Asselmann, E., Kunas, S.L., Wittchen, H.-U., & Martini, J. (2020). Changes in psychopathological symptoms during pregnancy and after delivery: A prospective-longitudinal study in women with and without anxiety and depressive disorders prior to pregnancy. *Journal of Affective Disorders*, 263, 480-490.

<https://doi.org/10.1016/j.jad.2019.11.112>

Changes in psychopathological symptoms during pregnancy and after delivery: A prospective-longitudinal study in women with and without anxiety and depressive disorders prior to pregnancy

Asselmann, E. ¹, Kunas, S. L. ², Wittchen, H.-U. ³ & Martini, J. ^{3,4}

Author affiliations:

¹ Department of Psychology, Faculty of Life Sciences, Humboldt University of Berlin,
Berlin, Germany

² Department of Psychiatry and Psychotherapy, Campus Charité Mitte, Charité
Universitätsmedizin Berlin, Berlin, Germany^[SEP]

³ Institute of Clinical Psychology and Psychotherapy, Technische Universität Dresden,
Dresden, Germany

⁴ Department of Psychiatry & Psychotherapy, Faculty of Medicine, Carl Gustav Carus
University Hospital, Technische Universität Dresden, Dresden,
Germany

Corresponding Author:

Eva Asselmann

Humboldt University of Berlin

Faculty of Life Sciences

Department of Psychology

Unter den Linden 6, 10099 Berlin, Germany

Phone: +49 30 2093 9430

E-Mail: eva.asselmann@hu-berlin.de

Abstract

Background: The role of anxiety and depressive disorders prior to pregnancy for changes in peripartum psychopathological symptoms has not been resolved yet. **Methods:** A regional-epidemiological sample of 306 women was prospectively followed up in seven waves from early pregnancy until 16 months postpartum. Lifetime DSM-IV anxiety and depressive disorders were assessed at baseline with the CIDI-V. Psychopathological symptoms (somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) were measured with the BSI three times during pregnancy and three times after delivery. **Results:** Multilevel analyses revealed that women with versus without lifetime anxiety ($\beta=0.22$ to $\beta=0.32$) and depressive ($\beta=0.24$ to $\beta=0.34$) disorders prior to pregnancy experienced higher peripartum psychopathological symptoms. All symptoms linearly decreased during pregnancy ($\beta=-0.02$ to $\beta=-0.07$ per month). Somatization ($\beta=-0.46$) was lower, whereas paranoid ideation ($\beta=0.26$) and obsession-compulsion ($\beta=0.21$) were higher after delivery than during pregnancy. Though, obsession-compulsion linearly decreased after delivery ($\beta=-0.02$). Lifetime anxiety disorders prior to pregnancy interacted with linear changes in anxiety ($\beta=-0.04$) and phobic anxiety ($\beta=-0.05$) during pregnancy. That is, only women with but not without anxiety disorders prior to pregnancy experienced a linear decline in anxiety and phobic anxiety during pregnancy. **Limitations:** Lifetime anxiety and depressive disorders were assessed in early pregnancy and might be biased. **Conclusions:** Peripartum psychopathological symptoms are higher in women with versus without lifetime anxiety and depressive disorders prior to pregnancy, but symptom changes only slightly vary by lifetime diagnostic status.

Key words: Psychopathology; childbirth; delivery; postpartum; symptom trajectory.

Highlights

- We examined changes in psychopathological symptoms over the peripartum period
- All psychopathological symptoms linearly decreased during pregnancy
- Symptoms of somatization were lower after delivery
- Symptoms of obsession-compulsion and paranoid ideation were higher after delivery
- Though, symptoms of obsession-compulsion linearly decreased after delivery
- (Phobic) anxiety during pregnancy only decreased in women with anxiety disorders

Introduction

Anxiety and depressive disorders belong to the most frequent mental disorders in women of reproductive age (Kessler et al., 2012). Both diagnostic classes are characterized by etiological similarities but also differences frequently co-occur, and prospectively relate to each other (Andrews et al., 2010; Asselmann et al., 2018a; Asselmann et al., 2018c; Beesdo-Baum et al., 2009; Bittner et al., 2007; Copeland et al., 2009; Goldberg et al., 2009; Kessler et al., 2011; Kessler et al., 2012). More specifically, anxiety and depressive disorders prior to pregnancy are associated with an increased risk for anxiety and depressive disorders during and after pregnancy (Biaggi et al., 2016; Martini et al., 2015) and may lead to various unfavorable outcomes in (expectant) mothers and their offspring (Asselmann et al., 2016a; Asselmann et al., 2018b; Asselmann et al., 2016b; Asselmann et al., 2016c; Ding et al., 2014; Martini et al., 2016; Martini et al., 2017; Petzoldt et al., 2016). Therefore, a major task is to unravel how changes in anxiety, depressive, and other psychopathological symptoms at individual stages of the peripartum period differ between women with and without a history of anxiety and depression. Such knowledge is crucial to improve an early recognition of pregnant women who are particularly likely to experience a (further) symptom escalation that might result into full-threshold psychopathology and associated adversities (Goodman et al., 2016; Viswasam et al., 2019).

Various studies revealed that anxiety and depressive symptoms during pregnancy and after delivery remained relatively stable or even decreased over time (Figueiredo and Conde, 2011; Grant et al., 2008; Heron et al., 2004; Leach et al., 2014; Moss et al., 2009; Schubert et al., 2017; Skouteris et al., 2009). Such favorable changes might be explained by a cascade of pregnancy-related bodily (e.g., cardiovascular, neural, endocrine, and inflammatory) changes that have inter alia been associated with alterations and improvements in stress responsivity

or mood (De Weerth and Buitelaar, 2005; Entringer et al., 2010; Glynn et al., 2001; Obel et al., 2005; Osborne and Monk, 2013).

Though, symptom trajectories considerably varied (Ahmed et al., 2019; Ahmed et al., 2018; Baron et al., 2017; Cents et al., 2013; Fredriksen et al., 2017; Korja et al., 2018; Luoma et al., 2015; Sutter-Dallay et al., 2012), and previous research identified several risk factors for more unfavorable trajectories such as persistently high or increasing symptoms (Baron et al., 2017; Biaggi et al., 2016). In this context, especially increased anxiety and depressive symptoms in early pregnancy as well as a history of psychopathology or psychiatric treatment have been associated with more unfavorable changes in anxiety and depressive symptoms over the peripartum period (Ahmed et al., 2019; Ahmed et al., 2018; Fredriksen et al., 2017; Grant et al., 2008; Heron et al., 2004; Korja et al., 2018; Luoma et al., 2015; Micali et al., 2011; Moss et al., 2009; Schubert et al., 2017; Skouteris et al., 2009).

However, many of these studies started in middle or late pregnancy and investigated the predictive role of concurrent anxiety and depressive symptoms (during pregnancy) or a self-reported history of disorder (Baron et al., 2017; Biaggi et al., 2016). This impedes studying the role of anxiety and depression status for changes in psychopathological symptoms over the entire peripartum period, since concurrent anxiety and depressive symptoms might already be affected by the pregnancy and self-reported diagnoses might be biased. Therefore, additional studies are needed that start as soon as the pregnancy has been confirmed and examine the role of full-threshold lifetime anxiety and depressive disorders (assessed with a standardized diagnostic interview according to ICD or DSM criteria) prior to pregnancy for symptom changes from early pregnancy until late postpartum (Martini et al., 2013). Comprehensive information on a history of clinically significant disorders promises to be particularly useful to early and precisely identify high-risk groups of pregnant women but has rarely been considered so far (Martini et al., 2015).

Moreover, previous research mostly focused on peripartum changes in overall anxiety and/ or depressive symptoms. In contrast, less is known on how peripartum changes of different anxiety, depressive, and other psychopathological symptoms vary between women with and without anxiety and depression liability. Especially anxiety disorders are a phenotypically highly heterogeneous group of disorders (Beesdo-Baum and Knappe, 2012; Craske et al., 2009; Shear et al., 2007). In the general population and (expectant) mothers, anxiety and depressive disorders are characterized by high comorbidities with other mental disorders and not only homotypic but also heterotypic continuities (that is, prospective associations with disorders of the same and other diagnostic classes; Asselmann et al., 2018c; Biaggi et al., 2016; Bittner et al., 2007; Copeland et al., 2009; Grant et al., 2008; Kessler et al., 2011; Kessler et al., 2012; Martini et al., 2015; Micali et al., 2011). It is thus plausible to assume that (expectant) mothers with versus without lifetime anxiety and depressive disorders prior to pregnancy are at increased risk for various types of psychopathology but that individual symptom changes differ from each other (e.g., for general versus phobic anxiety).

In this context, it is important to not only account for continuous but also discontinuous short- and long-term symptom changes during pregnancy and after delivery. The birth of a child constitutes one of the most striking experiences in life and leads to immediate and far-reaching bodily and socio-environmental changes. Therefore, (expectant) mothers might not only experience a gradual increase or decrease in symptoms over the peripartum period but also abrupt symptom changes after delivery. These changes might be either transient (lasting for a few weeks only) or enduring (lasting for several months or years) and vary between women with and without anxiety and depressive disorders prior to pregnancy. However, prospective-longitudinal study designs with multiple waves of

assessment from early pregnancy until late postpartum are necessary to test these assumptions.

Here, we use data from a prospective-longitudinal regional-epidemiological study among 306 pregnant women from Germany. Lifetime anxiety and depressive disorders according to DSM-IV were assessed in early pregnancy and diverse psychopathological symptoms were measured repeatedly (up to six times) from early pregnancy until up to 16 months postpartum. Based on these data, we examined how individual symptoms changed over the peripartum period and whether these changes differed between women with and without lifetime anxiety and depressive disorders prior to pregnancy, respectively. We considered continuous and discontinuous as well as short- and long-term changes, including (a) linear symptom changes during pregnancy (from 10 - 12 to 35 - 37 weeks of gestation), (b) linear symptom changes after delivery (from two to 16 months postpartum), (c) abrupt and transient short-term symptom changes after delivery (at two months postpartum), as well as (d) abrupt and enduring long-term symptom changes after delivery (from two to 16 months postpartum).

Our hypotheses are as follows: All types of psychopathological symptoms gradually decrease during pregnancy and after delivery and are lower after delivery than during pregnancy. However, these favorable changes are less pronounced in women with versus without lifetime anxiety and depressive disorders prior to pregnancy, respectively. More specifically, women with lifetime anxiety disorders prior to pregnancy experience a weaker decrease (or even increase) especially in anxiety and closely associated symptoms (anxiety, phobic anxiety, and obsession-compulsion) over the peripartum period. In contrast, women with lifetime depressive disorders prior to pregnancy experience a weaker decrease (or even increase) especially in depressive and closely associated symptoms (depression, somatization, and interpersonal sensitivity) during pregnancy and after delivery. Other trajectories (abrupt

and transient short-term changes after delivery) and changes in other symptoms (in hostility, paranoid ideation, and psychoticism) are additionally explored.

Method

Procedure

The prospective-longitudinal Maternal Anxiety in Relation to Infant Development (MARI) Study was conducted in 306 expectant mothers, sampled from the community in gynecological outpatient settings in the area of Dresden, Germany (study period: 01/ 2009 until 09/ 2012). These (expectant) mothers (and their infants) completed up to seven assessments: T1 (baseline): week 10 to 12 of gestation; T2: week 22 to 24 of gestation; T3: week 35 to 37 of gestation; T4: 10 days postpartum; T5: two months postpartum; T6: four months postpartum; and T7: 16 months postpartum.

Participants were assessed with standardized diagnostic interviews, questionnaires, and observations. Informed consent was obtained from all participants. The study was carried out in accordance with the Helsinki Declaration of 1975 (as revised in 2013) and approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (No: EK 94042007). More detailed information concerning the objectives, methods, design, and inclusion/ exclusion criteria as well as a detailed study flow chart have been previously published (Martini et al., 2015; Martini et al., 2013).

Sample

In total, 533 pregnant women were screened for inclusion and exclusion criteria in gynecological outpatient settings in the area of Dresden (Germany). Fifty women met the exclusion criteria (gestational age > 12 weeks: $N = 8$; aged younger than 18 or older than 40 years: $N = 8$; multiple pregnancy: $N = 2$; history of more than three spontaneous abortions, (induced) termination of pregnancy, still birth, or infant impairment: $N = 2$; invasive fertility treatment: $N = 9$; severe physical disease, microsomia, or skeletal malformation: $N = 6$; substance abuse or heroin substitution during the past six months: $N = 0$; severe psychiatric

illness: $N = 2$; expectation of leaving the area of Dresden: $N = 6$; insufficient mastery of the German language: $N = 7$). In addition, nine women did not participate due to spontaneous abortions before T1, ten because their partner did not agree, 154 due to a lack of time, and four due to unknown reasons.

Finally, 306 women were enrolled in the study, and 274 women could be retained until T7 (retention rate: 89.5 %). More specifically, 306 women participated at T1, 293 at T2, 278 at T3, 284 at T4, 281 at T5, 283 at T6, and 267 at T7. Due to spontaneous abortion or termination of pregnancy, the participation of eight women ended after T1. During the study, three women moved away, five women could not be reached anymore by phone, postal, or personal contact, nine women reported a lack of time or interest in a further participation, and seven women refused to be contacted again for additional follow-up assessments. Some retained women did not participate in single assessments, for example, due to preterm delivery, sickness, or a lack of time (T3: $N = 10$; T4: $N = 2$; T5: $N = 5$; T6: $N = 1$; T7: $N = 7$). Detailed information on sociodemographic, gynecological, and clinical characteristics of the study sample, including information on systematic drop out from T1 to T7, has been previously presented (Martini et al., 2015; Martini et al., 2013).

Assessment of maternal anxiety and depressive disorders

Maternal anxiety, depressive, and other mental disorders prior to, during, and after pregnancy were assessed at each wave (T1, T2, T3, T5, T6, and T7) except for T4 (shortly after delivery) using the Composite International Diagnostic Interview for Women (CIDI-V; Martini et al., 2009). The CIDI-V is a modified version of the WHO-CIDI (World Health Organization, 1990) and allows for a fully standardized assessment of symptoms, syndromes, and diagnoses of mental disorders according to DSM-IV-TR and ICD-10 criteria, including information on onset, recency, severity, comorbidity, and impairments. Moreover, the CIDI-

V accounts for a range of female-specific conditions and factors (e.g., the menstrual and reproductive history). The lifetime version was used at baseline (T1) and the interval version at follow-up (T2, T3, T5, T6, and T7). Cognitive probes and timelines were used to enhance the accuracy of respondents' reports for the respective reference period.

The psychometric properties of the CIDI have been shown to be good (Reed et al., 1998; Wittchen et al., 1998). For instance, test-retest reliabilities over an average period of 38 days were high with kappa values of $\kappa = 0.68$ for any major depressive disorder, $\kappa = 0.70$ for dysthymia, and $\kappa = 0.81$ for any anxiety disorder (Wittchen et al., 1998).

Diagnostic interviews were conducted by psychologists who were initially trained (for one week) and conducted a series of supervised practice interviews. All interviewers were closely monitored by experienced supervisors (clinical psychologists only; Martini et al., 2015; Martini et al., 2013). To encourage a further study participation, participants were interviewed by the same investigator throughout the study whenever possible.

Overall, 109 women did not meet criteria for any lifetime anxiety or depressive disorder prior to pregnancy. 149 women fulfilled criteria for any lifetime anxiety disorder (panic disorder, agoraphobia, social phobia, specific phobia, phobia not otherwise specified, obsessive-compulsive disorder, generalized anxiety disorder, or post-traumatic stress disorder) prior to pregnancy. 113 women met criteria for any lifetime depressive disorder (major depressive disorder or dysthymia) prior to pregnancy. Of these women, 65 were affected by both any lifetime anxiety disorder and any lifetime depressive disorder prior to pregnancy. To account for these comorbidities, both (a) any anxiety disorder prior to pregnancy and (b) any depressive disorder prior to pregnancy were included as predictors in all our models (see below). Detailed information on sociodemographic and clinical characteristics at baseline (T1; Martini et al., 2013) as well as rates of incident and recurrent or persistent anxiety and depressive disorders over the course of the study (until T7; Martini

et al., 2015) in women with pure anxiety, pure depressive, and comorbid anxiety and depressive disorders (as well as specific diagnoses) prior to pregnancy has been previously presented.

Assessment of psychopathological symptoms

Psychopathological symptoms were assessed at each wave (T1, T2, T3, T5, T6, and T7) except for T4 (shortly after delivery) with the German version of the Brief Symptom Inventory (BSI; Geisheim et al., 2002), a short version of the Symptom Checklist-90 that consists of 53 items, labeled from 0 (not at all) to 4 (extremely). The BSI includes the following subscales: somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Moreover, a global severity index can be built to indicate the average score across the entire inventory, with higher scores indicating higher severity. Reliability and validity of the BSI have been extensively studied and reported elsewhere (Derogatis, 2000; Derogatis and Melisaratos, 1983; Geisheim et al., 2002).

The BSI was embedded in the CIDI-V and checked for completeness immediately. Therefore, all women who participated at T1, T2, T3, T5, T6, and T7 provided full information on the BSI. The only exception was that twelve mothers at T7 did not answer the BSI at this wave due to a lack of time during the interview. Six of them fulfilled criteria for any lifetime anxiety disorder prior to pregnancy and five for any lifetime depressive disorder prior to pregnancy at baseline.

Statistical analyses

We used Stata 14 (StataCorp, 2015) for the analyses and applied multilevel analyses with measurement occasions (Level 1) nested within persons (Level 2). Because multilevel analyses enable to deal with missing data at individual time points, our models refer to the total baseline sample ($N = 306$), including women who did or did not participate in all subsequent waves. We built separate models per subscale (somatization, obsession–compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and global severity index) and modeled the effects as fixed effects.

More specifically, we simultaneously regressed the standardized score of the respective continuous symptom subscale of the BSI on linear age (in years at T1, centered ¹), quadratic age (centered linear age* centered linear age), cubic age (centered linear age* centered linear age* centered linear age), any anxiety disorder prior to pregnancy (yes (1) versus no (0), centered ¹), any depressive disorder prior to pregnancy (yes (1) versus no (0), centered ¹), and four event-related predictors that coded how the time point of the respective BSI assessment was related to the time point of delivery.

(1) *Linear changes during pregnancy*: This variable was built to indicate gradual symptom changes from early pregnancy (10 - 12 weeks of gestation) until late (35 - 37 weeks of gestation) pregnancy. It was coded with the time span (in months) between the respective assessment and delivery for all measurement occasions during pregnancy (T1, T2, and T3) and coded with 0 for all measurement occasions after delivery (T5, T6, and T7). Because a few women were not retained in the study until their child was born, we assumed an average

¹ In the analyses, these variables were centered to ensure that the intercept in the overall model referred to an average woman of the total sample (of average age as well as with or without anxiety and/ or depressive disorders).

length of pregnancy of 40 weeks for all women and subtracted the average week of gestation, in which the respective assessment was conducted, from this length. Because T1 was conducted between week 10 and 12 of gestation, T2 was conducted between week 22 and 24 of gestation, and T3 was conducted between week 35 and 37 of gestation, we coded this variable with $-29/4$ (-7.25) for T1, with $-17/4$ (-4.25) for T2, and with $-4/4$ (-1) for T3 (the number of weeks was divided by four, since time was measured in monthly increments).

(2) *Linear changes after delivery*: We generated this variable to analyze gradual symptom changes from early (two months) until late (16 months) postpartum. It was coded with the time span (in months) between the respective assessment and delivery for all measurement occasions after delivery (T5, T6, and T7) and coded with 0 for all measurement occasions during pregnancy (T1, T2, and T3). Because T5 was conducted two months postpartum, T6 was conducted four months postpartum, and T7 was conducted 16 months postpartum, we coded this variable with 2 for T5, with 4 for T6, and with 16 for T7.

(3) *Short-term changes after delivery*: We built this variable to examine transient short-term symptom changes in the first weeks postpartum. It was coded with 1 for T5 (conducted two months postpartum) and coded with 0 for all other measurement occasions (T1, T2, T3, T6, and T7), thus indicating the difference in symptoms between T5 and all other waves.

(4) *Baseline changes after delivery*: We generated this variable to investigate enduring long-term symptom changes after delivery. It was coded with 1 for all measurement occasions after delivery (T5, T6, and T7) and coded with 0 for all measurement occasions during pregnancy (T1, T2, and T3), thus indicating the difference between postpartum and prepartum symptoms.

We further examined whether changes in psychopathological symptoms varied as a function of lifetime anxiety and depressive disorders prior to pregnancy. To do so, we

included an interaction term between the respective event-related predictor and (a) any lifetime anxiety disorder prior to pregnancy (yes (1) versus no (0), centered) as well as (b) any lifetime depressive disorder prior to pregnancy (yes (1) versus no (0), centered). One interaction term was included at a time. In case of a significant interaction, we built separate models in women with and without the respective lifetime disorder prior to pregnancy to test how the event-related predictor was associated with the outcome in both groups.

Because each analysis refers to an individual research question, we did not adjust for multiple testing (Savitz and Olshan, 1995). However, we set the alpha level at .01.

Results

Correlations between individual psychopathological symptoms (averaged across all six waves) in the total sample are shown in Supplemental Table 1. Means and standard deviations for these symptoms at each wave and averaged across all six waves (unstandardized scores) in the total sample are presented in Table 1. Respective data for women with ($N = 149$, 48.69 %) and without ($N = 157$, 51.31 %) any lifetime anxiety disorder prior to pregnancy as well as women with ($N = 113$, 36.93 %) and without ($N = 193$, 63.07 %) any depressive disorder prior to pregnancy are shown in Table 2 and Table 3.

Insert Table 1, Table 2, and Table 3

Psychopathological symptoms by anxiety and depressive disorders prior to pregnancy

As shown in Table 4, women with any lifetime anxiety disorder prior to pregnancy ($\beta = 0.22$ to $\beta = 0.32$) and women with any lifetime depressive disorder prior to pregnancy ($\beta = 0.24$ to $\beta = 0.34$) experienced higher psychopathological symptoms over the peripartum period than women without the respective lifetime disorder prior to pregnancy. The only exceptions were that somatization, obsession-compulsion, and paranoid ideation did not differ between women with and without any lifetime anxiety disorder prior to pregnancy ($p > .01$) and that obsession-compulsion, depression, and hostility did not differ between women with and without any lifetime depressive disorder prior to pregnancy ($p > .01$).

Insert Table 4

Symptom changes over time

Examining linear changes in psychopathological symptoms during pregnancy and after delivery revealed that all of the examined symptoms gradually decreased from early until late pregnancy ($\beta = -0.02$ to $\beta = -0.07$ per month). Moreover, obsession-compulsion

decreased from two months until 16 months postpartum ($\beta = -0.02$ per month) but no other linear symptom changes after delivery were found ($p > .01$). Similarly, there was no evidence for any transient short-term changes in psychopathological symptoms two months after delivery ($p > .01$).

With respect to baseline changes in psychopathological symptoms after delivery, we found that somatization ($\beta = -0.46$) was lower, whereas obsession-compulsion ($\beta = 0.21$) and paranoid ideation ($\beta = 0.26$) were higher after delivery than during pregnancy. Figure 1 visualizes how individual psychopathological symptoms changed over time.

Insert Figure 1

Symptom changes by anxiety and depressive disorders prior to pregnancy

In addition, we examined whether changes in psychopathological symptoms over the peripartum period differed between women with and without any lifetime anxiety and depressive disorder prior to pregnancy, respectively. Findings revealed that any lifetime anxiety disorder prior to pregnancy interacted with linear changes in anxiety ($\beta = -0.04$, 99 % CI: -0.07, -0.01, $p = .003$) and phobic anxiety ($\beta = -0.05$, 99 % CI: -0.08, -0.02, $p < .001$) during pregnancy. That is, anxiety and phobic anxiety during pregnancy only decreased in women with any lifetime anxiety disorder prior to pregnancy (anxiety; $\beta = -0.06$, 99 % CI: -0.10, -0.03, $p < .001$; phobic anxiety: $\beta = -0.07$, 99 % CI: -0.11, -0.03, $p < .001$) but not in women without a history of anxiety ($p > .01$; Figure 2). However, there was no evidence that any other symptom changes differed between women with and without a lifetime history of anxiety or depression, respectively ($p > .01$).

Insert Figure 2

Discussion

The aim of this study was to examine (a) whether (expectant) mothers experience continuous and discontinuous short- and long-term changes in widespread psychopathological symptoms at different stages over the peripartum period and (b) whether these changes vary by lifetime anxiety and depressive disorders prior to pregnancy. For this purpose, a regional-epidemiological community sample of 306 women was prospectively followed up from early pregnancy until up to 16 months postpartum.

We found that women with lifetime anxiety disorders prior to pregnancy experienced higher psychopathological symptoms over the peripartum period than women without lifetime anxiety disorders prior to pregnancy. The same was true for women with versus without lifetime depressive disorders prior to pregnancy. These findings are in line with previous evidence that a history of mental disorders (including anxiety and depression) relates to an increased risk for anxiety and depressive symptoms and disorders during pregnancy and after delivery (Ahmed et al., 2019; Ahmed et al., 2018; Biaggi et al., 2016; Martini et al., 2015; Schubert et al., 2017). In particular, our results correspond to previous evidence from the MARI study that anxiety and depressive disorders prior to pregnancy were associated with elevated rates of clinically significant, full-threshold anxiety and depressive disorders (Martini et al., 2015) as well as pregnancy- and child-related fears and anxieties (Martini et al., 2016) during pregnancy and after delivery. Our findings might be due to multiple factors, including less favorable bodily (e.g., cardiovascular, neuroendocrine, and inflammatory; e.g., Winkel et al., 2015) and psychosocial (e.g., lower self-esteem and lower social support; e.g., Asselmann et al., 2016) changes in women with heightened anxiety and depression vulnerability (Biaggi et al., 2016; Hodgson and Coe, 2019). Though, a few associations between lifetime anxiety or depressive disorders and individual symptoms in our study were not or only marginally significant. One might speculate whether these symptoms

varied as a function of specific clinical features (e.g., specific diagnoses of anxiety or depressive disorders, severity, comorbidity, duration, and persistence; Martini et al., 2015).

Moreover, all types of symptoms declined from early until late pregnancy. This corresponds to our hypotheses and previous evidence that psychopathological symptoms remained stable or even improved over the peripartum period (Figueiredo and Conde, 2011; Grant et al., 2008; Heron et al., 2004; Leach et al., 2014; Moss et al., 2009; Schubert et al., 2017; Skouteris et al., 2009). In contrast to many previous studies, our study started as soon as the pregnancy was confirmed, which enabled us to model change trajectories from week ten of gestation onwards. Therefore, our findings considerably extend previous evidence. The fact that psychopathological symptoms especially improved during pregnancy might be explained by a range of complex pregnancy-related bodily (e.g., cardiovascular, neuroendocrine, and inflammatory) changes that have been associated with alterations and improvements in stress responsivity and mood (Osborne and Monk, 2013; De Weerth and Buitelaar, 2005; Entringer et al., 2010; Glynn et al., 2001; Obel et al., 2005). Besides, women with increasing psychopathological symptoms during pregnancy might have been more likely to end their study participation (selective drop out). However, the retention rate was high (89.5 % until last follow-up) and similar for women with and without anxiety and depressive disorders prior to pregnancy (Martini et al., 2015; Martini et al., 2013).

In addition, mothers experienced lower somatization but higher obsessive-compulsive and paranoid symptoms after delivery than during pregnancy. At the same time, postpartum obsessive-compulsive symptoms gradually decreased over time. As suggested by previous research, postpartum obsessive-compulsive symptoms such as unwanted, intrusive thoughts of infant-related harm are common and particularly pronounced in the first weeks after delivery (Abramowitz et al., 2007; Brok et al., 2017; Fairbrother and Woody, 2008). Inter alia, this might be explained by specific neuroendocrine changes (e.g., in estrogen and

progesterone; Forray et al., 2010) but also novel role expectations and responsibility, for example, to protect the newborn (Abramowitz et al., 2007). Moreover, former studies evidenced increased rates of psychosis after delivery (Jones et al., 2014; Wesseloo et al., 2015), which corresponds to our results. In this respect, it has been previously discussed whether some women might be particularly susceptible to abrupt neuroendocrine changes (affecting inter alia the dopaminergic system; Maguire, 2020) as well as sleep loss after childbirth (Lewis et al., 2018; Sharma and Mazmanian, 2003). The fact that somatization symptoms were lower after delivery might be due to the possibility that many women had experienced specific, pregnancy-related bodily changes and associated somatic complaints that improved immediately after delivery (Body and Christie, 2016; Lagadec et al., 2018).

There was little evidence that the course of psychopathological symptoms during pregnancy and after delivery differed between women with and without lifetime anxiety and depressive disorders prior to pregnancy, respectively. However, only women with but not without a lifetime history of anxiety experienced improvements in anxiety and phobic anxiety over the course of pregnancy. As shown in Figure 2, women with versus without any lifetime anxiety disorder prior to pregnancy initially experienced higher levels of anxiety and phobic anxiety in early pregnancy but symptom levels around birth were similar in both groups. These findings are particularly noteworthy, since anxiety and depressive symptoms and disorders have often been associated with less favorable changes in peripartum symptoms (Ahmed et al., 2019; Ahmed et al., 2018; Fredriksen et al., 2017; Grant et al., 2008; Heron et al., 2004; Korja et al., 2018; Luoma et al., 2015; Micali et al., 2011; Moss et al., 2009; Schubert et al., 2017; Skouteris et al., 2009). The majority of these previous studies examined the predictive role of concurrent anxiety or depressive symptoms (in pregnancy) or a self-reported history of psychopathology. In contrast, we focused on lifetime anxiety and depressive disorders prior to pregnancy that were assessed with a standardized diagnostic

interview according to DSM criteria shortly after the pregnancy was confirmed. These methodological differences might explain seemingly contradictory results. One might further speculate whether women with a history of anxiety disorders often tended to experience specific pregnancy- and child-related (instead of other) fears and anxieties during the peripartum period (Martini et al., 2016).

Strengths and limitations

Our study has several strengths but is not without limitations: First, lifetime anxiety and depressive disorders prior to pregnancy (according to DSM-IV) were assessed in early pregnancy with a standardized diagnostic interview (CIDI-V). Cognitive probes and timelines were used to maximize the accuracy of participants' reports. However, retrospective memory and recall biases might have occurred. For example, currently healthy women with mild or short-term anxiety or depressive disorders several years ago might not have fully recalled their past symptoms, leading to a potential underestimation of lifetime psychopathology (Andrews et al., 1999; Moffitt et al., 2010).

Second, anxiety, depressive, and other psychopathological symptoms during pregnancy and after delivery were measured at up to six time points with a well-established questionnaire (BSI). Though, the BSI is relatively short, which impedes to distinguish between measurement errors and true changes over time. Moreover, the BSI primarily focuses on internalizing symptoms. Thus, additional studies are needed to examine the role of anxiety and depressive disorders prior to pregnancy for changes in other (e.g., externalizing) symptoms. Especially ecological momentary assessments might be useful to measure short-term fluctuations hereon in time to experience across different situations in everyday life (Doyle et al., 2015; Giesbrecht et al., 2012).

Third, our study is based on a prospective-longitudinal design. That is, lifetime disorders were assessed in early pregnancy (at baseline) and psychopathological symptoms were measured three times during pregnancy and three times after delivery. Based on these data, we simultaneously modeled continuous and discontinuous short- and long-term changes in psychopathological symptoms during pregnancy and after delivery. However, more subtle changes (e.g., quadratic or cubic effects) were not assessed and require further investigation based on larger samples, if they are theoretically plausible to assume.

Fourth, larger studies are also needed to examine the role of specific lifetime diagnoses of anxiety and depressive disorders prior to pregnancy (including their clinical features and previous treatment due to these disorders) for changes in peripartum psychopathological symptoms. For example, only nine women were diagnosed with obsessive-compulsive disorder at baseline (Martini et al., 2013). The role of specific diagnoses was therefore not considered herein.

Fifth, 89.5 % of the total sample could be retained from baseline until last follow-up and all women who participated at individual waves (except for twelve women at T7) provided information on the BSI. Although the retention rate was high and similar for women with and without anxiety and depressive disorders prior to pregnancy (Martini et al., 2015; Martini et al., 2013), systematic drop out might have occurred. For instance, women with increasing symptoms and impairments might have been more likely to end their participation, leading to an underestimation of peripartum psychopathological symptoms.

Sixth, our findings stem from a regional-epidemiological sample from Dresden but might not be generalizable to pregnant women in general (Martini et al., 2015; Martini et al., 2013).

Conclusions

Our findings suggest that pregnant women experience improvements with respect to a wide variety of psychopathological symptoms over the course of their pregnancy. Symptoms of somatization are lower, whereas symptoms of obsession-compulsion and paranoid ideation are higher after delivery than during pregnancy. Obsessive-compulsive symptoms gradually improve but other symptoms remain largely unchanged after delivery. Women with (versus without) lifetime anxiety and depressive disorders prior to pregnancy experience higher overall levels but similar changes in psychopathological symptoms over the peripartum period. The only exception is that anxiety and phobic anxiety during pregnancy more strongly improve in women with versus without a lifetime history of anxiety disorders prior to pregnancy.

Additional research is needed to examine the underlying individual (e.g., psychobiological changes such as alterations in sex and stress hormones) and socio-environmental (e.g., family- and work-related changes) mechanisms to explain these changes. In particular, larger epidemiological studies may investigate the role of specific diagnoses and clinical features of anxiety and depressive disorders prior to pregnancy (e.g., specific diagnosis, severity, comorbidity, onset, persistence, and recurrence) for changes in psychopathological symptoms over the peripartum period in further detail.

Role of the funding source

All authors had complete freedom to direct the analysis and its reporting without influence from the sponsors. There was no editorial direction or censorship from the sponsors.

Ethical standards

The authors assert that all procedures contributing to this work have been approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (No: EK 94042007) and comply with the Helsinki Declaration of 1975, as revised in 2013.

Conflict of interest

Prof. Dr. Hans-Ulrich Wittchen reports the following items that might be perceived as a potential conflict of interest: Prof. Dr. Hans-Ulrich Wittchen is on the advisory board of the Lundbeck Institute Skodsborg, Denmark and has also received grant support from there. All other authors declare that they have no financial relationships that might be perceived as a potential conflict of interest.

Acknowledgements

This work has been supported by the Institute of Clinical Psychology and Psychotherapy, Technische Universität Dresden and by the Lundbeck Institute Skodsborg, Denmark. Parts of the field work were additionally funded by the Friends and Sponsors (Gesellschaft der Freunde und Förderer) of the Technische Universität Dresden.

Principle investigators are Jun.-Prof. Dr. Julia Martini and Prof. Dr. Hans-Ulrich Wittchen. Core staff members of the project are Dipl.-Psych. Yvonne Hansche, Dr. Michael Höfler, Dipl.-Psych. Julia Niehoff, Dr. Johanna Petzoldt, Dipl.-Math. Jens Strehle, Dr. Gesine

Wieder, Dipl.-Psych. Susanne Müllender, and Dipl.- Psych. Julia Wittich. Advisors/consultants to the project are Prof. Dr. Katja Beesdo-Baum, Dr. Franziska Einsle, and Prof. Dr. Susanne Knappe.

Contributors

Julia Martini and Hans-Ulrich Wittchen were responsible for the concept, design, and methods of the study and supported and supervised the data collection of the overall study program. Eva Asselmann and Julia Martini took the lead on preparing and writing this paper. Eva Asselmann conducted the analyses and wrote the manuscript draft. Stefanie Kunas, Hans-Ulrich Wittchen, and Julia Martini provided critical revision and contributed to the interpretation of findings.

References

- Abramowitz, J.S., Nelson, C.A., Rygwall, R., Khandker, M., 2007. The cognitive mediation of obsessive-compulsive symptoms: a longitudinal study. *Journal of Anxiety Disorders* 21, 91-104.
- Ahmed, A., Bowen, A., Feng, C.X., Muhajarine, N., 2019. Trajectories of maternal depressive and anxiety symptoms from pregnancy to five years postpartum and their prenatal predictors. *BMC Pregnancy and Childbirth* 19, 26.
- Ahmed, A., Feng, C., Bowen, A., Muhajarine, N., 2018. Latent trajectory groups of perinatal depressive and anxiety symptoms from pregnancy to early postpartum and their antenatal risk factors. *Archives of Women's Mental Health* 21, 689-698.
- Andrews, G., Anstey, K., Brodaty, H., Issakidis, C., Luscombe, G., 1999. Recall of depressive episode 25 years previously. *Psychological Medicine* 29, 787-791.
- Andrews, G., Hobbs, M.J., Borkovec, T.D., Beesdo, K., Craske, M.G., Heimberg, R.G., Rapee, R.M., Ruscio, A.M., Stanley, M.A., 2010. Generalized worry disorder: a review of DSM-IV generalized anxiety disorder and options for DSM-V. *Depression and Anxiety* 27, 134-147.
- Asselmann, E., Hertel, J., Schmidt, C.O., Homuth, G., Nauck, M., Beesdo-Baum, K., Grabe, H.J., Pané-Farré, C.A., 2018a. Interplay between RGS2 and childhood adversities in predicting anxiety and depressive disorders: Findings from a general population sample. *Depression and Anxiety* 35, 1104-1113.
- Asselmann, E., Hoyer, J., Wittchen, H.-U., Martini, J., 2016a. Sexual problems during pregnancy and after delivery among women with and without anxiety and depressive disorders prior to pregnancy: a prospective-longitudinal study. *The Journal of Sexual Medicine* 13, 95-104.

- Asselmann, E., Venz, J., Wittchen, H.-U., Martini, J., 2018b. Maternal anxiety and depressive disorders prior to, during and after pregnancy and infant interaction behaviors during the Face-to-Face Still Face Paradigm at 4 months postpartum: A prospective-longitudinal study. *Early Human Development* 122, 45-53.
- Asselmann, E., Wittchen, H.-U., Erler, L., Martini, J., 2016b. Peripartum changes in social support among women with and without anxiety and depressive disorders prior to pregnancy: a prospective-longitudinal study. *Archives of Women's Mental Health* 19, 943-952.
- Asselmann, E., Wittchen, H.-U., Petzoldt, J., Martini, J., 2016c. Peripartum changes in partnership quality among women with and without anxiety and depressive disorders prior to pregnancy: a prospective-longitudinal study. *Archives of Women's Mental Health* 19, 281-290.
- Asselmann, E., Wittchen, H.U., Lieb, R., Beesdo-Baum, K., 2018c. Sociodemographic, clinical, and functional long-term outcomes in adolescents and young adults with mental disorders. *Acta Psychiatrica Scandinavica* 137, 6-17.
- Baron, E., Bass, J., Murray, S.M., Schneider, M., Lund, C., 2017. A systematic review of growth curve mixture modelling literature investigating trajectories of perinatal depressive symptoms and associated risk factors. *Journal of Affective Disorders* 223, 194-208.
- Beesdo-Baum, K., Höfler, M., Gloster, A.T., Klotsche, J., Lieb, R., Beauducel, A., Bühner, M., Kessler, R.C., Wittchen, H.u., 2009. The structure of common mental disorders: a replication study in a community sample of adolescents and young adults. *International Journal of Methods in Psychiatric Research* 18, 204-220.
- Beesdo-Baum, K., Knappe, S., 2012. Developmental epidemiology of anxiety disorders. *Child and Adolescent Psychiatric Clinics* 21, 457-478.

- Biaggi, A., Conroy, S., Pawlby, S., Pariante, C.M., 2016. Identifying the women at risk of antenatal anxiety and depression: a systematic review. *Journal of Affective Disorders* 191, 62-77.
- Bittner, A., Egger, H.L., Erkanli, A., Jane Costello, E., Foley, D.L., Angold, A., 2007. What do childhood anxiety disorders predict? *Journal of Child Psychology and Psychiatry* 48, 1174-1183.
- Body, C., Christie, J.A., 2016. Gastrointestinal diseases in pregnancy: nausea, vomiting, hyperemesis gravidarum, gastroesophageal reflux disease, constipation, and diarrhea. *Gastroenterology Clinics* 45, 267-283.
- Brok, E.C., Lok, P., Oosterbaan, D.B., Schene, A.H., Tendolkar, I., 2017. Infant-Related Intrusive Thoughts of Harm in the Postpartum Period: A Critical Review. *The Journal of Clinical Psychiatry* 78, e913-e923.
- Cents, R., Diamantopoulou, S., Hudziak, J., Jaddoe, V., Hofman, A., Verhulst, F., Lambregtse-van den Berg, M., Tiemeier, H., 2013. Trajectories of maternal depressive symptoms predict child problem behaviour: the Generation R study. *Psychological Medicine* 43, 13-25.
- Copeland, W.E., Shanahan, L., Costello, E.J., Angold, A., 2009. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. *Archives of General Psychiatry* 66, 764-772.
- Craske, M.G., Rauch, S.L., Ursano, R., Prenoveau, J., Pine, D.S., Zinbarg, R.E., 2009. What is an anxiety disorder? *Depression and Anxiety* 26, 1066-1085.
- De Weerth, C., Buitelaar, J.K., 2005. Physiological stress reactivity in human pregnancy—a review. *Neuroscience & Biobehavioral Reviews* 29, 295-312.

Derogatis, L., 2000. Brief Symptom Inventory (BSI): Administration, scoring, and procedure manual (3rd ed.). National Computer Services., Minneapolis, MN.

Derogatis, L.R., Melisaratos, N., 1983. The Brief Symptom Inventory: an introductory report. *Psychological Medicine* 13, 595-605.

Ding, X.-X., Wu, Y.-L., Xu, S.-J., Zhu, R.-P., Jia, X.-M., Zhang, S.-F., Huang, K., Zhu, P., Hao, J.-H., Tao, F.-B., 2014. Maternal anxiety during pregnancy and adverse birth outcomes: a systematic review and meta-analysis of prospective cohort studies. *Journal of Affective Disorders* 159, 103-110.

Doyle, C., Werner, E., Feng, T., Lee, S., Altemus, M., Isler, J.R., Monk, C., 2015. Pregnancy distress gets under fetal skin: Maternal ambulatory assessment & sex differences in prenatal development. *Developmental Psychobiology* 57, 607-625.

Entringer, S., Buss, C., Shirtcliff, E.A., Cammack, A.L., Yim, I.S., Chicz-DeMet, A., Sandman, C.A., Wadhwa, P.D., 2010. Attenuation of maternal psychophysiological stress responses and the maternal cortisol awakening response over the course of human pregnancy. *Stress* 13, 258-268.

Fairbrother, N., Woody, S.R., 2008. New mothers' thoughts of harm related to the newborn. *Archives of Women's Mental Health* 11, 221-229.

Figueiredo, B., Conde, A., 2011. Anxiety and depression symptoms in women and men from early pregnancy to 3-months postpartum: parity differences and effects. *Journal of Affective Disorders* 132, 146-157.

Forray, A., Focseneanu, M., Pittman, B., McDougale, C.J., Epperson, C.N., 2010. Onset and exacerbation of obsessive-compulsive disorder in pregnancy and the postpartum period. *The Journal of Clinical Psychiatry* 71, 1061-1068.

- Fredriksen, E., von Soest, T., Smith, L., Moe, V., 2017. Patterns of pregnancy and postpartum depressive symptoms: Latent class trajectories and predictors. *Journal of Abnormal Psychology* 126, 173-183.
- Geisheim, C., Hahlweg, K., Fiegenbaum, W., Frank, M., Schröder, B., von Witzleben, I., 2002. Das Brief Symptom Inventory (BSI) als Instrument zur Qualitätssicherung in der Psychotherapie. *Diagnostica* 48, 28-36.
- Giesbrecht, G.F., Campbell, T., Letourneau, N., Kooistra, L., Kaplan, B., Team, A.S., 2012. Psychological distress and salivary cortisol covary within persons during pregnancy. *Psychoneuroendocrinology* 37, 270-279.
- Glynn, L.M., Wadhwa, P.D., Dunkel-Schetter, C., Chicz-DeMet, A., Sandman, C.A., 2001. When stress happens matters: effects of earthquake timing on stress responsivity in pregnancy. *American Journal of Obstetrics and Gynecology* 184, 637-642.
- Goldberg, D., Krueger, R., Andrews, G., Hobbs, M., 2009. Emotional disorders: Cluster 4 of the proposed meta-structure for DSM-V and ICD-11: Paper 5 of 7 of the thematic section: 'A proposal for a meta-structure for DSM-V and ICD-11'. *Psychological Medicine* 39, 2043-2059.
- Goodman, J.H., Watson, G.R., Stubbs, B., 2016. Anxiety disorders in postpartum women: a systematic review and meta-analysis. *Journal of Affective Disorders* 203, 292-331.
- Grant, K.-A., McMahon, C., Austin, M.-P., 2008. Maternal anxiety during the transition to parenthood: a prospective study. *Journal of Affective Disorders* 108, 101-111.
- Heron, J., O'Connor, T.G., Evans, J., Golding, J., Glover, V., Team, A.S., 2004. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders* 80, 65-73.

Hodgson, D., Coe, C., 2019. Perinatal Programming. CRC Press, London.

Jones, I., Chandra, P.S., Dazzan, P., Howard, L.M., 2014. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. *The Lancet* 384, 1789-1799.

Kessler, R.C., Ormel, J., Petukhova, M., McLaughlin, K.A., Green, J.G., Russo, L.J., Stein, D.J., Zaslavsky, A.M., Aguilar-Gaxiola, S., Alonso, J., 2011. Development of lifetime comorbidity in the World Health Organization world mental health surveys. *Archives of General Psychiatry* 68, 90-100.

Kessler, R.C., Petukhova, M., Sampson, N.A., Zaslavsky, A.M., Wittchen, H.U., 2012. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International Journal of Methods in Psychiatric Research* 21, 169-184.

Korja, R., Nolvi, S., Kataja, E.-L., Scheinin, N., Junttila, N., Lahtinen, H., Saarni, S., Karlsson, L., Karlsson, H., 2018. The courses of maternal and paternal depressive and anxiety symptoms during the prenatal period in the FinnBrain Birth Cohort study. *PloS one* 13, e0207856.

Lagadec, N., Steinecker, M., Kapassi, A., Magnier, A.M., Chastang, J., Robert, S., Gaouaou, N., Ibanez, G., 2018. Factors influencing the quality of life of pregnant women: a systematic review. *BMC Pregnancy and Childbirth* 18, 455.

Leach, L.S., Christensen, H., Mackinnon, A., 2014. Pregnancy and levels of depression and anxiety: A prospective cohort study of Australian women. *Australian & New Zealand Journal of Psychiatry* 48, 944-951.

Lewis, K.J., Di Florio, A., Forty, L., Gordon-Smith, K., Perry, A., Craddock, N., Jones, L., Jones, I., 2018. Mania triggered by sleep loss and risk of postpartum psychosis in women with bipolar disorder. *Journal of Affective Disorders* 225, 624-629.

Luoma, I., Korhonen, M., Salmelin, R.K., Helminen, M., Tamminen, T., 2015. Long-term trajectories of maternal depressive symptoms and their antenatal predictors. *Journal of Affective Disorders* 170, 30-38.

Maguire, J., 2020. Hormonal and immunological factors in postpartum psychosis, In: Payne, J.L., Osborne, L.M. (Eds.), *Biomarkers of Postpartum Psychiatric Disorders*. Elsevier, San Diego, pp. 159-179.

Martini, J., Asselmann, E., Einsle, F., Strehle, J., Wittchen, H.-U., 2016. A prospective-longitudinal study on the association of anxiety disorders prior to pregnancy and pregnancy- and child-related fears. *Journal of Anxiety Disorders* 40, 58-66.

Martini, J., Petzoldt, J., Einsle, F., Beesdo-Baum, K., Höfler, M., Wittchen, H.-U., 2015. Risk factors and course patterns of anxiety and depressive disorders during pregnancy and after delivery: a prospective-longitudinal study. *Journal of Affective Disorders* 175, 385-395.

Martini, J., Petzoldt, J., Knappe, S., Garthus-Niegel, S., Asselmann, E., Wittchen, H.-U., 2017. Infant, maternal, and familial predictors and correlates of regulatory problems in early infancy: The differential role of infant temperament and maternal anxiety and depression. *Early Human Development* 115, 23-31.

Martini, J., Wittchen, H.-U., Soares, C.N., Rieder, A., Steiner, M., 2009. New women-specific diagnostic modules: the Composite International Diagnostic Interview for Women (CIDI-VENUS). *Archives of Womens Mental Health* 12, 281-289.

Martini, J., Wittich, J., Petzoldt, J., Winkel, S., Einsle, F., Siegert, J., Höfler, M., Beesdo-Baum, K., Wittchen, H.-U., 2013. Maternal anxiety disorders prior to conception,

psychopathology during pregnancy and early infants' development: a prospective-longitudinal study. *Archives of Women's Mental Health* 16, 549-560.

Micali, N., Simonoff, E., Treasure, J., 2011. Pregnancy and post-partum depression and anxiety in a longitudinal general population cohort: The effect of eating disorders and past depression. *Journal of Affective Disorders* 131, 150-157.

Moffitt, T.E., Caspi, A., Taylor, A., Kokaua, J., Milne, B., Polanczyk, G., Poulton, R., 2010. How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. *Psychological Medicine* 40, 899-909.

Moss, K.M., Skouteris, H., Wertheim, E.H., Paxton, S.J., Milgrom, J., 2009. Depressive and anxiety symptoms through late pregnancy and the first year post birth: an examination of prospective relationships. *Archives of Women's Mental Health* 12, 345-349.

Obel, C., Hedegaard, M., Henriksen, T.B., Secher, N.J., Olsen, J., Levine, S., 2005. Stress and salivary cortisol during pregnancy. *Psychoneuroendocrinology* 30, 647-656.

Osborne, L.M., Monk, C., 2013. Perinatal depression—the fourth inflammatory morbidity of pregnancy?: theory and literature review. *Psychoneuroendocrinology* 38, 1929-1952.

Petzoldt, J., Wittchen, H.U., Einsle, F., Martini, J., 2016. Maternal anxiety versus depressive disorders: specific relations to infants' crying, feeding and sleeping problems. *Child: Care, Health and Development* 42, 231-245.

Reed, V., Gander, F., Pfister, H., Steiger, A., Sonntag, H., Trenkwalder, C., Sonntag, A., Hundt, W., Wittchen, H.-U., 1998. To what degree does the Composite International Diagnostic Interview (CIDI) correctly identify DSM-IV disorders? Testing validity issues in a clinical sample. *International Journal of Methods in Psychiatric Research* 7, 142-155.

- Savitz, D.A., Olshan, A.F., 1995. Multiple comparisons and related issues in the interpretation of epidemiologic data. *American Journal of Epidemiology* 142, 904-908.
- Schubert, K.O., Air, T., Clark, S.R., Grzeskowiak, L.E., Miller, E., Dekker, G.A., Baune, B.T., Clifton, V.L., 2017. Trajectories of anxiety and health related quality of life during pregnancy. *PloS one* 12, e0181149.
- Sharma, V., Mazmanian, D., 2003. Sleep loss and postpartum psychosis. *Bipolar Disorders* 5, 98-105.
- Shear, M.K., Bjelland, I., Beesdo, K., Gloster, A.T., Wittchen, H.U., 2007. Supplementary dimensional assessment in anxiety disorders. *International Journal of Methods in Psychiatric Research* 16, S52–S64.
- Skouteris, H., Wertheim, E.H., Rallis, S., Milgrom, J., Paxton, S.J., 2009. Depression and anxiety through pregnancy and the early postpartum: an examination of prospective relationships. *Journal of Affective Disorders* 113, 303-308.
- StataCorp, 2015. *Stata Statistical Software: Release 14*. StataCorp LP, College Station, TX.
- Sutter-Dallay, A., Cosnefroy, O., Glatigny-Dallay, E., Verdoux, H., Rascle, N., 2012. Evolution of perinatal depressive symptoms from pregnancy to two years postpartum in a low-risk sample: the MATQUID cohort. *Journal of Affective Disorders* 139, 23-29.
- Viswasam, K., Eslick, G.D., Starcevic, V., 2019. Prevalence, onset and course of anxiety disorders during pregnancy: A systematic review and meta analysis. *Journal of Affective Disorders* 255, 27-40.
- Wesseloo, R., Kamperman, A.M., Munk-Olsen, T., Pop, V.J., Kushner, S.A., Bergink, V., 2015. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. *American Journal of Psychiatry* 173, 117-127.

Wittchen, H.-U., Lachner, G., Wunderlich, U., Pfister, H., 1998. Test-retest reliability of the computerized DSM-IV version of the Munich Composite International Diagnostic Interview (M-CIDI). *Social Psychiatry and Psychiatric Epidemiology* 33, 568-578.

World Health Organization, 1990. Composite International Diagnostic Interview (CIDI): (a) CIDI-interview (version 1.0), (b) CIDI-user manual, (c) CIDI-training manual (d) CIDI-computer programs. World Health Organization, Geneva.

(a)

(b)

(c)

(d)

(e)

(f)

(g)

(h)

Figure 1: Changes in psychopathological symptoms during pregnancy and after delivery in the total sample.

Note. The first line indicates linear changes in psychopathological symptoms from early until late pregnancy. It is based on the sum of the coefficients of the intercept and the event-related predictor “linear changes during pregnancy”, multiplied by its values at T1, T2, and T3. A continuous line was drawn in case of a significant linear change effect during pregnancy. The second line indicates linear changes in psychopathological symptoms from two months until 16 months postpartum. It is based on the sum of the coefficients of the intercept and the event-related predictors “linear changes after delivery” and “baseline changes after delivery”, multiplied by their values at T5, T6, and T7. A continuous line was drawn in case of a significant linear change or baseline change effect after delivery, respectively.

(a)

(b)

(c)

(d)

Figure 2: Changes in anxiety and phobic anxiety during pregnancy and after delivery in women with and without any lifetime anxiety disorder prior to pregnancy.

Note. For detailed information on both lines, please see Figure 1.

Table 1

Means and standard deviations for individual psychopathological symptoms at each wave and averaged across all six waves in the total sample

Symptom	T1		T2		T3		T5		T6		T7		Grand mean	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Somatization	0.48	0.42	0.26	0.31	0.36	0.33	0.16	0.27	0.13	0.21	0.12	0.28	0.25	0.34
Obsession-compulsion	0.53	0.51	0.46	0.42	0.46	0.37	0.52	0.47	0.50	0.45	0.39	0.42	0.48	0.45
Interpersonal sensitivity	0.47	0.53	0.37	0.40	0.34	0.39	0.31	0.36	0.33	0.39	0.28	0.45	0.35	0.43
Depression	0.28	0.41	0.17	0.30	0.17	0.29	0.16	0.30	0.17	0.27	0.19	0.36	0.19	0.33
Anxiety	0.31	0.38	0.24	0.27	0.24	0.28	0.18	0.26	0.16	0.25	0.16	0.26	0.22	0.29
Hostility	0.53	0.47	0.39	0.36	0.37	0.36	0.35	0.35	0.31	0.33	0.30	0.37	0.38	0.38
Phobic anxiety	0.16	0.32	0.09	0.21	0.10	0.23	0.11	0.20	0.07	0.18	0.05	0.19	0.10	0.23
Paranoid ideation	0.32	0.45	0.22	0.38	0.17	0.30	0.17	0.26	0.21	0.31	0.18	0.31	0.21	0.35
Psychoticism	0.14	0.28	0.08	0.20	0.08	0.19	0.08	0.24	0.09	0.22	0.09	0.24	0.10	0.23
Global severity index	0.37	0.31	0.25	0.23	0.27	0.22	0.22	0.23	0.21	0.21	0.19	0.24	0.26	0.25

Note. BSI = Brief Symptom Inventory. *M* = Mean. *SD* = Standard Deviation.

Table 2

Means and standard deviations for individual psychopathological symptoms at each wave and averaged across all six waves in women with and without lifetime anxiety disorders prior to pregnancy

Symptom	T1		T2		T3		T5		T6		T7		Grand mean	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Somatization														
No anxiety disorder	0.46	0.42	0.25	0.28	0.34	0.33	0.14	0.21	0.12	0.19	0.08	0.15	0.24	0.31
Anxiety disorder	0.49	0.42	0.26	0.34	0.38	0.34	0.18	0.31	0.13	0.22	0.16	0.38	0.27	0.37
Obsession-compulsion														
No anxiety disorder	0.47	0.46	0.43	0.38	0.44	0.37	0.52	0.44	0.46	0.39	0.35	0.38	0.45	0.41
Anxiety disorder	0.59	0.55	0.50	0.46	0.49	0.37	0.52	0.50	0.54	0.51	0.43	0.47	0.51	0.48
Interpersonal sensitivity														
No anxiety disorder	0.39	0.44	0.32	0.35	0.26	0.33	0.25	0.25	0.29	0.33	0.21	0.33	0.29	0.35
Anxiety disorder	0.56	0.61	0.42	0.44	0.42	0.43	0.37	0.43	0.36	0.44	0.36	0.54	0.42	0.49
Depression														
No anxiety disorder	0.24	0.33	0.13	0.22	0.13	0.21	0.13	0.21	0.14	0.20	0.14	0.27	0.15	0.25
Anxiety disorder	0.33	0.47	0.20	0.37	0.21	0.34	0.20	0.37	0.20	0.33	0.24	0.43	0.23	0.39
Anxiety														
No anxiety disorder	0.23	0.28	0.19	0.20	0.19	0.22	0.15	0.22	0.13	0.19	0.11	0.18	0.17	0.22
Anxiety disorder	0.41	0.44	0.28	0.31	0.29	0.32	0.21	0.28	0.20	0.29	0.21	0.32	0.27	0.34

Hostility														
No anxiety disorder	0.47	0.40	0.32	0.29	0.30	0.30	0.30	0.31	0.28	0.30	0.26	0.31	0.33	0.33
Anxiety disorder	0.59	0.52	0.46	0.42	0.45	0.40	0.41	0.37	0.33	0.36	0.36	0.42	0.44	0.43
Phobic anxiety														
No anxiety disorder	0.09	0.20	0.07	0.13	0.08	0.16	0.10	0.18	0.06	0.15	0.02	0.06	0.07	0.16
Anxiety disorder	0.23	0.40	0.11	0.26	0.13	0.28	0.12	0.22	0.09	0.21	0.09	0.26	0.13	0.29
Paranoid ideation														
No anxiety disorder	0.25	0.42	0.18	0.29	0.15	0.26	0.14	0.20	0.19	0.29	0.14	0.26	0.18	0.30
Anxiety disorder	0.40	0.48	0.27	0.45	0.19	0.34	0.20	0.30	0.24	0.34	0.22	0.35	0.26	0.39
Psychoticism														
No anxiety disorder	0.12	0.25	0.06	0.15	0.05	0.14	0.04	0.10	0.06	0.12	0.05	0.13	0.06	0.16
Anxiety disorder	0.17	0.31	0.11	0.25	0.11	0.24	0.12	0.33	0.13	0.28	0.13	0.32	0.13	0.29
Global severity index														
No anxiety disorder	0.31	0.27	0.22	0.17	0.23	0.19	0.19	0.16	0.19	0.16	0.15	0.16	0.22	0.20
Anxiety disorder	0.42	0.34	0.29	0.28	0.30	0.25	0.26	0.28	0.24	0.25	0.24	0.30	0.30	0.29

Note. BSI = Brief Symptom Inventory. *M* = Mean. *SD* = Standard Deviation.

Table 3

Means and standard deviations for individual psychopathological symptoms at each wave and averaged across all six waves in women with and without lifetime depressive disorders prior to pregnancy

Symptom	T1		T2		T3		T5		T6		T7		Grand mean	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Somatization														
No depressive disorder	0.44	0.42	0.22	0.28	0.35	0.32	0.13	0.25	0.10	0.18	0.08	0.15	0.23	0.31
Depressive disorder	0.53	0.41	0.32	0.35	0.38	0.36	0.20	0.29	0.17	0.24	0.18	0.42	0.30	0.37
Obsession-compulsion														
No depressive disorder	0.51	0.49	0.43	0.38	0.44	0.35	0.47	0.43	0.47	0.41	0.33	0.38	0.45	0.41
Depressive disorder	0.55	0.53	0.52	0.47	0.50	0.41	0.61	0.52	0.55	0.51	0.49	0.48	0.54	0.49
Interpersonal sensitivity														
No depressive disorder	0.41	0.50	0.32	0.37	0.32	0.40	0.27	0.31	0.27	0.32	0.21	0.35	0.30	0.39
Depressive disorder	0.58	0.56	0.45	0.43	0.37	0.37	0.37	0.42	0.42	0.47	0.41	0.57	0.44	0.48
Depression														
No depressive disorder	0.24	0.35	0.15	0.29	0.15	0.25	0.15	0.23	0.15	0.22	0.15	0.28	0.17	0.28
Depressive disorder	0.34	0.49	0.20	0.32	0.20	0.33	0.19	0.38	0.20	0.34	0.26	0.46	0.23	0.39
Anxiety														
No depressive disorder	0.28	0.35	0.21	0.25	0.22	0.26	0.16	0.23	0.12	0.17	0.12	0.20	0.19	0.26
Depressive disorder	0.38	0.41	0.29	0.29	0.27	0.31	0.21	0.30	0.23	0.33	0.23	0.33	0.27	0.33
Hostility														
No depressive disorder	0.50	0.46	0.37	0.37	0.35	0.36	0.35	0.34	0.30	0.31	0.26	0.32	0.36	0.37

Depressive disorder	0.57	0.48	0.42	0.35	0.41	0.36	0.37	0.36	0.32	0.36	0.39	0.43	0.41	0.40
Phobic anxiety														
No depressive disorder	0.13	0.27	0.07	0.15	0.09	0.20	0.10	0.18	0.05	0.14	0.03	0.15	0.08	0.19
Depressive disorder	0.22	0.39	0.13	0.28	0.12	0.27	0.12	0.22	0.10	0.24	0.07	0.24	0.13	0.28
Paranoid ideation														
No depressive disorder	0.26	0.42	0.20	0.37	0.17	0.30	0.15	0.20	0.18	0.25	0.16	0.29	0.19	0.32
Depressive disorder	0.42	0.48	0.25	0.39	0.16	0.30	0.21	0.34	0.27	0.39	0.21	0.34	0.26	0.39
Psychoticism														
No depressive disorder	0.12	0.27	0.07	0.19	0.07	0.18	0.06	0.16	0.07	0.15	0.06	0.14	0.08	0.19
Depressive disorder	0.18	0.30	0.10	0.23	0.10	0.22	0.11	0.34	0.13	0.30	0.15	0.35	0.13	0.29
Global severity index														
No depressive disorder	0.33	0.29	0.23	0.21	0.25	0.21	0.20	0.18	0.19	0.16	0.15	0.18	0.23	0.22
Depressive disorder	0.42	0.34	0.30	0.26	0.29	0.24	0.26	0.28	0.26	0.27	0.26	0.31	0.30	0.29

Note. BSI = Brief Symptom Inventory. *M* = Mean. *SD* = Standard Deviation.

Table 4

Psychopathological symptoms by lifetime anxiety and depressive disorders prior to pregnancy as well as changes in psychopathological symptoms over time

Symptom	Intercept				Anxiety disorder prior to pregnancy				Depressive disorder prior to pregnancy				Linear changes during pregnancy				Linear changes after delivery				Short-term changes after delivery				Baseline changes after delivery			
	β	99%CI	p		β	99%CI	p		β	99%CI	p		β	99%CI	p		β	99%CI	p		β	99%CI	p		β	99%CI	p	
Somatization	0.04	-0.13	0.21	.573	0.05	-0.09	0.19	.468	0.25	0.10	0.40	.001	-0.06	-0.08	-0.04	<.001	0.00	-0.01	0.01	.746	0.09	-0.05	0.23	.190	-0.46	-0.62	-0.30	<.001
Obsession-compulsion	-0.05	-0.24	0.13	.443	0.11	-0.06	0.29	.205	0.23	0.04	0.41	.016	-0.02	-0.04	-0.01	.009	-0.02	-0.03	-0.01	<.001	0.01	-0.12	0.13	.907	0.21	0.07	0.35	.003
Interpersonal sensitivity	-0.15	-0.33	0.03	.033	0.27	0.11	0.44	.001	0.33	0.15	0.50	<.001	-0.05	-0.07	-0.03	<.001	-0.01	-0.02	0.00	.223	-0.05	-0.18	0.08	.447	0.08	-0.07	0.23	.279
Depression	-0.22	-0.40	-0.04	.002	0.22	0.05	0.38	.011	0.21	0.04	0.38	.017	-0.06	-0.07	-0.04	<.001	0.01	0.00	0.02	.282	-0.01	-0.14	0.12	.888	0.11	-0.04	0.26	.162
Anxiety	-0.06	-0.24	0.11	.366	0.32	0.17	0.47	.000	0.29	0.14	0.45	<.001	-0.04	-0.06	-0.02	<.001	0.00	-0.01	0.01	.800	0.05	-0.08	0.19	.444	-0.17	-0.33	-0.01	.038
Hostility	-0.18	-0.36	0.00	.010	0.28	0.12	0.44	.001	0.14	-0.03	0.30	.099	-0.07	-0.09	-0.05	<.001	0.00	-0.01	0.01	.995	0.12	-0.02	0.26	.087	-0.03	-0.19	0.13	.687
Phobic anxiety	-0.14	-0.32	0.03	.038	0.22	0.07	0.37	.004	0.26	0.10	0.41	.001	-0.04	-0.06	-0.02	<.001	-0.01	-0.02	0.00	.219	0.14	0.00	0.28	.057	-0.01	-0.17	0.15	.937
Paranoid ideation	-0.31	-0.49	-0.13	<.001	0.21	0.04	0.37	.014	0.24	0.06	0.41	.007	-0.07	-0.09	-0.05	<.001	-0.01	-0.02	0.00	.224	-0.15	-0.28	-0.02	.023	0.26	0.11	0.41	.001
Psychoticism	-0.22	-0.40	-0.04	.002	0.22	0.05	0.39	.010	0.25	0.07	0.42	.005	-0.04	-0.06	-0.03	<.001	0.00	-0.01	0.01	.879	-0.07	-0.20	0.06	.268	0.16	0.02	0.31	.029
Global severity index	-0.16	-0.34	0.02	.022	0.27	0.09	0.44	.003	0.34	0.15	0.52	<.001	-0.06	-0.08	-0.05	<.001	-0.01	-0.01	0.00	.265	0.02	-0.09	0.13	.721	-0.02	-0.15	0.11	.726

Note. BSI = Brief Symptom Inventory. β : standardized β -coefficient from multilevel mixed-effect models; *CI*: confidence interval; adjusted for linear, quadratic, and cubic age.

Supplemental Table 1

Correlations between individual psychopathological symptoms averaged across all six waves (grand means)

Symptom	Somatization	Obsession-compulsion	Interpersonal sensitivity	Depression	Anxiety	Hostility	Phobic anxiety	Paranoid ideation	Psychoticism
	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>
Somatization									
Obsession-compulsion	0.42								
Interpersonal sensitivity	0.38	0.55							
Depression	0.38	0.58	0.68						
Anxiety	0.47	0.51	0.53	0.54					
Hostility	0.42	0.52	0.63	0.59	0.53				
Phobic anxiety	0.41	0.36	0.44	0.44	0.53	0.40			
Paranoid ideation	0.35	0.44	0.62	0.56	0.47	0.54	0.42		
Psychoticism	0.39	0.50	0.59	0.72	0.52	0.54	0.50	0.53	
Global severity index	0.66	0.76	0.79	0.81	0.76	0.77	0.63	0.72	0.76

Note. BSI = Brief Symptom Inventory.