The prevalence of antenatal and postnatal co-morbid anxiety and depression: a meta-analysis

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To date, the precise prevalence of co-morbidity of anxiety and depression in the perinatal period is not well known. We aimed to estimate the prevalence of co-morbid anxiety and depression in the antenatal and postnatal periods. Systematic searches of multiple electronic databases were conducted for studies published between January 1950 and January 2016. We included 66 (24 published and 42 unpublished) studies incorporating 162 120 women from 30 countries. Prevalence of self-reported antenatal anxiety symptoms and mild to severe depressive symptoms was 9.5% [95% confidence interval (CI) 7.8–11.2, 17 studies, n = 25592 and of co-morbid anxiety symptoms and moderate/severe depressive symptoms was 6.3% (95% CI 4.8–7.7, 17 studies, n = 27 270). Prevalence of a clinical diagnosis of any antenatal anxiety disorder and depression was 9.3% (95% CI 4.0–14.7, 10 studies, n = 3918) and of co-morbid generalized anxiety disorder and depression was 1.7% (95% CI 0.2–3.1, three studies, n = 3085). Postnatally between 1 and 24 weeks postpartum, the prevalence of co-morbid anxiety symptoms and mild to severe depressive symptoms was 8.2% (95% CI 6.5–9.9, 15 studies, n = 14731), while co-morbid anxiety symptoms and moderate/severe depressive symptoms was 5.7% (95% CI 4.3–7.1, 13 studies, n = 20 849). The prevalence of a clinical diagnosis of co-morbid anxiety and depression was 4.2% (95% CI 1.9-6.6, eight studies, n = 3251). Prevalence rates did not differ with regard to year of publication, country income, selection bias and attrition bias. The results suggest that co-morbid perinatal anxiety and depression are prevalent and warrant clinical attention given the potential negative child developmental consequences if left untreated. Further research is warranted to develop evidence-based interventions for prevention, identification and treatment of this co-morbidity.

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Introduction

Epidemiological studies consistently demonstrate high rates of co-morbidity between anxiety and depressive disorders (Broekman *et al.* 2014; Falah-Hassani *et al.* 2016). In a cohort study conducted in the Netherlands among those with a depressive disorder, 67% had a current co-morbid anxiety disorder (Lamers *et al.* 2011). Of those with a current anxiety disorder, 63% had a current depressive disorder. Further, in 57% of co-morbid cases, anxiety preceded depression, and in 18% depression preceded anxiety. Data from the US-based National Comorbidity Survey of more than 8000 community-living persons confirm that co-morbid anxiety disorders often predate depressive disorders (Kessler *et al.* 1996).

Co-morbid anxiety and depression have been associated with sociodemographic factors such as female

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gender, not having a partner, lower socio-economic status and lower educational level (de Graaf et al. 2002; Alonso et al. 2004; Fichter et al. 2010), and with vulnerability factors such as parental psychiatric history, childhood trauma, negative life events and neuroticism (de Graaf et al. 2002). They are further associated with important clinical factors including earlier age at onset of first disorder, more severe and persistent symptomatology (Lamers et al. 2011), increased disability and impaired functioning (Kessler & Frank, 1997; Fichter et al. 2010), higher health care utilization (Kessler et al. 1994), poorer response to treatment (Merikangas et al. 2003; Rush et al. 2005) and increased risk to commit suicide (Tavares et al. 2012). Individuals experiencing co-morbidity also have fewer social interactions and demonstrate greater social dysfunction (Nakayama et al. 2014).

Despite high rates of co-morbidity between anxiety and depressive disorders and women's increased vulnerability to experience these conditions during the perinatal period, the precise prevalence of this comorbidity is not well known. Estimates of the prevalence of co-morbid perinatal anxiety and depression have varied across studies. Previous studies have

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reported the prevalence of co-morbid anxiety and depression to be between 4 and 8% in pregnancy (Fisher et al. 2010; Grant et al. 2012) and between 2% and 13% in the first 6 months postpartum (Reck et al. 2008; Austin et al. 2010; Tavares et al. 2012). The identification and management of co-morbid anxiety and depression in the perinatal period are important given the well-documented adverse effects of anxiety and depression on maternal and child outcomes. Primary care practitioners and those providing care across the perinatal period have an opportunity to assess maternal mental health. However, little is known about their ability to recognize and manage perinatal anxiety (Ford et al. 2017). For non-perinatal anxiety in primary care settings, health care providers fail to diagnose anxiety disorders in half of cases (Olariu et al. 2015). Moreover, only a small proportion of obstetricians and midwives screen for anxiety during pregnancy (Coleman et al. 2008). The aim of this systematic review and meta-analysis was to estimate the prevalence of co-morbid anxiety and depression in the antenatal and postnatal periods.

Method

Search strategy and study eligibility

The protocol and reporting of the results of this systematic review and meta-analysis were based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al. 2009). Comprehensive literature searches were conducted in PubMed, Embase, PsycINFO, Web of Science, Scopus, ResearchGate and Google Scholar from their inception until January 2016 using predefined search terms (online Supplementary Table S1). We used Medical Subject Headings (MeSH) terms and text words in PubMed, and Emtree terms and text words in Embase. The titles and abstracts of all identified citations were screened for relevance and the full texts of potentially relevant articles were obtained and assessed for eligibility. In addition, the reference lists of relevant articles were hand-searched.

Studies were eligible for inclusion if they: (a) assessed antenatal or postnatal anxiety and depressive symptoms using a validated diagnostic or self-report instrument; (b) reported the results of peer-reviewed research based on cross-sectional or cohort studies; and (c) reported the results for co-morbid anxiety and depressive symptoms or the authors provided the reviewers with the requested data in order to estimate the prevalence of co-morbid anxiety and depressive symptoms. Studies were excluded if they: (a) were conducted among self-selected volunteers; (b) over-sampled psychiatric patients; (c) recruited

women experiencing a medically high-risk pregnancy; (d) reported results only for a subsample of a study population; (e) reported results only for a subgroup of anxiety disorders, e.g. panic disorder, except generalized anxiety disorder; (f) reported mean data only; (g) reported combined prevalence of either anxiety or depression; or (h) did not report a cut-off point for anxiety or depressive symptoms. Study authors were contacted by email for additional information, particularly those who reported only mean data, not cut-off data, or had missing information. We made efforts to ensure that all of the studies included in the meta-analyses used relatively representative samples. Volunteers are generally healthier than the general population. The generalizability of the results of self-selected volunteers to childbearing women is limited (Leung et al. 2013).

Data extraction and quality assessment

We extracted individual details of the included studies such as year of publication, country, study population, recruitment method, sample size, measure of anxiety and depression, cut-off points and timing of measurement, and prevalence of co-morbid anxiety and depression. The risk of bias in the included studies was independently rated by two reviewers (K.F.-H. and R.S.) using criteria adapted from the Effective Public Health Practice Project Quality Assessment Tool (Armijo-Olivo *et al.* 2012). Three domains were assessed: selection bias, detection bias and attrition bias (online Supplementary Table S2). Any disagreements in quality ratings were resolved by discussion (K.F.-H. and R.S.), and if necessary with the involvement of another author (C.-L.D.).

Data synthesis and meta-analysis

Many studies reported an estimate for the prevalence of antenatal or postnatal co-morbid anxiety and depressive symptoms for more than one time point for the same participants. In order to include each study only once in a meta-analysis, an overall prevalence of antenatal or postnatal co-morbid anxiety and depressive symptoms was estimated using an average sample size and an average number of events. The prospective cohort studies included in the current meta-analysis determined the prevalence of co-morbid anxiety and depressive symptoms rather than the incidence. We therefore combined both cross-sectional and cohort studies in a single analysis. Anxiety and depression were measured using diverse scales and cut-off scores and at differing antenatal or postnatal time periods. We performed subgroup analyses for studies on self-reported depressive symptoms and clinically diagnosed depression. We also performed subgroup analyses for studies on self-reported mild to severe

depressive symptoms and self-reported moderate to severe depressive symptoms. Following published recommended cut-off points, mild to severe depressive symptoms were defined as Edinburgh Postnatal Depression Scale (EPDS) >9, Center for Epidemiologic Studies Depression Scale (CES-D) >16, Hospital Anxiety and Depression Scale (HADS) >8, Depression Anxiety and Stress Scale (DASS) >10, Hopkins Symptom Checklist-25 (HSCL-25) >1.75, or Self-Rating Scale for Depression (SRDS) >40. Moderate to severe depressive symptoms were defined as EPDS >12, CES-D >20, HADS >11, DASS >14, or Beck Depression Inventory (BDI) >20. Furthermore, we performed subgroup analyses for studies on trait anxiety, self-report anxiety symptoms, any clinically diagnosed anxiety disorder, and generalized anxiety disorder.

We used a random-effects meta-analysis to combine the estimates of different studies (Higgins & Green, 2009). The presence of heterogeneity across the studies was assessed by the I^2 statistic (Higgins & Thompson, 2002). An I^2 statistic less than 25% indicates small inconsistency and more than 50% indicates large inconsistency (Higgins & Thompson, 2002). We used meta-regression to assess the differences between subgroups (Higgins & Green, 2009). We performed subgroup analyses according to year of publication, country of study, pregnancy trimester, postpartum time period, selection bias and attrition bias. Stata, version 13 (StataCorp LLC, USA) was used for the meta-analyses.

Results

Study characteristics

The study selection process is presented in online Supplementary Fig. S1. The literature search yielded 23 464 references, of which 22 685 were excluded following title and abstract screening by the first author (K.F.-H.). Overall, 779 full papers were retrieved and assessed by two reviewers. Of these, 77 studies were relevant following full-text screening. From these 77 studies, a further 11 were excluded from the meta-analyses: five studies were conducted among self-selected volunteers (Wenzel et al. 2005; Moss et al. 2009; McFarland et al. 2011; McPhie et al. 2015; Sockol & Battle, 2015), two used non-validated tools to assess anxiety or depressive symptoms (Milgrom et al. 2008; Farr et al. 2014), one reported mean anxiety and depressive symptoms scores (van Bussel et al. 2009), one estimated prevalence of co-morbid postpartum anxiety and depressive symptoms after the first year of postpartum (Nguyen et al. 2015), one recruited women who already sought psychiatric treatment (Swanson et al. 2011), and finally one study measured both anxiety and depression with a single scale but did not give separate scores for anxiety and depression (Karmaliani et al. 2009).

In total, 66 studies (n = 162120 women) on antenatal or postnatal co-morbid anxiety and depressive symptoms were included in the meta-analyses. Forty-two authors provided via email additional information to determine co-morbidity and enable study inclusion. Characteristics of the included studies are provided in online Supplementary Tables S3-S5. There were 44 studies that provided data on the prevalence of antenatal co-morbid anxiety and depressive symptoms and 36 studies that provided postnatal data. Three studies reported an estimate for the prevalence of co-morbid anxiety and depressive symptoms either at pregnancy or postpartum (online Supplementary Table S5). The included studies were conducted in 30 different countries spanning six continents. The countries with the largest number of included studies were the USA (n=13), Australia (n=8), Brazil (n=4), Canada (n=4) and the Netherlands (n=4). There were two studies from France, Germany, Greece, Italy, New Zealand, Norway, Portugal, Singapore, Tanzania, UK and Vietnam, and one study from Bangladesh, Croatia, Ghana, Hong Kong, Hungary, Ireland, Israel, Japan, Nigeria, Poland, Romania, Saudi Arabia, Switzerland and Turkey.

Prevalence of antenatal co-morbid anxiety and depression

Table 1 presents the prevalence of co-morbid anxiety and depression in the 1st, 2nd and 3rd trimesters of pregnancy. Meta-analytic pooling of the estimates yielded the prevalence of co-morbid anxiety symptoms and mild to severe depressive symptoms to be 11.6% [95% confidence interval (CI) 9.0–14.2, two studies, n =595] for the 1st trimester, 10.6% (95% CI 7.2-14.0, six studies, n = 9337) for the 2nd trimester, and 9.5% (95% CI 6.1–13.0, six studies, n = 3922) for the 3rd trimester (Table 1). The overall pooled prevalence for co-morbid anxiety symptoms and mild to severe depressive symptoms across the three trimesters was 9.5% (95% CI 7.8–11.2, 17 studies, *n* = 25 592, Fig. 1). The prevalence of co-morbid anxiety symptoms and moderate to severe depressive symptoms was 4.1% (95% CI 2.8–5.5, two studies, n = 812) for the 1st trimester, 7.5% (95% CI 3.6–11.3, five studies, n = 8570) for the 2nd trimester, and 6.6% (95% CI 3.7–9.5, five studies, *n* =8756) for the 3rd trimester (Table 1). The overall pooled prevalence for co-morbid anxiety symptoms and moderate to severe depressive symptoms across the three trimesters was 6.3% (95% CI 4.8-7.7, 17 studies, n = 27270, Table 1 and online Supplementary Fig. S2). The overall prevalence for co-morbid self-

 Table 1. Prevalence of antenatal co-morbid anxiety and depression

Time period 1st trimester			All studies					Studies w	Studies without high risk of selection or attrition bias				
	Measure	Outcome	No. of studies	Sample	Prevalence, %	95% CI	I ² , %	No. of studies	Sample	Prevalence, %	95% CI	I ² , %	
	Self-report	Depressive symptoms + trait anxiety	0					0					
		Mild to severe depressive symptoms + anxiety symptoms	2	595	11.6	9.0–14.2	99	2	595	11.6	9.0–14.2	99	
		Moderate to severe depressive symptoms + anxiety symptoms	2	812	4.1	2.8–5.5	99	1					
	Clinical	Depression + any anxiety disorder	1					1					
	diagnosis	Depression + generalized anxiety disorder	1					1					
2nd trimester	Self-report	Depressive symptoms and trait anxiety	2	2088	7.9	6.7-9.0	95	1					
	1	Mild to severe depressive symptoms + anxiety symptoms	6	9337	10.6	7.2–14.0	95	5	7541	9.8	5.5–14.1	95	
		Moderate to severe depressive symptoms + anxiety symptoms	5	8570	7.5	3.6–11.3	98	2	1342	9.4	7.9–11.0	99	
	Clinical	Depression + any anxiety disorder	4	2274	14.7	0.0-29.6	99	3	1363	8.3	0.0 - 19.1	99	
	diagnosis	Depression + generalized anxiety disorder	1					1					
3rd trimester	Self-report	Depressive symptoms + trait anxiety	2	596	8.2	6.0-10.4	95	2	596	8.2	6.0-10.4	95	
	-	Mild to severe depressive symptoms + anxiety symptoms	6	3922	9.5	6.1–13.0	91	5	1705	10.5	6.9–14.1	83	
		Moderate to severe depressive symptoms + anxiety symptoms	5	8756	6.6	3.7–9.5	97	4	6539	8.0	2.6–13.5	97	
	Clinical	Depression and any anxiety disorder	4	1372	3.7	1.3-6.0	84	3	881	3.8	0.2 - 7.4	89	
	diagnosis	Depression + generalized anxiety disorder	1					1					
1st, 2nd or 3rd	Self-report	Depressive symptoms + trait anxiety	5	2820	8.1	5.7-10.5	78	4	1758	8.6	5.7-11.6	74	
trimester		Mild to severe depressive symptoms + anxiety symptoms	17	25 592	9.5	7.8–11.2	95	14	22 804	9.8	7.8–11.8	95	
		Moderate to severe depressive symptoms + anxiety symptoms	17	27 270	6.3	4.8–7.7	97	11	15 891	7.6	5.5–9.8	97	
	Clinical	Depression + any anxiety disorder	10	3918	9.3	4.0-14.7	98	7	2428	6.9	2.8-11.0	95	
	diagnosis	Depression + generalized anxiety disorder	3	3085	1.7	0.2-3.1	79	3	3085	1.7	0.2-3.1	79	

CI, Confidence interval.

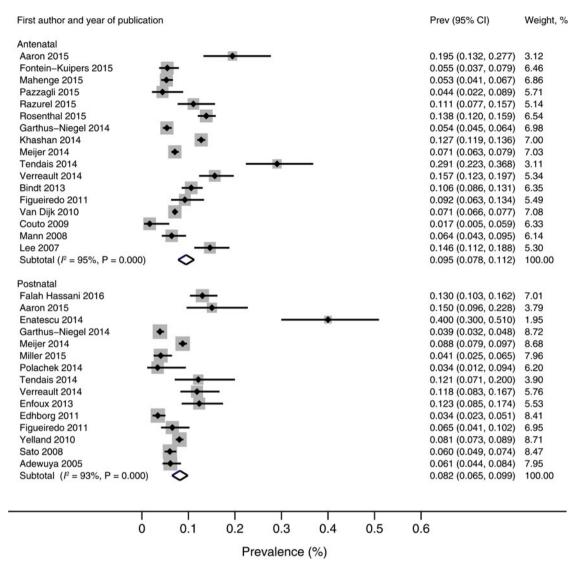


Fig. 1. Prevalence (Prev) of antenatal and postnatal (1-24 weeks) co-morbid mild to severe depressive and anxiety symptoms. CI, Confidence interval.

reported trait anxiety and depressive symptoms across the three trimesters was 8.1% (95% CI 5.7-10.5, five studies, n = 2820). The overall prevalence for a clinically diagnosed co-morbid anxiety and depression disorder across the three trimesters was 9.3% (95% CI 4.0-14.7, 10 studies, n = 3918, Table 1 and online Supplementary Fig. S3) and co-morbid generalized anxiety disorder and depression was 1.7% (95% CI 0.2–3.1, three studies, n = 3085).

Prevalence of postnatal co-morbid anxiety and depression

Table 2 shows the prevalence of co-morbid anxiety and depression at 1-4 weeks, 5-12 weeks, 1-24 weeks, and >24 weeks postpartum. The prevalence of postnatal (1-24 weeks postpartum) co-morbid trait anxiety and

depressive symptoms was 9.4% (95% CI 6.2-12.6, three studies, n = 1013). Meta-analytic pooling of the estimates yielded the prevalence of co-morbid anxiety symptoms and mild to severe depressive symptoms to be 7.6% (95% CI 3.7–11.4, 5 studies, n = 1941) for 1-4 weeks postpartum, 8.2% (95% CI 5.5-10.9, eight studies, n = 4632) for 5–12 weeks postpartum, and 8.2% (95% CI 6.5–9.9, 15 studies, *n* = 14731, Table 2 and Fig. 1) for 1-24 weeks postpartum. The prevalence of co-morbid anxiety symptoms and moderate to severe depressive symptoms was 6.3% (95% CI 2.2-10.5, three studies, n = 1814) for 1–4 weeks postpartum, 5.8% (95% CI 4.1–7.5, nine studies, n = 7705) for 5–12 weeks postpartum, and 5.7% (95% CI 4.3-7.1, 13 studies, n = 20849, Table 2 and online Supplementary Fig. S2) for 1–24 weeks postpartum. The prevalence of a clinically diagnosed co-morbid anxiety and

 Table 2. Prevalence of postnatal co-morbid anxiety and depression

Time period 1–4 weeks postpartum			All stud	lies				Studies w	Studies without high risk of selection or attrition bias				
	Measure			Io. of rudies Sample	le Prevalence, %	95% CI	I ² , %	No. of studies	Sample	Prevalence, %	95% CI	I ² , %	
	Self-report							1					
		Mild to severe depressive symptoms + anxiety symptoms	5	1941	7.6	3.7–11.4	91	5	1941	7.6	3.7–11.4	91	
		Moderate to severe depressive symptoms + anxiety symptoms	3	1814	6.3	2.2–10.5	90	2	1314	3.4	2.5–4.4	95	
	Clinical diagnosis	Depression + any anxiety disorder	0					0					
	· ·	Depression + generalized anxiety disorder	0					0					
5-12 weeks	Self-report	Depressive symptoms + trait anxiety	3	987	8.1	2.0-14.2	92	3	987	8.1	2.0-14.2	92	
postpartum	•	Mild to severe depressive symptoms + anxiety symptoms	8	4632	8.2	5.5–10.9	92	7	2415	9.9	6.1–13.6	92	
		Moderate to severe depressive symptoms and anxiety symptoms	9	7705	5.8	4.1–7.5	92	6	2262	8.0	3.7–12.4	94	
	Clinical diagnosis	Depression + any anxiety disorder	5	1207	3.5	1.8-5.3	65	4	908	4.1	1.7-6.4	72	
		Depression + generalized anxiety disorder	1					1					
1-24 weeks	Self-report	Depressive symptoms + trait anxiety	3	1013	9.4	6.2-12.6	58	3	1013	9.4	6.2-12.6	58	
postpartum		Mild to severe depressive symptoms + anxiety symptoms	15	14 731	8.2	6.5–9.9	93	12	8132	8.5	6.4–10.6	91	
		Moderate to severe depressive symptoms + anxiety symptoms	13	20 849	5.7	4.3–7.1	95	10	15 406	6.4	4.6–8.1	95	
	Clinical diagnosis	Depression + any anxiety disorder	8	3251	4.2	1.9-6.6	94	7	2952	4.6	1.9-7.3	95	
		Depression + generalized anxiety disorder	1					1					
>24 weeks	Self-report	Depressive symptoms + trait anxiety	1					0					
postpartum		Mild to severe depressive symptoms + anxiety symptoms	2	1828	5.2	4.2–6.2	97	2	1828	5.2	4.2–6.2	97	
		Moderate to severe depressive symptoms + anxiety symptoms	2	1692	3.1	2.3–3.9	97	1					
	Clinical diagnosis	Depression + any anxiety disorder	3	1515	8.0	0.6-15.5	89	2	1427	2.5	1.7-3.3	94	
	5	Depression + generalized anxiety disorder	0					0					

CI, Confidence interval.

depression disorder was 3.5% (95% CI 1.8-5.3, five studies, n = 1207) for 5–12 weeks postpartum and 4.2% (95% CI 1.9–6.6, eight studies, n = 3251, Table 2 and online Supplementary Fig. S3) for 1–24 weeks postpartum.

Prevalence of antenatal or postnatal co-morbid depression and anxiety

The prevalence rates of co-morbid depression and anxiety at 1st, 2nd or 3rd trimester of pregnancy, or 1-24 weeks postpartum as well as at 1st, 2nd or 3rd trimester of pregnancy, or 1-52 weeks postpartum are presented in Table 3. The prevalence of antenatal (1st, 2nd or 3rd trimester) or postnatal (1-24 weeks postpartum) co-morbid trait anxiety and depressive symptoms was 8.1% (95% CI 5.9–10.3, six studies, n = 2847, Table 3), co-morbid anxiety symptoms and mild to severe depressive symptoms was 8.6% (95% CI 7.2-9.9, 25 studies, $n = 33\,370$), co-morbid anxiety symptoms and moderate to severe depressive symptoms was 6.0% (95% CI 4.9–7.2, 24 studies, n = 122406), and clinically diagnosed co-morbid anxiety and depression disorder was 7.9% (95% CI 4.6-11.1, 16 studies, n = 6516).

Sensitivity analysis

Excluding studies with high risk of selection or attrition bias did not change significantly the prevalence estimates for self-reported co-morbid anxiety and depressive symptoms or a clinically diagnosed anxiety and depression disorder (Tables 1-3). Further, the prevalence of co-morbid anxiety and depressive symptoms or a clinically diagnosed anxiety and depression disorder did not differ with regard to year of publication ($\geq 2011 \ v. \leq 2010$), country income, selection bias and attrition bias (Table 4).

Discussion

This is the first systematic review and meta-analysis to estimate the prevalence of co-morbid anxiety and depression in the perinatal period. Included were 66 studies involving 162 120 women from 30 different countries. Overall, the prevalence rate for self-report anxiety and mild to severe depressive symptoms in the 1st trimester was 11.6%, decreasing slightly as the pregnancy progressed to 9.5% in the 3rd trimester. The prevalence of co-morbid symptoms across the three trimesters was 9.5%. Postnatally, 7.6% of women experienced anxiety and mild to severe depressive symptoms in the first 4 weeks following childbirth, with rates stabilizing at approximately 8.2% at 24 weeks. Similar patterns at lower rates were found for anxiety and moderate to severe depressive symptoms both antenatally and postnatally. When

diagnostic interviews were employed, the prevalence rate for a co-morbid anxiety and depression disorder during the 2nd trimester was 14.7%, decreasing significantly to approximately 3.7% in the 3rd trimester for an overall 9.3% rate across the pregnancy. The prevalence for a co-morbid anxiety and depression disorder continued to decrease postnatally and ranged from 3.5% to 4.2% in the first 24 weeks and then increased to 8.0% after 24 weeks postpartum. Very few studies provided data for co-morbid generalized anxiety disorder and depression either antenatally or postnatally. Overall, our findings demonstrate co-morbid anxiety and depression affects approximately one in 10 women during their pregnancy and one in 12 women postnatally. Given the well-documented negative effects of perinatal anxiety and depression on child cognitive, behavioral and emotional development, co-morbid anxiety and depression are an important public health issue that warrant further attention.

In understanding the results, it is important to note that the majority of studies assessed anxiety and depression using self-report instruments that measured symptoms rather than 'gold standard' diagnostic clinical interviews. While the sensitivity and specificity of these self-report instruments vary substantially, the most frequently used measures in this review were the State-Trait Anxiety Inventory (STAI) (Grant et al. 2008) for anxiety and the EPDS (Bergink et al. 2011) for depression. Self-report measures do have limitations, such as potentially inflated prevalence estimates, but they also have high clinical utility. Health professionals in obstetrics, midwifery, public health and primary care practices often have limited clinical expertise and time for diagnostic interviews. Since research clearly suggesting informal surveillance misses at least 50% of cases (Gavin et al. 2005), selfreport measures are crucial for systematic identification. The varying prevalence rates between the included studies may further be attributed to diverse recruitment strategies, inclusion and exclusion criteria, data collection methods, and follow-up time periods. Language or translation complexities and variations in conveying psychiatric symptoms are other potential methodological issues (Bandelow & Michaelis, 2015). While our results are not consistent with another systematic review that found rates of perinatal anxiety among World Bank-categorized low- and middleincome countries to be significantly greater than those reported in high-income countries (Dennis et al. 2017), in our review there were very few studies included from low- to middle-income countries. Additional research addressing perinatal mental health in low- and middle-income countries is required.

It is noteworthy that many of the studies included in this review presented perinatal anxiety and depression

Table 3. Prevalence of antenatal or postnatal co-morbid anxiety and depression

			All studies						Studies without high risk of selection or attrition by			
Time period	Measure	Outcome	No. of studies	Sample ^a	Prevalence, %	95% CI	I ² , %	No. of studies	Sample	Prevalence, %	95% CI	I ² , %
1st, 2nd or 3rd trimester or 1–24 weeks	Self-report	Depressive symptoms + trait anxiety	6	2847	8.1	5.9–10.3	75	5	1785	8.5	5.8–11.2	72
postpartum		Mild to severe depressive symptoms + anxiety symptoms	25	33 370	8.6	7.2–9.9	94	21	26 313	8.8	7.3–10.4	95
		Moderate to severe depressive symptoms + anxiety symptoms	24	122 406	6.0	4.9–7.2	98	16	23 057	6.7	5.2–8.3	97
	Clinical diagnosis	Depression + any anxiety disorder	16	6516	7.9	4.6–11.1	97	13	5122	6.2	3.8–8.6	95
1st, 2nd or 3rd trimester or 1–52 weeks	Self-report	Depressive symptoms + trait anxiety	6	2675	7.9	5.9–9.9	68	4	925	7.9	4.5–11.2	72
postpartum		Mild to severe depressive symptoms + anxiety symptoms	25	33 324	8.5	7.2–9.9	95	21	26 267	8.8	7.2–10.4	95
		Moderate to severe depressive symptoms + anxiety symptoms	24	122 231	6.0	4.8–7.2	98	15	22 189	6.6	4.9–8.2	97
	Clinical diagnosis	Depression + any anxiety disorder	19	9467	7.4	5.1–9.8	97	16	8073	5.9	4.1–7.6	94

CI, Confidence interval.

^a We used an average sample sizes for the studies that reported two or more time points. Because of attrition, sample sizes were smaller for longer follow-ups.

Table 4. Prevalence of antenatal (1st, 2nd or 3rd trimester) or postnatal (1–24 weeks) anxiety and depressive symptoms and that of anxiety and depression disorder according to year of publication, country income, and methodological quality of included studies

		Anxiety and depressive symptoms						Anxiety and depression disorder						
Study characteristic	Level	No. of studies	Sample	Prevalence, %	95% CI	р	No. of studies	Sample	Prevalence, %	95% CI	р			
Publication year	<2010	10	19 415	5.6	3.7–7.5	0.19	8	3972	9.5	3.4–15.7	0.42			
	>2011	33	128 129	7.9	6.7-9.1		8	2544	6.1	2.8-9.4				
Country income	Low to middle	7	3740	7.1	4.3–9.9	0.98	6	2643	8.7	4.6–12.8	0.76			
	High	36	143 804	7.4	6.3-8.5		10	3873	7.3	3.3-11.4				
Selection bias	Low	2	5297	4.8	4.2 - 5.3	0.84	4	2095	9.4	3.7-15.1	0.49			
	Moderate	33	46 441	8.0	6.6-9.5		9	3027	4.5	2.8-6.2				
	High	8	95 806	5.9	4.3-7.6		3	1394	15.0	0.0-36.6				
Attrition bias	Low	30	126 960	7.5	6.3-8.7	0.56	14	6156	8.0	4.5-11.5	0.88			
	Moderate	9	11 934	7.5	5.9-9.2		2	360	6.6	4.02				
	High	4	8650	5.1	1.6-8.5		0							

CI, Confidence interval.

data separately for each condition. To ensure comprehensiveness of the meta-analysis, 44 study authors provided additional, unpublished information to enable us to calculate the prevalence rate of co-morbidity and permit study inclusion. Of the few studies that specifically published results for co-morbid anxiety and depression, a similar relationship between anxiety and depression was found in comparison with nonpostpartum samples. An Australian study found that a third of pregnant and postpartum women with major depression had co-morbid anxiety (Austin et al. 2010). Similarly, in a Canadian population-based study, 18% of women reported depressive symptoms at 8 weeks postpartum of which 52% also experienced co-morbid anxiety (Falah-Hassani et al. 2016). In a US population-based study incorporating 4451 postpartum women, 18.0% reported anxiety symptoms, of which 35% also reported depressive symptoms (Farr et al. 2014). These results confirm a significant amount of overlap between anxiety and depressive symptoms.

Because co-morbid anxiety and depression are associated with higher symptom severity, suicidality, chronicity and treatment resistance, identifying risk factors is an important first step in developing prevention interventions. Co-morbidity has many origins. The genetic factors contributing to anxiety and depression are shared (Taporoski et al. 2015). Environmental experiences, such as stressful life events and a lack of social support, also contribute to both (Norhayati et al. 2015; Biaggi et al. 2016). The factors leading to co-morbid anxiety and depression v. a single disorder seem multifactorial (Moscati et al. 2016). Previous studies have found that, in comparison with individuals with a single disorder, those with co-morbid anxiety and depression were more likely to be lower educated, not married and younger. Further, they were more likely to have neuroticism, a positive parental psychiatric history and a history of childhood trauma (Blazer et al. 1994; de Graaf et al. 2002).

To date, very few studies have examined co-morbidity risk factors in the perinatal population. In an Australian population-based survey of 4366 women, symptoms of co-morbid anxiety and depression were associated with young maternal age, not being married, not having completed secondary school, having a health care card, and experiencing one or more social health issues (Yelland et al. 2010). In another population-based study involving a sample of 522 Canadian women (Falah-Hassani et al. 2016), immigration within past 5 years, maternal vulnerable personality, childcare stress and perceived stress predicted a higher risk of co-morbidity. Conversely, high breastfeeding self-efficacy, maternal self-esteem and partner support were associated with a lower risk of developing co-morbidity (Falah-Hassani et al. 2016). These two perinatal studies provide beginning evidence that some risk factors may be similar to nonpostpartum populations but they also highlight unique factors that require further exploration to assist in preventive strategies. When examining co-morbidity risk factors it is important to note that there is growing evidence to suggest anxiety disorders often precede depressive disorders. Because a reversed pattern depressive disorders preceding anxiety disorders may represent a different etiologic pathway, it is also essential to evaluate whether risk factors of co-morbidity with preceding anxiety are different from

co-morbidity with preceding depression. A large study conducted in the Netherlands found that a pattern of depressive disorder preceding anxiety disorder was more likely among those who were female, were higher educated, experienced childhood parental divorce and suffered childhood emotional neglect (de Graaf *et al.* 2003).

While the US Preventive Services Task Force now endorses screening for perinatal depression (Siu et al. 2016), not identifying anxiety symptoms as well underestimates the prevalence of mental health disorders and the need for perinatal mental health services. Matthey et al. (2003) suggest that there is a 'hierarchical diagnostic custom' where depression takes precedence in clinical practice even when anxiety symptoms are a prominent feature resulting in cases of anxiety being untreated. Given the possible adverse effects of co-morbid perinatal anxiety and depression on maternal and infant outcomes, primary care practitioners, obstetricians and midwives should screen pregnant women and those who are in the postpartum period for depression as well as for anxiety, and facilitate treatment of both conditions.

Conclusions

The prevalence of maternal co-morbid anxiety and depression in the antenatal and postnatal periods was estimated among 162 120 women from 30 countries. Results suggest that co-morbidity across the perinatal period is prevalent and merits clinical attention similar to that given to perinatal depression. Research to develop evidence-based interventions to prevent co-morbid anxiety and depression in the perinatal period is warranted in order to promote healthy child development.

Supplementary material

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Declaration of Interest

None.

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