively recruited at university-affiliated prenatal clinics in France. Exclusions: personal history of psychotic illness, multiple pregnancy, in vitro fertilization for current pregnancy, > 1 week of hospitalization due to pregnancy complications, planned cesarean section delivery. Women later excluded if premature birth or unplanned cesarean section. Age, mean = 29.6 y (SD = 4.2); 64% primiparas; 73% ≥ 12 y education; 96% married.	497	497/945 Eligible women (53%) participated. Anxiety disorders were considered as a single diagnostic category because of the relatively low prevalence of each specific anxiety disorder. Information regarding psychotropic or other treatment during pregnancy not reported.
Uguz et al, 2007[46] (Turkey)	SCID-I for *DSM-IV* (interviewers not specified)	Third trimester (35.08 ± 3.77 wk)	Pregnant women in third trimester consecutively recruited from university-affiliated obstetric clinics in Turkey. Age, 27.23 ± 5.55, y; all married; 71% with primary school as highest education level; 86.2% unemployed housewives; 57.4% had at least 1 live birth. Comparison group: consecutively recruited nonpregnant women with diagnosed OCD who presented to psychiatric outpatient clinics of the same centers. All married and matched with pregnant women for age and educational level, and had not received psychotropic drugs in past 4 wk.	434 Pregnant women 58 Nonpregnant comparison women with OCD	434/566 Eligible women (76.7%) participated. No participants received pharmacotherapy during pregnancy.
Uguz et al, 2010[47] (Turkey)	SCID-I for *DSM-IV* (psychiatrists)	Any point in pregnancy	Pregnant women systematically recruited from obstetric clinic in Turkey. Exclusions: severe medical problems, fetal malformation, uncontrolled pregnancy complications. Comparison group of nonpregnant premenopausal women recruited from hospital personnel and relatives without gynecologic or other medical illnesses. 99.3% Married; 74.8% primary school education; duration of pregnancy for pregnant group, 23.26 ± 9.56 wk. No significant difference for age, education, marital status, and number of children between pregnant and control groups.	309 Pregnant 107 Comparison subjects	309/364 Eligible women (85%) participated. Information regarding psychotropic or other treatment during pregnancy not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Vesga-López et al, 2008[29] (United States)	Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV* version (lay interviewers)	Any point during pregnancy (for currently pregnant women)	Women aged 18–50 y from the National Epidemiologic Survey on Alcohol and Related Conditions (2001–2002). Past year pregnant women: 59.4% white, 14.3% black, 7.7% Asian, 15.7% Hispanic; 81.2% married or cohabiting; 55.5% college or higher; 67.1% less than $20,000.	14,549 Total 1,524 Pregnant in past year (of which 453 were currently pregnant, 994 postpartum, 77 unknown status or no live children) Comparison group of 13,025 nonpregnant women	Largest nationally representative survey to date to include information on psychiatric disorders in pregnant women. Information regarding psychotropic or other treatment during pregnancy not reported. Did not collect data on month of pregnancy at assessment.
Zar et al, 2002[48] (Sweden)	Prescreened for anxiety disorders, then Anxiety Disorder Interview Schedule-Revised for *DSM-IV* (interviewers not specified)	32 Weeks' gestation	Pregnant women (in gestational week 28) recruited from county hospital obstetric clinic in Sweden. No exclusions. Age, mean = 27 y (range, 17–40) in nulliparous group and mean = 30 y (range, 20–42) in parous group.	506	506/613 Eligible women (83%) screened; 386 interviewed. 67 Screen-negative women who were not interviewed were determined as comparable to the 67 screen-negative women who were interviewed. Information regarding psychotropic or other treatment during pregnancy not reported.
Risk factor studies					
Adewuya et al, 2006[30] (Nigeria)	(see in prevalence studies)				
Borri et al, 2008[32] (Italy)	(see in prevalence studies)				
Buist et al, 2011[49] (United States)	CIDI for *DSM-IV* (GAD criteria adjusted to require only 1 mo of symptoms during pregnancy to meet diagnostic threshold rather than 6 mo as required in the *DSM*) (interviewers not specified)	2 Time points: at < 17 weeks' gestation and again at 28–32 weeks' gestation	Sample of English- or Spanish-speaking pregnant women (< 17 wk of singleton pregnancy) with history of MDD or PTSD in last 5 y, or antidepressant use in last year recruited from obstetric services in United States. Exclusions: insulin-dependent diabetes, plans to move or terminate the pregnancy. Randomly selected 1 of 3 women who do not have these characteristics to serve as controls. 74% White, 14% Hispanic, 8% black; 87% married or cohabiting; 56% ≥ 16 y education; 43% nulliparous.	2,793	Attrition rates of 15% and 16% for overall sample at times 1 and 2, respectively. Higher attrition among women with GAD both before and during pregnancy (25% and 28% for 2 time points, respectively). Sample selected for MDD, PTSD, and antidepressant use bias. Antidepressant use in pregnancy was 12%. Potential confounding effect of medication use on GAD.
Fadzil et al, 2013[33] (Malaysia)	(see in prevalence studies)				
Felice et al, 2007[35] (Malta)	(see in prevalence studies)				
Labad et al, 2005[50] (Spain)	SCID for *DSM-IV* (psychiatrists)	Prior OCD diagnosis made at anxiety disorder clinic	Women with OCD diagnosis consecutively recruited from OCD outpatient clinic in Spain. Exclusions: psychotic disorder, cognitive deficit. Age, 35.3 ± 13.2 y.	46 (17 with prior pregnancies; 12 with pregravid OCD)	46/47 (98%) Participation rate. No antiobsessive treatment among participants during pregnancy. Demographic characteristics other than age not reported.
Seng et al, 2009[40] (United States)	(see in prevalence studies)				

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Seng et al, 2011[42] (United States)	(see in prevalence studies)				
Smith et al, 2006[44] (United States)	(see in prevalence studies)				
Uguz et al, 2007[46] (Turkey)	(see in prevalence studies)				
Onset and/or course studies					
Bandelow et al, 2006[51] (Germany)	Prior diagnosis of panic disorder confirmed by SCID for *DSM-IV* (interviewer not specified)	Prior panic disorder diagnosis	Clinical sample of women with preexisting panic disorder with or without agoraphobia consecutively selected and recruited from clinic admission lists at anxiety disorder clinic in Germany. Excluded women with history of other psychiatric disorders, including anxiety disorders other than panic disorder and MDD (unless secondary to panic disorder). Age, 43.4 ± 12.5 y; all Caucasian.	128 Women (93 with at least 1 pregnancy)/195 pregnancies Comparison group: 35 never pregnant women with preexisting panic disorder	128/204 Eligible women (62.7%) participated. Small number of women (≤7 [exact number not reported for pregnancy]) received antipanic medications during pregnancy, and 7 women received psychotherapy treatment.
Buist et al, 2011[49] (United States)	(see in risk factors studies)				
Cohen et al, 1994[52] (United States)	Prior diagnosis of pregravid panic disorder per *DSM-III-R* criteria made by clinical interview at anxiety disorder clinic (clinician at anxiety disorders clinic)	Panic disorder diagnosis made prior to pregnancy	Women with pregravid panic disorder recruited from outpatient perinatal psychiatry clinics. Age, mean = 31.9 y (range, 24–40). Duration of illness,7.8 ± 4.5 y.	49	Sample biased toward having more severe pregravid symptoms because of clinical setting. Participants tended to have previous failed attempts to discontinue medications. Discontinuation attempts neither controlled nor systematic. 24 Women (50%) conceived on antipanic medication; 32 (65%) took antipanic medication at some point in pregnancy; 15 (31%) for entire pregnancy.
Cohen et al, 1996[53] (United States)	SCID for *DSM-III-R* (trained psychiatrist)	Prospectively assessed at 11, 23, and 37 weeks' gestation for current panic disorder diagnosis according to SCID	Pregnant women with pregravid panic disorder consecutively recruited from outpatient perinatal psychiatry clinic. All married; mean age of 34 y (range, 30–40); 4 nulliparous and 6 multiparous. 8/10 Women met panic disorder criteria at baseline; 1 met criteria for MDD; 8 had history of comorbid panic disorder and MDD.	10	7/10 Women (70%) conceived on antipanic medication. Sample may have been biased toward more symptomatic women. Multiparity/primiparity not controlled for. Comorbidities present. Varying levels of pharmacologic treatment.
Dannon et al, 2006[54] (Israel)	Semistructured diagnostic interview for *DSM-IV* (psychiatrist)	Prior panic disorder diagnosis at psychiatric clinic	Women between the ages of 20 and 35 y with history of panic disorder referred to tertiary referral center and treated to remission with paroxetine 6 y earlier in initial study. Exclusions (at enrollment in original study): aged < 18 y; comorbid Axis I diagnosis, including schizophrenia, bipolar disorder, or substance abuse; unstable medical disease; prior treatment with paroxetine. Women with comorbid MDD were included if depression began after onset of panic symptoms.	68	*Relapse* defined as occurrence of a panic attack in any phase of study. No mention of any assessment of nonmedication treatment at any phase of study.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Forray et al, 2010[55] (United States)	SCID for *DSM-IV* (interviewer not reported)	Prior OCD diagnosis at entry to anxiety disorder clinic	Female anxiety disorder clinic patients between 18 and 69 y with OCD diagnosis recruited from clinic database. Exclusions: lifetime history of psychotic disorder, or substance dependence disorder in past year. For the ever pregnant group: age, 40.8 ± 10.8 y; 92% white; 79% married; 40.8% high school or less education.	126 Total 78 Women had at least 1 pregnancy (ever pregnant), and 48 women were never pregnant	Information regarding psychotropic or other treatment during pregnancy not reported.
Guler et al, 2008[56] (Turkey)	SCID-I for *DSM-IV* (psychiatrists)	Third trimester (31.50 ± 6.51 wk)	Subsample of women from Guler et al.[37] Pregnant women in third trimester consecutively recruited from 2 university-affiliated prenatal clinics in Turkey. Women with panic disorder diagnosis at initial assessment were recruited. Exclusions: comorbid psychiatric illness, current mental health treatment, suicide risk. All married, 92% unemployed housewives; 77% primary school as highest level of education; gestational age at diagnosis of panic disorder, mean = 31.54 wk (SD = 6.51).	13 (7 with pregravid history of panic attack and 6 with no pregravid history of panic attacks—panic disorder began during week 6 to 28 of gestation)	No participants received pharmacotherapy or psychotherapy during pregnancy.
Klein et al, 1994[57] (United States)	SADS-LA for *DSM-III-R* (interviewer not specified)	Prior panic disorder diagnosis made at anxiety disorder clinic	Women of childbearing age with diagnosed panic disorder and who had at least 1 full-term pregnancy with panic disorder predating a pregnancy recruited from an anxiety disorder clinic's record of women. Demographic data not reported.	20 Women (results analyzed for 33 full-term pregnancies)	20/28 Eligible women (71.4%) participated. 8 Pregnancies (24%) involved antipanic medications in first trimester but not in second and third trimesters The pregnancies occurred from 2 mo to 23 y before the interview. Time differential may have affected recall. 3/20 Women diagnosed without SADS-LA. Lack of systematic interrater reliability for interviews.
Labad et al, 2005[50] (Spain)	(see in risk factors studies)				
Labad et al, 2010[58] (Spain)	SCID for *DSM-IV* (psychiatrists)	Prior OCD diagnosis made at anxiety disorder clinic	Consecutively recruited female patients at OCD clinic meeting *DSM-IV* criteria for OCD. Exclusions: schizophrenia, history of psychoactive substance abuse. Age, mean = 36 y (range, 18–74).	90 (35 with children)	90/92 (98%) Participation rate. Most were taking psychotropic drugs for OCD. Demographic characteristics other than age not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Maina et al, 1999[59] (Italy)	SCID for *DSM-III-R* (interviewer not specified)	OCD diagnosis within 2 y prior to study enrollment and diagnosis confirmed at enrollment	Male and female patients with a principal diagnosis of OCD together with a YBOCS rating > 16 and who had their onset of OCD within the past 2 y were consecutively recruited from university-affiliated outpatient psychiatric clinic in Italy. Exclusion: concurrent major depression, schizophrenia, organic brain syndrome, and neurologic disease. Age of females, 28.9 ± 8.7 y; education, 10.3 ± 3.4 y; 57.6% married; 33.3% single. Comparison/control: in addition, a random sample of subjects selected from general practitioner rolls and matched with the patients for age, sex, marital status, SES, and years of education (and with no history of psychiatric illness as assessed by SCID) were also enrolled as control group (mixed male and female groups).	68 Total (33 women, 16 of whom had children)	68/71 Eligible patients (95.8%) enrolled in study. Information regarding psychotropic or other treatment during pregnancy not reported.
Neziroglu et al,[60] 1992 (United States)	Clinical interview for *DSM-III-R* (psychiatrist or psychologist, then diagnosis confirmed by second psychiatrist or psychologist)	Prior OCD diagnosis made at anxiety disorder clinic	Female anxiety disorder clinic patients with prior OCD diagnosis. Of women with children: age, mean = 41 y (range, 20–78).	106 Total (59 had at least 1 child, 42 childless, 5 childless: 4 with abortions and 1 miscarriage)	Limited demographic information reported. Information regarding psychotropic or other treatment during pregnancy not reported.
Northcott and Stein,[61] 1994 (Canada)	Clinical interview for *DSM-III-R* (psychiatrist or psychologist)	Prior panic disorder diagnosis made at anxiety disorder clinic	Women who developed panic disorder before, during, or between pregnancies recruited from anxiety disorder clinic patient database. No exclusions specified. Age, 40 ± 8 y (range, 22–59).	97	97/138 (70%) Return rate on mailed questionnaires. Information regarding psychotropic or other treatment during pregnancy not reported.
Uguz et al, 2007[46] (Turkey)	(see in prevalence studies)				
Rambelli et al, 2010[80] (Italy)	SCID for *DSM-IV* (psychiatrist or psychologist with long-standing SCID experience)	12–15 wk	Subsample from Borri et al.[32] Composed of pregnant women presenting for first ultrasound at clinic in Italy and who completed through the 6-mo postpartum assessment. Exclusions: no fixed residence. Age, 32.7 ± 3.74 y; 92% married or cohabiting; 85% employed; 46.5% high school; 45.4% college or higher; 92.7% middle SES; 67.7% first pregnancy.	600 (24 with current panic disorder at 12 to 15 weeks' pregnancy)	1,066/2,598 Eligible women (49.9% participation rate) participated at baseline. Lack of data on nonparticipants. 466/1,066 (43.7%) Women dropped out by 6-mo postpartum follow-up. Completers were slightly older and more educated. Information regarding psychotropic or other treatment during pregnancy not reported.
Uguz et al, 2011[62] (Turkey)	SCID for *DSM-IV* (interviewer not specified)	Any time in pregnancy	Women attending 2 outpatient clinics in Turkey for routine prenatal care were screened for OCD. The first consecutive 52 patients who met the criteria for OCD and who reported onset prior to current pregnancy were included in the study. Exclusions: schizophrenia or related disorder, gestational complications, history of neurologic disease, concomitant severe medical illness. Age, 27.1 ± 5.3 y; all married; 81% primary school as highest educational level; 92% unemployed housewives; 19.2% primigravidas. Duration of pregnancy, 29.5 + 8.2 wk.	52	All eligible women participated. Information regarding psychotropic or other treatment during pregnancy not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
van Veen et al,[63] 2009 (Netherlands)	MINI for *DSM-IV* (interviewer not specified)	Prior diagnosis	Female patients with social phobia who had previously participated in research projects were recruited from 2 university medical centers in Netherlands. Excluded women with an endocrine disorder of any kind. Age, 42 ± 11.7 y, 75% employed; 76% medium or high level of education; 86% had received treatment for social phobia during lifetime, 45% in current treatment.	64 Total (41 with prior pregnancy)	64/140 (46%) Response rate to survey. Subanalyses were carried out with very small sample sizes. Information regarding psychotropic or other treatment during pregnancy not reported.
Villeponteaux et al, 1992[64] (United States)	Prior panic disorder diagnosis per *DSM-III-R* made at anxiety disorder clinic (interviewer not specified)	Prior panic disorder diagnosis	Women who had experienced pregnancy after the onset of panic disorder were recruited by mail from anxiety disorder clinic patient database. Excluded women who took psychotropic medication during pregnancy. Demographic data not reported.	22 Women (44 pregnancies)	57/108 Delivered questionnaires (53% response rate) returned. 22 Returned questionnaires provided relevant data and were included in study. Excluded women taking medication and thus may have excluded more severely ill patients.
Vulink et al, 2006[65] (The Netherlands)	Prior OCD diagnosis by MINI for *DSM-IV* (psychiatrist)	Prior OCD diagnosis	Recruited from database of female anxiety disorder clinic outpatients with primary diagnosis of OCD. Age, 37.1 ± 10.6 y.	101 Total (52 had ever been pregnant)	101/350 Questionnaires (29%) returned and completed. Some participants took psychotropic medications during pregnancy, but number not specified. 3 Participants discontinued SSRIs during pregnancy.
Williams and Koran, 1997[66] (United States)	Prior diagnosis by clinical interview at anxiety disorder clinic per *DSM-III-R* criteria (psychiatric resident, then reviewed by psychiatrist)	Prior OCD diagnosis	Female anxiety disorder clinic outpatients with OCD identified by chart review and invited to participate. Exclusions: no chart diagnosis of schizophrenia, schizoaffective disorder, mental retardation, or organic brain syndrome. Age, 44.9 ± 10.8 y (prior pregnancy group), 35.9 ± 9.8 y (no prior pregnancy group); mostly white.	57 Total (38 with prior pregnancy and 19 without prior pregnancy)	57/72 (79%) Participation rate. Non-use of psychotropic medication inferred but not confirmed in all cases.
Wisner et al, 1996[67] (United States)	Prior panic disorder diagnosis made at psychiatric clinic, then SADS used to assess current psychiatric diagnoses per Research Diagnostic Criteria SADS-L used to investigate lifetime episodes at 5-y follow-up (interviewers not specified)	Prior panic disorder diagnosis	Women with panic disorder who were pregnant or had children under age 3 y were identified through medical records and selected if panic disorder predated 1 or more pregnancies or was a first lifetime episode associated with a pregnancy. Age, 34 ± 4.8 y; 86% white, 73% married; 3 had minimal medication exposure.	22 Women (45 pregnancies)	3 Women with minimal medication exposure during pregnancy.
Outcome studies					
Andersson et al, 2004[68] (Sweden)	Screened with PRIME-MD Patient Questionnaire, then screen-positive women administered the PRIME-MD Clinician Evaluation Guide for *DSM-IV* by phone (1 research nurse, 4 obstetricians)	Second trimester (16–18 wk)	Subsample of Andersson et al.[31] Consecutively recruited pregnant women attending routine ultrasound screening at 2 obstetric clinics in northern Sweden. Excluded women with fetal malformation or missed abortion by ultrasound, multiple births, and subjects with incomplete medical record data regarding newborns. 96% Married or cohabiting; 43.5% expecting first child.	1,465 (204 with 1 or more PRIME-MD diagnosis, 170 with depressive disorder, 86 with anxiety disorder)	11 Subjects (5.4%) with diagnosis received some sort of treatment, only 2 pharmacologic: 1 received antianxiety treatment (SSRI) at time of evaluation, and 1 started SSRI later in pregnancy.
Buist et al, 2011[49] (United States)	(See risk factors studies)				

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Coelho et al, 2011[69] (United Kingdom)	SCID for *DSM-IV* (trained psychologists and mental health clinicians)	20 wk	Pregnant women presenting for 20-wk prenatal ultrasound scan in United Kingdom. Women who screened positive for high worry or social phobia symptoms invited for diagnostic interview. Random sample of low scorers on screening also invited for interview. Age, 30.75 ± 4.43 y; 96.3% married or cohabiting; 89.3% white; 79% high SES.	246 (56 GAD, 68 social phobia, 28 both disorders, and 94 no prenatal GAD or social phobia)	304/619 Screen-positive women (49%) participated and 123/202 screen-negative women (61%) participated. Information regarding psychotropic or other treatment during pregnancy not reported.
Gezginc et al, 2008[70] (Turkey)	SCID for *DSM-IV* (interviewer not specified)	Prior OCD diagnosis confirmed by SCID at study entry gestational week: 29.48 + 6.75)	Pregnant women with OCD and control group of pregnant women with no mental disorders and similar demographic characteristics recruited from 2 university obstetric clinics in Turkey. Exclusions: pregnancy complications, depression during pregnancy, psychotropic medication during pregnancy. OCD group: age, 29.44 ± 6.75 y; Duration of OCD, 8.0 ± 5.7 y; gestation, 29.48 ± 6.75 wk; all married; 84% unemployed housewives; 72% with primary school education as highest level. No significant differences between OCD group and controls on demographic factors.	50 Total (25 with OCD; 25 controls)	How participants were recruited is not specified, and participation rate not reported. Excluded women with psychotropic use during pregnancy.
Giardinelli et al, 2012[36] (Italy)	(see in prevalence studies)				
Grant et al, 2008[71] (Australia)	MINI for *DSM-IV* (interviewer not specified)	Third trimester (35–39 wk)	Pregnant women consecutively recruited from prenatal clinics in Sydney. Exclusions: multiple gestation, pregnancy complications, substance abuse problems, chronic psychiatric disorders. Selected sample in which women at high and low-moderate risks for developing anxiety and/or depression during the postpartum period were equally represented. Age, 31.97 ± 4.43 y (range, 20–43); mostly middle class; 93% Caucasian, highly educated; 90% partnered; 70% expecting first baby. 51% High risk and 49% low risk for developing anxiety or depression in the postpartum period.	100 (21 with anxiety disorder in pregnancy)	149/273 Eligible women (54.5%) in initial sample. Final sample of 100 after exclusions for medical reasons, withdrawals, and incomplete data. Sample overrepresented women at high risk for postpartum depression or anxiety. Information regarding psychotropic or other treatment during pregnancy not reported.
Grant et al, 2009[72] (Australia)	MINI for *DSM-IV* (trained research officers)	Third trimester (35–39 wk)	Subsample of Grant et al,[71] composed of women who met criteria for at least 1 anxiety disorder during the last 6 months of pregnancy and their 7-month-old infants who completed assessments. Control group of women with no anxiety disorder in pregnancy. See Grant et al[71] for inclusion/exclusion criteria. Age, 31.41 ± 5.17 y (pregnant women), 32.18 ± 4.20 y (controls); mostly Caucasian and partnered.	88 (17 with anxiety disorder in pregnancy and 71 controls)	88/149 Originally enrolled women (59%) participated. Sample overrepresented women at high risk for postpartum depression or anxiety. Information regarding psychotropic or other treatment during pregnancy not reported.
Grant et al, 2010[73] (Australia)	MINI for *DSM-IV* (trained research assistants)	Third trimester (35–39 wk)	Subsample of Grant et al[71] composed of women and their 7-month-old infants who completed assessments. See Grant et al[71] for inclusion/exclusion criteria. Age, 31.77 ± 4.33 y; 84.4% tertiary education; 94.8% Caucasian; 92.2% partnered; 71.4% primiparous.	77 (14 with prenatal anxiety disorder and 63 controls)	77/149 Originally enrolled women (51.7%) participated. Sample overrepresented women at high risk for postpartum depression or anxiety. Information regarding psychotropic or other treatment during pregnancy not reported.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Grant et al, 2010[74] (Australia)	MINI for *DSM-IV* (trained research assistants)	Third trimester (35–39 wk)	Subsample of Grant et al[71] sample composed of women and their 7-month-old infants who completed assessments. See Grant et al[71] for inclusions/exclusion criteria. Age, 31.94 ± 4.25 y; 85.7% tertiary education; 94% Caucasian; 91.6% partnered; 72.6% primiparous.	84 (16 with prenatal anxiety disorder and 68 controls)	84/159 Originally enrolled women (52.8%) participated. Sample overrepresented women at high risk for postpartum depression or anxiety. Information regarding psychotropic or other treatment during pregnancy not reported.
Hunter et al, 2012[75] (United States)	SCID for *DSM-IV* (physician or master's-level social worker)	Lifetime and pregnancy anxiety disorders retrospectively diagnosed postpregnancy (postdelivery: 76 ± 38 d)	Recruited from state birth registry, local obstetric clinics or local infant care treatment program, and self-referral. Exclusions: known birth defects, chromosomal abnormality, and infant major neurologic disorder; prenatal exposure to nicotine, nonnicotine substance use, and parental psychotic illness. 82% married or cohabiting; 52% non-Hispanic Caucasian, 30% Hispanic Caucasian.	242 (46 with prenatal anxiety disorder and 169 without)	Dyads were classified relative to maternal history of anxiety and maternal prenatal antidepressant use. Small sample sizes in the antidepressant-exposed groups limited additional subgroup analyses. Disorders included were agoraphobia, GAD, OCD, panic disorder, and PTSD (specific phobia and social phobia were excluded). 27 (11%) With antidepressant exposure during pregnancy.
Lilliecreutz et al, 2011[76] (Sweden)	Women screened positive for blood/injection phobia were administered diagnostic interview to determine if they met *DSM-IV* criteria for blood/injection phobia (experienced psychotherapist administered by phone)	12–16 Weeks' gestation	Subsample of the 110 pregnant women who met diagnostic criteria for blood/injection phobia in Lilliecreutz and Josefsson[38] and a randomly selected subsample of nonphobic women from same study who were matched on age and parity. Mostly married or cohabiting; equal number of primiparas and multiparas.	330 Total (110 with blood/injection phobia and 220 controls)	Information regarding psychotropic or other treatment during pregnancy not reported.
Lilliecreutz et al, 2011[77] (Sweden)	Women screened positive for blood/injection phobia were administered diagnostic interview to determine if they met *DSM-IV* criteria for blood/injection phobia (experienced psychotherapist administered by phone)	12–16 Weeks' gestation	Subsample of the 110 pregnant women who met diagnostic criteria for blood/injection phobia in Lilliecreutz and Josefsson[38] and a randomly selected subsample of nonphobic pregnant women from same study who were matched on age and parity. Mostly married or cohabiting; equal number of primiparas and multiparas.	220 Total (110 with blood/injection phobia and 110 nonphobic controls)	1 Woman in phobia group used antidepressant; none in control group did. Missing cortisol values at 1 or more collection points.
Mauri et al, 2010[78] (Italy)	SCID for *DSM-IV* (psychiatrist or psychologist)	12–15 wk	Subsample from Borri et al,[32] composed of pregnant women presenting for first ultrasound at clinic in Italy and who completed through the 12-mo postpartum assessment. Exclusions: age, < 18 y; no fixed residence. Age, 32.27 ± 3.95 y; 92% married or cohabiting; 82.8% employed; 48% high school; 42% college or higher; 91% middle SES; 66% first pregnancy.	500 (information regarding percentage of sample with any anxiety disorder or specific anxiety disorders not provided)	1,066/2,598 Eligible women participated (49.9% participation rate) at baseline. Lack of data on nonparticipants. 566/1,066 Women (53.1%) dropped out by 12 mo in postpartum period, leaving 500 for study analysis. Dropouts were significantly younger, more frequently unemployed, and more with specific phobia. Information on psychotropic use not reported except to say that women who required it had the possibility to receive psychotropic or psychological treatment.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Monk et al, 2004[79] (United States)	SCID for *DSM-IV* (licensed psychologist)	24–26 wk	Pregnant, nonsmoking women with singleton fetuses ranging in age from 33 to 39 weeks' gestation recruited from large urban hospital. Exclusions: any maternal or fetal complications, including hypertension, diabetes mellitus, suspected fetal growth restriction, or a fetal structural anomaly on ultrasound. Original sample of 64: age, 27 ± 6 y; 59% Latina, 23% white, 11% African American, 7% Asian or Dominican Indian; 69% married or cohabiting; 49% primiparas; 52% working outside the home at least half of time; diverse range of incomes (low to high).	57 Total composed of 5 groups: (1) 11 anxiety disorder (3 simple phobia, 3 social phobia, 3 agoraphobia without panic disorder, and 2 GAD), (2) 11 depression, (3) 11 no diagnosis but high anxiety symptoms, (4) 13 no diagnosis but medium anxiety symptoms, and (5) 11 no diagnosis but low anxiety symptoms	57/64 (89%) Subjects from original sample remained eligible for analysis. The majority of women with anxiety disorders was diagnosed with phobias and thus actually may experience their high anxiety on an intermittent basis. 2 Participants were taking SSRIs. Analyses were run with and without these 2 participants.
Rambelli et al, 2010[80] (Italy)	(see in onset and course studies)				
Rogal et al, 2007[39] (United States)	(see in prevalence studies)				
Seng et al, 2011[81] (United States)	Life Stressor Checklist to determine lifetime trauma exposure and NWS PTSD Module to diagnose PTSD per *DSM-IV* (interviews conducted via phone by survey research organization by diverse women experienced in mental diagnostic phone interviews. 10% of interviews monitored for quality and accuracy)	Before 28 wk	Subsample from Seng et al.[40] Inclusion: PTSD positive, PTSD negative, or nonexposed controls with prenatal and delivery records and live singleton births. 4 Cohorts: (1) 277 nonexposed to trauma, (2) 307 trauma-exposed, resilient/PTSD-negative controls, (3) 98 PTSD-positive women, and (4) 157 PTSD recovered.	839 (98 PTSD-positive; 277 nonexposed to trauma; 157 PTSD recovered; 307 trauma-exposed, resilient/PTSD-negative controls)	Only women expecting first child included and thus may not generalize to multigravid pregnant women. Information regarding psychotropic or other treatment during pregnancy not reported.
Sutter-Dallay et al, 2004[45] (France)	(see in prevalence studies)				
Uguz et al, 2013[82] (Turkey)	SCID for *DSM-IV* (interviewers not specified)	Anxiety disorders in pregnancy retrospectively diagnosed within first 8 wk of postpartum period	Perinatal patients recruited from outpatient psychiatry clinics in Turkey. Exclusions: history of medical illness or pregnancy-related complications, fetal malformations, maternal infection during pregnancy, history of bipolar disorder, schizophrenia, or related psychotic disorders, smoking or alcohol consumption during pregnancy, comorbid depression and anxiety disorders, and any psychotropic medication during pregnancy. Age, 30.09 ± 4.87 y; all married; 52% with primary school as highest educational level; 81% not employed; 23.3% primiparous.	90 Total (24 MDD, 19 panic disorder, 22 GAD, and 25 healthy pregnant controls)	Psychiatric diagnoses in pregnancy retrospectively diagnosed by SCID administered within first 8 wk of postpartum period. Symptom severity during pregnancy not assessed. Excluded women receiving any psychotropic medication.

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Table 1 (continued). Characteristics of Studies Included in Review of Anxiety Disorders During Pregnancy

Study	How Anxiety Disorder Diagnosed (by whom)	Assessment Point in Pregnancy[a]	Sample Recruitment and Characteristics[a]	Sample Size	Comments
Uguz et al, 2013[83] (Turkey)	SCID for *DSM-IV* (psychiatrists)	GAD in pregnancy retrospectively diagnosed in early postpartum period	Pregnant women aged 18 through 40 y and planning elective cesarean section deliveries at hospitals in Turkey were recruited. Women with GAD at early postpartum assessment and control women with no psychiatric diagnoses included in study. Exclusions: history of medical illnesses or pregnancy-related complications; any newborn malformation; history of maternal infection that could negatively affect fetal growth; mental retardation; multiple birth; existence of intrauterine growth restriction, low birth weight, preterm delivery, or emergency cesarean section; history of bipolar disorder, schizophrenia, or related psychotic disorders; comorbidity with depressive and other anxiety disorders; reported smoking or alcohol consumption in pregnancy; use of systemic corticosteroids in pregnancy; and the existence of hypoxia in baby during childbirth. Age, 29.84 ± 5.32 y, all married, 72.7% with primary school as highest educational level, 84% not employed, 18.2% primiparous. For women with GAD, duration of GAD during pregnancy, 35.84 ± 6.44 wk.	44 Total (19 GAD and 25 controls with no psychiatric diagnosis)	Participation rate not reported. Information regarding psychotropic or other treatment during pregnancy not reported. Sample consisted of women with elective cesarean deliveries.
Warren et al, 2006[84] (United States)	SCID for *DSM-IV* (interviewer not specified)	SCID at a few months in postpartum period	Recruited mothers with panic disorder in early postpartum period via advertising and from a list of volunteers obtained from birth record, as part of larger study of infants and mothers with panic disorder. Exclusions: infant with major medical problem, trauma, or abuse or mother who reported abusing alcohol or drugs during pregnancy or in postpartum period. Control group of mothers without a lifetime history of anxiety disorders or other major psychopathology and without recent alcohol abuse/dependency. Mostly Caucasian and middle to upper class, 26 primiparas.	25 Mothers with panic disorder and 33 controls	Medical records available for only 58 eligible participants from initial 83 participants. No information on frequency and severity of panic attacks during pregnancy. 2 Panic disorder mothers took psychotropic medication during pregnancy. 1 Control mother took phenobarbital during pregnancy.
Intervention studies					
Lilliecreutz et al, 2010[85] (Sweden)	Diagnostic interview to determine if subjects met *DSM-IV* criteria for blood/injection phobia (psychotherapist)	"Early pregnancy"	Recruited following referral by obstetrician to Department of Psychosocial Obstetrics and Gynecology Department due to blood/injection phobia. Treatment group: age, mean = 28.5 y (SD = 5.03), 70% first-time mothers, 93% normal spontaneous vaginal delivery. Untreated phobic control group: age, mean = 30.5 y (SD = 4.09), 54.3% first-time mothers, 76% normal spontaneous vaginal delivery. Healthy controls: age, mean = 30.7 years (SD = 4.22), 60% nulliparous, 80% normal spontaneous vaginal delivery.	30 Intervention group As controls, 46 pregnant women with untreated blood/injection phobia and 70 healthy pregnant women were used (from Lilliecreutz and Josefsson 2008 prevalence study[38])	30/41 Eligible women (73.2%) agreed to intervention. No participants received pharmacotherapy or other psychotherapy during pregnancy.

[a]Values shown are mean ± SD unless stated otherwise.

Abbreviations: CIDI = Composite International Diagnostic Interview, GAD = generalized anxiety disorder, MDD = major depressive disorder, MINI = MINI-International Neuropsychiatric Interview, OCD = obsessive-compulsive disorder, PRIME-MD = Primary Care Evaluation of Mental Disorders, PTSD = posttraumatic stress disorder, SADS = Schedule for Affective Disorders and Schizophrenia, SADS-L = Schedule for Affective Disorders and Schizophrenia-Lifetime version, SADS-LA = Schedule for Affective Disorders and Schizophrenia-Lifetime version-modified for the study of anxiety disorders, SCID = Structured Clinical Interview for DSM, SES = socioeconomic status, SSRI = selective serotonin reuptake inhibitor, YBOCS = Yale-Brown Obsessive Compulsive Scale.

conducted the diagnostic interviews, and, in the remaining studies, interviews were conducted by research nurses, other health care professionals, or trained lay people. Few studies provided information regarding interviewer training or the qualifications criteria by which interviewers (especially those who were not mental health professionals) had been deemed competent.

Reports provided information on the following anxiety disorders: panic disorder (25 reports), GAD (17 reports), OCD (23 reports), agoraphobia (6 reports), specific phobia (10 reports), social phobia (14 reports), PTSD (14 reports), any phobia (1 reports), and any anxiety disorder (18 reports). Twenty reports provided information on prevalence, 16 on course, 10 on comorbid disorders, 10 on risk factors, and 22 on outcomes. Only 1 study tested an intervention for an anxiety disorder in pregnancy.

Prevalence of Anxiety Disorders in Pregnancy

Twenty reports representing 18 samples examined the prevalence of 1 of more anxiety disorders during pregnancy (see Table 2). Studies were conducted in 9 different countries: 7 studies (representing 5 samples) in United States, 7 in Europe, 3 in Eurasia, 1 in Africa, 1 in Asia, and 1 in Latin America. Most studies used samples recruited from hospital- or community-based prenatal clinics. One study[36] recruited participants from a prenatal class, and another sample[29] was derived from a large US epidemiologic survey. Diagnostic interviews were conducted during the first trimester of pregnancy (1 study), second trimester (3 studies), and third trimester (6 studies) and at any point during pregnancy (10 studies). Studies did not provide information enabling determination of whether prevalence varies in relation to stage of pregnancy, neither did they discriminate between anxiety disorders existing prior to pregnancy or with pregnancy onset. With the exception of 1 study[35] in which diagnostic interviews were administered at 2 separate time points in pregnancy, each study examined prevalence of anxiety disorders only once during pregnancy.

Sample sizes ranged from 172 to 14,549 pregnant women. Most studies used random or consecutive sampling, 1 used convenience sampling,[39] and 3 did not report sampling method.[30,33,34] As per the review inclusion criteria, all studies utilized a diagnostic interview to determine anxiety disorder diagnoses. With the exception of 1 study[35] that used *ICD-10* diagnostic criteria for anxiety disorders, all used *DSM-IV* anxiety disorder diagnostic criteria. Only 5 studies[30,41,44,46,47] utilized a relevant comparison group of nonpregnant women.

One study[30] excluded women who were currently receiving any mental health treatment, which may have decreased prevalence by excluding the most ill women. This study, which was carried out in Nigeria, nevertheless had the highest prevalence of any anxiety disorder found in the review. Two studies[37,46] stated that no participants were taking psychotropic medications during pregnancy. None of the remaining studies reported on mental health treatment during pregnancy of the participants.

Prevalence estimates reported. Prevalence estimates varied widely, both for specific disorders and for overall prevalence of any anxiety disorder in pregnancy. Prevalence estimates for any anxiety disorder ranged from 4.4% to 39%. Prevalence of specific anxiety disorders ranged from 0%–10.5% for GAD (11 studies), 0.2%–5.7% for panic disorder (12 studies), 0%–5.2% for OCD (11 studies), 3.2%–19.9% for specific phobia (7 studies), 0.4%–6.4% for social phobia (10 studies), 0.9% for agoraphobia without history of panic to 17.2% for any agoraphobia (5 studies), and 0%–7.9% for PTSD (11 studies). In studies in which presence of any anxiety disorders was assessed, some or all anxiety disorders were included. For example, inclusion of specific phobia in determining prevalence of anxiety disorders greatly increases the prevalence, as specific phobias are the most common anxiety disorder, although arguably not the most debilitating. Forest plots were produced to give a graphical representation of the studies and to convey the extent of heterogeneity between prevalence estimates (see Supplementary eFigure 1 at PSYCHIATRIST.COM).

Comparisons of rates between pregnant women and controls. Only 4 studies[29,30,41,47] utilized control or comparison groups to compare prevalence of anxiety disorders in pregnant versus nonpregnant women. Two studies showed no differences in prevalence between pregnant and nonpregnant women, and 2 showed significant differences. Uguz et al[47] compared the prevalence of each of the specific *DSM-IV* anxiety disorders as well as that of any anxiety disorder among pregnant and nonpregnant and found no significant differences in rates between the 2 groups. Similarly, in a study using data from the large US epidemiologic survey,[29] there were no significant differences in the prevalence of individual anxiety disorders or in presence of any anxiety disorder between pregnant women and nonpregnant women. Conversely, in a small study of pregnant women in Nigeria,[30] having any anxiety disorder was significantly more common among pregnant women compared to nonpregnant women, and the rate for social phobia was significantly higher in the pregnant women compared to controls. There were nonsignificant increases in the rate of other anxiety disorders among pregnant women. Lastly, in a study of PTSD, Seng et al[41] compared 1,581 pregnant prenatal clinic patients to a subsample of 2,000 women in a similar age range from the US National Women's Study. The prevalence of PTSD in the pregnant sample was more than twice as high as that found in the comparison group.

Psychiatric Disorders Comorbid With Anxiety Disorders in Pregnancy

Ten of the included studies reported psychiatric diagnoses comorbid with anxiety disorders in pregnancy (Supplementary eTable 1), revealing substantial comorbidity of major depression with anxiety disorders, as well as high rates of having more than 1 anxiety disorder among pregnant women. No information was reported on whether comorbidities with anxiety disorders during pregnancy differed from those in nonpregnant populations. No studies

Table 2. Prevalence of Anxiety Disorders During Pregnancy

Study	N	Prevalence, %					
		GAD	Panic Disorder	OCD	Phobia	PTSD	Any Anxiety Disorder
Adewuya et al, 2006[30] (Nigeria)	172 (plus 172 nonpregnant controls)	Pregnant, 10.5 Nonpregnant, 5.2 ($\chi^2_1 = 3.256$, $P = .071$) OR = 2.12; 95% CI, 0.92–4.85	Pregnant, 5.2 Nonpregnant, 1.7 ($\chi^2_1 = 3.108$, $P = .078$) OR = 3.11; 95% CI, 0.83–11.69	Pregnant, 5.2 Nonpregnant, 1.7 ($\chi^2_1 = 3.108$, $P = .078$) OR = 3.11; 95% CI, 0.83–11.69	Specific phobia Pregnant, 9.3 Nonpregnant, 5.8 ($\chi^2_1 = 1.898$, $P = .221$) OR = 1.66; 95% CI, 0.73–3.77 Social phobia Pregnant, 6.4 Nonpregnant, 1.7 ($\chi^2_1 = 4.765$, $P = .029$) OR = 3.85; 95% CI, 1.05–14.65	Pregnant, 0.6 Nonpregnant, 0.0 ($\chi^2_1 = 1.003$, $P = .317$) OR = 1.01; 95% CI, 0.99–1.02	Pregnant, 39 Nonpregnant, 16.3 (includes panic disorder, specific phobia, social phobia, GAD, OCD, PTSD, anxiety disorder due to medical condition) ($\chi^2_1 = 22.119$, $P < .001$)
Andersson et al, 2003[31] (Sweden)	1,556	0.3	0.2	1.3	Social phobia, 0.4	NR	6.6 (includes GAD, panic disorder, OCD, social phobia, and anxiety NOS)
Borri et al, 2008[32] (Italy)	1,066	1.9	4	1.6	Specific phobia, 10.7 Social phobia, 3.8 Agoraphobia without panic, 1.5%	0.7	21.7 (includes panic disorder, agoraphobia without panic, social phobia, specific phobia, OCD, PTSD, GAD, and anxiety disorder NOS) Any anxiety disorder (specific phobia excluded), 13.7
Fadzil et al, 2013[33] (Malaysia)	175	0	5.7	0	Agoraphobia without panic attacks, 2.9 Social phobia, 0.6	0	9.1 (includes panic disorder, agoraphobia without panic attacks, social phobia, OCD, PTSD, and GAD)
Farias et al, 2013[34] (Brazil)	239	10.5	0.4	3.4	Agoraphobia, 17.2 Social phobia, 4.6	1.7	NR
Felice et al, 2007[35] (Malta)	229	At both 18.6 wk and 36 wk, 0.4%	0.4	0.4	All phobias, 1.8	NR	4.4 (includes phobia, panic disorder, GAD, OCD, and mixed anxiety and depressive disorder) (note: mixed anxiety and depressive disorder = 1.3%)
Giardinelli et al, 2012[36] (Italy)	590	1.4	5.4	3.4	Specific phobia, 3.6 Social phobia, 4.1	0.8	21 (includes panic disorder, specific phobia, social phobia, GAD, OCD, and PTSD)
Guler et al, 2008[37] (Turkey)	512	NR	2.5	NR	NR	NR	NR
Lilliecreutz and Josefsson, 2008[38] (Sweden)	1,529	NR	NR	NR	Specific (blood/injection) phobia, 7.2	NR	NR
Rogal et al, 2007[39] (United States)	1,100	NR	NR[a]	NR	NR	3	NR
Seng et al, 2009[40] (United States); and Seng et al, 2011[42] (United States)	1,581	NR	NR	NR	NR	Overall, 7.9 (95% CI, 6.6–9.3) Predominantly private-payer settings, 2.7 Predominantly public-payer settings, 13.9 African American, 13.4 Non–African American, 3.5	NR

(continued)

Table 2 (continued). Prevalence of Anxiety Disorders During Pregnancy

Study	N	Prevalence, %					
		GAD	Panic Disorder	OCD	Phobia	PTSD	Any Anxiety Disorder
Seng et al, 2010[41] (United States)	3,148 total (1,581 perinatal clinic sample and 2,000 comparison group)	NR	NR	NR	NR	Full perinatal sample, 7.9 (8.4% among trauma-exposed perinatal women) Full comparison group, 3.1 (4.4% among trauma-exposed comparison women)	NR
Smith et al, 2004[43] (United States)	387	NR	NR	NR	NR	3	NR
Smith et al, 2006[44] (United States)	948	NR	NR	NR	NR	3.5	NR
Sutter-Dallay et al, 2004[45] (France)	497	8.5	1.4	1.2	Agoraphobia, 14 Social phobia, 2	0	24 (includes GAD, panic disorder, OCD, agoraphobia, and social phobia)
Uguz et al, 2007[46] (Turkey)	434	NR	NR	3.5	NR	NR	NR
Uguz et al, 2010[47] (Turkey)	309 Pregnant women (plus 107 nonpregnant premenopausal controls)	Pregnant, 3.6 Nonpregnant, 3.7 (P = 1.00)	Pregnant, 1.9 Nonpregnant, 0.9 (OR = 2.07; 95% CI, 0.25–17.06; P = .683)	Pregnant, 5.2 Nonpregnant, 2.8 (OR = 1.84; 95% CI, 0.55–6.21; P = .425)	Specific phobia Pregnant, 3.2 Nonpregnant, 4.7 OR = 0.68; 95% CI, 0.24–1.96; P = .547) Social phobia Pregnant, 3.2 Nonpregnant, 2.8 (OR = 1.15; 95% CI, 0.32–2.92; P = 1.000)	Pregnant, 0 Nonpregnant, 0	Pregnant, 15.5 Nonpregnant, 15 (OR = 1.04; 95% CI, 0.62–1.75; P = 1.000) (includes OCD, GAD, PTSD, social phobia, and specific phobia)
Vesga-López et al, 2008[29] (United States)	13,478 Total[b] (453 currently pregnant and comparison group of 13,025 nonpregnant women)	Pregnant, 1.3 Nonpregnant, 1.8 (OR = 0.70; 95% CI, 0.26–1.85; AOR = 1.87; 95% CI, 0.67–5.25; P = NS)	Pregnant, 1.4 Nonpregnant, 3 (OR = 0.45; 95% CI, 0.13–1.58; AOR = 0.74; 95% CI, 0.21–2.60; P = NS)	NR	Specific phobia Pregnant, 8.3 Nonpregnant, 10.2 (OR = 0.80; 95% CI, 0.54–1.19; AOR = 1.04; 95% CI, 0.40–2.71; P = NS) Social phobia Pregnant, 3 Nonpregnant, 2.8% (OR = 1.08; 95% CI, 0.58–2.01; AOR = 1.11; 95% CI, 0.36–3.39; P = NS)	NR	Pregnant, 12.2 Nonpregnant, 14.9 (OR = 0.80; 95% CI, 0.57–1.11; AOR = 1.31; 95% CI, 0.73–2.36; P = NS) (includes panic disorder, social phobia, specific phobia, and GAD)
Zar et al, 2002[48] (Sweden)	453	0.9	1.3	0.2	Agoraphobia without history of panic, 0.9 Specific phobia, 19.9 Social phobia, 2.7	1.3	26.9 (includes GAD, panic disorder, OCD, agoraphobia, specific phobia, social phobia, and PTSD)

[a]PD not diagnosed by diagnostic interview and therefore not included.
[b]Sample also included 994 postpartum women and 77 with unknown status or no live children who were not included in this analysis.
Abbreviations: GAD = generalized anxiety disorder, NR = not reported, NS = nonsignificant, OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder.

in our review reported specifically on comorbidities with GAD or any phobias.

Onset of Anxiety Disorders in Pregnancy

Seven studies provided information regarding onset of OCD in pregnancy[46,50,55,58–60,66] and 4 regarding onset of panic disorder[56,61,67,80] (Supplementary eTable 2). Studies were small and data were collected retrospectively. Onset of OCD in pregnancy ranged from 0% to 15.4%. An additional study reported development of obsessive-compulsive symptoms in 39% of women during pregnancy.[60] Onset of panic disorder ranged from 0% to 53.8%. These wide ranges are most likely due to differing study designs and populations.

Course of Anxiety Disorders in Pregnancy

Several studies examined the course of OCD or panic disorder in pregnancy, and 1 looked at the course of social phobia. All studies were composed of samples of women with the relevant preexisting disorder. Most included women recruited from anxiety disorder clinic populations and thus may represent women with more severe anxiety disorders. With few exceptions,[53,54] these studies were limited by retrospective design. Women were asked to remember symptom severity from time periods ranging from earlier in current pregnancy to up to many years past in some studies. Consideration of potential confounders, such as psychotropic use or psychotherapeutic treatment, was absent in most of the studies. No studies were found that examined course of GAD, PTSD, or phobias other than social phobia during pregnancy.

Course of OCD in pregnancy. Six studies examined the course of OCD during pregnancy (Table 3). Four studies comprised anxiety disorder clinics patients, which may overrepresent women with more severe illness and comorbidities. Two studies included pregnant women recruited from prenatal clinics who screened positive for OCD. Sample sizes were small, ranging from 12 to 78 women. All studies used retrospective reports to characterize the course of OCD. Four were limited by lack of information regarding treatment, including psychopharmacologic treatment.

In 5 of the 6 studies, the greatest proportion of participants (44%–83%) reported no change in OCD symptoms during pregnancy. Decrease of symptoms occurred in 8%–23%, and increase of symptoms occurred in 8%–46.1%. In 1 study,[55] a variable course of symptoms across pregnancies was observed for some women, with symptom increase in one pregnancy and no change or symptom decrease in another pregnancy.

Course of panic disorder in pregnancy. Nine studies examined the course of panic disorder during pregnancy (Table 3) using samples ranging from 7 to 93 women. With the exception of 2 studies,[53,54] all used retrospective reports of women regarding panic disorder symptoms in prior or current pregnancies. All study samples comprised anxiety disorder clinic patients, except for 1[56] that comprised obstetric clinic patients. Two studies examined panic disorder in samples of women without psychopharmacologic treatment during pregnancy, 1 study did not report psychotropic exposure, and 5 included women with psychotropic exposure for some or all of the pregnancy.

The course of panic disorder varied widely among the studies, with no consistent pattern. Four reported that the greatest proportion of participants experienced symptom improvement, 1 study reported worsening in the majority of women with panic disorder, and 4 reported little change in symptoms across pregnancy. Dannon et al[54] conducted a naturalistic study comparing panic disorder relapse rates among 2 groups of women with history of panic disorder who had been treated to remission with paroxetine 6 years earlier. Women with onset of panic disorder in a prior pregnancy (PD-P) and women with panic disorder onset while not pregnant (PD-NP) were compared. *Relapse* was defined as occurrence of a panic attack. Women with pregnancy-onset panic disorder had significantly higher risk of relapse with a subsequent pregnancy than nonpregnancy-onset women ($F_{4,76} = 11.8$, $P < .001$). Of women with subsequent pregnancies, 57% (n = 15/26) of the PD-P women relapsed during a subsequent pregnancy compared to 44.4% (n = 8/18) of PD-NP women who did so. The PD-NP women also had a higher rate of relapse during future pregnancies ($F_1 = 3.4$, $P < .035$). For both groups of women, there was (1) an increased risk of relapse during pregnancy,(2) a history of panic disorder onset during pregnancy that constituted a higher risk of relapse during a subsequent pregnancy, and (3) more severe relapse in women who relapsed during pregnancy compared with nonpregnant relapsers. Overall, the review revealed inconsistent, unpredictable courses that varied between women and between pregnancies for multiparous women. In general, panic disorder symptoms may worsen, improve, or stay the same during pregnancy.

Course of phobia in pregnancy. One study examined the course of phobia during pregnancy. van Veen and colleagues[63] retrospectively examined the course of social phobia across pregnancy in a sample of 41 women with prior pregnancies. Most women (59%) reported no change in social phobia symptoms during pregnancy. Subgroup analyses of women who reported social phobia symptoms in both pregnancy and postpartum showed that women reported statistically fewer symptoms in pregnancy compared to prior to pregnancy and in the postpartum period. In addition to retrospective recall, this study was limited by a low response rate (46%) and very small sample sizes in the subgroup analyses.

Risk Factors Associated With Anxiety Disorders in Pregnancy

Four studies[30,32,33,35] reported risk factors for a diagnosis of any anxiety disorder in pregnancy. Only 3 factors (being single, low SES, and primiparity) were examined as potential risk factors in more than 1 study, with conflicting findings found for each. Additional potential risk factors were examined in only 1 study each. The lack of comparable data makes combining of results impractical. Findings are presented in Supplementary eTable 3.

Table 3. Course of Anxiety Disorders Across Pregnancy

Study	Sample Size and Description[a]	How Data Were Collected	Symptom Decrease Across Pregnancy (improvement), n (%)	No Change in Symptoms Across Pregnancy, n (%)	Symptom Increase Across Pregnancy (worsening), n (%)	Comments
Obsessive-compulsive disorder						
Uguz et al, 2007[46]	13 Pregnant prenatal clinic patients with pregravid OCD	Retrospective reports during third trimester	3 (23.1)	4 (30.8)	6 (46.1)	Information about medication use not reported.
Uguz et al, 2011[62]	52 Pregnant prenatal clinic patients with pregravid OCD	Retrospective reports during pregnancy (mean ± SD = 29.5 + 8.2 weeks' pregnancy)	7 (13.5)	28 (53.8)	17 (32.7)	Participants with MDD or another anxiety disorder comorbid with OCD exhibited higher symptom severity compared to pure OCD patients. Information about medication use not reported.
Forray et al, 2010[55]	78 Anxiety disorder clinic patients with OCD and at least 1 prior pregnancy (132 total pregnancies)	Retrospective reports	29 (22.0) (pregnancies)	58 (43.9) (pregnancies)	45 (34.1) (pregnancies)	9 Women reported worsening of OCD symptoms in 1 pregnancy and improvement or no change during another. Information about medication use not reported.
Labad et al, 2005[50]	12 Clinic patients with pregravid OCD	Retrospective reports	1 (8)	10 (83.3)	1 (8)	No antiobsessive treatment among participants during pregnancy.
Vulink et al, 2006[65]	52 Anxiety disorder clinic patients with OCD and at least 1 prior pregnancy	Retrospective self-report questionnaire by mail	11 (21)	24 (46)	17 (33)	Low response rate (29%) to questionnaire, indicating possible response bias. Some participants on psychotropic medication in pregnancy, although specific information not reported.
Williams and Koran, 1997[66]	29 Anxiety disorder clinic patients with pregravid OCD	Retrospective standardized telephone interviews	4 (14)	20 (69)	5 (17)	Information about medication use not reported.
Panic disorder						
Bandelow et al, 2006[51]	93 Anxiety disorder clinic patients with panic disorder and at least 1 prior pregnancy (195 pregnancies total)	Retrospective reports	17 (8.7) (pregnancies)	165 (84.6) (pregnancies)	13 (6.7) (pregnancies)	Excluded women with history of other psychiatric disorders, including other anxiety disorders and MDD (unless secondary to panic disorder). Small number of women (≤7/exact number not reported for pregnancy) received antipanic medications during pregnancy, and 7 women received psychotherapy treatment. In previously pregnant women, panic manifestations were significantly fewer during pregnancy compared with the nonperinatal period.
Cohen et al, 1994[52]	49 Anxiety disorder clinic patients with pregravid panic disorder	Retrospective chart review using CGI scale to rate severity of symptoms for each trimester as well as the 3-mo interval just prior to conception	10 (20) (women)	28 (57) (women)	10 (20) (women)	32 Patients (65%) took antipanic medication at some point in pregnancy; 15 (31%) for entire pregnancy. Participants tended to have previous failed attempts to discontinue medications. 1 Woman had a mixed course—experiencing periods of heightened and reduced symptoms of panic during pregnancy. Tended to have previous failed attempts to discontinue medications.

(continued)

Table 3 (continued). Course of Anxiety Disorders Across Pregnancy

Study	Sample Size and Description[a]	How Data Were Collected	Symptom Decrease Across Pregnancy (improvement), n (%)	No Change in Symptoms Across Pregnancy, n (%)	Symptom Increase Across Pregnancy (worsening), n (%)	Comments
Cohen et al, 1996[53]	10 Pregnant anxiety disorder clinic patients with history of panic disorder	Prospective assessment of patients at 11-, 23-, and 37-wk gestation for current panic disorder CGI used to rate severity	1 (10) (women)[b]	8 (80) (women)[b]	1 (10) (women)[b]	70% Took antipanic medication at some point during pregnancy. Increases in medications were not associated with clinical improvement. 7 Of 10 patients met panic criteria at all trimester visits, 1 did not meet criteria at any prenatal point, and 2 met criteria at some but not all assessments. Comorbidities present. Varying levels of pharmacologic treatment. Lack of diversity in panic disorder severity.
Dannon et al, 2006[54]	44 Women with history of panic disorder referred to tertiary referral center and treated to remission with paroxetine 6 y earlier in an initial study	Prospective assessment of recurrence of panic attacks using a self-report questionnaire	NA	NA	23 (52.3) (women)	Participants had all received treatment for panic disorder in past and thus may represent women with more severe panic disorder.
Guler et al, 2008[56]	7 Pregnant obstetric clinic patients with pregravid history of panic attacks and diagnosed with panic disorder in third trimester of pregnancy	Retrospective questionnaire during third trimester Degree of severity change rated on scale of 1 (no change) to 10 (much more increased)	4 (57.1) (women)	2 (28.6) (women)	1 (14.3) (women)	Excluded women with current treatment or psychiatric comorbidities. None on antipanic medications during pregnancy.
Klein et al, 1995[57]	19 Anxiety disorder clinic patients with pregravid panic disorder for at least 1 prior pregnancy (representing 33 full-term pregnancies with complete data)	Retrospective interview	14 (74) (women)	4 (21) (women)	1 (5) (women)	8 Pregnancies (24%) involved antipanic medications in first trimester but not in second and third trimesters. The pregnancies occurred from 2 mo to 23 y before the interview. Time differential may have affected recall.
Northcott and Stein, 1994[61]	Anxiety disorder clinic patients (67 pregnancies) who developed panic disorder before, during, or between pregnancies	Retrospective questionnaire by mail	29 (43) (pregnancies)	16 (24) (pregnancies)	22 (33) (pregnancies)	Of 20 multiparous women, 9 (45%) reported no consistent pattern in symptom alteration across pregnancies. Psychotropic use not reported.
Villeponteaux et al, 1992[64]	23 Anxiety disorder clinic patients with pregravid panic disorder (44 pregnancies total)	Retrospective questionnaires asking about changes in panic attack severity and frequency in pregnancy	Panic attacks across women Severity or none, 12 (54.5) Frequency or none, 14 (63.6) Panic attacks across pregnancies Severity or none, 29 (66) Frequency, 29 (66)	Panic attacks across women Severity, 1 (4.5) Frequency, 2 (9) Panic attacks across pregnancies Severity, 4 (9.1) Frequency, 8 (18.2)	Panic attacks across women Severity, 2 (9) Frequency, 3 (13.6) Panic attacks across pregnancies Severity, 5 (11.4) Frequency, 7 (15.9)	Some patients reported variable course of panic attacks within and across pregnancies. Some patients did not answer questions. Excluded women taking medication (n = 3) and thus may have excluded more severely ill patients.
Wisner et al, 1996[67]	22 Anxiety disorder clinic patients (45 pregnancies) with panic disorder that predated 1 or more pregnancies or was a first lifetime episode associated with a pregnancy	Retrospective interviews	12 (27) (pregnancies)	31 (69) (pregnancies)[c]	2 (4.4) (pregnancies)	3 Women (14%) [3 pregnancies (6.7%)] had psychotropic medication exposure. 19 Women (86%) had comorbid agoraphobia; 14 (64%) had comorbid mood disorder (13 MDD; 1 schizoaffective disorder, depressed type). The pattern of panic attacks across gestations was consistent for only 5 of 14 multiparas.

[a]N refers to participants relevant to course description only. [b]Change indicated as ± 2 point change in CGI score. [c]For these 31 pregnancies, "no change" represented continuation of panic attacks present at pregnancy onset (n = 14), continuation of remission of panic attacks (n = 11), or no symptoms because it was the pregnancy prior to the first lifetime onset of panic disorder in the corresponding postpartum period (n = 6).

Abbreviations: CGI = Clinical Global Impressions Scale, MDD = major depressive disorder, NA = not assessed, OCD = obsessive-compulsive disorder.

Risk factors for PTSD were examined in 2 studies (3 publications). Seng et al[40] compared demographic, trauma history, and posttraumatic stress–related psychiatric characteristics across 5 mutually exclusive pregnant cohorts: nonexposed, trauma-exposed but PTSD-negative, partial PTSD, past PTSD, and current PTSD. The strongest risk factors ($P \leq .013$ for each) were worst antecedent trauma was childhood abuse; worst trauma was a previous miscarriage or abortion that was experienced as traumatic, cumulative SES risk factors, depression diagnosis, GAD diagnosis, and previous therapy or medication. Using the same sample, Seng et al[42] conducted additional analyses to compare African American women and non–African American women on risk for PTSD in pregnancy. Although PTSD in pregnancy was 4 times higher among African American women (13.4%) compared to non–African American women (3.5%), race was not a significant factor once trauma history was accounted for. The higher rates of PTSD in pregnant African American women were accounted for by greater trauma exposure, particularly child and adult abuse trauma. Having accessed treatment prior to pregnancy was a significant predictor of PTSD for non–African American women but not for African American women. In another study[44] of 948 low-income pregnant women, the following factors were significant predictors of PTSD: current depression, current panic disorder, current suicidality, sexual molestation, and serious physical attack or assault. When only women who reported a past traumatic event were included in analysis (n = 278), prior or current mental health treatment, current depression, current panic disorder, current suicidality, and sexual molestation were significant predictors of PTSD in pregnancy. Posttraumatic stress disorder was less likely in women who experienced a trauma more than a year ago, compared to women who experienced a trauma within the last year.

Buist et al[49] examined risk factors for GAD in a cohort of 2,793 pregnant women, comparing women with no GAD diagnosis to the following 3 groups: (1) GAD in 6 months prior to pregnancy only (group A), (2) GAD in pregnancy only (group B), and (3) GAD in 6 months prior to and during pregnancy (group C). Previous history of GAD was the strongest predictor of GAD in pregnancy. Women with 4 or more prior GAD episodes were significantly more likely to experience GAD in pregnancy (groups B and C). Both groups B and C had significantly lower social support compared to the no-GAD group. Group B had significantly more black women compared to the no-GAD group. Group C women were significantly more likely to have experienced childhood abuse and were significantly less educated compared to no-GAD women. Limitations of the study include a selected sample of women at high risk for depression, PTSD, and antidepressant use, with possible confounding effects of medication on GAD.

Uguz et al[46] looked at factors related to OCD in pregnant women during the third trimester of pregnancy. There were no significant differences between pregnant women with (n = 15) and without (n = 419) OCD with regard to age, educational level, employment status, number of gestations and live births, gestational weeks, duration of marriage, history of abortion, and the existence of gestational complications. There was, however a statistically significant difference between pregnant women with and without OCD with regard to family history of OCD. A family history of OCD was reported by 33.3% of pregnant women with OCD versus 2.4% of pregnant women without OCD ($P < .0001$). Another study[50] reported that neither past nor present history of major depressive episodes was associated with onset or worsening of OCD in pregnancy.

Outcomes Associated With Anxiety Disorders in Pregnancy

Nineteen studies (representing 16 samples) reported on outcomes associated with anxiety disorders in pregnancy. Findings are reported in Table 4.

Maternal outcomes. Ten studies (2 that utilized the same sample[76,77]) examined maternal outcomes associated with anxiety disorders during pregnancy. Six of the studies investigated prenatal anxiety disorders as a potential risk factor for postpartum depression (defined variably as either high symptom levels or diagnoses). Each reported a statistically significant association between anxiety disorders in pregnancy and subsequent postpartum depression. Findings from 1 of the studies[78] furthermore suggest that type of anxiety disorder may affect postpartum depression risk differentially: whereas a prenatal diagnosis of agoraphobia, specific phobia, OCD, PTSD, or GAD was not associated with postpartum depression symptoms or diagnoses, panic disorder and social phobia were significant predictors of both elevated Edinburgh Postnatal Depression Scale (EPDS) scores and *DSM-IV* diagnoses of minor or major depression at 1 month postpartum. Panic disorder (but not social phobia) was a significant risk factor for depression diagnosis during the first year postpartum.

Coelho and colleagues[69] looked specifically at GAD and social phobia as potential predictors of postpartum depression (EPDS score > 12) and found that, after controlling for prenatal depression diagnosis, other prenatal anxiety disorders, maternal age, SES status, and ethnicity, GAD was an independent predictor of postpartum depression at each of 5 time points assessed over the first 2 years after delivery. Social phobia during pregnancy also predicted postpartum probable depression, but only at 10 months postpartum.

Only 1 study[71] examined prenatal anxiety disorder diagnosis as a risk factor for postpartum anxiety disorders. In addition to examining major depression diagnosis as an outcome, Grant et al[71] also examined the association between prenatal anxiety disorders and postpartum anxiety disorder diagnosis. After adjustments were made for demographic characteristics and prenatal depressive disorder, having an anxiety disorder during pregnancy was associated with a nearly 5-fold increased likelihood of depression and an equally high increased likelihood of experiencing an anxiety disorder in the first 7 months postpartum.

Table 4. Outcomes Associated With Anxiety Disorders During Pregnancy

Study	Anxiety Disorder	Timing of Anxiety Disorder Diagnosis in Pregnancy	Outcome and When Assessed	Findings
Maternal outcomes				
Coelho et al, 2011[69]	GAD, social phobia	20 Weeks' gestation	EPDS score > 12 at 5 postpartum time points throughout the first 2 y after delivery	After controlling for other prenatal anxiety disorder, prenatal depression, maternal age, SES status, and ethnicity, GAD independently predicted probable postpartum major depression at 5 time points throughout the first 2 y after delivery (OR = 7.54 [95% CI, 3.17–17.97], $P < .005$ at 10–14 d; OR = 3.76 [95% CI, 1.20–11.81], $P < .05$ at 10–12 wk; OR = 10.69 [95% CI, 3.75–30.43], $P < .005$ at 10 mo; OR = 5.11 [95% CI, 1.87–14.00], $P < .005$ at 14 mo; and OR = 7.13 [95% CI, 2.46–20.68], $P < .005$ at 24 mo in postpartum period). Social phobia during pregnancy also predicted probably postpartum depression, but only at 10 mo in the postpartum period (OR = 5.89 [95% CI, 2.04–17.06], $P < .005$).
Gezginc et al, 2008[70]	OCD	At mean ± SD gestational week 29.48 ± 6.75	Quality of life measured by WHOQOL-BREF in pregnancy	Compared to control women, women with OCD in pregnancy had significantly lower quality of life ($P < .01$).
Giardinelli et al, 2012[36]	Any anxiety disorder (panic disorder, specific phobia, social phobia, GAD, OCD, and PTSD)	7 Months' gestation	EPDS score > 10 at 3 mo in the postpartum period	Prenatal anxiety disorder was a significant risk factor for elevated postpartum depression symptoms (OR = 3.09; 95% CI, 1.77–5.38; $P < .001$).
Grant et al, 2008[71]	Any anxiety disorder (panic disorder, agoraphobia, social phobia, PTSD, GAD, and mixed anxiety-depressive disorder)	Third trimester	First 7 mo of postpartum period prevalence of depression or anxiety disorder diagnosis	Prenatal anxiety disorder was associated with significantly higher odds of an anxiety disorder diagnosis during the first 7 mo of postpartum period (OR = 4.97; 95% CI, 1.31–18.88; $P = .02$) after adjustment was made for demographic characteristics (ethnicity, parity, partnership status) and prenatal depressive disorder. Prenatal anxiety disorder was also associated with a significantly increased likelihood of a diagnosis of depression during the first 7 mo of postpartum period (OR = 4.99; 95% CI, 1.37–18.15; $P = .02$) after adjustment was made for demographic factors and prenatal mood.
Grant et al, 2010[74]	Any anxiety disorder (panic disorder, agoraphobia, social phobia, PTSD, and GAD)	35–39 Weeks' gestation	Maternal sensitivity to infant distress during the still-face procedure at 7 mo in the postpartum period	There was no significant difference in maternal sensitivity across still-face episodes between women with anxiety disorder during pregnancy and nonanxious controls.
Lilliecreutz et al, 2011[76]	Specific phobia (blood/injection type)	12–16 Weeks' gestation	Fear of childbirth during pregnancy	Compared to controls, women with blood/injection phobia had higher incidence of fear of childbirth ($P < .001$).
Lilliecreutz et al, 2011[77]	Specific phobia (blood/injection type)	12–16 Weeks' gestation	Morning and evening maternal salivary cortisol at 25 and 36 weeks' gestation Maternal serum CRF, ACTH, and cortisol at 25 weeks' gestation	Pregnant women with blood/injection phobia had a higher output of cortisol compared with women without the phobia ($F_1 = 6.25$, $P = .014$), but there was no marked difference in the diurnal cortisol rhythm between groups. There were no statistically significant differences between women with blood/injection phobia and those without in serum concentrations of CRF, ACTH, and cortisol.

(continued)

Table 4 (continued). Outcomes Associated With Anxiety Disorders During Pregnancy

Study	Anxiety Disorder	Timing of Anxiety Disorder Diagnosis in Pregnancy	Outcome and When Assessed	Findings
Mauri et al, 2010[78]	Any anxiety disorder (panic disorder, agoraphobia without panic, social phobia, specific phobia, OCD, PTSD, GAD, anxiety disorder NOS)	First trimester	First month postpartum point prevalence and 12-mo postpartum period prevalence of probable depression (EPDS score >12) and of depression diagnosis (major or minor depression)	Having a prenatal anxiety disorder was associated with a significantly increased likelihood of postpartum depressive outcomes (EPDS score >12, minor or major depression diagnosis) at 1 mo in postpartum period, even after controlling for established risk factors. However, different anxiety diagnoses differed in their ability to predict these outcomes. Multivariate analyses with adjustment for established risk factors produced the following outcomes: Panic disorder and social phobia were each significant predictors of probable depression (EPDS score >12) at 1 mo in postpartum period (adjusted RR = 5.27; 95% CI, 2.0–13.91 for panic disorder; adjusted RR = 3.80; 95% CI, 1.34–10.46 for social phobia). The point prevalence of probable depression at 1 mo in postpartum period was 25% for those who had panic disorder and 20.7% for those who had social phobia at the first trimester of pregnancy. Panic disorder and social phobia were significant predictors of a diagnosis of minor or major depression at 1 mo in postpartum period (RR = 7.23 [95% CI, 2.31–22.66] for panic disorder; RR = 6.63 [95% CI, 2.11–20.85] for social phobia). The point prevalence of depression diagnosis at 1 mo in postpartum period was 17.9% for women who had panic disorder and 17.2% for women who had social phobia during pregnancy. PTSD was significantly associated with 1-y period prevalence of probable depression (EPDS score >12) (adjusted RR = 12.2; 95% CI, 1.10–13.85). Only panic disorder was associated with depression diagnosis 1-year period prevalence (adjusted RR = 3.10; 95% CI, 1.16–8.22), with 29.2% of women with panic disorder during pregnancy developing depression during the first year of postpartum period. In general, the effect sizes of anxiety disorders in predicting postpartum depression was stronger at 1 month than for the first year period prevalence (note: significance levels not given).
Rambelli et al, 2010[80]	Panic disorder	12–15 Weeks' gestation	Major or minor depression diagnosis at 1, 3, and 6 mo of postpartum period	After controlling for lifetime depression and other postpartum depression risk factors, panic disorder in pregnancy was a significant and independent risk factor for postpartum depression (RR = 4.25; 95% CI, 1.48–12.19). Women with panic disorder in pregnancy had 4.2 times greater risk of postpartum depression than women without panic disorder in pregnancy.
Sutter-Dallay et al, 2004[45]	Any anxiety disorder (GAD, panic disorder, OCD, agoraphobia, and social phobia)	Third trimester	EPDS score > 12 at 6 wk of postpartum period	Women with prenatal anxiety disorder were 2.7 times more likely to have high levels of postpartum depression symptoms, independent of maternal prenatal depression and other confounding factors (adjusted OR = 2.7; 95% CI, 1.1–6.3; $P = .03$).
Obstetric outcomes				
Andersson et al, 2004[68]	Any anxiety disorder (anxiety NOS, GAD, panic disorder, OCD, and social phobia)	Second trimester (16–18 wk)	Neonatal outcomes (umbilical artery pH, umbilical artery base deficit, Apgar score at 1 and 5 min, neonatal ICU, overall premature birth, spontaneous preterm birth, SGA, respiratory distress, asphyxia, and malformation)	There were no significant differences in any of the neonatal outcomes between women with an anxiety disorder in pregnancy and healthy controls.
Lilliecreutz et al, 2011[76]	Specific phobia (blood/injection type)	12–16 Weeks' gestation	Cesarean section, premature delivery, neonatal morbidity, small for gestational age	Compared to controls, women with blood/injection phobia had higher incidence of elective cesarean section ($P = .032$), premature delivery ($P = .028$), preeclampsia ($P = .008$), and premature contractions ($P = .035$), and their infants had higher neonatal morbidity ($P = .001$), were more often small for gestational age ($P = .009$), and had a longer postpartum hospital stay ($P = .001$).
Rogal et al, 2007[39]	PTSD	Any pregnancy time point	Preterm birth, birth weight	There were no statistically significant differences between women with PTSD diagnosis in pregnancy and those without PTSD in terms of preterm delivery or infant birth weight.

(continued)

Table 4 (continued). Outcomes Associated With Anxiety Disorders During Pregnancy

Study	Anxiety Disorder	Timing of Anxiety Disorder Diagnosis in Pregnancy	Outcome and When Assessed	Findings
Seng et al, 2011[81]	PTSD	Before 28 weeks	Gestational age, birth weight	A significant association was found between PTSD during pregnancy and lower birth weight and shorter gestation. Infants born to women with PTSD during pregnancy had a mean birth weight 283 g less than infants of trauma-exposed, resilient women and 221 g less than infants of nonexposed women ($F_{3,835}=5.4$, $P=.001$). PTSD was also associated with shorter gestation in multivariate models that took childhood abuse history into account. PTSD was not associated with infant gestational age in the subset of women with no abuse history but was significantly associated with infant gestational age in the subset of women with history of childhood abuse (note: specific statistics not reported).
Uguz et al, 2013[83]	GAD, panic disorder	Any pregnancy time point	Gestational age, birth weight	Compared 4 groups of pregnant women: women with MDD, GAD, panic disorder, and healthy controls. Infants of women with panic disorder had lower birth weight compared to infants of women with MDD ($P=.036$), GAD ($P=.010$), or controls ($P=.000$). Infants of women with panic disorder had significantly shorter gestational age compared to infants of women with GAD ($P=.030$) or of control women ($P=.000$). There was no difference between infants of GAD women and infants of control women in terms of gestational age or birth weight.
Warren et al, 2006[84] (United States)	Panic disorder	Any pregnancy time point	Premature birth, birth weight	Compared to controls, infants of mothers with panic disorder were not significantly more likely to be born prematurely or earlier than controls but did show smaller birth weight corrected for gestational age ($P=.03$), even after the researchers controlled for potentially confounding variables.
Fetal, neonatal, and infant outcomes				
Grant et al, 2009[72]	Any anxiety disorder (panic disorder, agoraphobia, social phobia, PTSD, and GAD)	35–39 Weeks' gestation	Infant cortisol reactivity to a standardized interactive stressor (still-face procedure) at age 7 mo	There was a significant difference between the infants of women with anxiety disorder during pregnancy and those without in their overall pattern of cortisol response to the still-face procedure at age 7 mo ($F_{3,180}=3.29$, $P=.02$). This effect was independent of the effects of prenatal depression symptoms and postpartum concurrent symptoms of anxiety and depression. Maternal sensitivity did not appear to moderate the association between prenatal anxiety diagnosis and infant cortisol response. However, differences between groups (anxiety disorder in pregnancy or not) in infant cortisol response was found at only 1 of 4 sampling points, raising the possibility of chance finding in this small study.
Grant et al, 2010[73]	Any anxiety disorder (panic disorder, agoraphobia, social phobia, PTSD, and GAD)	35–39 Weeks' gestation	Infant mental and psychomotor development at age 7 mo	7-Month-old infants of women with any anxiety disorder diagnosis during pregnancy did not differ from controls in either mental development or psychomotor development ($P>.10$).
Grant et al, 2010[74]	Any anxiety disorder (panic disorder, agoraphobia, social phobia, PTSD, and GAD)	35–39 Weeks' gestation	Infant response to a standardized interactive stressor (still-face procedure) at age 7 mo	There was no significant difference between the infants of women with anxiety disorder during pregnancy and nonanxious controls in their reactivity to the still-face procedure at age 7 mo. Maternal sensitivity to infant distress was associated with lower infant reactivity in both groups, but this interaction effect was significantly greater among infants of women who experienced anxiety disorder in pregnancy ($\beta=-.76$, $P<.05$).
Hunter et al, 2012[75]	Any anxiety disorder (panic disorder, GAD, OCD, agoraphobia, and PTSD)	Any pregnancy time point	Infant P50 auditory sensory gating at mean infant age of 76 d (SD = 38)	In the absence of prenatal exposure to antidepressants, infants born to a mother with an anxiety disorder had significantly greater impairment of P50 sensory gating than infants born to a mother with no identified anxiety disorder (Tukey-Kramer $P<.001$). Prenatal antidepressant exposure mitigated the effect of anxiety.

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Table 4 (continued). Outcomes Associated With Anxiety Disorders During Pregnancy

Study	Anxiety Disorder	Timing of Anxiety Disorder Diagnosis in Pregnancy	Outcome and When Assessed	Findings
Monk et al, 2004[79]	Any anxiety disorder (GAD, social phobia, simple phobia, agoraphobia without panic disorder)	24–26 Weeks' gestation	At 36 to 38 wk of pregnancy, psychophysiological measures (electrocardiogram, blood pressure, respiration, and fetal heart rate) were measured at baseline and during a Stroop challenge (a color-word matching task)	Although fetuses of women with diagnosed depression or with elevated subsyndromal anxiety (ie, did not meet criteria for an anxiety disorder but had high trait anxiety on self-report) showed significant fetal heart rate increases during the Stroop challenge test, fetuses of women with anxiety disorders had no significant response. Note: The anxiety disorders were grouped together, creating a very heterogeneous group that may have obscured patterns of fetal heart rate responses associated with different subtypes. The majority of the women with anxiety disorder were diagnosed with phobias and thus actually may have experienced their high anxiety on an intermittent basis, in contrast to depressed or high-anxiety women, who most likely had chronic levels of elevated anxiety.
Uguz et al, 2013[83]	GAD	GAD in pregnancy retrospectively diagnosed in early postpartum period	Brain-derived neurotrophic factor (BDNF) levels obtained from cord blood at delivery	Newborns of healthy mothers had approximately 2-fold higher BDNF levels compared to newborns of GAD mothers. Mean ± SD levels of infant cord blood BDNF in infants of women with and without GAD were 1.03 ± 0.38 ng/mL and 2.08 ± 0.91 ng/mL, respectively ($t = -5.14$, $P = .000$). Duration of GAD during pregnancy was the only variable correlating with infant BDNF levels ($r = -0.554$, $P = .014$). BDNF levels were unrelated to maternal age, number of children, duration of pregnancy, anxiety severity, and infant birth weight.

Abbreviations: ACTH = adrenocorticotropic hormone, CRF = corticotrophin-releasing factor, EPDS = Edinburgh Postnatal Depression Scale, FHR = fetal heart rate, GAD = generalized anxiety disorder, ICU = intensive care unit, MDD = major depressive disorder, NOS = not otherwise specified, OCD = obsessive-compulsive disorder, OR = odds ratio, PTSD = posttraumatic stress disorder, RR = relative risk, SES = socioeconomic status, SGA = small for gestational age, WHOQOL-BREF = World Health Organization Quality of Life Assessment-BREF.

Other maternal outcomes examined included quality of life, fear of childbirth, and cortisol levels in pregnancy. Gezgniç et al[70] reported a significantly lower quality of life in pregnant women with OCD compared to matched pregnant controls without OCD. In 2 studies comparing the same sample of women with blood/injection phobia in pregnancy to control women, both higher incidence of fear of childbirth[76] and higher salivary cortisol level during pregnancy[77] were found in the phobic women.

Obstetric outcomes. Six studies examined the association of obstetric outcomes with maternal anxiety disorders during pregnancy. Birth weight (or gestational size) and/or preterm delivery (or gestational age) were examined outcomes in all 6. There were mixed findings regarding whether anxiety disorders affect birth weight. Three reported no significant differences in regard to infant birth weight when comparing infants of control women without the condition to infants of women with any anxiety disorder,[68] PTSD,[39] or GAD.[82] Other studies, however, did find significant differences in infant birth weight or size for gestational age. Compared to women without the condition, women with blood/injection phobia in pregnancy were significantly more likely to have infants who were small for gestational age.[76] Birth weight was significantly lower in infants of women with PSTD in pregnancy compared to women without the diagnosis[81] and in infants of mothers with panic disorder in pregnancy than in infants of healthy control women.[84] In a study[82] that compared 4 groups of pregnant women (women with major depression, GAD, or panic disorder and healthy controls), infants of women with panic disorder had the lowest birth weights, significantly lower than infants of women with depression or GAD or healthy controls.

There were similarly mixed findings regarding anxiety disorders in pregnancy and gestational age at delivery or preterm birth. Three studies reported shorter gestational age or preterm birth among infants of women with panic disorder,[82] blood/injection phobia,[76] or women with PTSD.[81] Other studies reviewed reported no difference between infants of control women and infants of women with panic disorder,[84] PTSD,[39] or any AD.[68]

Additional obstetric outcomes were examined by Lilliecreutz and colleagues,[76] who reported that, compared to controls, women with blood/injection phobia had higher rates of elective cesarean section, premature delivery, preeclampsia, and premature contractions. Their infants had higher neonatal morbidity, were more often small for gestational age, and had a longer postpartum hospital stay. Andersson and colleagues[68] examined several obstetric and neonatal outcomes and found no significant differences in outcomes between women with anxiety disorder in pregnancy and healthy controls.

Fetal, neonatal, and infant outcomes. Six studies (3 utilizing the same sample[72–74]) examined fetal/infant outcomes associated with maternal anxiety disorders during pregnancy. One study[83] found significantly higher brain-derived neurotropic factor (BDNF) in the cord blood of newborns of mothers with no psychiatric disorder compared to mothers with GAD in pregnancy, suggesting a possible negative influence of GAD on fetal neurodevelopment through lower BDNF levels. In a study examining fetal heart rate in response to maternal stress,[79] the

Stroop Challenge test was administered at 36 to 38 weeks' gestation to 57 women, 11 with an anxiety disorder, 11 with a depression diagnosis, and 35 without psychiatric diagnosis. Participants were subdivided into 3 groups (high anxiety, middle anxiety, and low anxiety) based on the State Trait Anxiety Inventory. Fetuses of women with depression or with high anxiety, but who did not meet criteria for an anxiety disorder, showed significant fetal heart rate increases during the Stroop test; however, fetuses of women with anxiety disorders had no significant response. The study authors suggested that the lack of response among fetuses of mothers with anxiety disorder may have been due to (1) heterogeneity of disorders in the anxiety disorder group; (2) uneven distribution of birth weight among groups, with trend for heavier weight in infants in the anxiety disorder group, which may affect fetal heart rate reactivity; and (3) the fact that the majority of mothers with anxiety disorder were diagnosed with phobias and may actually experience their high anxiety on an intermittent basis, whereas depressed women and those with high-anxiety symptoms very likely have chronic levels of elevated anxiety.

In a prospective, longitudinal study, Grant and colleagues[72] examined outcomes in a sample of infants whose mothers (n = 17) met criteria for at least 1 anxiety disorder during the last 6 months of pregnancy and 71 control women with no diagnosis during pregnancy. At age 7 months, infants and mothers attended a 1-hour laboratory session in which they took part in the still-face procedure, a short interactive stress paradigm used in many research studies to induce and examine infant response to a mildly stressful event. Infant salivary cortisol level was measured upon arrival and at 15, 25, and 40 minutes following the still-face procedure, and maternal sensitivity to infant distress and nondistress was observed. There was a significant difference between infants of prenatally anxious mothers and infants of women with no anxiety disorder in their overall pattern of stress-induced cortisol response, independent of maternal depressive symptoms and concurrent (postpartum) symptoms of anxiety and depression. Although maternal sensitivity was also independently associated with infant cortisol response, it did not moderate the association between prenatal anxiety disorder and infant cortisol response. In 2 related studies using the same sample,[73,74] maternal prenatal anxiety disorder did not predict infant response/reactivity to the still-face procedure. Only the interaction between prenatal anxiety disorder and maternal sensitivity to the infant significantly predicted infant reactivity. In addition to the laboratory visit, the same mother-infant dyads received a home visit at which assessments of the 7-month-old infants' mental and psychomotor development were conducted using the Bayley Scales of Infant Development.[88] No significant differences were found between infants of mothers with anxiety disorders during pregnancy and infants of control mothers on either mental or psychomotor development.

A study by Hunter and colleagues[75] examined P50 auditory sensory gating in infants of mothers with or without an anxiety disorder diagnosis in pregnancy (N = 242), some with concurrent antidepressant exposure. P50 auditory sensory gating has been reported to be impaired in a number of psychiatric disorders characterized by attentional dysfunction[75] and is regarded as a putative marker for early attentional processes in infants. In this study, infant P50 auditory sensory gating was recorded during active sleep at a mean age of 76 days (SD = 38). Infants whose mothers had any anxiety disorder diagnosis during pregnancy but no prenatal antidepressant exposure had diminished P50 sensory gating in infancy; however, prenatal antidepressant exposure mitigated this effect. Infants born to a mother with an anxiety disorder untreated by an antidepressant had more impaired P50 sensory gating than infants born to a mother with no identified anxiety disorder in pregnancy, a finding that suggests prenatal treatment implications of both antidepressants and interventions to increase maternal sensitivity.

Interventions for Treatment of Anxiety Disorders in Pregnancy

No randomized controlled trials of treatment for anxiety disorders in pregnancy were identified. Only 1 treatment trial[85] was found: an open trial of group cognitive-behavioral therapy (CBT) for pregnant women with blood/injection phobia. Thirty women participated in a 2-session CBT group therapy led by a CBT therapist and a midwife. The 2 sessions, held 4 weeks apart, included education on and exposure to different functions of lancets, syringes, injection needles, and intravenous catheters and education on symptoms of phobic reactions and how to manage physical symptoms and associated cognitions. As homework, participants were given needles, lancets, and syringes to take home and look at and touch. At session 2, participants were exposed to a hierarchy of anxiety-provoking situations 1 or more times: pricking a finger, subcutaneous injection in the arm, vein puncture, and insertion of an intravenous catheter. Both CBT sessions included a 5-minute relaxation exercise. The main outcomes of degree of phobia were self-rated using the Injection Phobia Scale-Anxiety (IPSA) and the Injection Phobia Scale-Avoidance (IPSAV) before and after each group therapy session and at 3 months after delivery. Outcomes of women who received the treatment were compared against those of 2 control groups: pregnant women with untreated blood/injection phobia (n = 46) and healthy pregnant women (n = 70). Treatment group scores were significantly reduced on both the IPSA and IPSAV over the whole study period ($P < .001$ for each scale) and when scores before and after each of the 2 treatment sessions were compared ($P < .001$ for each session). Compared to the control groups, the CBT group had significantly higher scores of phobic symptoms compared to both untreated and healthy women before the first treatment session ($P < .001$). At the postpartum follow-up, the CBT group scored significantly lower than the untreated women, but higher than the healthy controls ($P < .001$). Overall, the treatment reduced pregnant women's level of phobic symptoms significantly, and improvements were maintained at 3-month postpartum follow-up.

DISCUSSION

Main Findings

Our review highlights several important findings. We found that the prevalence of anxiety disorders is high among pregnant women. However, there is considerable variability in prevalence estimates for specific disorders and for any anxiety disorder among the studies, and evidence to date is inconclusive as to whether anxiety disorder prevalence among pregnant women differs from that in nonpregnant populations. In addition, at present it is not possible to discern whether there are differences in rates of anxiety disorders at various stages of pregnancy.

A small number of studies provided information regarding onset and course of anxiety disorders in pregnancy, with OCD and panic disorder best studied. There was a wide range in the proportion of women experiencing pregnancy onset of OCD or panic disorder. Although most women with preexisting OCD reported no change in OCD symptoms during pregnancy, there was considerable variation. The course of panic disorder varied widely among the studies, with no consistent pattern detected. For both OCD and panic disorder, symptoms may worsen, improve, or stay the same during pregnancy, indicating the need for a watchful and individualized approach to management. Limitations of these studies include small sample sizes, retrospective design and inherent recall bias, and little control for potential confounders, including pharmacologic and psychotherapeutic treatment. Missing from the literature was any exploration of whether women with psychiatric illness who become pregnant and who may discontinue their psychiatric medications for fear of prenatal exposure of offspring to these agents have an increased risk of relapse during pregnancy. This represents an important area for future study.

Our review of risk factors for anxiety disorders in pregnancy revealed limited findings. Only 4 studies examined risk factors for any anxiety disorder, and only 3 potential factors (single marital status, low SES, and primiparity) were examined in more than 1 study–all with conflicting results. This lack of evidence indicates a clear need for further research to identify factors that increase risk for pregnant women so that targeted monitoring and preventive interventions can be implemented.

In terms of maternal outcomes associated with prenatal anxiety disorder, 6 studies reported statistically significant associations between prenatal anxiety disorders and postpartum depression, although there were mixed findings regarding specific anxiety disorders, indicating a need for further research to determine postpartum depression risk in regard to different specific anxiety disorders. Our finding that prenatal anxiety disorders increase risk for development of postpartum depression is supported by previous research that has shown that anxiety disorders often precede development of depression.[89–91] A recent study by Prenoveau et al[92] reported that postpartum GAD similarly raises risk for the development of postpartum major depressive disorder (MDD). These findings highlight the importance of identifying pregnant women with anxiety disorders and offering effective treatments to both treat maternal anxiety disorders and prevent postpartum MDD. Having a prenatal anxiety disorder was also found to be a risk factor for postpartum anxiety disorders in 1 study,[71] and other single studies reported lower quality of life in pregnant women with OCD[70] and greater fear of childbirth and higher salivary cortisol in pregnant women with blood/injection phobia.[76,77]

Six studies[39,68,76,81,83,84] examined effects of maternal prenatal anxiety disorders on obstetric/neonatal outcomes, with mixed findings regarding effects on infant birth weight/size or gestational age at delivery, indicating a clear need for more research on this important topic. A growing body of research has demonstrated that elevated maternal anxiety symptom levels in pregnancy are associated with adverse infant outcomes.[13b,14,16,19,93–95] Therefore, it is surprising that so few studies were found that examined the effects of diagnosed anxiety disorders on the fetus or infant. One[79] examined an effect of maternal anxiety disorder on the fetus, reporting that, whereas fetuses of mothers with prenatal depression or with high anxiety (but without an anxiety disorder) showed a significant heart rate increase, fetuses of mothers with anxiety disorder in pregnancy showed no significant response. Two studies examined 7-month-old infants' responses to a mild stressor. Infants of prenatally anxious mothers had significantly higher cortisol levels than infants of mothers without an anxiety disorder in pregnancy[72] but showed no significantly different behavioral response/reactivity to the stressor.[74] Another study[75] showed that infants of mothers with an anxiety disorder in pregnancy (and no antidepressant exposure) had decreased P50 sensory gating—a possible marker for early attentional processes in infants. This finding was mitigated by antidepressant treatment, demonstrating the importance of studying treated versus untreated illness.

Although it was beyond the scope of this review to fully investigate comorbidity of anxiety disorders with depression and other disorders, rates of comorbid psychiatric disorders were high in the 10 studies in our review in which comorbidity was reported. This finding is consistent with previous research showing that anxiety disorders and depression are highly comorbid in general populations[1,89,96,97] as well as in postpartum populations.[98–100] The high comorbidity of depression, multiple anxiety disorders, or both with anxiety disorders in pregnancy is of great clinical relevance, as such comorbidity increases chronicity, functional impairment, and suicidality and is associated with a less favorable prognosis than that with a single diagnosis.[99,101–104]

The review reveals a paucity of research regarding treatment for anxiety disorders in pregnancy. No randomized controlled trials were identified. The only study of anxiety disorder treatment in pregnancy was an open trial of a short intervention for needle/injection phobia. While it may be reasonable to assume that anxiety disorder treatments that are effective in nonpregnant populations might be effective for

pregnant women as well, there is a current lack of evidence. There is a need for studies of treatments specifically geared toward the needs of pregnant women.

There are several important limitations to the available data. First, there is significant heterogeneity among studies, including substantial diversity of populations studied, risk factors examined, outcomes analyzed, and confounders controlled for in statistical analyses. In addition, the methodological quality of the studies differed considerably. Although 57 studies were included, these represented the available literature addressing several research questions regarding multiple specific anxiety disorders as well as any anxiety disorder during pregnancy. Thus, the available research on anxiety disorders in pregnancy is actually quite limited, and there is a need for much further study to satisfactorily answer the research questions posed in this review. At present, there is a limited evidence base to guide current practice and decision making.

Strengths and Limitations

This review has a number of strengths. We conducted a systematic search using inclusive search strategies. We included studies using clearly defined criteria to minimize selection bias. Only studies in which anxiety disorders were diagnosed by using a clinical interview were included, thus ensuring an important indicator of quality. We acknowledge several limitations of our review as well. It included studies published only in English. We did not attempt to include gray literature but considered only published studies. In order to enhance generalizability, we excluded specific subpopulations for whom vulnerability to anxiety disorders during pregnancy may be greater. We excluded samples comprising specific subpopulations of pregnant women, such as adolescents younger than 17 years, disaster survivors, and women with abuse histories, substance abuse problems, or specific medical or gestational problems (eg, hyperemesis, previous still birth). In addition, most studies excluded women who could not read and understand the dominant language of country in which the study was conducted, thereby limiting inclusion of immigrant and refugee women for whom anxiety may be increased. Anxiety disorders in these specific populations represent areas for further study and review.

Recommendations and Implications

Although the evidence provided from this review is limited, it does identify several areas for additional research and may provide clinicians with some suggestions to guide management. Identification and treatment of anxiety disorders in pregnancy are especially important due to the potential impact of untreated anxiety disorders during pregnancy on maternal, obstetric, and fetal/child outcomes. As recommended screening for perinatal depression becomes integrated into obstetric and other practice settings,[105–107] screening for anxiety disorders should also be considered. Currently, there are no screening tools specific to anxiety and pregnancy, and it is unclear whether screening efforts to detect perinatal depression are adequate for the detection of prenatal anxiety disorders. As the course of anxiety disorders varies substantially among women, individualized risks and benefits of treatment interventions must be considered. At this time, treatment research is needed to determine the most effective treatments for anxiety disorders during pregnancy. Psychotherapies that are adapted specifically to the context of pregnancy would be attractive first-line treatments. However, some women with severe anxiety often require pharmacologic treatment. In the case of medication selection, it is rational to select medications with the most complete reproductive safety profiles and to have the patient engage in concurrent psychotherapy.

CONCLUSIONS

Although research on perinatal anxiety disorders lags greatly behind that of perinatal depression, studies of anxiety disorders in pregnancy have increased, with the majority of studies included in this review (46 studies) published in the past decade, compared to only 11 in the prior decades. This is good news. However, the findings of this review reveal that our current knowledge is limited and there is much we don't yet understand about anxiety disorders in pregnancy. Additional research is required to develop a solid evidence base on which to guide clinical practice.

Drug names: paroxetine (Paxil, Pexeva, and others).

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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.

Supplementary material follows this article.

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Supplementary Material

Article Title: Anxiety Disorders During Pregnancy: A Systematic Review

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List of Supplementary Material for the article

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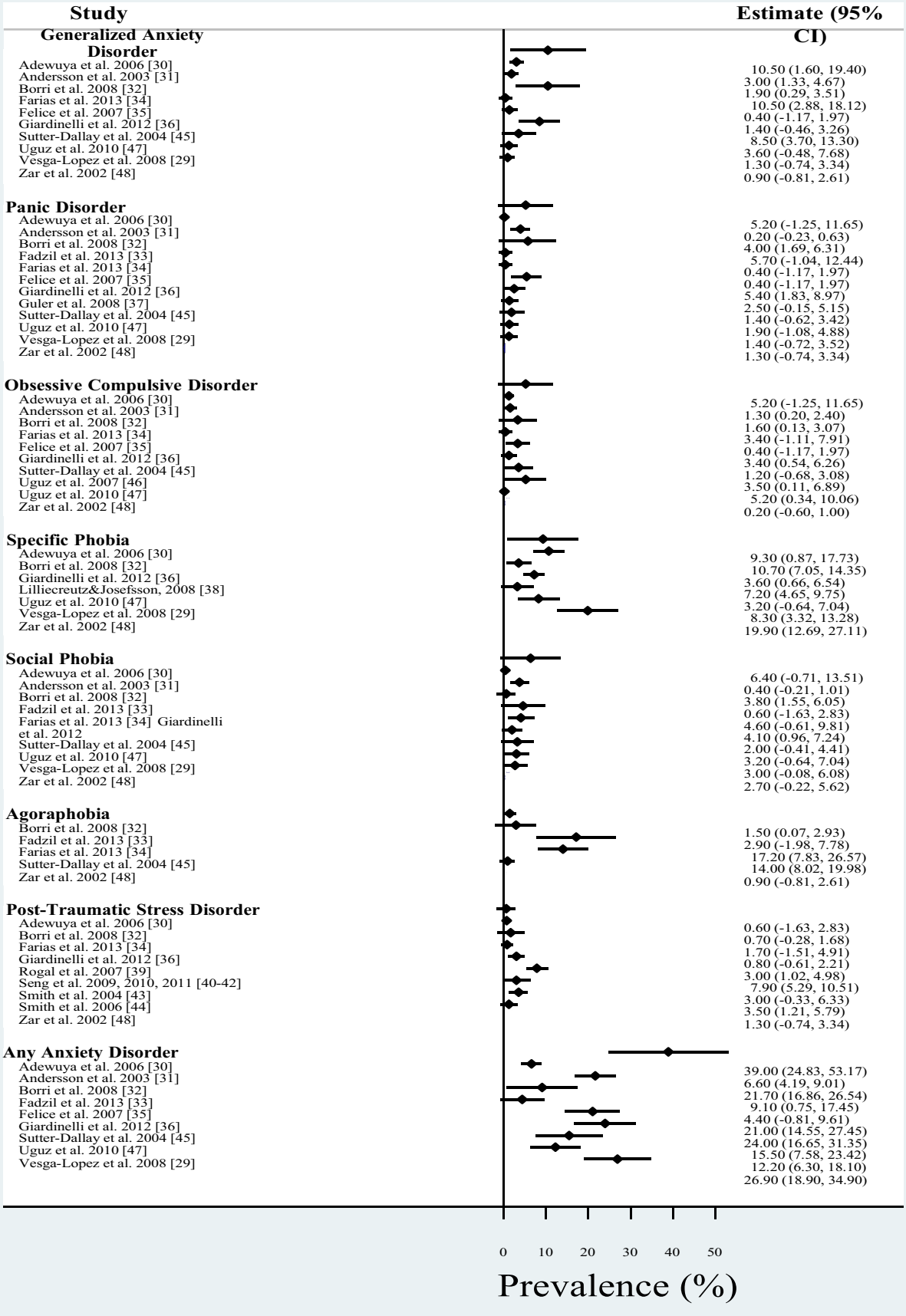
Supplementary eFigure 1: Forest Plot



Supplementary eTable 1: Psychiatric Diagnoses Comorbid with Anxiety Disorders in Pregnancy

Study	N[1]	MDD	Comorbid Anxiety Disorder	Alcohol or Illicit Drug Use
OCD				
Uguz et al. 2007	52	6 (11.5%)	19 (36.5%) any AD	-
Chaudron & Nirodi, 2010	7	4 (57%) mood or anxiety disorder		-
Panic Disorder				
Rambelli et al. 2010	43	18 (41.9%)	6 (14%) any anxiety disorder	
Warren, Racu, Gregg, & Simmens, 2006	25	2 (8%)	-	-
Wisner, Peindl, & Hanusa, 1996	22	13 (59%)	19 (86%) agoraphobia	-
PTSD				
Seng et al. 2009	125	44 (35%)	18 (14.4%) GAD	-
Smith et al. 2006	33	22 (66.7%)[2]	12 (36.4%)[2]PD	27.3%[3]
Rogal et al. 2007	31	7 (22.6%) MDD; 11 (35.5%) minor depression	9 (29%) PD	13 (41.9%)
Any Anxiety Disorder				
Borri et al. 2008	231	47 (20.3%) mood disorder	23 (10%) had 2 or more anxiety disorders	-
Sutter-Dallay et al. 2004	119	Women with one or more anxiety disorders were 4 times more likely to have MDD than those without an anxiety disorder (number and percent not reported)	25 (21%) 2 or more anxiety disorders	-

MDD = Major depressive disorder; PD = Panic disorder

[1] N refers to participants with relevant anxiety disorder in pregnancy

[2] Diagnosed using the Patient Health Questionnaire

[3] Determined by questionnaire

Supplementary eTable 2: New Onset of Anxiety Disorders among Women with Prior or Current Pregnancies

Study[a]	Sample Size and Criteria	Onset of Disorder in Pregnancy
OCD		
Forray et al. 2010[55]	78 clinic patients with OCD and prior pregnancy	12 (15.4%)
Labad et al. 2005[50]	17 clinic patients with OCD and prior pregnancy	1 (6%)
Labad et al. 2010[58]	35 clinic patients with OCD and at least one child	2 (5.7%)
Maina et al. 1999[59]	16 clinic patients with at least one child and who reported onset of OCD within the past 2 years	0 (0%)[b]
Neziroglu et al. 1992[60]	59 clinic patients with OCD and at least one child	23 (39.0%)[c]
Uguz et al. 2007[46]	15 pregnant women with OCD diagnosed at 3rd trimester	2 (13.3%) (both in 2nd trimester).
Williams and Koran 1997[66]	38 clinic patients with OCD and prior pregnancy	5 (13%)

Panic Disorder		
Guler, Koken et al. 2008[56]	13 pregnant women with PD diagnosed in 3rd trimester	7 (53.8%). Developed in weeks 6 – 28 of pregnancy.
Northcott and Stein 1994[61]	97 clinic patients who developed PD either before, during, or between pregnancies	3 (3%)
Rambelli et al. 2010[80]	43 pregnant women who met criteria for PD at 12-15 weeks gestation	5 (11%)
Wisner et al. 1996[67]	22 women with PD who were pregnant or had children under age 3 years	0 had first onset of PD during pregnancy. 2 (9.1%) developed new episode of PD during pregnancy.

[a] N refers to participants relevant to pregnancy onset only.
[b] One participant developed OCS during pregnancy but did not meet full OCD criteria until after delivery.
[c] This was the first pregnancy for 12 (52.2%), the second pregnancy for 8 (34.8%), and the third pregnancy for 3 (13%).
OCD = obsessive-compulsive disorder; OCS = obsessive-compulsive symptoms; PD = panic disorder

Supplementary eTable 3: Findings on Risk Factors for any Anxiety Disorder Diagnosis in Pregnancy (from Multivariate Analyses)

Factor	A Significant Risk Factor	Not a Significant Risk Factor
Low educational level	Borri et al. 2008[32] (OR = 2.34, 95% CI = 1.49-3.67; p < .001)	
Low socioeconomic status	Borri et al. 2008[32] (OR = 3.03, 95% CI = 1.51-6.06; p < .001)	Aduwuya et al. 2006[30]
Single marital status	Borri et al. 2008[32] (OR = 2.01, 95% CI = 1.2-3.29; p < .001)	Aduwuya et al. 2006[30]; Felice et al. 2007[35]
Age < 25 years	Aduwuya et al. 2006[30] (OR 4.62, 95% CI 2.39-8.92; p = sig.)	
Older age	Felice et al. 2007[35] (OR 1.135, 95% CI 1.01-1.27, p = .029)	
Primiparity	Aduwuya et al. 2006[30] (OR 3.90, 95% CI 2.00-7.59; p = sig.)	Felice et al. 2007[35]
Having a medical condition	Aduwuya et al. 2006[30] (OR 3.60, 95% CI 1.28-10.12; p = sig.)	
Depression	Fadzil et al. 2013[33] (AOR 6.66; 95% CI 1.79- 24.77, p = .005)	
Personal psychiatric history	Felice et al. 2007[35] (OR 2.28, 95% CI 1.29-4.02, p = .004)	
Gestational age < 20 weeks	Fadzil et al. 2013[33] (AOR 4.85; 95% CI 1.609 - 14.64; p = .005)	
Employment status		Borri et al. 2008[32]
Smoking		Felice et al. 2007[35]
Support from partner		Felice et al. 2007[35]
Support from mother		Felice et al. 2007[35]
Family psychiatric history		Felice et al. 2007[35]
Partner's reaction to pregnancy		Felice et al. 2007[35]