

Research paper

Mid-pregnancy insomnia is associated with concurrent and postpartum maternal anxiety and obsessive-compulsive symptoms: A prospective cohort study

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ABSTRACT

Background: Although many perinatal women are affected by anxiety, few studies have focused on perinatal anxiety and its potential triggers. The primary aim of this study was to examine concurrent and prospective associations between mid-pregnancy insomnia and perinatal anxiety. Furthermore, we compared psychosocial and reproductive characteristics between participants with and without mid-pregnancy insomnia and explored changes in the prevalence of obsessive-compulsive disorder (OCD) symptoms from mid-pregnancy to 8 weeks postpartum.

Methods: This study was part of the Norwegian Depression and Anxiety in the Perinatal Period (DAPP) prospective, population-based, cohort study. We analyzed hospital birth records and questionnaire responses from pregnancy week 17 and postpartum week 8 ($n = 530$). The Bergen Insomnia Scale was used to measure insomnia and the Hopkins Symptom Checklist to measure anxiety. OCD symptoms were measured based on questions from the Mini-International Neuropsychiatric Interview.

Results: Mid-pregnancy insomnia was significantly associated with both concurrent and postpartum anxiety in a linear mixed model adjusted for several potential confounders. Participants with mid-pregnancy insomnia had significantly higher levels of perinatal anxiety and postpartum OCD symptoms than participants with normal mid-pregnancy sleep. OCD symptoms affected more women after delivery than before (6.4% vs. 3.8% $p = 0.034$).

Limitations: Immigrants were underrepresented in our sample.

Conclusion: Our results suggest that mid-pregnancy insomnia is a marker for concurrent anxiety and predictor of postpartum anxiety. Future research should examine whether insomnia treatment starting in mid-pregnancy reduces both perinatal insomnia and anxiety. Health providers should also be aware that postpartum women have an increased risk of developing OCD symptoms.

1. Introduction

Most research on perinatal mental disorders has focused on depression (Fisher et al., 2016), whereas anxiety, despite being prevalent (Fairbrother et al., 2016), has often been overlooked (Howard et al., 2014) and under-treated (Smith et al., 2009). Perinatal anxiety has been acknowledged as an essential topic, and a growing number of

studies have addressed it (Field, 2018; Furtado et al., 2018), with an ongoing discussion regarding which instruments should be used for detection (Matthey, 2016; Sinesi et al., 2019).

Anxiety can be defined as specific anxiety and related disorders (ADs), including obsessive-compulsive disorder (OCD) (Fairbrother et al., 2019), as well as less specific symptoms of excessive worry, restlessness, and malaise. Maternal anxiety may have negative

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implications not only for the obstetric outcome (Schetter and Tanner, 2012) and the child's health and development (Glasheen et al., 2010; Hoffman et al., 2017), but also for the mother's relationship with both the infant (Dawson et al., 2000) and the other parent (Wenzel et al., 2005), but more research on perinatal anxiety is needed (Ali, 2018; Goodman et al., 2016; McGuinness et al., 2011).

Insomnia, a syndrome characterized by difficulties in sleep onset or continuity, poor sleep quality, and impaired daytime functioning (Reichner, 2015), is twice as frequent among women as men (Bei et al., 2015). During pregnancy, the prevalence of insomnia ranges from 13% early in the first trimester (Okun et al., 2015) up to 74% late in the third trimester (Fernández-Alonso et al., 2012). Insomnia can occur independently or in comorbidity with other psychiatric disorders (Morin and Benca, 2012) and is a risk factor for the development of anxiety in non-perinatal populations (Hertenstein et al., 2018). Thus, antenatal insomnia may be associated with perinatal anxiety. The few previous studies on the relationship between perinatal insomnia and anxiety are subject to limited access to covariates, small sample sizes, and the use of only antenatal measurements (Polo-Kantola et al., 2017); cross-sectional design and recruitment from psychiatric settings (Swanson et al., 2011); or assessments late in pregnancy (Osnes et al., 2019).

In a previous survey of perinatal women, we found that late-pregnancy insomnia was associated with postpartum anxiety (Osnes et al., 2019). Furthermore, 10% had symptoms of at least one AD, among which only OCD was clearly more prevalent after childbirth (4.2%) compared to during pregnancy (2.5%) (Osnes et al., 2019). Given that two-thirds of postpartum women with OCD symptoms have dysfunctional mother-infant behavior and postpartum OCD seems to become chronic if left untreated, it is essential to be aware of and treat such symptoms (Challacombe et al., 2016; McGuinness et al., 2011). In this study, we explored the association between antenatal insomnia and perinatal anxiety from as early as mid-pregnancy, a point when non-pharmacological treatment interventions for insomnia can be completed before delivery (Riemann et al., 2017). We also repeated the OCD measurements in a different sample.

Thus, the primary aim of this study was to examine concurrent and prospective associations between mid-pregnancy insomnia and anxiety during mid-pregnancy and 8 weeks after childbirth while adjusting for previously identified risk factors for both insomnia and perinatal anxiety (Furtado et al., 2019, 2018; Singareddy et al., 2012). Furthermore, we compared psychosocial and reproductive characteristics between participants with and without mid-pregnancy insomnia and explored changes in the prevalence of OCD symptoms from mid-pregnancy to 8 weeks postpartum.

2. Material and methods

2.1. Design, setting, and participants

This study is part of the Depression and Anxiety in the Perinatal Period (DAPP) study, a prospective cohort study targeting all women scheduled to deliver at Ålesund Hospital in Norway. The hospital serves a population of approximately 100 000 people, 1300 of whom on average give birth yearly. For data collection, we retrieved information from hospital birth records and administered questionnaires at week 17 of pregnancy (Questionnaire 1, Q1) and week 8 postpartum (Questionnaire 2, Q2). Fig. 1 illustrates the study timeline.

The public antenatal program in Norway provides a routine ultrasound examination free of charge at gestational week 17. The DAPP study's target population was all women undergoing that examination. The only two exclusion criteria at time of inclusion were being < 18 years of age and not being able to answer a questionnaire in Norwegian. Women with stillbirths were excluded before postpartum assessment (Q2). From November 2015 to April 2017, a total of 1748 women came to the hospital for the examination, 755 (43%) of whom provided

informed written consent to participate and were included in the study. Potential reasons for non-participation were invitation refusal, meeting exclusion criteria, time constraints, or undergoing the examination in the evening when recruiting personnel were absent. The women who had returned Q1 and delivered a live child were sent Q2 via postal mail in time to be answered eight weeks postpartum. The final study sample consisted of 530 participants who returned both questionnaires and submitted data regarding all variables included in the primary analyses (Fig. 2). The DAPP study was approved by the Regional Committees for Medical and Health Research Ethics (approval number 2014/1480/REC South East).

2.2. Measures

2.2.1. Anxiety measures

The main outcome, anxiety, was measured in Q1 and Q2 by the anxiety dimension of the Hopkins Symptom Checklist-25 (SCL-A) (i.e., the first 10 items) (Derogatis et al., 1974), assessing symptoms during the past 7 days (Brouwers et al., 2001). The score for each item ranges from 1, indicating "not at all", to 4, indicating "extremely". The Norwegian version of the SCL-A has been validated against the International Classification of Diseases (ICD) criteria for anxiety and depression (Sandanger et al., 1998); it shows good psychometric properties and reliable construct measurement (Veijola et al., 2003) and is widely used in population-based surveys in Norway (Statistics Norway, 2016). Cronbach's alpha for the SCL-A was 0.74 in Q1 and 0.78 in Q2.

The OCD measure, coded according to DSM-IV-TR diagnostics (American Psychiatric Association, 2000), was used in Q1 and Q2 as self-administered questions based on the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) as previously administered in an extensive Norwegian survey (Osnes et al., 2019). To measure infant-related obsessive-compulsive symptoms, we additionally asked the following question in Q2: "During the last month, have you experienced excessive/unreasonable/disturbing/troublesome thoughts or activities related to your newborn child?"

In Q1, participants reported whether a health professional had previously given them an AD diagnosis.

2.2.2. Insomnia measures

In Q1, participants completed the Bergen Insomnia Scale (BIS) to measure insomnia, the main predictor. The BIS includes six items with scores ranging from 0 to 7, reflecting the number of days with symptoms per week during the last month. The BIS was used both as a total score on a continuous scale and as a dichotomous score based on the DSM-IV-TR diagnostic criteria for the presence of insomnia (American Psychiatric Association, 2000). Absence of insomnia is referred to as normal sleep (Wassing et al., 2018). The BIS demonstrates good psychometric properties (Pallesen et al., 2008) and has been used in several studies of pregnant women (Dørheim et al., 2014; Osnes et al., 2019). Cronbach's alpha for the BIS was 0.81.

2.2.3. Depression measures

We included the Edinburgh Postnatal Depression Scale (EPDS), a 10-item scale that assesses symptoms of depression during the previous 7 days (Cox and Sagovsky, 1987), in Q1 and Q2. Although the EPDS was developed to screen for postpartum depression, it is also validated for use during pregnancy (Bergink et al., 2011).

In Q1, we included the Lifetime Major Depression Scale, which measures previous depression based on DSM-IV criteria (Kendler et al., 1993). It comprises five items relating to sadness, appetite change, lack of energy, self-blame, and poor concentration, which are given "Yes" or "No" responses. The scale has high reliability for gauging lifetime history of major depression (Kendler et al., 1993).

2.2.4. Reproductive and psychosocial measures

Q1 included the Relationship Satisfaction Scale, a 10-item, modified

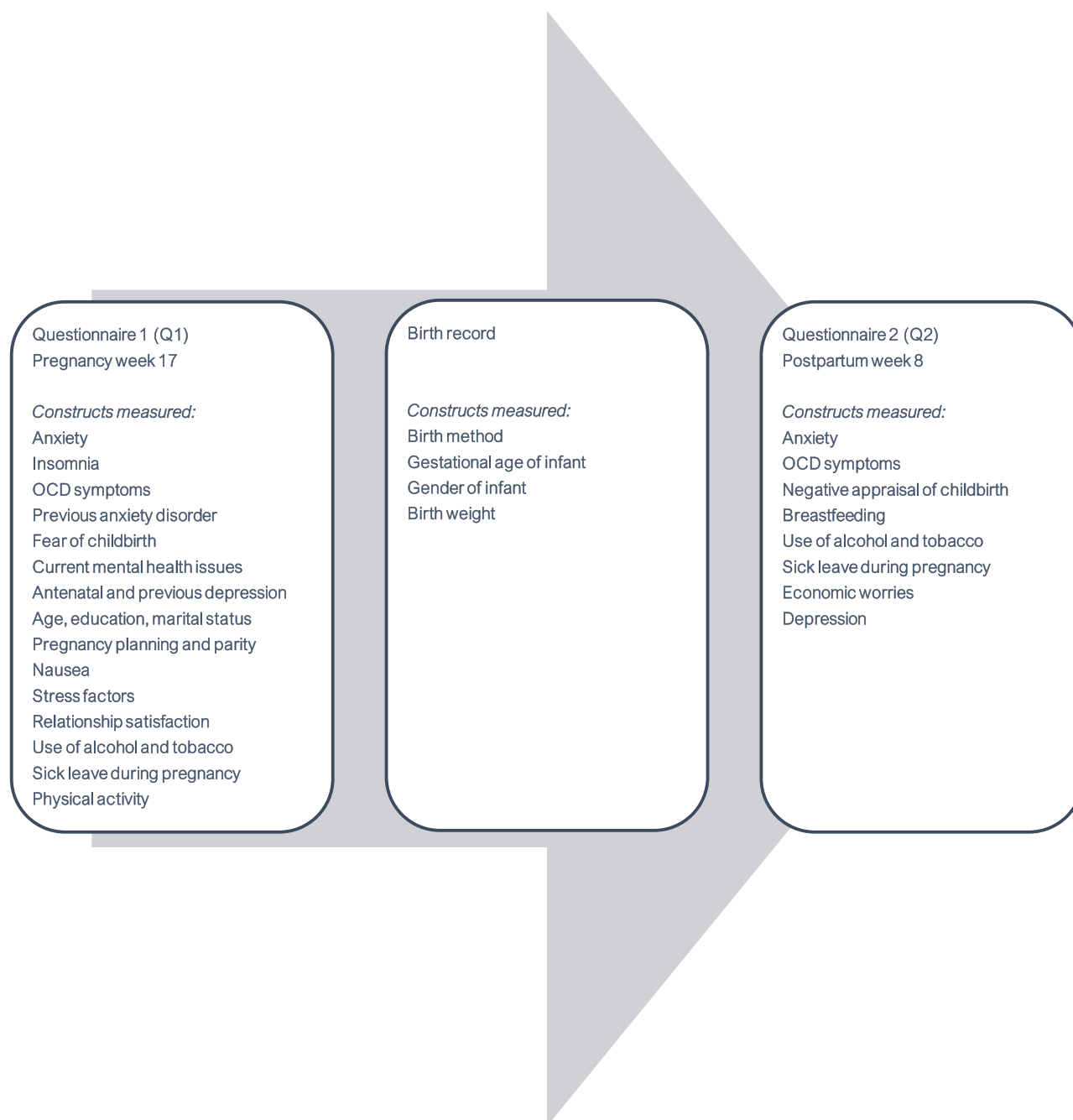


Fig. 1. Overview of the study timeline in the Depression and Anxiety in the Perinatal Period (DAPP) study.

version of Mehrabian's Marital Satisfaction Scale (Blum and Mehrabian, 1999), assessing partner closeness, problems, happiness, responsiveness, plans for quitting the relationship, satisfaction with the relationship, disagreements, feeling lucky with the other partner, views on child rearing, and thoughts regarding the other partner's satisfaction. The score for each item ranges from 1 to 4, and a greater score indicates lower satisfaction with the relationship. Q1 also measured stress factors experienced during the last year using 10 items selected from life event scales (Coddington, 1972; Swearingen and Cohen, 1985). The items regarded marital separation/divorce, severe problems in the relationship, family conflicts, traffic accidents, fire/theft, loss of a close relative, and other crises in life, with scores ranging from 1 (not so difficult) to 3 (very difficult).

In Q1, participants reported their age, marital status, education level, parity status, weight and height (i.e., body mass index), physical

activity, current mental health issues, whether their pregnancy was planned, and whether they had experienced a problematic degree of nausea during the first trimester. Participants were also asked questions regarding the use of alcohol, cigarettes, and dipping tobacco both during pregnancy (Q1) and after delivery (Q2), as well as whether they had been on sick leave from work, and if so, whether it was due to pregnancy-related problems (Q1) or mental issues (Q2). In Q2, we asked whether the participants breastfed, to be answered "Yes" (i.e., either exclusively or partly) or "No", and about worries regarding their personal economic situation. In Q1, we used six factors from the 33-item Wijma Delivery Expectancy/Experience Questionnaire (W-DEQ) version A (Wijma et al., 1998) to measure fear of childbirth (Garthus-Niegel et al., 2011), and we used the corresponding six factors from the W-DEQ version B in Q2 to measure negative cognitive appraisal of the recent childbirth (Korukcu et al., 2016).

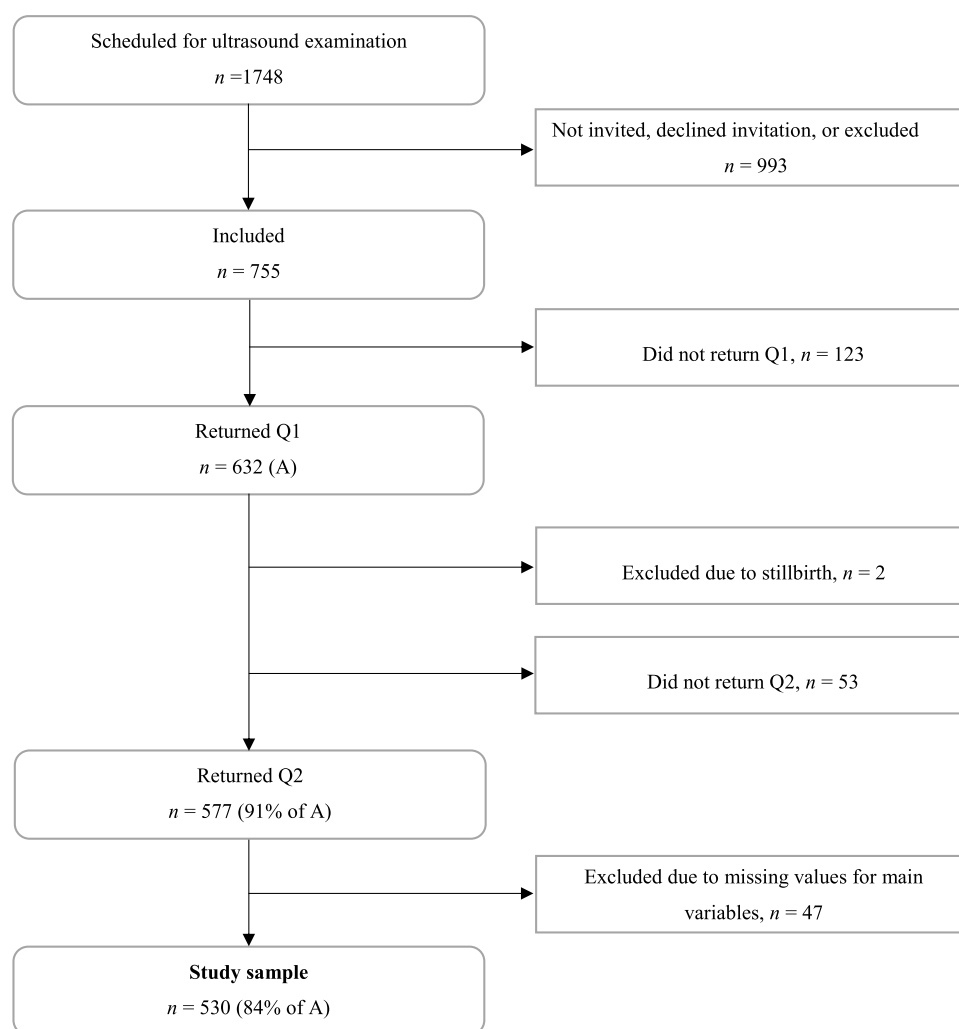


Fig. 2. An overview of inclusion, response rates, and study sample in the Depression and Anxiety in the Perinatal Period (DAPP) study. Q1: Questionnaire 1 in pregnancy week 17; Q2: Questionnaire 2 in postpartum week 8.

From hospital birth records, we retrieved data on emergency and elective cesarean sections, gestational age, and infant gender and birth weight.

2.3. Statistical analyses

Continuous data are presented as mean and standard deviation (SD) for normally distributed data, and also as medians with 25th and 75th percentiles for non-normally distributed data. Given the large sample size, we used *t*-tests to analyze between-group differences for both normally and non-normally distributed data. Data were assessed for normal distribution by visual inspection of Q-Q plots. We present categorical data as frequency and percentage and tested for differences in proportions using the chi-squared test. Paired samples *t*-tests and McNemar's tests were used to test differences in mean scores and proportions, respectively, before versus after delivery. Cronbach's alphas were calculated to test the internal validity of psychometric scales.

Linear mixed models (LMMs) were performed to investigate the associations between anxiety symptoms in Q1 and Q2 and insomnia, previous and antepartum depression, and reproductive and psychosocial variables. All covariates were measured in Q1, other than frequent economic worries, for which the value at Q2 was used as a proxy for the unmeasured value at Q1. We tested for interactions between time points (i.e., Q1 and Q2) and some chosen covariates (i.e., insomnia, previous AD, previous depression, antenatal depression, fear of childbirth,

current mental health issues, and nausea). The interactions were included if significant in the final model, i.e., if the variable was significantly more strongly associated with anxiety in Q1 than in Q2, or vice versa. Random intercepts for women were used to account for intra-women correlations. The SCL-A distributions in Q1 and Q2 were positively skewed and initially adjusted to range from 1, and then log-transformed before the LMM analyses. Case-wise deletion was used for handling missing values for the covariates.

Spearman's rho (r_s), the Pearson correlation coefficient, and Kendall's tau-b were used to explore whether any pair of independent variables were too highly correlated to be jointly entered into the regression model. The variance inflation factor (VIF) was also used to rule out multicollinearity.

The significance level was set to 0.05. Data analyses were performed using the SPSS statistical software package, version 25 (IBM Corp., 2017).

3. Results

3.1. Sample characteristics

Our study sample comprised 530 women. Table 1 presents socio-demographic characteristics and birth outcomes from the study sample and the Medical Birth Registry of Norway (Norwegian Institute of Public Health 2017). After returning Q1, a total of 55 women were

Table 1
Sociodemographic and birth outcome characteristics.

Characteristic	Study sample, <i>n</i> = 530 ^a <i>n</i> (%) or mean \pm SD	Medical Birth Registry of Norway (2017), <i>n</i> = 56 547 <i>n</i> (%) or mean \pm SD
Q1: Maternal age, years	30.5 \pm 4.4	30.9 \pm 4.9 ^b
Q1: Marital status		
Married/cohabitating	515 (97.1)	52 975 (93.7)
Has partner, live separately	4 (0.8)	
Single	11 (2.1)	
Q1: Education level		
Lower secondary	9 (1.7)	
Upper secondary	121 (22.8)	
Higher education (> 12 years)	400 (75.5)	
Parity		
Primiparous (including index pregnancy)	204 (38.5)	23 840 (42.2)
Multiparous	326 (61.5)	32 707 (57.8)
Q1: Body mass index	26.3 \pm 4.6	
Pregnancy was planned	445 (84.0)	
Nausea 1st trimester		
No nausea	89 (16.8)	
A little bothered	224 (42.3)	
Much bothered	217 (40.9)	
Q1: Physical exercise during pregnancy		
≥ 3 times per week	64 (12.5)	
1–3 times per week	238 (46.4)	
< 1 time per week	192 (37.4)	
Never	19 (3.7)	
Gestational age at birth, weeks	39.7 \pm 1.6	39.3 \pm 1.9
Emergency cesarean section	45 (8.5)	5 870 (10.4)
Elective cesarean section	23 (4.3)	3 159 (5.6)
Birth weight, g	3 654 \pm 518	3 489 \pm 591
Gender of child		
Girl	263 (49.7)	27 861 (48.5)
Boy	266 (50.3)	29 592 (51.5)
Breastfeeding		
Exclusively	423 (79.8)	
Partly	63 (11.9)	
Not breastfeeding	44 (8.3)	
Smoking in pregnancy	8 (1.5)	2 011 (3.9)
Dipping tobacco use in pregnancy	7 (1.4)	
Smoking after delivery	10 (1.9)	1 138 (2.2)
Dipping tobacco use after delivery	18 (3.4)	
Alcohol use in pregnancy	2 (0.4)	
Alcohol use after delivery	63 (11.9)	
Q1: Sick leave during pregnancy	271 (51.1)	
Q1: Sick leave due to pregnancy-related problems	231 (43.6)	
Q2: Sick leave during pregnancy	394 (74.3)	
Q2: Sick leave due to mental issues	35 (7.2)	
Q2: Economic worries		
Frequently	37 (7.0)	
Sometimes	153 (28.9)	
Rarely	242 (45.6)	
Never	98 (18.5)	

Q1: Questionnaire 1 at pregnancy week 17; Q2: Questionnaire 2 at postpartum week 8 in the Depression and Anxiety in the Perinatal Period (DAPP) study.

^a Due to missing values for some of the items, *n* varied between 511 (dipping tobacco use in pregnancy) and 530.

^b Maternal age at time of delivery.

either excluded due to stillbirth (*n* = 2) or did not return Q2 (*n* = 53) (Fig. 2). Compared to those who completed both questionnaires, these 55 women did not significantly differ in terms of insomnia, anxiety, or depression, but those who remained in the study had more frequent higher education (75.2% vs. 56.4% *p* = 0.004). We excluded the data of 47 women with missing values in the primary analyses (Fig. 1). The excluded women did not significantly differ from our study sample in regards to age or education level, or insomnia, anxiety, or depression scores in Q1 and Q2.

3.2. Prevalence and univariate analyses

Insomnia was present among 59.8% (*n* = 317) of participants in Q1. Table 2 presents comparisons between the participants with mid-pregnancy insomnia (*n* = 317) and the participants with normal mid-pregnancy sleep (*n* = 213).

There was a significant increase in the number of participants experiencing OCD symptoms from Q1 to Q2 [3.8% (*n* = 20) vs. 6.4% (*n* = 34), *p* = 0.034]. A total of 1.5% (*n* = 8) experienced OCD symptoms in both Q1 and Q2 (i.e., 76.5% of the women experiencing postpartum OCD symptoms did not experience them during pregnancy). In Q2, 47.1% (*n* = 16) of those with postpartum OCD symptoms reported having infant-specific obsessions or compulsions. There was little evidence of a difference in the rates of postpartum OCD symptoms between primiparous and multiparous women (*p* = 0.831).

3.3. Linear mixed model analyses for anxiety

Table 3 presents the results from the main analysis (i.e., for the LMM with the log-transformed SCL-A measured in Q1 and Q2 as the dependent variable). Among all independent variables entered into the model, bivariate correlations were < 0.7 and variation inflation factors were < 3. When testing for interactions with time (i.e., Q1 and Q2), insomnia, antenatal depression, and stress factors had significant interactions when tested one by one. When including these time-interactions in the same model, only antenatal depression remained significant (*p* < 0.001) for the interaction with time and was the only time-interaction kept in our final model (Table 3). For the other variables, a common estimate was found in Q1 and Q2 for the association with anxiety. Insomnia was significantly associated with antenatal and postpartum anxiety (*b* = 0.01, *p* = 0.001). To include the single women (*n* = 11), we also performed LMM analyses including relationship dissatisfaction instead of marital status. Relationship dissatisfaction was not significantly associated with perinatal anxiety (*p* = 0.406). A normal approximation was found to be reasonable for residual distributions from the LMM analyses.

4. Discussion

4.1. Main findings and implications

In this study, we found a significant, positive association between mid-pregnancy insomnia and both concurrent and postpartum anxiety after adjusting for several potential confounders. Mid-pregnancy insomnia was not more strongly associated with concurrent than with postpartum anxiety. Thus, mid-pregnancy insomnia may be both a marker for antenatal anxiety and a predictor of postpartum anxiety. In addition, participants with mid-pregnancy insomnia had significantly higher levels of both perinatal anxiety and postpartum OCD symptoms compared to participants with normal mid-pregnancy sleep. Therefore, antenatal insomnia could be an important intervention target, and screening for insomnia during mid-pregnancy could be an efficient strategy for detecting women who are struggling with or at risk of developing anxiety, not least of all because reporting insomnia symptoms may feel less stigmatizing.

Over-active arousal systems are claimed to be a shared pathway for

Table 2

Comparisons of psychosocial and reproductive characteristics between participants with insomnia and participants with normal sleep based on insomnia measures in pregnancy week 17 (Q1), $n = 530^a$.

Variable	Insomnia, $n = 317$ n (%) or mean \pm SD/ median (25–75 perc.) ^b	Normal sleep, $n = 213$ n (%) or mean \pm SD/ median (25–75 perc.) ^b	p value
Q1: Previous anxiety and related disorder	37 (11.7)	15 (7.0)	0.108 ^c
Q1: Anxiety, SCL-A	13.7 \pm 3.3 13.0 (11.0–15.0)	12.2 \pm 2.2 12.0 (10.5–13.0)	< 0.001 ^d
Q2: Anxiety, SCL-A	13.1 \pm 3.2 12.0 (11.0–14.5)	12.0 \pm 2.2 11.0 (10.0–13.0)	< 0.001 ^d
Q1: OCD symptoms	12 (3.8)	8 (3.8)	1.000 ^c
Q2: OCD symptoms	27 (8.5)	7 (3.3)	0.026 ^c
Q1: Previous depression	131 (41.3)	56 (26.3)	0.001 ^c
Q1: Depression, EPDS	5.3 \pm 4.2 4.0 (2.0–7.0)	3.2 \pm 3.0 3.0 (1.0–5.0)	< 0.001 ^d
Q2: Depression, EPDS	4.7 \pm 4.1 4.0 (2.0–6.0)	3.6 \pm 3.2 3.0 (1.0–6.0)	0.001 ^d
Q1: Current mental health issues	29 (9.1)	10 (4.7)	0.079 ^c
Q1: Fear of childbirth	14.7 \pm 6.0	12.8 \pm 5.6	< 0.001 ^d
Q2: Negative appraisal of childbirth	11.7 \pm 6.2	9.9 \pm 5.5	0.001 ^d
Q1: Nausea (much bothered)	145 (45.7)	72 (33.8)	0.008 ^c
Q1: Maternal age, years	30.8 \pm 4.6	30.1 \pm 4.1	0.108 ^d
Q1: Higher education (> 12 years)	240 (75.7)	160 (75.1)	0.958 ^c
Multiparous	202 (63.7)	124 (58.2)	0.236 ^c
Q1: Body mass index	27.1 \pm 4.8 26.1 (23.5–29.7)	25.1 \pm 3.8 24.5 (22.4–27.1)	< 0.001 ^d
Q1: Relationship dissatisfaction	14.5 \pm 4.1 14.0 (11.0–17.0)	13.8 \pm 3.7 13.0 (11.0–16.0)	0.047 ^d
Q1: Stress factors during the last year	1.9 \pm 2.8 0.0 (0.0–3.0)	1.3 \pm 2.2 0.0 (0.0–2.0)	0.010 ^d
Emergency cesarean section	31 (9.8)	14 (6.6)	0.255 ^c
Elective cesarean section	15 (4.7)	8 (3.8)	0.747 ^c

Q1: Questionnaire 1 at pregnancy week 17; Q2: Questionnaire 2 at postpartum week 8; SCL-A: Anxiety scale from the Hopkins Symptom Checklist; EPDS: Edinburgh Postnatal Depression Scale.

^a Due to missing values for some of the items, total n varied between 524 (body mass index) and 530.

^b Median (25–75 percentile) is given for non-normally distributed data.

^c Chi-squared test.

^d t -test.

Table 3

Estimated regression coefficients (b) with 95% confidence intervals (CI) and p values from a linear mixed model analysis with anxiety measured by the log-transformed SCL-A in pregnancy week 17 (Q1) and postpartum week 8 (Q2) as the dependent variable ($n = 530$)^a.

Variable	Estimate (b)	95% CI	p value
Insomnia	0.01	0.00 to 0.14	0.001
Previous anxiety and related disorder	0.26	0.10 to 0.41	0.001
Previous depression	0.18	0.08 to 0.27	< 0.001
Depression			
At Q1	0.08	0.07 to 0.10	< 0.001
At Q2	0.06	0.04 to 0.07	< 0.001
Difference Q2 – Q1 (interaction)	–0.03	–0.04 to –0.02	< 0.001
Maternal age	–0.01	–0.02 to 0.00	0.111
Higher education	–0.04	–0.14 to 0.06	0.445
Multiparous	0.01	–0.08 to 0.10	0.819
Married or cohabitating	0.25	–0.03 to 0.52	0.076
Planned pregnancy	–0.01	–0.13 to 0.11	0.924
Fear of childbirth	0.01	0.00 to 0.02	0.028
Nausea (much bothered) during first trimester	0.11	0.02 to 0.19	0.015
Current mental health issues	0.04	–0.15 to 0.23	0.673
Frequent economic worries	0.11	–0.06 to 0.29	0.202
Stress factors in last year	0.01	–0.01 to 0.03	0.457

SCL-A: Anxiety scale from the Hopkins Symptom Checklist.

^a The covariates were measured in Q1, except the variable “frequent economic worries” measured in Q2. It was included in the model because we expect the economic situation to be comparable in Q1 and Q2.

insomnia and anxiety (Riemann et al., 2015, 2010), indicating that the negatively toned cognitive activity related to insomnia could trigger arousal and distress, which may lead to developing anxiety (Harvey, 2002). Cognitive behavioral therapy for insomnia (CBT-I) has been reported to be safe and effective during pregnancy (Manber et al., 2018) and decreases both insomnia and anxiety in non-perinatal populations (Belleville et al., 2011; Ye et al., 2015). It is possible that CBT-I could also improve or prevent perinatal anxiety when provided to pregnant women with insomnia (Manber et al., 2019); however, further research is required on this topic.

A significantly higher proportion of participants in this study reported OCD symptoms following delivery than during mid-pregnancy, increasing from 3.8% in week 17 of pregnancy to 6.4% in week 8 postpartum, with both rates being higher than the 1-year OCD prevalence (1.2%) in the general population (Ruscio et al., 2010). Concordantly, in a meta-analysis, Russell et al. (2013) showed that postpartum women are at a greater risk of experiencing OCD than both pregnant women and the general female population.

In this study, half of the women exhibiting postpartum OCD symptoms experienced obsessions or compulsions regarding the infant. Because such ego-dystonic obsessions are often aggressive, women might be reluctant to tell others about them due to shame or fear of reprisals (Brandes et al., 2004). Therefore, health professionals should normalize such symptoms so that women feel safe to disclose them (Fairbrother and Abramowitz, 2016). It is also important to differentiate between symptoms of OCD and of psychosis (McGuinness et al., 2011). Evaluations of measures to best assess OCD among postpartum women were published recently (Thiséus et al., 2019), and cognitive behavioral therapy was reported as being effective for postpartum OCD (Challacombe et al., 2017; Marchesi et al., 2016).

4.2. Strengths and limitations

The present study has several strengths. To the best of our knowledge, this is the first prospective study examining the association between mid-pregnancy insomnia and perinatal anxiety. Furthermore, this study did not only target participants attending a routine examination that is experienced by most pregnant women in Norway (suggesting low first wave selection bias), but also had a large sample size. Moreover, the response rate for the final questionnaire was exceptionally high (91%) and we were able to adjust for various known risk factors for both insomnia and perinatal anxiety.

This study also has several methodological limitations. First, the data on insomnia, anxiety, and OCD were based on self-reported instruments. Second, less than half of the women attending the ultrasound examination at the hospital ultimately participated, and reasons why were not recorded (i.e., whether they declined to participate, were excluded at time of inclusion, or did not receive an invitation). Third, we only invited Norwegian-speaking women to participate, which limits the generalizability of the findings, as rates of perinatal anxiety and gestational risk factors may differ among non-Norwegian-speaking residents and immigrants with minority status (Liu et al., 2016; Rubertsson et al., 2014).

5. Conclusion

The present study found a significant association between mid-pregnancy insomnia and both concurrent and postpartum anxiety, which may aid healthcare workers in identifying women who are suffering from or at risk of developing anxiety using antenatal insomnia as an indicator. Future researchers should explore whether detection and subsequent treatment of insomnia during pregnancy can reduce the rate of both perinatal insomnia and anxiety. Healthcare professionals should be aware of the increased risk of developing OCD symptoms postpartum and that these symptoms often involve the infant.

Contributors' statements

Rannveig S. Osnes designed and coordinated the DAPP study, performed the statistical analyses, and drafted the manuscript. Malin Eberhard-Gran, Håvard Kallestad, Gunnar Morken, and John Olav Roaldset contributed to the planning and completion of the DAPP study, interpreted the results, and critically reviewed the manuscript. Turid Follstad supervised the statistical analyses, interpreted the results, and critically reviewed the manuscript. All authors approved the final manuscript as submitted.

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Declaration of Competing Interest

There are no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2020.01.140](https://doi.org/10.1016/j.jad.2020.01.140).

References

- Ali, E., 2018. Women's experiences with postpartum anxiety disorders: a narrative literature review. *Int. J. Womens. Health* 10, 237–249. <https://doi.org/10.2147/IJWH.S158621>.
- American Psychiatric Association, 2000. Diagnostic and statistical manual of mental disorders: dsm-iv-tr. 10.1176/appi.books.9780890423349.5847.
- Bei, B., Coe, S., Baker, F.C., Trinder, J., 2015. Sleep in women: a review. *Aust. Psychol.* 50, 14–24. <https://doi.org/10.1111/ap.12095>.
- Belleville, G., Cousineau, H., Levrier, K., St-Pierre-Delorme, M.E., 2011. Meta-analytic review of the impact of cognitive-behavior therapy for insomnia on comorbid anxiety. *Clin. Psychol. Rev.* 31, 638–652. <https://doi.org/10.1016/j.cpr.2011.02.004>.
- Bergink, V., Kooistra, L., Lambregtse-van den Berg, M.P., Wijnen, H., Bunevicius, R., van Baar, A., Pop, V., 2011. Validation of the edinburgh depression scale during pregnancy. *J. Psychosom. Res.* 70, 385–389. <https://doi.org/10.1016/j.jpsychores.2010.07.008>.
- Blum, J.S., Mehrabian, A., 1999. Personality and temperament correlates of marital satisfaction. *J. Pers.* 67, 93–125. <https://doi.org/10.1111/1467-6494.00049>.
- Brandes, M., Soares, C.N., Cohen, L.S., 2004. Postpartum onset obsessive-compulsive disorder: diagnosis and management. *Arch. Womens. Ment. Health* 7, 99–110. <https://doi.org/10.1007/s00737-003-0035-3>.
- Brouwers, E.P.M., van Baar, A.L., Pop, V.J.M., 2001. Does the edinburgh postnatal depression scale measure anxiety? *J. Psychosom. Res.* 51, 659–663. [https://doi.org/10.1016/S0022-3999\(01\)00245-8](https://doi.org/10.1016/S0022-3999(01)00245-8).
- Challacombe, F.L., Salkovskis, P.M., Woolgar, M., Wilkinson, E.L., Read, J., Acheson, R., 2017. A pilot randomized controlled trial of time-intensive cognitive-behaviour therapy for postpartum obsessive-compulsive disorder: effects on maternal symptoms, mother-infant interactions and attachment. *Psychol. Med.* 47, 1478–1488. <https://doi.org/10.1017/S0033291716003573>.
- Challacombe, F.L., Salkovskis, P.M., Woolgar, M., Wilkinson, E.L., Read, J., Acheson, R., 2016. Parenting and mother-infant interactions in the context of maternal postpartum obsessive-compulsive disorder: effects of obsessional symptoms and mood. *Infant Behav. Dev.* 44, 11–20. <https://doi.org/10.1016/j.infbeh.2016.04.003>.
- Coddington, R.D., 1972. The significance of life events as etiologic factors in the diseases of children. i-a survey of professional workers. *J. Psychosom. Res.* 16, 7–18. [https://doi.org/10.1016/0022-3999\(72\)90018-9](https://doi.org/10.1016/0022-3999(72)90018-9).
- Cox, J.L., Sagovsky, J.M.H.R., 1987. Detection of postnatal depression development of the 10-item edinburgh postnatal depression scale. *Br. J. Psychiatry* 150, 782–786.
- Dawson, G., Ashman, S.B., Carver, L.J., 2000. The role of early experience in shaping behavioral and brain development and its implications for social policy. *Dev. Psychopathol.* 12, 695–712. <https://doi.org/10.1017/S0954579400004089>.
- Derogatis, L.R., Lipman, R.S., Rickels, K., Uhlenhuth, E.H., Covi, L., 1974. The hopkins symptom checklist (HSCL): a self-report symptom inventory. *Behav. Sci.* 19, 1–15.
- Dørheim, S.K., Bjorvatn, B., Eberhard-Gran, M., 2014. Can insomnia in pregnancy predict postpartum depression? a longitudinal, population-based study. *PLoS ONE* 9 (4). <https://doi.org/10.1371/journal.pone.0094674>.
- Fairbrother, N., Abramowitz, J.S., 2016. Obsessions and compulsions during pregnancy and the postpartum period. In: Wenzel, A. (Ed.), *The Oxford Handbook of Perinatal Psychology*. Oxford University Press, pp. 167–181.
- Fairbrother, N., Corbyn, B., Thordarson, D.S., Ma, A., Surm, D., 2019. Screening for perinatal anxiety disorders: room to grow. *J. Affect. Disord.* 250, 363–370. <https://doi.org/10.1016/j.jad.2019.03.052>.
- Fairbrother, N., Janssen, P., Antony, M.M., Tucker, E., Young, A.H., 2016. Perinatal anxiety disorder prevalence and incidence. *J. Affect. Disord.* 200, 148–155. <https://doi.org/10.1016/j.jad.2015.12.082>.
- Fernández-Alonso, A.M., Trabalón-Pastor, M., Chedraui, P., Pérez-López, F.R., 2012. Factors related to insomnia and sleepiness in the late third trimester of pregnancy. *Arch. Gynecol. Obstet.* 286, 55–61. <https://doi.org/10.1007/s00404-012-2248-z>.
- Field, T., 2018. Postnatal anxiety prevalence, predictors and effects on development: a narrative review. *Infant Behav. Dev.* 51, 24–32. <https://doi.org/10.1016/j.infbeh.2018.02.005>.
- Fisher, S.D., Wisner, K.L., Clark, C.T., Sit, D.K., Luther, J.F., Wisniewski, S., 2016. Factors associated with onset timing, symptoms, and severity of depression identified in the postpartum period. *J. Affect. Disord.* 203, 111–120. <https://doi.org/10.1016/j.jad.2016.05.063>.
- Furtado, M., Chow, C.H.T., Owais, S., Frey, B.N., Van Lieshout, R.J., 2018. Risk factors of new onset anxiety and anxiety exacerbation in the perinatal period: a systematic review and meta-analysis. *J. Affect. Disord.* 238, 626–635. <https://doi.org/10.1016/j.jad.2018.05.073>.
- Furtado, M., Lieshout, R.J.V., Ameringen, M.V., Green, S.M., Frey, B.N., 2019. Biological and psychosocial predictors of anxiety worsening in the postpartum period: a longitudinal study. *J. Affect. Disord.* 250, 218–225. <https://doi.org/10.1016/j.jad.2019.02.064>.
- Garthus-Niegel, S., Størksen, H.T., Torgersen, L., Von Soest, T., Eberhard-Gran, M., 2011. The wjima delivery expectancy/experience questionnaire - a factor analytic study. *J. Psychosom. Obstet. Gynecol.* 32, 160–163. <https://doi.org/10.3109/0167482X.2011.573110>.
- Glasheen, C., Richardson, G.A., Fabio, A., 2010. A systematic review of the effects of

- postnatal maternal anxiety on children. *Arch. Womens. Ment. Health* 13, 61–74. <https://doi.org/10.1007/s00737-009-0109-y>.
- Goodman, J.H., Watson, G.R., Stubbs, B., 2016. Anxiety disorders in postpartum women: a systematic review and meta-analysis. *J. Affect. Disord.* 203, 292–331. <https://doi.org/10.1016/j.jad.2016.05.033>.
- Harvey, A., 2002. A cognitive model of insomnia. *Behav. Res. Ther.* 40, 869–893. [https://doi.org/10.1016/S0005-7967\(01\)00061-4](https://doi.org/10.1016/S0005-7967(01)00061-4).
- Hertenstein, E., Feige, B., Gmeiner, T., Kienzler, C., Spiegelhalter, K., Johann, A., Jansson-Fröjmark, M., Palagini, L., Rücker, G., Riemann, D., Baglioni, C., 2018. Insomnia as a predictor of mental disorders: a systematic review and meta-analysis. *Sleep Med. Rev.* 43, 96–105. <https://doi.org/10.1016/j.smrv.2018.10.006>.
- Hoffman, C., Dunn, D.M., Njoroge, W.F.M., 2017. Impact of postpartum mental illness upon infant development. *Curr. Psychiatry Rep.* 19, 1–6. <https://doi.org/10.1007/s11920-017-0857-8>.
- Howard, L.M., Molyneux, E., Dennis, C.L., Rochat, T., Stein, A., Milgrom, J., 2014. Non-psychotic mental disorders in the perinatal period. *Lancet* 384, 1775–1788. [https://doi.org/10.1016/S0140-6736\(14\)61276-9](https://doi.org/10.1016/S0140-6736(14)61276-9).
- IBM Corp., 2017. IBM spss statistics for windows, version 25.0.
- Kendler, K., Neale, M., Kessler, R., Heath, A., Eaves, L., 1993. The lifetime history of major depression in women. Reliability of diagnosis and heritability. *Arch. Gen. Psychiatry* 50, 863–870.
- Korukcu, O., Bulut, O., Kukulcu, K., 2016. Psychometric evaluation of the wijma delivery expectancy/experience questionnaire version b. *Health Care Women Int* 37, 550–567. <https://doi.org/10.1080/07399332.2014.943838>.
- Liu, C.H., Giallo, R., Doan, S.N., Seidman, L.J., Tronick, E., 2016. Racial and ethnic differences in prenatal life stress and postpartum depression symptoms. *Arch. Psychiatr. Nurs.* 30, 7–12. <https://doi.org/10.1016/j.apnu.2015.11.002>.
- Manber, R., Bei, B., Simpson, N., Asarnow, L., Rangel, E., 2018. Cognitive behavioral therapy is effective for insomnia during pregnancy: a randomized controlled trial in an ethnically diverse sample. *Sleep* 41, A154.
- Manber, R., Bei, B., Simpson, N., Asarnow, L., Rangel, E., Sit, A., Lyell, D., 2019. Cognitive behavioral therapy for prenatal insomnia. *Obstet. Gynecol.* 00, 1. <https://doi.org/10.1097/AOG.0000000000003216>.
- Marchesi, C., Ossola, P., Amerio, A., Daniel, B.D., Tonna, M., De Panfilis, C., 2016. Clinical management of perinatal anxiety disorders: a systematic review. *J. Affect. Disord.* 190, 543–550. <https://doi.org/10.1016/j.jad.2015.11.004>.
- Matthey, S., 2016. Anxiety and stress during pregnancy and the postpartum period. In: Wenzel, A. (Ed.), *The Oxford Handbook of Perinatal Psychology*. Oxford University Press, pp. 132–149.
- McGuinness, M., Blissett, J., Jones, C., 2011. OCD in the perinatal period: is postpartum ocd (ppOCD) a distinct subtype? a review of the literature. *Behav. Cogn. Psychother.* 39, 285–310. <https://doi.org/10.1017/S1352465810000718>.
- Morin, C.M., Benca, R., 2012. Chronic insomnia. *Lancet* 379, 1129–1141. [https://doi.org/10.1016/S0140-6736\(11\)60750-2](https://doi.org/10.1016/S0140-6736(11)60750-2).
- Norwegian Institute of Public Health, 2017. Medical birth registry of norway [WWW document]. URL <http://statistikkbank.fhi.no/mfr/> (accessed 12.18.18).
- Okun, M.L., Buysse, D.J., Hall, M.H., 2015. Identifying insomnia in early pregnancy: validation of the insomnia symptoms questionnaire (ISQ) in pregnant women. *J. Clin. Sleep Med.* 11, 645–654. <https://doi.org/10.5664/jcs.4776>.
- Osnes, R.S., Roaldset, J.O., Follestad, T., Eberhard-Gran, M., 2019. Insomnia late in pregnancy is associated with perinatal anxiety: a longitudinal cohort study. *J. Affect. Disord.* 248, 155–165. <https://doi.org/10.1016/j.jad.2019.01.027>.
- Pallesen, S., Bjorvatn, B., Nordhus, I.H., Sivertsen, B., Hjørnevik, M., Morin, C.M., 2008. A new scale for measuring insomnia: the bergen insomnia scale. *Percept. Mot. Ski.* 107, 691–706. <https://doi.org/10.2466/PMS.107.1.691-706>.
- Polo-Kantola, P., Aukia, L., Karlsson, H., Karlsson, L., Paavonen, E.J., 2017. Sleep quality during pregnancy: associations with depressive and anxiety symptoms. *Acta Obstet. Gynecol. Scand.* 96, 198–206. <https://doi.org/10.1111/aogs.13056>.
- Reichner, C.A., 2015. Insomnia and sleep deficiency in pregnancy. *Obstet. Med.* 8, 168–171. <https://doi.org/10.1177/1753495x15600572>.
- Riemann, D., Baglioni, C., Bassetti, C., Bjorvatn, B., Dolenc Groselj, L., Ellis, J.G., Espie, C.A., Garcia-Borreguero, D., Gjerstad, M., Gonçalves, M., Hertenstein, E., Jansson-Fröjmark, M., Jennum, P.J., Leger, D., Nissen, C., Parrino, L., Paunio, T., Pevernagie, D., Verbraecken, J., Weef, H.G., Wichniak, A., Zavalko, I., Arnardottir, E.S., Deleanu, O.C., Strazisar, B., Zoetmulder, M., Spiegelhalter, K., 2017. European guideline for the diagnosis and treatment of insomnia. *J. Sleep Res.* 26, 675–700. <https://doi.org/10.1111/jsr.12594>.
- Riemann, D., Nissen, C., Palagini, L., Otte, A., Perlis, M.L., Spiegelhalter, K., 2015. The neurobiology, investigation, and treatment of chronic insomnia. *Lancet Neurol* 14, 547–558. [https://doi.org/10.1016/S1474-4422\(15\)00021-6](https://doi.org/10.1016/S1474-4422(15)00021-6).
- Riemann, D., Spiegelhalter, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., Nissen, C., 2010. The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep Med. Rev.* 14, 19–31. <https://doi.org/10.1016/j.smrv.2009.04.002>.
- Robertsson, C., Hellström, J., Cross, M., Sydsjö, G., 2014. Anxiety in early pregnancy: prevalence and contributing factors. *Arch. Womens. Ment. Health* 17, 221–228. <https://doi.org/10.1007/s00737-013-0409-0>.
- Ruscio, A.M., Stein, D.J., Chiu, W.T., Kessler, R.C., 2010. The epidemiology of obsessive-compulsive disorder in the national comorbidity survey replication. *Mol. Psychiatry* 15, 53–63. <https://doi.org/10.1038/mp.2008.94>.
- Russell, E.J., Fawcett, J.M., Mazmanian, D., 2013. Risk of obsessive-compulsive disorder in pregnant and postpartum women: a meta-analysis. *J. Clin. Psychiatry* 74, 377–385. <https://doi.org/10.4088/JCP.12r07917>.
- Sandanger, I., Moum, T., Ingebrigtsen, G., Dalgard, O.S., Sørensen, T., Bruusgaard, D., 1998. Concordance between symptom screening and diagnostic procedure: the hopkins symptom checklist-25 and the composite international diagnostic interview i. *Soc. Psychiatry Psychiatr. Epidemiol.* 33, 345–354.
- Schetter, C.D., Tanner, L., 2012. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. *Curr. Opin. Psychiatry* 25, 141–148. <https://doi.org/10.1097/YCO.0b013e3283503680>.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for dsm-iv and ICD-10. *J. Clin. Psychiatry* 59, 22–33. [https://doi.org/10.1016/S0924-9338\(99\)80239-9](https://doi.org/10.1016/S0924-9338(99)80239-9).
- Sinesi, A., Maxwell, M., Carroll, R.O., Cheyne, H., 2019. Anxiety scales used in pregnancy: systematic review. *BJPsych Open* 5, 1–13. <https://doi.org/10.1192/bjo.2018.75>.
- Singareddy, R., Vgontzas, A.N., Fernandez-Mendoza, J., Liao, D., Calhoun, S., Shaffer, M.L., Bixler, E.O., 2012. Risk factors for incident chronic insomnia: a general population prospective study. *Sleep Med* 13, 346–353. <https://doi.org/10.1016/j.sleep.2011.10.033>.
- Smith, M.V., Howell, H., Wang, H., Poschman, K., Yonkers, K.A., 2009. Success of mental health referral among pregnant and postpartum women with psychiatric distress. *Gen. Hosp. Psychiatry* 31, 155–162. <https://doi.org/10.1016/j.genhosppsych.2008.10.002>.
- Statistics Norway, 2016. Statistisk sentralbyrå - Statistics Norway [WWW Document]. URL <https://www.ssb.no/en/helse/statistikk/helseforhold/hvert-3-aar> (accessed 6. 19.19).
- Swanson, L.M., Pickett, S.M., Flynn, H., Armitage, R., 2011. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. *J. Women's Heal.* 20, 553–558. <https://doi.org/10.1089/jwh.2010.2371>.
- Swearingen, E.M., Cohen, L.H., 1985. Measurement of adolescents' life events: the junior high life experiences survey. *Am. J. Community Psychol.* 13, 69–85. <https://doi.org/10.1007/BF00923260>.
- Thiséus, J., Perrin, S., Cervin, M., 2019. Intrusive thoughts and compulsive behaviors in postpartum women: psychometric properties of the parental thoughts and behaviors checklist. *Psychiatry Res* 278, 194–198. <https://doi.org/10.1016/j.psychres.2019.06.015>.
- Veijola, J., Jokelainen, J., La, K., Joukamaa, M., Kokkonen, P., Ja, M., 2003. The hopkins symptom checklist-25 in screening dsm-iii-r axis-I disorders. *Nord. J. Psychiatry* 57, 119–123.
- Wassing, R., Benjamins, J.S., Talamini, L.M., Schalkwijk, F., Van Someren, E.J.W., 2018. Overnight worsening of emotional distress indicates maladaptive sleep in insomnia. *Sleep* 1–8. <https://doi.org/10.1093/sleep/zsy268>.
- Wenzel, A., Haugen, E.N., Jackson, L.C., Brendle, J.R., 2005. Anxiety symptoms and disorders at eight weeks postpartum. *J. Anxiety Disord.* 19, 295–311. <https://doi.org/10.1016/j.janxdis.2004.04.001>.
- Wijma, K., Wijma, B., Zar, M., 1998. Psychometric aspects of the W-DEQ; a new questionnaire for the measurement of fear of childbirth. *J. Psychosom. Obstet. Gynaecol.* 19, 84–97. <https://doi.org/10.3109/01674829809048501>.
- Ye, Y.Y., Zhang, Y.F., Chen, J., Liu, J., Li, X.J., Liu, Y.Z., Lang, Y., Lin, L., Yang, X.J., Jiang, X.J., 2015. Internet-based cognitive behavioral therapy for insomnia (ICBT-i) improves comorbid anxiety and depression - A meta-analysis of randomized controlled trials. *PLoS ONE* 10, 1–11. <https://doi.org/10.1371/journal.pone.0142258>.