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**SLEEPING PROBLEMS DURING PREGNANCY,  
PARENTAL PERINATAL DEPRESSIVE  
SYMPTOMS AND CHILDREN'S EMOTIONAL  
PROBLEMS**

FINDINGS FROM THE CHILD-SLEEP AND FINNBRAIN  
BIRTH COHORTS

**Johanna T. Pietikäinen**

ACADEMIC DISSERTATION

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Rakkaille tyttärilleni Lauralle, Lotalle ja Saimille  
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# ABSTRACT

**Background and Objective:** Depression affects up to 10–15% of women during pregnancy and the first postnatal year. Insomnia during pregnancy is a risk factor for postnatal depression, but it is unclear which insomnia symptoms and at which stage of pregnancy we should screen for preventive purposes. While maternal perinatal depression and its consequences for children's emotional development have received attention, the longitudinal pattern of both maternal and paternal depressive symptoms and the father's contribution to the risk of emotional symptoms in the offspring is less clear. The aims of this doctoral study were to investigate a) how risk factors, including prenatal sleep, associate with postnatal depressive symptoms (PDS), b) how the accumulation of such risk factors increases the risk of PDS, c) the longitudinal pattern of maternal and paternal depressive symptoms from pregnancy until two years postnatally, and d) how persistent depressive symptoms associate with children's emotional problems at the ages of 2 and 5 years.

**Materials and methods:** This thesis consists of four individual studies from two Finnish birth cohorts. Studies I, III and IV were based on the CHILD-SLEEP birth cohort (n = 1667 mothers, n = 1598 fathers in late pregnancy and n = 949 children at the age of 2 years) and Study II on the FinnBrain birth cohort (n = 3808 mothers in early pregnancy). In Studies I and II, logistic regression analysis was performed, with a higher level of depressive symptoms (CES-D  $\geq 10$  (CS) or EPDS  $\geq 11$  (FB)) as the dependent variable and various insomnia symptoms as independent variables. In addition, in Study II, odd ratios were calculated for various PDS risk factor combinations and heat maps were constructed to visualize the accumulation of the PDS risk. In Study III, latent trajectory analyses were performed to examine the longitudinal pattern of maternal and paternal depressive symptoms. In Study IV, associations of maternal and paternal depressive symptom trajectories with children's emotional problems at the ages of 2 and 5 years were examined with a general linear model.

**Results:** In Studies I and II, we found associations between several insomnia symptoms in late pregnancy and PDS after adjusting for background variables and prenatal depressive symptoms: poor general sleep quality, short sleep of  $\leq 7$  h and long sleep latency of  $> 20$  min. In addition, in the cumulative models of Study II, we found that long sleep latency ( $\geq 20$  min) in early pregnancy, decreased functioning in middle pregnancy, and insufficient sleep time during late pregnancy associated with PDS. The accumulation of several risk factors such as a history of depression, anxiety and multiparity substantially increased the risk of PDS,

and the best model comprising background variables as well as measurements from early, middle and late pregnancy was able to predict 21.2% of PDS (Nagelkerke 0.21). In Study III, three stable depressive symptom trajectories were found for both mothers and fathers: stable low (n = 1053, 63.1% mothers, n = 1201, 74.9% fathers), stable intermediate (n = 470, 28.1% mothers, n = 362, 22.6% fathers) and stable high (n = 147, 8.8% mothers, n = 41, 2.6% fathers). Depression in one parent also associated with increased depressive symptoms in the spouse ( $\chi^2 = 104.6$ ,  $p < 0.001$ ). In Study IV, we constructed combined parental depressive symptom trajectories and found a group with a higher level of persistent maternal depressive symptoms or depressive symptoms in both parents to associate with an increased risk of children's emotional problems, whereas paternal depressive symptoms did not increase this risk for children if the mother was non-depressive. A higher level of maternal depressive symptoms was associated with a higher level of children's emotional problems in a dose-dependent manner at the ages of both 2 and 5 years, whereas no such pattern was found in relation to a higher level of paternal depressive symptoms. Importantly, persistent subclinical maternal depressive symptoms increased the risk of externalizing and internalizing problems among both 2- and 5-year-olds.

**Conclusions:** Long sleep latency in early pregnancy and several insomnia symptoms in late pregnancy might be vulnerability markers for an increased risk of PDS and thus potential screening items in order to better detect women at increased risk of PDS. The accumulation of risk factors in PDS should be taken into account when deciding when preventive interventions are necessary, and this study is the first to use heat maps to visualize such an accumulation. Maternal depressive symptoms should preferably be detected during pregnancy and treated with low threshold counselling and psychotherapeutic interventions as the first-line treatment. The screening of both parents is recommendable if one of them presents with depressive symptoms during the perinatal period. Individual, group and couple therapeutic interventions should be developed in the public sector in order to respond to the growing need for non-pharmacological treatments for perinatal mental health disorders.

# TIIVISTELMÄ

**Tausta ja tavoitteet:** Raskausaikana ja synnytyksen jälkeisenä vuotena noin 10-15 % naisista sairastuu masennukseen. Raskausaikainen unettomuus on synnytyksen jälkeisen masennuksen riskitekijä, mutta ei tiedetä mitä unettomuusoireita ja missä raskauden vaiheissa tulisi seuloa, jotta masennusta voitaisiin ennaltaehkäistä. Vaikka lasten tunne-elämän oireiden yhteydestä äidin masennusoireisiin on kertynyt tutkimustietoa, molempien vanhempien masennuksen kulku sekä isän osuus lapsen tunne-elämän oireiden syntymisessä on epäselvä. Tämän väitöskirjatutkimuksen tavoitteina oli tutkia a) kuinka riskitekijät, raskausaikainen unettomuus mukaan luettuna, liittyvät synnytyksen jälkeisiin masennusoireisiin, b) miten kyseisten riskitekijöiden kasaantuminen lisää synnytyksenjälkeisten masennusoireiden riskiä, c) äitien ja isien masennusoireiden pitkittäistä kulkua loppuraskaudesta lapsen toiseen elinvuoteen asti, sekä d) kuinka vanhempien pitkäkestoiset masennusoireet liittyvät 2- ja 5-vuotiaiden lasten tunne-elämän ongelmiin.

**Aineisto ja menetelmät:** Tämä väitöskirja koostuu neljästä osatyöstä, joiden aineisto perustuu kahteen suureen suomalaiseen syntymäkohorttiin. Osatyöt I, III ja IV perustuvat CHILD-SLEEP (CS) syntymäkohorttiin (n = 1667 äitiä, n = 1598 isää loppuraskaudessa ja n = 949 lasta kahden vuoden iässä) ja osatyö II FinnBrain (FB) -kohorttiin (n = 3808 äitiä alkuraskaudessa). Osatöissä I ja II synnytyksen jälkeisiä masennusoireita (CES-D  $\geq 10$  (CS) tai EPDS  $\geq 11$  (FB)) käytettiin logistisessa regressiossa riippuvina muuttujina ja eri unettomuusoireita riippumattomina muuttujina. Tämän lisäksi osatyössä II laskettiin vetosuhteet (odds ratio) lukuisille synnytyksen jälkeisten masennusoireiden riskitekijäyhdistelmille ja riskin kasaantumista havainnollistettiin lämpökartta (heat map) -kuvilla. Osatyössä III tehtiin latentti trajektorianalyysi äitien ja isien pitkittäisten masennusoireiden tutkimiseksi. Osatyössä IV tutkittiin lineaarisella mallinnuksella äitien ja isien masennustrajektorien yhteyksiä kaksi- ja viisivuotiaiden lasten tunne-elämän ongelmiin.

**Tulokset:** Osatöissä I ja II löydettiin yhteys synnytyksen jälkeisten masennusoireiden ja useiden loppuraskauden unettomuusoireiden välille: huono unenlaatu, lyhyt uni  $\leq 7$ h ja unensaantivaikeus  $> 20$  minuuttia ennustivat synnytyksen jälkeisiä masennusoireita. Analyysit oli mukautettu taustatekijöillä ja raskausaikaisella masennuksella. Tämän lisäksi osatyön II kumulatiivisissa malleissa (T1+T2+T3) havaittiin alkuraskauden unensaantivaikeuden ( $\geq 20$ min), keskiraskauden huonontuneen toimintakyvyn ja loppuraskauden riittämättömän unen ennustavan synnytyksen jälkeisiä masennusoireita. Riskitekijöiden kuten

masennushistorian, ahdistuneisuuden ja monisyntyäjäyden, kumuloituminen kasvattivat synnytyksen jälkeisten masennusoireiden riskiä huomattavasti. Paras ennustemalli, joka sisälsi taustamuuttujat sekä mittaustulokset alkua-, keski- ja loppuraskaudesta pystyi ennustamaan 21.2% (Nagelkerke 0.21) synnytyksen jälkeisistä masennusoireista. Osatyössä III sekä äideille että isille löydettiin kolme tasaista masennustrajektoria: stabiili matala (n = 1053, 63.1% äidit, n = 1201, 74.9% isät), stabiili keskitaso (n = 470, 28.1% äidit, n = 362, 22.6% isät) ja stabiili korkea (n = 147, 8.8% äidit, n = 41, 2.6% isät). Masennusoireet toisella vanhemmalla yhdistyivät puolison masennusoireisiin ( $\chi^2 = 104.6$ ,  $p < 0.001$ ). Osatyössä IV yhdistimme vanhempien masennustrajektorit ja havaitsimme äitien lievienkin pitkäkestoisten masennusoireiden sekä molempien vanhempien masennusoireiden nostavan riskiä kaksi- ja viisivuotiasten lasten tunne-elämän oireille. Isän masennusoireet eivät lisänneet lasten tunne-elämän oireiden riskiä jos äiti oli masennusoireeton. Äitien masennusoireiden lisääntyessä lasten tunne-elämän oireet lisääntyivät annosriippuvaisella tavalla sekä kaksi- että viisivuotiaille lapsilla, kun taas isien masennusoireet eivät lisänneet lapsen oireita vastaavalla tavalla. Tärkeä löydös oli, että äitien subkliiniset masennusoireet lisäsivät lasten riskiä internalisoiviin ja eksternalisoiviin ongelmiin sekä kahden että viiden vuoden iässä.

**Loppupäätelmät:** Unensaantivaikeus alkuraskaudesta sekä useat unettomuusoireet loppuraskaudesta voivat olla haavoittuvuusmerkkejä riskille sairastua synnytyksen jälkeiseen masennukseen ja siten potentiaalisia seulontakohteita kyseisten äitien paremmalle löytämiselle. Riskitekijöiden kasaantumisen merkitys pitäisi ottaa huomioon päätettäessä milloin ennaltaehkäisevät toimet ovat tarpeellisia. Tämä tutkimus käytti ensimmäistä kertaa lämpökarttoja visualisoimaan synnytyksen jälkeisen masennuksen riskin kasaantumista. Äitien masennusoireet pitäisi havaita mieluiten jo raskausaikana ja hoitaa matalalla kynnyksellä, psykoterapeuttiset hoitomuodot etulinjassa. Molempien vanhempien seulonta masennusoireiden suhteen on suositeltavaa, jos toisella vanhemmista havaitaan masennusoireita. Julkiselle sektorille tulisi kehittää yksilö-, pari- ja ryhmäterapeuttisia hoitomuotoja, jotta raskaus- ja vauva-ajan mielenterveyshäiriöiden lääkkeettömien hoitomuotojen lisääntyneeseen tarpeeseen pystyttäisiin vastaamaan.

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# LIST OF ORIGINAL PUBLICATIONS

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- I. Pietikäinen JT, Polo-Kantola P, Pölkki P, Saarenpää-Heikkilä O, Paunio T, Paavonen EJ. Sleeping problems during pregnancy – a risk factor for postnatal depressiveness. *Archives of Women’s Mental Health* 2019;22(3):327-337. doi: 10.1007/s00737-018-0903-5.
- II. Pietikäinen JT, Härkänen T, Polo-Kantola P, Karlsson H, Paunio T, Karlsson L, Paavonen EJ. Estimating the cumulative risk of postnatal depressive symptoms: the role of insomnia symptoms across pregnancy. (Submitted manuscript 2020).
- III. Kiviruusu O, Pietikäinen JT, Kylliäinen A, Pölkki P, Saarenpää-Heikkilä O, Marttunen M, Paunio T, Paavonen EJ. Trajectories of mother’s and father’s depressive symptoms from pregnancy to 24 months postpartum. *Journal of Affective Disorders* 2020;260:629–637. doi: 10.1016/j.jad.2019.09.038
- IV. Pietikäinen JT, Kiviruusu O, Kylliäinen A, Pölkki P, Saarenpää-Heikkilä O, Paunio T, Paavonen EJ. Maternal and paternal depressive symptoms and children’s emotional problems at age two and five years: a longitudinal study. *Journal of Child Psychology and Psychiatry* 2020;61(2): 195–204. doi:10.1111/jcpp.13126.

The publications are referred to throughout the text by their Roman numerals and have been reprinted with the permission of their copyright holders.

This thesis also contains unpublished material.

# ABBREVIATIONS

etc.	et cetera
i.e.	id est
e.g.	exempli gratia
ACE	Adverse childhood experience
ACG	Actigraphy
ADHD	Attention Deficit/ Hyperactivity Disorder
AIC	Akaike information criterion
ALSPAC	Avon Longitudinal Study of Parents and Children
AOR	Adjusted odds ratio
BCT	Behavioural Couple Therapy
BDI	Beck Depression Inventory
BITSEA	The Brief Infant Toddler Social Emotional Assessment
BNSQ	The Basic Nordic Sleep Questionnaire
CBT	Cognitive behavioural therapy
CBT-I	Cognitive behavioural therapy for insomnia
CES-D	Center for Epidemiological Studies Depression Scale
CI	Confidence interval
CS	The CHILD-SLEEP cohort
DIS	Difficulty initiating sleep
DNA	Deoxyribonucleic acid
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	Electroencephalogram
EFCT	Emotionally focused couples therapy
EGDS	The Edinburgh Gotland Depression Scale
EPDS	The Edinburgh Postnatal Depression scale
ES	Effect size
ESS	The Epworth Sleepiness Scale
FB	The FinnBrain cohort
FTF	The Five to Fifteen Questionnaire
GBTM	Group-based trajectory models
GDM	Gestational diabetes mellitus
GMM	Growth mixture modelling
GMDS	The Gotland Male Depression Scale
GR	Glucocorticoid receptor
GWAS	Genome-wide association study
GW	Gestational week
GUSTO	Growing Up in Singapore Towards Healthy Outcomes
HAM-D	Hamilton Rating Scale for Depression
HIC	High-income country
HPA	Hypothalamus–pituitary–adrenal axis
HRSD	Hamilton Rating Scale for Depression

ICD	International Statistical Classification of Diseases and Related Health Problems
IPT	Interpersonal psychotherapy
LCA	Longitudinal latent class analysis
LCGA	Latent class growth analysis
LMIC	Low- and middle-income country
LTE	The List of Threatening Experiences questionnaire
MDD	Major depressive disorder
NICE	The National Institute for Health and Care Excellence
OR	Odds ratio
OSA	Obstructive sleep apnoea
PDS	Postnatal depressive symptoms
PHQ	The Patient Health Questionnaire
PMAD	Perinatal mood and anxiety disorders
PPD	Postpartum depression
PSQI	Pittsburgh Sleep Quality Index
PSS	The Global Measure of Perceived Stress Scale
PSG	Polysomnography
RCT	Randomized controlled trial
REM	Rapid eye movement
RLS	Restless legs syndrome
RNA	Ribonucleic acid
RR	Risk ratio
SCID	The Structured Clinical Interview for DSM-IV
SD	Standard deviation
SDB	Sleep disordered breathing
SDQ	The Strengths and Difficulties Questionnaire
SNRI	Selective serotonin and norepinephrine reuptake inhibitors
SSRI	Selective serotonin reuptake inhibitors
STAI	Spielberger Trait Anxiety Scale
SWA	Slow-wave activity
SWS	Slow-wave sleep

Antenatal/Prenatal = before birth/delivery

Postnatal/Postpartum= after birth/delivery

Perinatal/peripartum = around the time of delivery, used to refer to the time from the beginning of pregnancy until one year after delivery in perinatal psychiatry

# 1 INTRODUCTION

Depression has become the most common complication of childbirth (Accortt and Wong, 2017), affecting approximately 10–15% of women (Gavin et al., 2005; O’Hara and McCabe, 2013). The prevalence of depression during the perinatal period, from conception until 12 months postpartum, is rising (Pearson et al., 2018). However, based on studies by Cox et al. (2016) and Gavin et al. (2015), less than 50% of ante- or postnatal depression is recognized in primary care and, alarmingly, less than 10% receive adequate treatment. Suicide is now causing more maternal deaths in developed countries than obstetric complications, haemorrhages and embolisms in the perinatal period (Cantwell et al., 2011; Palladino et al., 2011). Furthermore, from the child’s perspective, pregnancy and the first months and years are perhaps the most important ones in life, as changes in foetal programming and other disturbances during the time of rapid development and maturation can have lasting effects (O’Donnell and Meaney, 2017). Thus, Meaney (Meaney, 2018) justifiably emphasizes maternal mental health as an issue for population health.

Paternal perinatal depression is increasingly being acknowledged. A recent meta-analysis (Rao et al., 2020) estimated 9.7% of fathers to be depressed during pregnancy and 8.75% during the first postnatal year. However, the longitudinal pattern of evolution of depressive symptoms over time is not well known concerning either parent. Trajectories are a way of conceptualizing changes in these longitudinal symptoms. Maternal depressive symptom trajectories have been constructed in several studies (reviewed by Baron, Bass, Murray, Schneider, & Lund, 2017; Santos, Tan, & Salomon, 2017), but reports on paternal depressive symptom trajectories are scarce.

Several risk factors for postnatal depression have been identified including social, psychological and biological risks (Howard et al., 2014). Paternal risk factors for depression during this sensitive period are less understood (Bruno et al., 2020). Furthermore, the extent to which the accumulation of maternal risk factors increases the risk of PPD is also poorly understood. Because insomnia is treatable and thus a modifiable risk factor for PPD, as well as an integral component of many prenatal and postnatal psychiatric disorders such as depression, it is important both in terms of prevention and treatment. More studies have been called for on this subject (Meltzer-Brody et al., 2018b).

Maternal depression rates peak during the first postnatal months, and one in four children has been estimated to be exposed to maternal depression or anxiety (Abel et al., 2019). Unfortunately, these same months are also a

sensitive period for children's emotional development (Heim and Binder, 2012). We already know that maternal depression affects child neonatal outcomes (Jarde et al., 2016) and cognitive capacity (Liu et al., 2017; Sloman et al., 2019), and is a risk factor for an insecure mother–infant attachment relationship (Atkinson et al., 2000; Badovinac et al., 2018; Barnes and Theule, 2019). The problems arising can have lasting consequences: the offspring of depressed parents have been found to have higher rates of problems concerning health, mental disorders and addictions, even when entering middle age (Weissman et al., 2006). The role of fathers in children's emotional problems, however, has received much less attention (Cui et al., 2020), and longitudinal studies taking into account the influence of both mothers and fathers are rare.

Interestingly, the infants of mothers suffering from depression and/or anxiety during pregnancy have been found to have regulatory problems, such as problems with sleep and more fussing/crying (Field, 2017; Field et al., 2007; O'Connor et al., 2007). Boys with a reactive temperament seem particularly susceptible (Netsi et al., 2015). Infant sleep problems and thus impaired parental sleep can precede and worsen almost all maternal perinatal mental health disorders (Lawson et al., 2015; Posmontier, 2008). Moreover, paternal depression rates tend to follow maternal rates (Dudley et al., 2001; Goodman, 2004). Thus, a negative loop of parental and child sleep problems, mood symptoms and dysregulation can start (Sadeh et al., 2010), in some cases leading to continuing parental depressive symptoms and children's emotional problems.

Impaired parenting is thought to be the main modifiable mechanism in the transmission of depression and anxiety to the next generation. Fortunately, parenting interventions such as Incredible Years (Gardner and Leijten, 2017; Menting et al., 2013) and the Strongest Families Smart Website (Sourander et al., 2018, 2016) have been shown to mitigate children's social, internalizing and behavioural problems. Several preventive interventions such as Family Talk (Beardslee et al., 1996) for families with a depressed parent have also been developed (Beardslee, 2019; Solantaus et al., 2010). Importantly, Nurture and Play is one of the programmes developed for prenatally depressed mothers (Salo et al., 2019). Such interventions would be wise to be taken into use with a low threshold, and emphasis should be on the early programmes. Moreover, the treatment of parental mental disorders during pregnancy and lactation requires special knowledge considering the risks and benefits of each treatment modality. Recognizing this, perinatal psychiatry, or mother–infant psychiatry, is pursuing recognition as an independent sub-speciality of adult psychiatry (Payne, 2019).

The present study investigated maternal and paternal longitudinal depressive symptom trajectories, sleeping problems during pregnancy as a

risk factor for postnatal depressive symptoms, and the effects of persistent parental depression on children's emotional problems in the Finnish CHILD-SLEEP and FinnBrain birth cohorts. In this literature review, I limit the examination of children's emotional problems to ages from 0–5 years. Data from these new birth cohorts collected between 2011 and 2015 are essential in order to develop effective clinical interventions that match the needs of the Finnish population.

## 2 REVIEW OF THE LITERATURE

### 2.1 PERINATAL DEPRESSION

#### 2.1.1 DIAGNOSIS AND DEFINITION

Depressive disorders are characterized by enduring low mood, loss of energy, markedly decreased interest in activities, several somatic and cognitive symptoms, insomnia symptoms and recurrent thoughts concerning death. The diagnostic criteria for a depressive episode of the International Classification of Diseases, 10<sup>th</sup> Edition (ICD-10) (World Health Organization, 1993), and those for major depressive disorder (MDD) of the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition (DSM-V) (American Psychiatric Association, 2013), are presented in Table 1.

The DSM-5 and ICD-10 categorize the severity of depressive symptoms differently; ICD-10 specifies an episode as mild (four to five symptoms), moderate (six to seven symptoms) or severe with/without psychotic features (at least eight symptoms, including all three main criteria from **Table 1**), whereas DSM-5 categorizes mild/moderate and severe MDD primarily based on the degree of functional impairment. Both ICD-10 and DSM-5 also take into account the course of disease (single or recurrent episode, remission), but only DSM-5 allows the use of the specifiers “with mixed features” and “with anxious distress”, in which, respectively, the patient may present subsyndromal manic or anxious symptoms in addition to depressive symptoms. Dysthymia refers to mild/subclinical depressive symptoms that persist for at least two years. In this thesis, dysthymia is not considered as part of increased depressive symptoms. The term ‘depressive symptoms’ refers to a questionnaire-based score above a cut-off level commonly referring to the risk of clinical depression. Furthermore, the term ‘clinical depression’ is reserved for depression confirmed with an interview. Bipolar depression is beyond the scope of this review.

There are no specific diagnostic codes for perinatal depression in either DSM-5 or ICD-10, but the DSM-5 specifier “with peripartum onset” can be used in addition to MDD in case the current or most recent episode has started during pregnancy or in the first four postpartum weeks, and ICD-10 defines postpartum onset as within 6 weeks of delivery. In clinical practice and clinical research, the definition of postpartum onset is often extended up to 3 months or even 1 year after delivery (Stewart and Vigod, 2019).

In ICD-10, the codes for mild and severe puerperal mental disorders (F53.0 Mild mental and behavioural disorders associated with the

puerperium, not elsewhere classified, F53.1, F53.8, F53.9) are also usable in the case of otherwise non-specified disorders (WHO, 1993).

In ICD-11 (WHO, 2018) (World Health Organization, 2018), the codes 6E20 for mental or behavioural disorders associated with pregnancy, childbirth and puerperium without psychotic symptoms and 6E21 for corresponding disorders with psychotic features are introduced, and puerperium is defined as symptom onset within approximately 6 weeks after delivery. ICD-11 states that symptoms should involve significant mental or behavioural features to justify the use of the codes 6E20–21. However, if the symptoms would meet the requirements for a specific mental health disorder, that diagnosis should also be assigned.

Globally, major depressive disorder is one of the top five causes of disabling diseases (GBD 2016 Disease and Injury Incidence and Prevalence Collaborators, 2017). In a Finnish population-based survey of men and women over 30 years old (Markkula et al., 2015), the overall prevalence of MDD was 7.4% (95% CI 5.7–9.0), being 4.4% (95% CI 2.1–6.7) in men and 10.0% (95% CI 8.2–11.8) in women. The highest MDD prevalence (9.6%, 95% CI 7.1–12.1) was in the age group 30–44 years. Women were at two-fold higher risk (OR 2.33; 95% CI 1.6–3.4) when compared to men.

**Table 1. The diagnostic criteria for major depressive disorder (DSM-5) and depressive episode (ICD-10-DCR)**

DSM –V	ICD-10
≥ 2 weeks	≥ 2 weeks
At least five symptoms off which at least one is either 1. or 2.	At least four symptoms of which two are either 1., 2. or 3.
1. Depressed mood	1. Depressed mood
2. Markedly decreased interest or pleasure	2. Loss of interest or pleasure
3. Significant change in weight or appetite	3. Decreased energy or increased fatigability
4. Insomnia or hypersomnia	4. Change in appetite with corresponding weight change
5. Psychomotor agitation or retardation	5. Disturbed sleep
6. Fatigue or loss of energy	6. Psychomotor agitation or retardation
7. Excessive or inappropriate guilt or feelings of worthlessness	7. Unreasonable Ideas of guilt and worthlessness
8. Diminished ability to think or concentrate	8. Diminished ability to think or concentrate
9. Recurrent thought of death, suicidal ideation or suicide attempt	9. Recurrent thought of death or self-harm, suicidal behaviour of any type
	10. Loss of confidence and self-esteem
Impairment: Clinically significant distress or impairment in social, occupational or other areas	Impairment: Grades of symptom severity (mild/ moderate/ severe) are associated with varying levels of functional impairment
Exclusion : Hypomanic or manic episodes, symptoms related to psychoactive substance use or organic mental disorders	Exclusion: Hypomanic or manic episodes, symptoms related too psychoactive substance use or organic mental disorders
Specifier 'with peripartum onset': onset of the current or most recent episode of major depression occurs during pregnancy or in the first four weeks postpartum	

DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (American Psychiatric Association, 2013); ICD-10-DCR = International Classification of Diseases, 10th revision, Diagnostic Criteria for Research (World Health Organization (WHO), 1992)

## 2.1.2 MATERNAL PERINATAL DEPRESSIVE SYMPTOMS

### 2.1.2.1 Screening and prevalence, subtypes

From one country and continent to another, maternal depression during pregnancy and postpartum appears to be universal and common: from 13% to 19% in developed countries (O'Hara and McCabe, 2013), the most recent meta-estimate being 11.9% (Shorey et al., 2018). Prevalence estimates of maternal perinatal depression vary depending on the assessment method used, the sample characteristics and the study location. In a meta-analysis by O'Hara and Swain (1996), the estimated prevalence of postpartum depression was 13% (at least two weeks after delivery), and interestingly, the difference between questionnaire and interview-based estimates was small (14% vs 12%, respectively). More recently, in their literature review, Norhayati et al. (2015) estimated the prevalence to be 5.2–74.0% (based on questionnaires)/0.1–62.0% (interview) in developed countries and 1.9–82.1% (questionnaire)/1.0–26.3% (interview) in developing ones. Shorey et al. (2018) reported in their meta-analysis, which only included healthy mothers without a life-time history of depression, overall prevalence rates of 17% for postnatal depression; the incidence was 14%, 16% and 20% at 0–3 months, 4–6 months and 7–12 months postpartum, respectively. The difference between the structured interview vs questionnaire-based prevalence was also small (18% vs 17%) in this study.

Postnatal depression should to be distinguished from **postpartum blues**, which affects 50–85% of women. The symptoms of postpartum blues include depressive mood, affective lability, interpersonal sensitivity, insomnia, anxiety and tearfulness. Unlike in depression, however, these symptoms typically resolve within 10 days postpartum (O'Hara et al., 1990).

The prevalence of prenatal depression has been estimated to be from 10% to 17% (Howard et al., 2014; Underwood et al., 2017a). Wisner et al. (2013) found in their study on US women (n = 10000) that 40% of depression episodes began postnatally, while about one-third began during pregnancy and one quarter before pregnancy. This is in line with a review of longitudinal studies concerning perinatal depression by Underwood et al. (2016): 39% of women having prenatal depression went on to also have postnatal depression, whereas 47% of those with postnatal depression had also had depression prenatally. In low- and middle-income (LMIC) countries, prevalence estimates are even higher, from 15.6% to 19.8% (Fisher et al., 2012), and up 42% in women migrating from LMIC (Collins et al., 2011; Fellmeth et al., 2017).

Recently, based on a large multicentre consortium, several subtypes of perinatal depression have been proposed (Putnam et al., 2017). Putnam et al. introduced five distinct subgroups of PPD (severe anxious depression,

moderate anxious depression, anxious anhedonia, pure anhedonia and resolved depression). The onset of depressive symptoms in the first 8 weeks postnatally was associated with more severe depression, characterized as the subtype “anxious anhedonia”. Notably, over 20% of women with PPD who reported the onset of symptoms during the first 8 postnatal weeks had very severe depressive symptoms in the EPDS assessment. This proportion of severely ill mothers was almost four times higher when compared to women for whom the onset of depression already occurred during pregnancy.

The idea of a **reproductive subtype of depression** is not new, as Payne et al. (2009 and 2019) reported that a subgroup of women and their close relatives might be particularly sensitive to hormonal fluctuations in the brain and suffer from severe episodes of depression in premenstrual, puerperal and perimenopausal time periods. The hormonal levels *per se* seem to be within normal limits in these women, but the sensitivity and affective response to changing hormonal levels appear to differ from other women (Payne et al. 2009). Payne and coauthors also reported that one type of reproductive depression is a risk factor for other types. For example, postpartum depression can be associated with later perimenopausal depression. The recurrence risk of postnatal depression in later pregnancies is high: approximately 40% of women have a relapse, with a clustering of cases near delivery (Cooper and Murray, 1995; Wisner et al., 2004).

The Structured Clinical Interview for DSM-IV (SCID) has been considered as the gold standard for the clinical diagnosis of depression. Several screening scales have also been used to detect perinatal depression in particular, with the Edinburgh Postnatal Depression Scale (EPDS) (Cox, 2019; Cox et al., 1987) being the most common choice. The EPDS has been validated to detect both pre- and postnatal depression (Eberhard-Gran et al., 2001; Kozinszky and Dudas, 2015). Thresholds used for further evaluation and in research vary, but women scoring >12–13 (range 0–30) have been proposed to be assessed for clinical depression. In the initial study by Cox et al. (1987), an EPDS cut-off of 12/13 was reported to have a sensitivity of 86% and specificity of 78% to detect major and minor depression according to research diagnostic criteria. Other used scales include the CES-D (Radloff, 1977), PHQ-9 (Kroenke et al., 2001), Hamilton Rating Scale for Depression (Hamilton, 1960), and BDI-II (Beck et al., 1961). The UK NICE guidelines (National Institute for Health and Care Excellence, 2014) recommend the use of the Whooley questions (Spitzer et al., 1994; Whooley et al., 1997): “During the past month, have you often been bothered by feeling down, depressed or hopeless?”, “During the past month, have you often been bothered by having little interest or pleasure in doing things?” and a third question if the response to either of the previous questions has been yes, “Is this something you need or want help with?” Howard et al. (2018) found in a sample of 9963 women at the first prenatal appointment that the EPDS detected depression better than the Whooley questions when both were compared

with the SCID interview. However, the difference was not large and both tools had high specificity. Furthermore, Tandon et al. (2012) compared the EPDS, 20-item CES-D and BDI-II in a perinatal population and found all three scales to be highly accurate ( $AUC \geq 0.95$ ) in detecting major depression in the population.

There is a consensus that perinatal mental health disorders are underdiagnosed and undertreated (Flynn et al., 2006; Woolhouse et al., 2009). Marcus et al. (2009) have estimated that only approximately one in five women experiencing depressive symptoms, either during pregnancy or postpartally, seek treatment. Of the women who do receive treatment, the vast majority do not receive adequate treatment and do not report improvement in symptoms (Flynn et al., 2006). Goodman & Tyer-Viola (2010) conducted a study on 491 women. Of the 113 (23%) women with a positive screening score for either anxiety or depression during pregnancy, less than half (41%,  $n = 41$ ) were detected by physicians in a routine prenatal appointment. Of the detected women, only 17 (37%) received documented mental health treatment, and postnatally, only 25.5% of the women with a positive screening score received treatment and only 2% were referred. Other researchers have come to similar conclusions: less than half of the cases are recognized in primary care and less than 10% receive adequate treatment (Cox et al., 2016; Ko et al., 2012). It is difficult for many women to disclose their mental difficulties to their health-care practitioners. In a recent Australian study ( $n = 1597$ ) (Forder et al., 2020), 20.7% of women indicated they had not always responded honestly to questions concerning their mental health. The main reasons for women not disclosing the symptoms in the Folder study were a tendency to normalize symptoms, fear of adverse repercussions and health-care involvement, and negative perceptions of themselves and others. In addition, in a review by Jones (2019) concerning barriers to help seeking during the perinatal period, stigma, structural reasons (provider unavailable) and instrumental factors such as cost were reported to be the main barriers.

In Finland, a population-based study on 511 422 women reported a depression prevalence of 0.1% based on national hospital discharge registries (Räsänen et al., 2013). In Finnish birth cohort studies, ante/postnatal depression prevalences of 21.6%/12.0% (prenatally CES-D  $\geq 16$ /postnatally BDI  $\geq 14$ ) in the PREDO study (Girchenko et al., 2017; Wolford et al., 2017) and 9.5%/10.3% (EPDS  $\geq 10$ ) in the KuBiCo study (Ruohomäki et al., 2018) have been reported, depending on the scale used and the cut-off level. Thus, there also appears to be a gap between diagnosed and treated women in Finland.

### 2.1.2.2 Maternal perinatal depressive symptom trajectories

The severity, duration and recurrence of depression can vary over time. Mixture models provide a means to group individuals with similar development patterns based on repeated observations of individual-level attributes across time. To date, dozens of maternal depressive symptom trajectories have been identified in numerous studies. However, the statistical approaches have varied (Warren et al., 2015), including latent group-based trajectory models (GBTM), growth mixture models (GMM) and longitudinal latent profile analysis. Of these, longitudinal latent profile analysis does not make any assumptions concerning the general pattern of growth or form of change (Gibson, 1959). Maternal trajectory studies have previously been reviewed by Santos et al. (2017) and Baron et al. (2017) (growth curve mixture models).

A summary of maternal trajectory studies is presented in **Table 2**.

**Table 2.** Maternal depressive symptom trajectory studies of >400 participants

<b>Author; year; country</b>	<b>N; timeframe</b>	<b>Measures; analysis</b>	<b>Trajectory labels and size</b>
Ahmed et al. (2018), Canada	615; early (gw 17) and late (gw 30) pregnancy, early postpartum (4 weeks)	EPDS; GBTM	#4: 1) Low stable (49.6%); 2) Moderate-stable (42.3%); 3)4) Postpartum (3.6%); 4) Antepartum (4.6%)
Barker et al. (2013), UK (ALSPAC)	12 152; gw 32, postnatally: 8 weeks, 8, 21, 33 months	EPDS; LCA	#3: 1) Low (54%); 2) Medium (36%); 3) Clinical (10%)
Barthell et al. (2017), West Africa	776; gw 28; postnatally 3, 12, 24 months	PHQ-9; GMM	#3: 1) Asymptomatic (91.5%); 2) Recurrent risk (4.3%); 3) Postnatal risk (4.3%)
Bayrampour et al. (2016), Canada	1445; <gw 25, gw 34–36, postnatally: 4 and 12 months	EPDS; GBTM	#5: 1) Minimal (26.3%); 2) Mild (51.4%); 3) Postpartum (9.6%); 4) Antepartum (10.2%); 5) Chronic (2.4%)
Campbell et al. (2007), USA	1261; postnatally: 1 month, 6, 15, 24, 36 and 54 months, 7 years	CES-D (20 item); LCGA	#6: 1) Low-stable (45.6%); 2) Moderate-stable (36.4%); 3) Intermittent depression (3.6%); 4) Moderate-increasing (6.2%); 5) High-decreasing (5.6%); 6) High-chronic (2.5%)
Campbell et al. (2009), USA	1357; postnatally: 1 month, 6, 15, 24, 36 and 54 months, 7, 9, 11 and 12 years	CES-D (20 item); GMM	#5: 1) Never depressed (48.5%); 2) Stable subclinical (30.8%); 3) Early decreasing (5.1%); 4) Moderately elevated (10.9%); 5) Chronic (4.7%)
Cents et al. (2013), Netherlands	4167; early/mid-pregnancy, postnatally: 2, 6, 36 months	BSI; GBTM	#4: 1) No (34%); 2) Low (54%); 3) Moderate (11%); 4) High (1.5%)
Denckla et al. (2018), UK (ALSPAC)	12 121; gw 18 and 32, postnatally: 8 weeks, 8, 21, 33, 61 months	EPDS; GMM	#4: 1) Resilient (74.3%); 2) Improving (9.2%); 3) Emergent (4%); 4) Chronic (11.5%)
Drozd et al. (2018), Norway	1374; postnatally: 1.5, 4, 6 and 12 months	EPDS; GMM	#2: 1) Low risk (91.0%); 2) High risk (9%)
Fisher et al. (2019), USA	507, all depressive; postnatally 4–8	SIGH-ADS <sub>25</sub> ; GBTM	#3: 1) Gradual remission (50.4%); 2) Partial improvement (41.8%); 3) Chronic severe (7.8%)

Review of the literature

	weeks, 3, 6 and 12 months		
Fredriksen et al. (2017), Norway	1036; gw 21, 28 and 36; postnatally 6 weeks, 6 and 12 months	EPDS; GMM	#4; 1) <i>Minimum symptoms</i> (82.9%); 2) <i>Moderate persistent</i> (10.5%); 3) <i>Pregnancy only</i> (4.4%); 4) <i>Postpartum only</i> (2.2%)
Garman et al. (2019), South Africa	446; 2, 6, 18 weeks postpartum	EPDS; LCGA	#4; 1) <i>Chronic low</i> (71.1%); 2) <i>Late postpartum</i> (10.1%); 3) <i>Early postpartum</i> (14.4%); 4) <i>Chronic high</i> (4.5%)
Giallo et al. (2014), Australia	4879; postnatally 3–12 months, 2–3, 4–5 and 6–7 years	Kessler-6; LCGA	#2; 1) <i>Minimal depressive symptoms</i> (84%); 2) <i>Persistently high depressive symptoms</i> (16%)
Giallo et al. (2015a), Australia	4164; postnatally 3–12 months, 2–3, 4–5 and 6–7 years	Kessler-6; LCA	#3; 1) <i>Minimal depressive symptoms</i> (74.6%); 2) <i>Subclinical depressive symptoms</i> (20.8%); 3) <i>Persistent and increasingly high depressive symptoms</i> (4.6%)
Giallo et al. (2015b), Australia	1085; gw 10–24, gw 30–32; postnatally 3, 6, 9, 12 and 18 months, 4 years	EPDS; LCA	#3; 1) <i>No or few symptoms</i> (61%); 2) <i>Persistent subclinical symptoms</i> (30%); 3) <i>Persistent and increasingly high symptoms</i> (9%)
Glasheen et al. (2013), USA	577 high-risk sample; first, second and third trim; postnatally 8 and 18 months	CES-D; GMM	#2; 1) <i>Low symptom group</i> (16.5%); 2) <i>High symptom group</i> (83.5%)
Hammerton et al. (2015) (ALSPAC), UK	10 559; gw 18 and 32, postnatally: 8 weeks, 8 months, 1 y 9 months, 2 y 9 m, 5, 6, 8 and 11 years	EPDS; LCGA	#5; 1) <i>Minimal class</i> (40%); 2) <i>Mild class</i> (30%); 3) <i>Increasing class</i> (6%); 4) <i>Sub-threshold class</i> (18%); 5) <i>Chronic-severe class</i> (5%)
Kingsbury et al. (2018), Australia	2435; first trimester; postnatally 6 months, 5, 14, 21, 27 years	DSSI depression subscale; LCGM	#3; 1) <i>Low depression trajectory</i> (48.4%); 2) <i>Middle depression trajectory</i> (41.4%); 3) <i>High depression trajectory</i> (9.8%)
Kingston et al. (2018), Canada	1983; <gw 25, gw 34–36, postnatally: 4 months, 1 year	EPDS; LLCA	#4; 1) <i>Low level</i> (46.7%); 2) <i>Early postpartum</i> (10.9%); 3) <i>Subclinical</i> (18.8%); 4) <i>Persistent high</i> (5.6%)
Korja et al. (2018), Finland	3202; gw 14, gw 24, gw 34	EPDS; GMM	#5; 1) <i>Consistently low</i> (67%); 2) <i>Consistently high</i> (2%); 3) <i>Moderate</i> (24%); 4) <i>Moderate and decreasing</i> (4%); 5) <i>Moderate and increasing</i> (2%)
Lee et al. (2014), USA	844 overweight/obese; 1–24 months postpartum (5 assessments)	EPDS; LCGA	#3; 1) <i>Stable low</i> (82.5%); 2) <i>Decreasing</i> (7.3%); 3) <i>Increasing</i> (10.2%)
Matijasevich et al. (2015), Brazil	4321; 3, 12, 24, 48 months and 6 years postpartum	EPDS; GBTM	#5; 1) <i>Low</i> (34.8%); 2) <i>Moderate-Low</i> (40.9%); 3) <i>Increasing</i> (9%); 4) <i>Decreasing</i> (9.9%); 5) <i>High chronic</i> (5.4%)
McCall-Hosenfeldt et al. (2016), USA	3006; third trimester; postnatally 1, 6 and 12 months	EPDS; GBTM	#6; 1) <i>Trajectory 1</i> (6.5%); 2) <i>Trajectory 2</i> (42.2%); 3) <i>Trajectory 3</i> (36.5%); 4) <i>Trajectory 4</i> (1.7%); 5) <i>Trajectory 5</i> (11.9%); 6) <i>Trajectory 6</i> (1.3%). <i>Trajectory 4 showed increased dep. symptoms, otherwise relatively stable level of dep.; traj. 1 lowest – traj. 6 highest</i>
Mora et al. (2009), USA	1735; gw 15; postnatally 3, 11 and 25 months	CES-D (20 item); GMM	#5; 1) <i>Never</i> (71%); 2) <i>Antepartum</i> (6%); 3) <i>Postpartum</i> (9%); 4) <i>Chronic</i> (7%); 5) <i>Late</i> (7%)
Sutter-Dallay et al. (2012), France	579; 8 months gestation; postnatally 3 days, 6 weeks, 3,	CES-D 20; GBTM	#4; 1) <i>Postpartum</i> (4%); 2) <i>Never</i> (72.0%); 3) <i>Antepartum</i> (21.0%); 4) <i>Chronic</i> (3.0%)

	6, 12, 18, 24 months		
<i>van der Waerden et al. (2015), France</i>	1807; 3rd trim, postnatally: 4, 8, 12, 24 months, 3, 4, 5 years	EPDS, CES-D; GBTM	#5; 1) No symptoms (60.2%); 2) High pregnancy (4.7%); 3) High preschool (4.9%); 4) Persistent intermediate (25.2%); 5) Persistent-high (5.0%)

BSI = Brief Symptom Inventory; EPDS = Edinburgh Postnatal Depression Scale; CES-D = Center for Epidemiological Studies Depression Scale; PHQ-9 = The Patient Health Questionnaire; SIGH-ADS<sub>29</sub> = Depression scale incorporating the Hamilton Rating Scale for Depression; LCA = Longitudinal latent class analysis; LCGA = latent class growth analysis; GMM = Growth mixture modelling; GBTM = Group-based trajectory models

Fisher et al. (2019) only investigated mothers with PPD symptoms and found four factors to predict whether the mothers belonged to the chronic severe vs remitting groups: parity, education, baseline global functioning and depression severity.

In summary, all the studies have identified a large group of mothers with a low level of depressive symptoms, and most have also identified a smaller group with a high/chronic level of depressive symptoms. Some have identified subgroups with emerging depression postnatally and/or a subgroup with moderate/subclinical depressive symptoms. Significant heterogeneity in the scales and statistical methods used is apparent.

## 2.1.3 PATERNAL PERINATAL DEPRESSIVE SYMPTOMS

### 2.1.3.1 Screening and prevalence

Paternal perinatal depression has been far less studied than maternal depression. Prevalence estimates have varied from 1% to 46% depending, for example, on the study setting, location and the status of maternal mental health problems (Cameron et al., 2016; Dudley et al., 2001; Goodman, 2004; Wee et al., 2011). Paternal prevalence estimates appear to vary depending on the location of the study: the highest meta-estimates have been from North America (13.0%) and the Western Pacific region (10.1%), and the lowest from Europe (5.5%) (Cameron et al., 2016; Rao et al., 2020). In a meta-analysis by Paulson and Bazemore (2010), the meta-estimate for paternal prenatal and postpartum depression was 10.4% (95% CI 8.5–12.7%), and in an updated version, Cameron et al. (2016) reported a slightly lower meta-estimate of 8.4% (95% CI 7.2–9.6%). The most recent meta-estimate by Rao et al. (2020) is 8.8% within the first postnatal year. Interestingly, Paulson and Bazemore (2010) found depression prevalence rates to vary depending on the timing of the assessment and reported an increase in paternal depressive symptoms from 3 to 6 months postpartum up to 26%. Similarly, Cameron et al. (2016) and Rao et al. (2020) reported the highest postnatal depression rates at 3 to 6 months postnatally (13.0% and 9.2%, respectively). However, in the study

by Rao et al., meta-estimates for paternal depression during pregnancy were even higher.

Prenatal prevalence rates have been reported to vary from 2% to 19% (Wee et al., 2011). In the latest meta-analysis by Rao et al. (2020), the estimate was 9.8% in all three trimesters and, more specifically, 13.6% in the first, 11.3% in the second and 10.1% in the third trimester. In a large (n = 3523) study from New Zealand, 2.3% (n = 82) of fathers had elevated depressive symptoms prenatally and 4.3% (n = 153) postnatally (Underwood et al., 2017b). The prevalence of prenatal depression was thus similar to male depression rates in the general population. However, partnered men were likely to exhibit fewer depressive symptoms than the average population. Overall, Underwood et al. speculated that prenatal depression might be of less concern for fathers when compared to mothers.

Garfield et al. (2014) compared resident fathers to nonfathers in a large (n = 10 623), 23-year follow-up study. They reported that before fatherhood, resident fathers showed a decrease in depression scores and had less depression than nonfathers. However, after entering fatherhood, resident fathers displayed a 68% increase in depression scores during the first 5 years.

The same scales have been used to assess paternal and maternal depression (for example, EPDS, CES-D, HADS, BDI, at least 20 different scales). However, as for mothers, the cut-off levels used for fathers have varied significantly between studies and also differed from those used to assess maternal depression (Cameron et al., 2016; Pérez C. et al., 2017). The EPDS has also been validated for men, but the cut-off level has varied between 9–13, and lower cut-off scores have been suggested when compared to women (Matthey et al., 2001).

Brownhill et al. (2005) have proposed that the repeated finding of maternal depression being twice as common as in males could be the result of the more atypical depressive symptoms occurring in men (aggressiveness, irritability, substance use) and the fact that conventional scales better capture “classic” maternal symptoms of depression such as depressed mood. Interestingly, the Edinburgh Gotland Depression Scale (EGDS) (Agebjörn and Linder, 2015; Psouni et al., 2017) combines items from the EPDS (Cox et al., 1987) and the Gotland Male Depression Scale (GMDS) (Carlberg et al., 2018; Walinder and Rutz, 2001; Zierau et al., 2002) and assesses not only classic symptoms of depression but also acting out symptoms, the “depressive equivalents” (**Table 3**). In the Swedish validation study for the EGDS (Svenlin, 2015) against the SCID interview, the revised version of the scale (cut-off score  $\geq 8$ ) had a sensitivity of 91.7% and a specificity of 85.0. These results are, however, preliminary and should be replicated and validated further before wide-scale clinical usage.

**Table 3.** Comparison of the GMDS and EPDS items. From Fletcher, Garfield and Matthey (2015): *Fathers' Perinatal Mental Health*, from the book *Identifying perinatal depression and anxiety: Evidence-based practice in screening, psychosocial assessment and management*, pp. 228-241, edited by Milgrom and Gemmill, publisher John Wiley & Sons, Incorporated. Reproduced with permission from the publisher.

<b>Question focus in GMDS</b>	<b>Question focus in EPDS</b>
1. Stress	1. Ability to laugh
2. Aggression	2. Enjoyment
3. Feelings of emptiness	3. Self-blame
4. Inexplicable tiredness	4. Anxiety
5. Irritability	5. Panic
6. Difficulty with everyday decisions	6. Feeling overwhelmed
7. Sleep problems	7. Sleep problems
8. Morning anxiety	8. Sadness
9. Alcohol use or hyperactivity	9. Tearfulness
10. Family history of depression	10. Self-harm
11. Others perceive you as difficult	
12. Others perceive you as gloomy	
13. Others perceive you as complaining	

### **2.1.3.2 Paternal perinatal depressive symptom trajectories**

There have been several longitudinal studies with varying sample sizes and assessment points addressing paternal depressive symptoms, with the large ALSPAC study (n > 12 000) (Ramchandani et al., 2005, 2008b) perhaps being the most important. Studies on paternal depression trajectories are rare: Molgora et al. (2017) reported the only purely depressive symptom trajectory study also extending to the postnatal period.

A summary of paternal depressive symptom trajectory studies is presented in **Table 4**.

**Table 4.** Paternal depressive symptom trajectory studies

Authors, year, study, country	N; timeframe	Measures, analysis	Trajectory labels and size
Korja et al. (2019), Finland	2076; gw 14, 24, 34	EPDS, GMM	#5: 1) Consistently low (71%); 2) Consistently high (3%); 3) Moderate and stable (15%); 4) Moderate decreasing (9%); 5) Moderate increasing (2%)
Molgora et al. (2017), Italy	126; 7–8 months of pregnancy, postnatally: 40 days, 5–6 months and 12 months	EPDS, GMM	#3: 1) Resilient (52%); 2) Distress (37%); 3) Emergent depression (11%)
Vänskä et al. (2017), Finland	773; gw 18–30, postnatally: 2 and 12 months	GHQ-36, BDI-13, Mental health trajectories, mixture modelling	#5: 1) Stable low (79%); 2) Moderate increasing (9%); 3) Prenatal (5%); 4) Early fatherhood (3%); 5) Heterogeneous high level of problems (4%)

GMM = growth mixture modelling, GHQ = General Health Questionnaire; BDI = Beck Depression Inventory.

All of the paternal trajectory studies have reported a large group of fathers with a low symptom level throughout the study period. Interestingly, Molgora et al. (2017) and Vänskä et al. (2017) reported a group of fathers with an increasing symptom level towards the end of the first or second postnatal year. For comparison, Vänskä et al. (2011) reported *maternal* (n = 805) mental health trajectories as follows: 1) stable low (75.7%), 2) prenatal (5.8%), 3) early postpartum (8.7%), 4) late postpartum (5.6%) and 5) heterogeneous high (4.2%).

Kim & Swain (2007) and Areias et al. (1996) have also reported the same patterns: paternal depression appears to increase later than maternal depression, perhaps reflecting the reaction of paternal depression to maternal mental health symptoms, which tend to increase earlier.

#### 2.1.4 RISK FACTORS FOR PARENTAL PERINATAL DEPRESSIVE SYMPTOMS

Maternal and paternal risk factors for postnatal depression can be divided into biological, social and psychological risk factors. Here, I outline the most important risk factors for both parents. However, the rapidly expanding literature concerning the biological mechanisms underlying PPD is only

briefly outlined here and reviewed in detail elsewhere (Meltzer-Brody et al., 2018b; O'Donnell and Meaney, 2020; Payne and Maguire, 2019).

#### **2.1.4.1 Maternal risk factors**

##### **Biological risk factors**

Biological factors have an undisputable role in the aetiology of perinatal depression. However, the heritability of depression appears to be modest when compared to other psychiatric disorders. The heritability rate of major depression has been estimated to be 31–42% in twin studies, while in family studies, the offspring of a parent with major depression have had a 2- to 3-fold higher risk of developing major depression themselves (Sullivan, Neale, and Kendler 2000). Interestingly, heritability appears to be higher in more severe forms of depression and in women (42%) than in men (29%), and some genetic risk factors for major depression appear to be sex-specific (Kendler et al. 2006; Shadrina, Bondarenko, and Slominsky 2018).

In a Swedish study by Viktorin et al. (Viktorin et al. 2016) comprising 3427 female twins and a population-based cohort of 580 006 sisters, the heritability of perinatal depression was 54% (95% CI 35–70%) in the twin setting and 44% (95% CI 35–52%) in the sibling design, while the heritability of nonperinatal depression was 32% (95% CI 24–41%). Importantly, 33% of genetic variance in perinatal depression was not shared with nonperinatal depression. A large PACT consortium study currently involving over 17 000 participants is ongoing: the aim is to conduct the first genome-wide association study (GWAS) in order to determine the genetic basis of postpartum depression (Guintivano et al. 2019; Putnam et al. 2015, 2017).

Epigenetic changes refer to mechanisms such as histone modification, DNA methylation and RNA signalling by which the environment can alter the way genes are used in the genome without changing the gene sequence. O'Donnell and Meaney (O'Donnell and Meaney 2020) have reviewed current knowledge of these epigenetic mechanisms in terms of developmental and psychopathological aspects. For example, in rodent models, high maternal grooming/licking in the early development of pups has been shown to lead to a relative increase in the glucocorticoid receptor (GR) in the hippocampal region of adult offspring, and thus to greater feedback inhibition of the HPA axis, resulting in lower stress-induced secretion of adrenal glucocorticoid and more modest responses to stress. Conversely, prolonged maternal separation leads to increased HPA axis activation via multiple epigenetic mechanisms. In humans, lower hippocampal GR expression was detected in suicide completers who had a history of childhood maltreatment (Labonte et al. 2012; Zouk et al. 2006).

Quintivano et al. (2014) (Guintivano et al. 2014) have suggested that the postpartum depression risk is due to oestrogen-mediated epigenetic changes

in the hippocampal area. Women who are vulnerable to postpartum psychiatric disorders might thus be particularly sensitive to oestrogen-mediated signalling without differences in the absolute level of steroid hormones in the blood. Different methylations patterns in two oestrogen-regulated genes, HP1BP3 and TTC9B, predicted postpartum depression with high sensitivity (80%) (Osborne et al. 2016). Mehta et al. (Mehta et al. 2019) showed in a manipulation experiment how a large proportion of 116 previously identified sex steroid-sensitive genes were significantly associated (via gene expression/DNA methylation) with changes in depressive symptoms, oestradiol levels and neocortex serotonin transporter binding. These results give hope for the development of potential biomarkers of the PPD risk for future clinical use.

A rapid decrease in allopregnanolone levels at the time of delivery and the failure of GABA<sub>A</sub> receptors to adapt has been suggested to trigger postnatal depression (Maguire and Mody 2008). This has led to the development of the first FDA-approved treatment for PPD: brexanolone, a positive allosteric modulator of GABA<sub>A</sub> receptors, administered as a 60-h continuous infusion (Meltzer-Brody, Colquhoun, et al. 2018; Powell et al. 2020).

Increased parity, obstetric complications, chronic and medical illnesses, a young maternal age and multiple births have been considered to be other biological risk factors for developing perinatal depression (Howard et al. 2014; Lockwood Estrin et al. 2019). Recently, the maternal microbiome has also been associated with perinatal mental health and stress, but the results are preliminary (Redpath, Rackers, and Kimmel 2019).

Sleep disruption as a risk factor for perinatal depression is outlined in section 2.2.

### **Psychosocial risk factors**

Psychosocial risk factors have an important contribution to the development of postpartum depression, whereas postpartum psychosis might be more biologically triggered (Di Florio et al., 2013). A previous history of depression or other mental health disorders, particularly an anxiety disorder, is the strongest risk factor for perinatal depression (Guintivano et al., 2018; Wisner et al., 2013). Anxiety during pregnancy, poor social support, low partner support and marital difficulties, a low socio-economic status, a migration status, and unwanted pregnancy are other often-reported risk factors (Howard et al., 2014; Vliegen et al., 2014).

Importantly, a history of trauma and adverse life events, including a history of abuse and PTSD, have also been shown to be more significant in women developing perinatal mood disorders when compared to mood disorders in other periods (Guintivano et al., 2018; Onoye et al., 2009). Intimate partner violence (IPV) in both high-income and low-income countries (Rogathi et al., 2017) is a major risk factor. In a study by Palladino et al. (2011) in the US, 54.3% of pregnancy-associated suicides and 45.3% of

homicides were IPV associated. In a meta-analysis by Howard et al. (2013), partner violence during pregnancy increased the risk of postnatal depressive symptoms three-fold (95%CI 2.7–3.6). Personality disorders and disordered personality traits strongly associate with perinatal mood disorders and anxiety and predict long-lasting symptoms (Börjesson et al., 2005; Crowley et al., 2020). In a recent review (Li et al., 2020), mood lability during the early postpartum period predicted psychopathology up to 14 months postpartum, and maternal emotional dysregulation was also a risk for mother–baby interaction.

#### **2.1.4.2 Paternal risk factors**

Maternal depression is considered to be the most important risk factor for paternal depression (Fletcher et al., 2015; Goodman, 2004; Wee et al., 2011). In a meta-analysis by Cameron et al. (2016), paternal depression rates were not moderated by any sociodemographic characteristics such as a young or advanced paternal age, educational level, parity or a history of depression, but this might have been due to the low number of studies reporting sociodemographic information accepted into the analysis. In contrast, Edward et al. (2015) noted in their literature review that a history of depression was a risk factor for fathers, and others have also reported a young or advanced age (Nilsen et al., 2013), higher social deprivation, a low household income, stressful life events, smoking and a lack of social support (Deater-Deckard et al., 1998; Leung et al., 2017), as well as unemployment, renting and marital conflict (Nath et al., 2016), to associate with paternal postnatal depression. The sample sizes of the studies accepted into these meta-analyses/reviews have been relatively small (mean  $n < 200$ ), with the exception of the ALPSPAC study ( $n > 10\,000$ ) (Ramchandani et al., 2008b) and the studies by Pryor, Morton, Bandara, Robinson, & Grant, 2014 (Growing up in New Zealand,  $n = 4400$ ), J. F. Paulson, Dauber, & Leiferman (2006) (Early Childhood Longitudinal Study, US,  $n = 5089$ ) and Van Den Berg et al. (2009) (Generation R, Netherlands,  $n = 5463$ ).

As for mothers, reduced satisfaction with the couple relationship and marital conflict appear to be other important risk factors for fathers (Deater-Deckard et al., 1998; Giallo et al., 2013; Wee et al., 2011). Unintended pregnancy (Leathers and Kelley, 2000) and a difficult infant temperament/infant excessive crying (Van Den Berg et al., 2009) are other reported risk factors for paternal depression.

In a study by Dudley et al. (2001), while mothers appeared to be more influenced by their own personality, as well as perinatal and infant-related factors, depressed fathers were more influenced by the state of the marital relationship, their perception of the mother’s personality style and coping,

unresolved maternal issues (such as past sexual abuse) and the mother's view of the relationship with the father. However, the father's own past issues should also be taken account. In a recent review, Bruno et al. (2020) describe psychodynamic hypotheses such as the reactivation of distressing childhood memories, identification with their own father or fear of losing the attention of the partner underlying paternal depression.

The hormonal and neurobiological changes in the father's brain are beyond the scope of this literature review. However, testosterone levels in men have been shown to decrease during the transition to parenthood; the decrease has been associated with sensitive caregiving and investment in the partner relationship (Gettler et al., 2011; Mascaro et al., 2014). In line with this, a higher paternal testosterone level seems to protect the father from depressive symptoms, but is a risk factor for mothers and babies (Saxbe et al., 2017). Several neurobiological changes in the paternal brain have been reported (Swain et al. 2014, Kim et al. 2015). Changes appear to occur in different brain areas in mothers and fathers (Atzil et al., 2012; Rajhans et al., 2019), probably reflecting their different roles in parental caregiving behaviour. Hormonal and neurobiological changes in the paternal brain are important in the sense that they have been linked to paternal emotional responses to infant cries (Fleming et al., 2002; Storey et al., 2000), and children's oxytocin levels have been shown to mimic parental oxytocin levels and social reciprocity (Feldman et al., 2013). Thus, despite the traditional thinking of paternal depression as a more psychological disorder than maternal PPD, hormonal and neurobiological changes related to parental transformation seem to also dispose fathers to the onset of depressive symptoms.

### **2.1.5 CONNECTION BETWEEN MATERNAL AND PATERNAL DEPRESSIVE SYMPTOMS**

There appears to be a consensus that maternal and paternal depressive symptoms are connected. All the studies in a meta-analysis by Paulson and Bazelmor (2010) that examined the correlation between parental depressive symptoms found a positive association ( $r = 0.308$ , 95%CI 0.228–0.384). However, the direction of the connection has been unclear. Most studies have reported maternal depression to predict paternal depression (Cameron et al., 2016; Dudley et al., 2001; Goodman, 2004). However, Paulson et al. (2016), for example, reported prenatal depression in fathers ( $n = 78$ ) to predict worsening depressive symptomatology in mothers six months postnatally, but not vice versa. In a recent Norwegian study ( $n = 1036$  mothers and  $n = 836$  fathers) (Fredriksen et al., 2019) that also measured partner-related attachment, maternal depressive symptoms in late pregnancy were found to

predict a higher level of depressive symptoms in fathers 6 weeks postnatally with a small effect size, but no other longitudinal effects or effects in the opposite direction. However, when they investigated couples with an insecure attachment style, they also found such processes earlier in pregnancy, as well as throughout the first postnatal year. From this perspective, Emotional Focused Couples Therapy (EFCT) (Johnson, 2004) introduces a welcome perspective to emotional insecurities and couple conflicts. The attachment theory framework for the treatment of childbearing depression (Whiffen and Johnson, 1998) and couple conflict during the perinatal period describes how vicious circles can form in couple communication, particularly if one partner is fearful–avoidant and the other is fearful–dismissive. Ideally, in times when couples face stress, such as the transition to parenthood, securely attached partners can turn to each other for comfort and security. However, if one or both partners are insecurely attached, the relationship can break down if an accusative-clingy versus avoidant/dismissive communication circle negatively enforces itself for long enough and the couple is unable to adjust, meet each other at an emotional level and repair the relationship. It is also common for the fearful–avoidant partner, usually the mother, to become depressed. If marital problems appear to arise in the context of perinatal depression, couple intervention has proved to be an effective treatment choice. In a recent meta-analysis by Rathgeber et al. (2019) measuring relationship satisfaction, both EFCT and behavioural couple therapy (BCT) reached medium effect sizes at the post-test (EFCT:  $g = 0.73$ , BCT:  $g = 0.53$ ). A review by Wiebe and Johnson (2016) describes advances in research concerning EFCT.

In Australia, a national helpline, “Perinatal Anxiety and Depression Australia” (PANDA), has been established. A recent paper reported the issues male callers ( $n = 129$ ) were most concerned about, which were maternal mental health (70%), relationship breakdown (57%), their own mental health (43%) and the effect of the maternal mental state on their infant. In the UK, the National Health Service (NHS England, 2018) has planned to incorporate a family-oriented perspective into the treatment of perinatal mental disorders. A new policy recommends the assessment of paternal depressive symptoms if the mother is referred to perinatal mental health services, and the offering of psychotherapeutic interventions in the family and couple context. Fletcher et al. (2015) introduced and suggested a father-inclusive model of care for specialized perinatal mental health units, where fathers could be reached via mobile or Internet-based programs. This could increase the treatment rates for both parents in the perinatal period.

## **2.2 SLEEPING PROBLEMS AS A RISK FACTOR FOR POSTNATAL DEPRESSION**

### **2.2.1 INSOMNIA**

#### **2.2.1.1 Definition and prevalence**

Insomnia can be defined as subjective difficulty falling asleep, staying asleep or sleep being non-restorative. The diagnostic criteria for non-organic insomnia (ICD-10) (WHO, 1993) and Insomnia Disorder (DSM-V) (APA, 2013) are presented in **Table 5**. Comorbidity with psychiatric and medical conditions is high; individuals with insomnia are over five times more likely (OR 5.6, 95% CI 5.1–6.3) to also suffer from depression or anxiety and twice as likely (OR 2.2, 95% CI 1.6–3.1) to develop congestive heart failure when compared to individuals without insomnia (Ohayon, 2002; Pearson, 2006). Importantly, when sleep disorder is considered to be part of a medical or psychiatric condition, based on DSM-V and ICD-10, a separate diagnosis is needed for the primary condition, whereas the sleep problem is considered to be secondary insomnia.

In **Table 5**, the diagnostic criteria for insomnia according to DSM-5 and ICD-10 are presented.

**Table 5. The diagnostic criteria for insomnia**

DSM-5	ICD-10
<p><b>Insomnia Disorder G47.00</b></p> <p>A. A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms</p> <ol style="list-style-type: none"> <li>1. Difficulty initiating sleep.</li> <li>2. Difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakening.</li> <li>3. Early-morning awakening with inability to return to sleep.</li> </ol> <p>B. The sleep disorder causes clinically significant distress or impairment in social, occupational, educational, academic, behavioural, or other important areas of functioning.</p> <p>C. The sleep difficulty occurs at least three nights per week.</p> <p>D. The sleep difficulty is present for at least three months.</p> <p>E. The sleep difficulty occurs despite adequate opportunity for sleep.</p> <p>F. The insomnia is not better explained by and does not occur exclusively during the course of another sleep-wake disorder (e.g. narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep-wake disorder, a parasomnia).</p> <p>G. The insomnia is not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication).</p> <p>H. Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia</p> <p><i>Specify if:</i></p> <ul style="list-style-type: none"> <li>With nonsleep disorder mental comorbidity, including substance use disorders</li> <li>With other medical comorbidity</li> <li>With other sleep disorder</li> </ul> <p><i>Specify if:</i></p> <ul style="list-style-type: none"> <li>Episodic: Symptoms last at least 1 month but less than 3 months</li> <li>Persistent: Symptoms last 3 months or longer</li> <li>Recurrent: Two (or more) episodes within the space of 1 year</li> </ul> <p>Note: Acute and short-term insomnia (i.e. symptoms lasting less than 3 months but otherwise meeting all criteria with regard to frequency, intensity, distress, and/or impairment) should be coded as another specified insomnia disorder</p>	<p><b>Non-organic insomnia</b></p> <p>Diagnostic criterions:</p> <ol style="list-style-type: none"> <li>A. The individual complains of difficulty falling asleep, difficulty maintaining sleep, or non-refreshing sleep</li> <li>B. The sleep disturbance occurs at least three times a week for at least one month</li> <li>C. The sleep disorder results in marked personal distress or interference with personal functioning in daily living</li> <li>D. There is no known causative organic factor, such as a neurological or other medical condition, psychoactive substance use disorder, or a medication</li> </ol> <p>F51.01 Non-organic/ Primary insomnia (&gt;3 months)</p> <p>F51.02 Adjustment insomnia (1–3 months)</p>

DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> edition; ICD-10 = International Classification of Diseases, 10<sup>th</sup> edition

In population-based studies, approximately 30% of heterogeneous adult samples from different countries have reported symptoms of insomnia. The prevalence decreases to 9–15% when daytime consequences are taken into account and 6% according to DSM-IV classification (Ohayon, 2002).

During pregnancy, insomnia symptoms typically increase compared to non-pregnant stages, and approximately 50% or more of women report sleep disturbances (Dørheim et al., 2012; National Sleep Foundation, 2007; Sedov et al., 2018). In a survey by the US National Sleep Foundation (National

Sleep Foundation, 2007), pregnant women were more likely to have a good night's sleep only a few nights a month or less when compared to nonpregnant women (40% vs 29%), and to experience any symptom of insomnia at least a few nights a week (84% vs 64%). In the Finnish population, Polo-Kantola et al. (2017) found that 15% of mothers reported poor sleep quality after gw 30, and Hedman et al. (2002) (N = 325) reported 30.3% of mothers prenatally (third trimester) and 20.5% postnatally (3 mo after delivery) to suffer from restless sleep.

Several scales have been used to rate insomnia symptoms. The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and Insomnia Severity Index (ISI) (Bastien et al., 2001) are the most common sleep questionnaires, whereas the Basic Nordic Sleep Questionnaire (BNSQ) (Partinen and Gislason, 1995) and Bergen Insomnia Scale (BIS) (Pallesen et al., 2008) are also widely used in the Nordic countries. In addition to questionnaires, actigraphy and polysomnography have been used to gain more detailed objective information about the sleep architecture during pregnancy (Christian et al., 2019b; Garbazza et al., 2020; Zhu et al., 2018). However, subjective sleep and objective sleep do not always concur; the subjective perception of poor night sleep might be more important (Bei et al., 2010).

## **2.2.2 CHANGES IN SLEEP DURING PREGNANCY**

Women go through major anatomical, physiological and psychological changes during pregnancy, and maternal sleep also changes as pregnancy proceeds (Lee, 1998; Mindell et al., 2015; Santiago et al., 2001). For a comprehensive review of the clinical evaluation of insomnia symptoms during pregnancy, please see Barger et al. (2013). Briefly, sleep disruption can already start in the first trimester, when the rising progesterone level and increasing glomerular filtration rate can cause a frequent need to urinate. Other reasons for awakenings in early pregnancy include nausea, backaches, oesophageal reflux, leg cramps, the bed partner and children in the family (Baratte-Beebe, 1999). During pregnancy, unresolved attachment issues tend to surface as the mothers start to mentally prepare for parenthood (Raphael-Leff 1993/2001). This can manifest as emotional turmoil and distress and affect sleep.

The sleep architecture also starts to change. In polysomnographic studies, a decrease in the amount of deep sleep (slow wave sleep stages 3–4) has been reported when compared to nonpregnant women, and deep sleep continues to decrease during the second and third trimesters (Barger et al., 2013; Garbazza et al., 2020). Other typical pregnancy-related changes in objective sleep include increases in wake after sleep onset (WASO) and the number of

arousals, as well as decreases in the amount of REM sleep and in REM latency (Garbazza et al., 2020). During the second trimester, oesophageal reflux and foetal movement may start to disrupt sleep, but women may generally feel less tired during the daytime. In the third trimester, physical discomfort, a frequent need to urinate, leg cramps, joint pains and vivid frightening dreams, among other reasons, disrupt sleep; 65–80% of women report these symptoms (Baratte-Beebe, 1999).

Pregnant women tend to have the longest total sleep time (TST) in early pregnancy when compared to prepregnancy period (Lee et al., 2000b). In the third trimester, women sleep approximately 7 hours, with 2–3 awakenings per night, but some report only 3 to 4 hours of sleep (Facco et al., 2010b; Greenwood and Hazendonk, 2004). Due to decreases in sleep efficacy (SE), sleep is perceived as nonrestorative across pregnancy (Wilson et al., 2011).

Importantly, initiation insomnia is generally considered to be rare during pregnancy, and as Barger et al. (2015) suggest, if detected, it needs evaluation for anxiety about labour and delivery, marital problems, depression or feeling unsafe.

Sleep disturbances thus usually worsen as pregnancy proceeds and can continue to the postnatal period, particularly in first-time mothers (Lee et al., 2000b; Palagini et al., 2019). Postnatally, infant care needs continue to disrupt maternal sleep, although sleep fragmentation decreases during postnatal weeks 2–16 (Montgomery-Downs et al., 2010).

Mothers also suffer from restless legs syndrome, which may cause initiation insomnia; the symptoms may start early in pregnancy and peak (23–37%) in the third trimester, typically resolving after delivery (Hedman et al., 2002; Manconi et al., 2004). RLS symptoms may associate with iron deficiency anaemia and should be screened for in the obstetric setting, because the treatment differs from other sleep disorders. Iron and folate supplementation may alleviate the symptoms (Abbott et al., 2014; Lee et al., 2001). Sleep disordered breathing (SDB) and the prevalence of obstructive sleep apnoea (OSA) and snoring typically increase in pregnancy, particularly in obese women (Facco et al., 2010b; Silvestri and Aricò, 2019). RLS, SDB and OSA are, however, beyond the scope of this literature review.

### ***2.2.2.1 Consequences of sleeping problems during pregnancy for the mother and foetus***

Prenatal sleep disturbances have direct consequences for maternal and foetal health. Christian et al. (2019b) reviewed current knowledge concerning the consequences of poor sleep during pregnancy for maternal health, whereas Warland et al. (2018) reviewed the foetal consequences. Maternal

sleep-disordered breathing (SDB) during pregnancy has been shown to associate with gestational hypertension/pre-eclampsia (pooled aOR 2.34, 95% CI 1.60–3.09) and gestational diabetes (GDM) (aOR 1.86, 95% CI 1.30–2.42) (Pamidi et al., 2014). Short sleep duration (<7 h) and frequent snoring (>3x/week) have also been associated with glucose intolerance and GDM (Facco et al., 2010a). In a recent review and meta-analysis by Warland et al. (2018), short sleep duration was associated with a lower birth weight (SGA) (ES 1.3, 95%CI 0.9–2.0) and preterm birth (ES 1.4, 95%CI 1.0–2.1).

Importantly, poor sleep quality during pregnancy has been shown to have an association with inflammation and to predict preterm birth in African American women, whereas among Caucasian women, no such association has been seen (Blair et al., 2015). Similarly, in a study by Christian, Carroll, Porter, & Hall, (2019), African American women of the same parity had more frequent sleep disturbances and poorer sleep efficacy and sleep quality than white women. More studies are required to determine whether a poorer socioeconomic status or racial differences can explain such a difference.

Poorer obstetric outcomes, such as longer labour and a 4- to 5-fold higher likelihood of caesarean delivery, have been reported among women who slept less than 6 hours or had severely disrupted sleep in the third trimester (Lee and Gay, 2004). Maternal overweight is a risk: these women are more likely to develop preeclampsia, snore more frequently, experience excessive daytime sleepiness, insomnia symptoms, a shorter sleep duration and poor sleep quality (Facco et al., 2010b). Interestingly, in animal models, rat puppies of REM-sleep-derived dams showed a delay in maturation and impairment in neural networks regulating the sleep–wake profile (Aswathy et al., 2018). This could in turn postnatally subject the mother to various sleep problems by causing additional parental sleep disruption and fragmentation.

### **2.2.3 SLEEPING PROBLEMS ACROSS PREGNANCY AND DEPRESSION**

Almost all psychiatric problems are also tied to pre- and postnatal sleep difficulties (Lawson et al., 2015). Several reviews (González-Mesa et al., 2019; Okun, 2016, 2015; Ross et al., 2005) have investigated the connection between disturbed prenatal sleep and postnatal depression. Recently, the first meta-analyses of the subject (Emamian et al., 2019; González-Mesa et al., 2019) were also published. Based on these, at least poor sleep quality during late pregnancy seems to associate with postnatal depressive symptomatology: Gonzalez-Mesa report an odds ratio of 1.49 (95% CI 1.19–1.79).

In **Table 6** studies (n > 40) investigating the connection between prenatal insomnia and postnatal depressive symptoms are reviewed.

**Table 6.** *Insomnia studies during pregnancy vs postpartum depression in which the number of participants was >40.*

Study, Country	Design, follow-up	Sleep scale /timing /results	Depression scale /timing	Prevalence antenat. dep Mean (SD)	Prev. of postnatal dep Mean (SD)	Finding
Alipour 2012t, Iran	Prospective two-group cohort n = 156, Group 1: EPDS >10 3 months postpartum (n = 55) Group 2: EPDS ≤10 3 months postpartum (n = 101)	PSQI / at gw 28 and 38	EPDS / 3 months postpartum	NR	EPDS > 10 35.2% (n = 55)	- Inappropriate sleep quality at 28 weeks (OR = 3.9) and 38 weeks (OR = 3.4) increases the risk of postpartum depressive symptoms nearly four-fold (p = 0.03).
Bei et al. 2010, Australia	Prospective cohort study, n = 44, 45.5% nulliparous	PSQI and actigraphy /3 <sup>rd</sup> trimester and 1 week postpartum  Subj. sleep (n = 37)  PSQI <sub>total</sub> - prior preg: 2.84 (SD 2.83) - 3 <sup>rd</sup> trim: 6.90 (SD 2.92) - postpartum: 8.05 (SD 3.84)	Positive Negative Affect Schedule (PANAS), the Hospital Anxiety Depression scale (HADS) and the Depression Anxiety Stress Scale (DASS) /3 <sup>rd</sup> trimester and 1 week postpartum Cut-off: ≥2 HADS/PANAS subscales	HADS <sub>total</sub> = 8.46 (SD 5.36) HADS <sub>depr</sub> = 3.59 (SD 2.99)  DASS <sub>total</sub> = 8.30 (SD 6.45) DASS <sub>depr</sub> = 2.16 (SD 2.60)	HADS <sub>total</sub> = 6.51 (SD 4.87) HADS <sub>depr</sub> = 3.00 (SD 2.71)  DASS <sub>total</sub> = 6.97 (SD 6.10) DASS <sub>depr</sub> = 1.22 (1.57)	- 3 <sup>rd</sup> trimester objectively measured poorer sleep associated with lower positive affect postnatally - 3 <sup>rd</sup> trimester subjectively poorer sleep was associated with worse HADS <sub>total</sub> (R <sup>2</sup> = 0.25) and HADS <sub>depr</sub> postnatally
Coo Calcagni et al. 2012, Australia	Prospective cohort study, n = 72	PSQI, actigraphy /3 <sup>rd</sup> trimester (T1), within 2 first	DASS, HADS /within first 2 weeks postpartum	Group 1 HADS <sub>depr</sub> = 2.75 (SD 2.20)	Group 1 HADS <sub>depr</sub> = 3.78 (SD 2.97)	- Objective sleep and mood were better in multiparous than

	<p>Group 1: nulliparous (n = 37)</p> <p>Group 2: multiparous (n = 35)</p>	<p>postpartum weeks (T2)</p> <p>T1: PSQI<sub>total</sub> Group 1, 6.13 (SD 2.83)</p> <p>Group 2, 6.91 (SD 3.10)</p> <p>T2: PSQI<sub>total</sub> Group 1, 8.32 (SD 3.14)</p> <p>Group 2, 8.19 (SD 4.04)</p>	<p>Group 2 HADS<sub>depr</sub> = 3.91 (3.27)</p>	<p>Group 2 HADS<sub>depr</sub> = 3.38 (3.39)</p> <p>nulliparous women at 2 weeks postpartum - However, the role of parity might be limited in the interaction between sleep and mood</p>
<p>Chung et al. 2018, Taiwan</p>	<p>Chart review (matched control)</p> <p>Group 1: pregnant women with sleep disorder (n = 9838)</p> <p>Group 2: pregnant women without sleep disorder (n = 19 676)</p>	<p>ICD-9-based sleep disorder diagnosis in NHIRD database 2% (n = 20 140) pregnant women with medical records)</p>	<p>ICD-9-based depression diagnosis</p>	<p>Group 1: 0.2% (n = 20)</p> <p>Group 2: 0.05% (n = 10)</p> <p>- Prenatal sleep disorder increased risk of PPD by 5.36-fold when compared to control cases - PPD in women with sleep disorder: ≤6 w postpartum (5.46); 6–12 w 3.49- and &gt; 12 w 3.42-fold higher risk when compared to control group - If primiparous had sleep disorder; 10.1-fold higher risk</p>
<p>Coo S. et al. 2014, Australia</p>	<p>Prospective cohort study, n = 122</p> <p>T1: 3rd trimester T2: 7–10 days postpartum T3: 10–12 weeks</p>	<p>PSQI /T1–T3</p>	<p>EPDS /T1–T3</p>	<p>- Poor sleep quality, daytime dysfunction due to it, and the global PSQI score were associated with a low perceived ability to</p>

postpartum						
Dorheim et al. 2014, Norway	Prospective cohort study, n = 2088 Group 1: ≤10 EPDS (n = 1657) Group 2: >10 EPDS postpartum (n = 162) Group 3: >10 EPDS during pregnancy, <10 EPDS postpartum (n = 153) Group 4: >10 EPDS pregnancy and postpartum (n = 116)	Bergen Insomnia Scale and 3 questions from PSQI /at gw 32, 8 weeks postpartum at gw 32 BIS 17.2 and prev. of insomnia 61.6% (DSM-IV criteria)	EPDS, cut-off 10, Lifetime Major Depression Scale / at gw 32, 8 weeks postpartum	EPDS > 10 12.9% (n = 269)	EPDS > 10 13.3% (n = 278)	cope practically and emotionally with motherhood-related issues and with negative expectations about the future - Insomnia at gw 32 was associated with PPD 8 weeks postpartum only in women with a history of depression - Risk factors at gw 32 for PPD and postnatal insomnia: high EPDS scores and anxiety, fear of delivery, previous depression, primiparity, higher educational level
Gao et al 2019, China	Prospective cohort study, n = 1152	PSQI gw 23	EPDS ≥ 9/ gw 23, 3 months postpartum	EPDS ≥ 9	EPDS ≥ 9	- Poor prenatal sleep quality associated with prenatal (AOR 3.42) and postnatal (AOR 2.40) depressive symptoms
Goyal et al. 2007, USA	Prospective cohort study, n = 124, all primiparous	General Sleep Disturbance Scale/ third trimester	CES-D (20 items), third trimester, 1, 2 and 3 months postpartum	3 <sup>rd</sup> trim: CESD ≥ 16, n = 32 (25.8% of all)	3 months postpartum CES-D ≥ 16, n = 19 (15.3% of all)	- Sleep disturbance during 3 <sup>rd</sup> trim. and depressive symptoms 3 months postpartum were associated - Long sleep latency

					recommended as the screening question
Khazaie et al. 2013, Iran	RCT, n = 61, participants were seeking treatment for sleep disturbance at a psychiatric outpatient clinic	Global Sleep Assessment Questionnaire Actigraph /worn 72 h at gw 26–30 and after 2 and 6 weeks of treatment	Structured psychiatric interview (DSM-IV-TR), EPDS / 2 weeks and 6 weeks postpartum	NR	Two weeks postpartum: Group 1: EPDS 6.5 (SD 5.2) Group 2: EPDS 6.8 (SD 5.5) Group 3: 11.7 (SD 7.8)  Six weeks postpartum: Group 1: EPDS 5.1 (SD 1.8), Group 2: EPDS 5.3 (SD 2) Group 3: 7.9 (SD 1.3)
Marques 2011, Portugal	Prospective/retrospective cohort study, prenatal n = 581, postnatally n = 381 (65.7%)	Author developed questions, actigraph (n = 60) /3 <sup>rd</sup> trimester and min. 3 months postnatally	Psychiatric interview: Portuguese version of the Diagnostic Interview for Genetic Studies; BDI-II, Profile of Mood States (POMS) /3 <sup>rd</sup> trimester and min 3 months postnatally	DSM-IV: 1.1% (n = 6) had major depressive disorder in pregnancy ICD-10: 2.8% (n = 15)	- Insomnia in pregnancy was not a risk factor for PPD (ICD-10 or DSM-IV) but significantly predicted postpartum depressive symptomatology (PDS) - Negative affect (NA) significantly predicted PDS and PPD (OR 4.6/5.3 for DSM-IV/ICD-10, respectively) - Controlling NA, positive affect and life-time depression, insomnia lost its predictive role (mediators?)
Okun 2009, USA	Prospective	PSQI / late	HRSD (gw 36 and	0%; prenatally	HRSD ≥ 15, n = - Poor sleep at gw 36

<p>cohort study (three groups) n = 56 All had a history of depression &lt;5 years, not currently depressed</p> <p>Group 1: PPD relapse within 4 postpartum weeks (n = 5) Group 2: PPD relapse between postpartum weeks 5 to 28 (n = 14) Group 3: no relapse (n = 32)</p>	<p>pregnancy (gw 36)</p>	<p>postpartum) and clinical evaluation by DSM-IV criteria weekly for the first 20 postpartum weeks</p> <p>Early recurrence: PSQI 5.00 (SD 0.00) at gw 36</p> <p>Late recurrence: PSQI 10.00 (4.00) at gw 36</p>	<p>depressed women were excluded</p>	<p>19 (37%)</p>	<p>was related to late recurrence (&gt;4 weeks postpartum) of PPD</p> <p>- Women who had an early PPD relapse (&lt;4 weeks postpartum) did not have poor sleep at gw 36</p>
<p>Paulson and Miller-Graff 2019, USA</p> <p>Prospective cohort study, n = 83, high-risk sample</p> <p>T1: during pregnancy (3–15 gw n = 41; 16–27 gw n = 23; 28–39 n = 19)</p> <p>T2: 6 weeks postpartum</p> <p>T3: 4 months postpartum</p>	<p>PSQI (19 items), cut-off <math>\leq</math> 5</p> <p>T1: Poor sleep quality 56.25% (n = 45)</p>	<p>CES-D (20 items); cut-off 16</p>	<p>T1: CES-D mean 14.54 (SD 10.23) (n = 83)</p>	<p>T2: CES-D mean 11.68 (SD 8.77) (n = 81)</p> <p>T3: CES-D mean 11.71 (10.00)</p>	<p>- Prenatal sleep difficulties were associated with a worsening trajectory in maternal perinatal post-traumatic stress symptoms</p> <p>- Depressive symptoms remained stable over the perinatal period</p>
<p>Suri et al. 2017, USA</p> <p>Prospective cohort study,</p>	<p>HRDS item 4, score <math>\geq</math> 2</p>	<p>HRDS, SCID interview</p>	<p>0%</p>	<p>13% (n = 39)</p>	<p>- 3 HDRS items (work activities, early insomnia</p>

<p>n = 300 All participants had a history of SCID-diagnosed MDD, but euthymic at baseline T1: &gt;60 days before delivery T2: &gt;60 days after delivery</p>	<p>"complaints of nightly difficulty falling asleep"</p>	<p>(4-fold risk) and suicidality) predicted PPD</p>
<p>Tham et al. 2016, Singapore</p>	<p>EPDS, cut-off 10</p> <p>PSQI / Time 1: 26-28 weeks of pregnancy 26.7% had PSQI <math>\geq 7</math> (M = 8.91, SD2.06)</p>	<p>20.1% had EPDS <math>\geq 10</math> (M = 13.30, SD 3.50)</p> <p>28.8% had EPDS <math>\geq 10</math> (M = 13.11, SD 2.06)</p> <p>- Poor subjective sleep quality during pregnancy was an independent risk factor for borderline-high postnatal depressive symptoms (OR 2.66, 95% CI: 1.52-4.68)</p>
<p>Tomfohr 2015, Canada</p>	<p>EPDS, cut-off 12</p> <p>PSQI /T1-T4</p> <p>T1: at &lt;gw 22 T2: at gw 32 T3: 3 mo postpartum T4: 6 mo postpartum</p>	<p>NR</p> <p>NR</p> <p>- Four trajectory groups: 1) high sleep quality throughout (21.5%) 2) mild decrease in sleep quality (59.5%) 3) significant decrease in sleep quality (12.3%) 4) poor sleep quality throughout (6.7%) - Group 3 and 4 had the highest risk of postpartum dep. symptoms</p>
<p>Wilkie &amp; Shapiro, 1992, Scotland</p>	<p>EPDS, cut-off 10</p> <p>Author developed questions / 3rd trim., first 10 days postpartum</p>	<p>NR</p> <p>NR</p> <p>Greater sleep disruption in the third trimester was associated with higher blues symptoms</p>

	primiparous)	3 <sup>rd</sup> trim: 90% state sleep is much worse than normal			postnatally (r 0.40, p = 0.046 with Kendall scores)
Wu et al.2014, China	Prospective cohort study, T0 = 3 <sup>rd</sup> trimester (N = 293) T1 = three months postpartum (n = 223)	PSQI /3 <sup>rd</sup> trim.	EPDS, psychiatric interview /SCID-1)	9.4% depressed (n = 21)	- Third-trimester sleep quality was related to postnatal depressive symptoms (regression coefficient 0.82, s.e. 0.13, 95% CI 0.61, 1.10; p < 0.01)
Zhou 2018, China	Prospective cohort study, n = 228 T1: 3 <sup>rd</sup> trimester T2: One month postpartum	PSQI /T1	EPDS /T2	-	- Poor subjective sleep quality (OR = 2.39, 95% CI 1.07, 5.556, p = 0.044) during pregnancy predicted postnatal depressive symptoms.

EPDS = Edinburgh Postnatal Depression scale; HADS = Hospital Anxiety and Depression scale; PSQI = Pittsburgh Sleep Quality Index; OS = objective sleep, SS = subjective sleep; MAAACL = Multiple Affect Adjective Check List; NR = not responded; HRSD = Hamilton Rating Scale for Depression; PANAS = Positive Negative Affect Schedule; DASS = Depression Anxiety Stress Scale; BDI-II = Beck Depression Inventory; PDS = Postpartum depressive symptomatology; NA = negative affect; PPD = Postpartum depression; RCT = Randomized controlled trial; ISI = Insomnia Severity Index; BIS = Bergen Insomnia Scale; NHRD = National Health Insurance Research Database of Taiwan; SCID 1 = structured clinical interview patient edition (SCID-I/P); MD D =Major Depressive Disorder

† Original article written in Persian; only the abstract is available in English.

In summary, most of the studies have had a relatively small number of participants, and insomnia symptoms have either been measured only in late pregnancy or the pregnancy time points have not been differentiated. Studies investigating insomnia symptoms in a longitudinal study design starting from early pregnancy are lacking.

#### **2.2.4 MECHANISMS CONNECTING INSOMNIA AND DEPRESSION**

The connection between sleep and depressive symptoms has been under discussion for decades. Insomnia symptoms are part of the diagnostic criteria for depression. However, the insomnia also seems to precede first-onset and later depressive episodes. In non-pregnant populations, sleep disruption has been shown to precede depression (Baglioni et al., 2011; Gehrman et al., 2010; Hertenstein et al., 2019), with the latest meta-estimate of OR 2.8 (95% CI 1.6–5.2) (Hertenstein et al., 2019). In a study by Ohayon & Roth (2003), 40% of depressed patients reported insomnia before the first depressive episode, whereas 56% had insomnia preceding depression relapse. Blanken et al. (2020) reported that complaints of sleep onset difficulties in particular mediated the relationship between insomnia and first-onset MDD.

Several mechanisms linking insomnia and depression have been suggested. Palmer & Alfano (2017) reviewed the connection and mechanisms underlying sleep and emotions: sleep seems to influence both emotion generation and regulation via several potential behavioural and neurological mechanism such as situation selection (for example, the tendency of sleep-deprived individuals to avoid certain social situations that might elicit emotions), modification (for example, modifying an already happened situation by using humour in a tense situation), attention deployment (directing attention to/away from an emotional triggering stimulus), cognitive change (changing the meaning of an emotional situation) and response modulation (direct alteration of the response to an emotional stimulus).

The physiological model of insomnia considers hyperarousal, the co-occurring arousal of both sleep- and wake-promoting brain areas, as a central element of insomnia (Troxel and Buysse, 2010). Functional neuroimaging studies have confirmed the failure of arousal mechanisms to reduce activity during sleep onset (Nofzinger et al., 2004). Wassing et al. (2016) reported in their work that hyperarousal can result from an inadequate resolution of emotional distress, which is probably due to restless rapid-eye-movement (REM) sleep. REM sleep and disturbances concerning it thus appear to partly link emotional distress resolution and depression. In PSG studies, depression has indeed been linked to dysregulated REM sleep regulation: a shortened REM latency, increased REM sleep duration and increased REM density, as

well as a decrease in slow wave sleep production (Palagini et al., 2013). Interestingly, these PSG findings resemble those recorded from healthy pregnant women (shortened REM latency, decrease in SWS) (Garbazza et al., 2020). Furthermore, in recordings from the third pregnancy trimester, higher progesterone levels have associated with more WASO (wake after sleep onset) and arousals (Wilson et al., 2011). Postnatally, new mothers with depressive symptoms had a significantly shorter REM latency than new healthy mothers, but they also had approximately 1 h less sleep and 12% lower sleep efficiency (Lee et al., 2000a).

Most sleep research has been performed either on males or on non-pregnant women. However, as reviewed by Barba-Müller, Craddock, Carmona, & Hoekzema (2019) and Glynn, Howland, & Fox (2018), drastic functional and structural changes take place during pregnancy and the postnatal period in the maternal brain when compared to non-parous women; brain regions responsible, for example, for maternal caregiving behaviours, reward signalling and Theory of Mind (ToM) networks show substantial neuroplasticity simultaneously with unique changes in neuroendocrinology. We are just beginning to gain a sense of the sophisticated interplay between maternal and foetal systems, although the phenomenon of foetal microchimerism (cells containing male DNA in the blood of pregnant women decades after giving birth to a son) was already introduced in 1979 (Bianchi et al., 1996; Herzenberg et al., 1979). For example, in animal and human studies (Chan et al., 2012), it has been shown that some foetal cells are able to migrate to the maternal brain, and from animal studies we know that such foetal cells can attach to areas previously associated with maternal behaviour and undergo a neuronal maturation process there, conceivably participating in communication and neuronal circuits (Zeng et al., 2010). Thus, the maternal neuroendocrinological milieu, including serotonin and sleep systems, may have unique characteristics differing from the non-pregnant/male brain.

Some insight into the impact of gonadal hormones on sleep, brain maturation and vulnerability to mental disorders can be gained from studies from another developmental junction/crisis characterised by large hormonal shifts in sex steroids: adolescence. Studies investigating adolescent sleep have shown a close relationship between slow wave sleep, cortical plasticity and maturation (Tesler et al., 2013). The amplitude of slow waves is highest shortly before puberty, and the authors suggested that slow-wave activity (SWA) could be used as a novel tool to find early deviations from the normal development pattern and thus improve the detection and treatment of mental disorders in children and adolescents. Furthermore, oestradiol in females may directly influence neurons in brain areas responsible for sleep-wake states and the circadian clock (Franco et al., 2020; Hadjimarkou et al., 2008; Mong and Cusmano, 2016; Yan and Silver, 2016). Insomnia symptoms

typically emerge in girls aged 11–12 years, coinciding with the burst of gonadal steroids and start of puberty (Calhoun et al., 2014). It would be of interest to know whether those individuals who are particularly sensitive to oestrogen and other gonadal hormones are also the ones most prone to insomnia, sleep problems, stress-related emotion dysregulation and mental disorders in pregnancy and postpartum. Interestingly, in non-pregnant adults, the severity of depressive illness has also been linked to the initiation, density and duration of SWS (Gehrman et al., 2010; Perlis et al., 1997). In the future, a closer examination of SWS and SWA in different pregnancy stages and brain areas could increase our understanding of the pathophysiology of perinatal mental disorders.

Other mechanisms by which sleep influences mood states and depression during pregnancy have been proposed, including systemic inflammation, a blunted melatonin response and circadian rhythm disruption, oxidative stress, and genetics (reviewed by Christian, Carroll, Teti, et al., 2019; Meltzer-Brody, Howard, et al., 2018; Willis, Hatch, & Wise, 2019). Finally, while Rieman et al. (2001) pointed out that most of antidepressant medications inhibit REM sleep (and thus probably promote SWS), the connection between sleep and mood is most probably bidirectional, adding complexity to the picture.

## **2.3 PARENTAL DEPRESSION AND CHILDREN'S EMOTIONAL PROBLEMS**

Many children have to deal with parents with mental disorders. According to one estimate, in the US, at least 15 million children live with a parent who has had an episode of major depression in the previous year (England and Sim, 2009a). Abel et al.(2019) estimated in an UK study involving more than 545 000 children that the overall prevalence of maternal mental disorder was 23.2%, the incidence peaking at 0–3 months postnatally (26.7 per 100 person years, 95% CI 26.4–27.1). Adverse childhood experiences (ACE) such as a parental mental disorder potentially have long-lasting and considerable effects, particularly on children's learning/behavioural problems (Burke et al., 2011).

Although most studies have concerned maternal depression, parental mental disorders have been shown to associate, for example, with children's preterm birth (Grigoriadis et al., 2013), cognitive delays (Bennett et al., 2015; Liu et al., 2017; Slomian et al., 2019; Tuovinen et al., 2018) and poor physical health (Pierce et al., 2019), the effect lasting even to middle age (Weissman et al., 2006). Poorer academic and social performance in offspring is another well-established consequence (England and Sim, 2009a; Stein et al., 2014).

Stein et al. (2014) reviewed the effects of parental depression/mental illness on children. They concluded that there is substantial and strong evidence associating perinatal disorders with a range of negative child outcomes, many of which may persist until adolescence. The effect sizes have been from small to moderate if there has not been a severe or chronic maternal disorder or comorbid disorders.

Studies concerning gender differences in outcomes between boys and girls have yielded somewhat mixed results. Morbidity and mortality appear to be more increased in male fetuses and infants when born in disadvantageous environments, whereas female fetuses and infants appear to be more adaptive; the trade-off for females is an increased susceptibility to anxiety and mood disorders in pre-adolescence (Sandman et al., 2013). DeBrujin et al. (2009) found maternal emotional disturbances in early pregnancy to more strongly affect boys, whereas girls were affected later during pregnancy (Sandman et al. 2013; DeBrujin et al. 2009). Briggs-Gowan et al. (2004, 2001) reported different cut-off levels among girls and boys when evaluating emotional problems and competence in toddlers: girls have consistently had higher competence scores, whereas boys have had more emotional problems in some studies.

### **2.3.1 EFFECTS OF MATERNAL DEPRESSION ON OFFSPRING**

The literature concerning the effects of maternal depression in particular on the offspring is extensive and only briefly outlined here. Goodman et al. (2011) reported in their meta-analytic review that maternal depression was associated with higher levels of children's internalizing, externalizing, general psychopathology and negative affect/behaviour, and with lower levels of positive affect/behaviour, the effect sizes being small in magnitude. The research suggests that both the chronicity and severity of maternal depression are important (Brennan et al., 2000; Stein et al., 2014). However, as Barker et al. (2012) argue, additional risk factors related to maternal mental health problems (such as a low income, inadequate living conditions, single parenthood, partner cruelty and a low educational level) explained a substantial proportion of the increase in internalizing and externalizing problems in the offspring.

#### ***2.3.1.1 Prenatal maternal depression***

Several reviews have brought together results concerning maternal depression during pregnancy and child outcomes (Field, 2011; Gentile, 2017; Tien et al., 2019; Waters et al., 2014). While there appears to be a consensus that maternal prenatal depression has an effect on children's conduct problems and antisocial behaviour (externalizing problems), the results concerning children's internalizing problems (such as depression, anxiety and somatic symptoms) are more conflicting. While Walters et al. (2014) stated in their review that effects of prenatal depression on infant development and children's emotional problems are best explained by cumulative exposure to maternal depression and other risk factors, O'Donnell et al. (2014) argued that in their study, based on the large ALSPAC cohort, exposure to maternal depression or anxiety during pregnancy, in particular, associated with a two-fold increase in probable mental disorders in children in a 14-year follow-up. Prenatal anxiety might indeed be even more harmful than depression (Glover, 2014; O'Donnell and Meaney, 2017). However, disentangling the effect of different exposures is challenging, as children exposed to maternal prenatal depression are often also exposed to anxiety and various other risk factors such as poverty, domestic violence, parental substance abuse and childhood maltreatment. All in all, Madigan et al. (2018) calculated a meta-estimate of OR 1.8 (95% CI 1.6–2.0) for children's socioemotional problems if the mother had prenatal depression.

Several mechanisms by which maternal prenatal depression influences child development have been suggested. O'Donnell and Meaney (2017) discussed the foetal programming hypothesis in their review: do intrauterine signals programme future adverse neurodevelopment in offspring by altering

tissue differentiation in the foetal brain? They found little evidence to support this hypothesis, but concluded that exposure to maternal anxiety, depression and stress seems to lead to a “metaplastic” state in the foetal brain, which increases sensitivity to postnatal influences and care. They also reviewed the known influences of maternal prenatal depression on offspring brain development: cortical thinning (Sandman et al., 2015) and increased functional connectivity between the amygdala and other brain areas (temporal cortex, insula, anterior cingulate) in girls but not in boys (Soe et al., 2018). Importantly, cortical thinning is suggested to be an endophenotype of depression and to partly mediate the connection between maternal prenatal depression and later offspring externalizing behaviour. There also appear to be sensitive periods. In a recent imaging study, Zou et al. (2019) described how children had a period at the age of two months when they were sensitive to maternal depressive symptoms, and at the age of ten years, the effects of maternal depression could still be observed in MRI imaging. The effect of prenatal stress on foetal and child brain development have been further reviewed by Lautarescu et al. (2020).

The hypothalamus–pituitary–adrenal (HPA) axis functions differently during pregnancy compared to other times in a woman’s life (reviewed by Glover 2014). As pregnancy progresses, the maternal HPA axis becomes gradually less responsive to stress. However, even though the maternal cortisol level might not increase, depression, anxiety and stress can cause the placenta to alter foetal exposure to maternal cortisol by decreasing the amount and activity of the enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type II (11 $\beta$ -HSD2), which converts cortisol to its inactive form, cortisone. The less 11 $\beta$ -HSD2 there is, the more cortisol transfers through the placenta to the foetal side. Based on animal models, prenatal stress such as depression can downregulate 11 $\beta$ -HSD2. Increased cortisol levels can thus disturb the function of the foetal HPA axis and alter brain development (Lautarescu et al., 2020).

Direct genetic factors have an important role in the transmission of risk to the offspring. In a study by Hannigan et al. (2018) comprising over 22 000 mothers and over 35 000 children, intergenerationally shared genetic factors were found to explain 41% of the variance in children’s internalizing problems and 37% of the variance in children’s externalizing problems. In recent years, epigenetic studies have also increased, and maternal prenatal depression appears to associate with foetal epigenetic changes, with potentially lasting changes (Nemoda and Szyf, 2017). Furthermore, Suarez (2018) have shown such epigenetic changes to be associated with internalizing problems in boys.

Lastly, inflammation and alterations in the immune system (Karlsson et al., 2017; Slopen et al., 2015) and gut microbiota (Heiss and Olofsson, 2019; Rackers et al., 2018) are other potential mechanisms of transmission.

### **2.3.1.2 Postnatal maternal depression**

After delivery, the quality of postnatal care and exposure to maternal affect and behaviours, as well as other environmental factors, start to moderate the association between maternal depression and behavioural outcomes in the offspring (Charrois et al., 2017). The concept of sensitive periods in children's development has long been accepted (Heim and Binder, 2012). The term 'sensitive period' refers the enhanced neural plasticity in a given developmental period.

The downside of this plasticity is vulnerability; stressors or trauma might have particularly disadvantageous consequences during a sensitive period. Furthermore, during a critical period, certain experiences are necessary for normal brain development. If the critical period ends and such experiences are still missing, as Heim and Binder (2012) put it: "the window of opportunity has closed" and brain development has adopted a certain trajectory. The first postnatal months and the first year seem to be a sensitive period in terms of emotional processing (Bagner et al., 2010).

Murray et al. (1999) evaluated the quality of mother-child attachment 2 months postnatally and after a 5-year follow-up period. They concluded that exposure to maternal depression in the first months after delivery may have a long-lasting effect on a child's psychological adjustment. This is understandable both in terms of symptoms of maternal depression (passiveness, withdrawal, negative affect, hostility, decreased playfulness and positive interaction with the child) and the idea of sensitive and critical periods for a child's emotional development. The effect can be long-lasting: Netsi et al. (2018) showed in a sample of 8287 children that maternal postnatal depression doubled the risk of children's behavioural problems at the age of 3.5 years. Persistent and severe postnatal depression was also associated with lower mathematical grades at the age of 16 and an increased risk of offspring depression at the age of 18 (OR 7.4, 95% CI 2.9–19.1). To further complicate the picture, interactions between genes and the environment are probably important determinants of the consequences of early life stress or maternal postnatal depression for the child. Belsky (2010) and Holmberg & Lersch (2010) pointed out that the same alleles that can increase the risk of disadvantageous outcomes in a negative environment such as abuse in childhood can also be beneficial in a positive environment. Thus, these alleles might markedly increase susceptibility to changes in the environment. In the case of a similar negative environment, complex interactions between a child's genetic background, gender, age, the gonadal steroid status and HPA axis reactivity determine what the consequences are for a particular child (Heim and Binder, 2012). Slomian et al. (2019) reviewed associations between maternal postnatal depression and maternal health, children's physical and emotional health, and the developing mother-child attachment relationship.

The quality of the parent–child attachment relationship has indeed an important influence. In a recent meta-analysis by Badovinac et al. (2018), maternal depression was significantly ( $n = 1727$ ,  $g = 0.27$ , 95% CI 0.13–0.40) associated with disorganized attachment in two- to five-year-old children. The findings of other studies are in line with these results (Atkinson et al., 2000; Barnes and Theule, 2019; Martins and Gaffan, 2000). Interestingly, prenatal depression has been reported to have an association with disorganized attachment, independent of postnatal depression (Hayes et al., 2013). Furthermore, insecure attachment in children was moderately (meta-estimate of  $r = .31$ ,  $p < .001$ , 95% CI 0.29–0.34) associated with later depressive symptoms in the offspring (Spruit et al., 2020). Parental depression has also been shown to adversely influence the marital/ parental relationship, and the children are exposed to more divorces and emotionally cold/controlling behaviour. In fact, marital discord has been reported to mediate the relationship between parental depressive symptoms and children’s internalizing symptoms (Cummings et al., 2005). Crittendon et al. (2015) also pointed to the need to evaluate the whole family system in case a child or one family member has symptoms of mental disorder; in many cases, the parent without a diagnosis of mental disorder can distort information about the diagnosed parent in ways that harm the child.

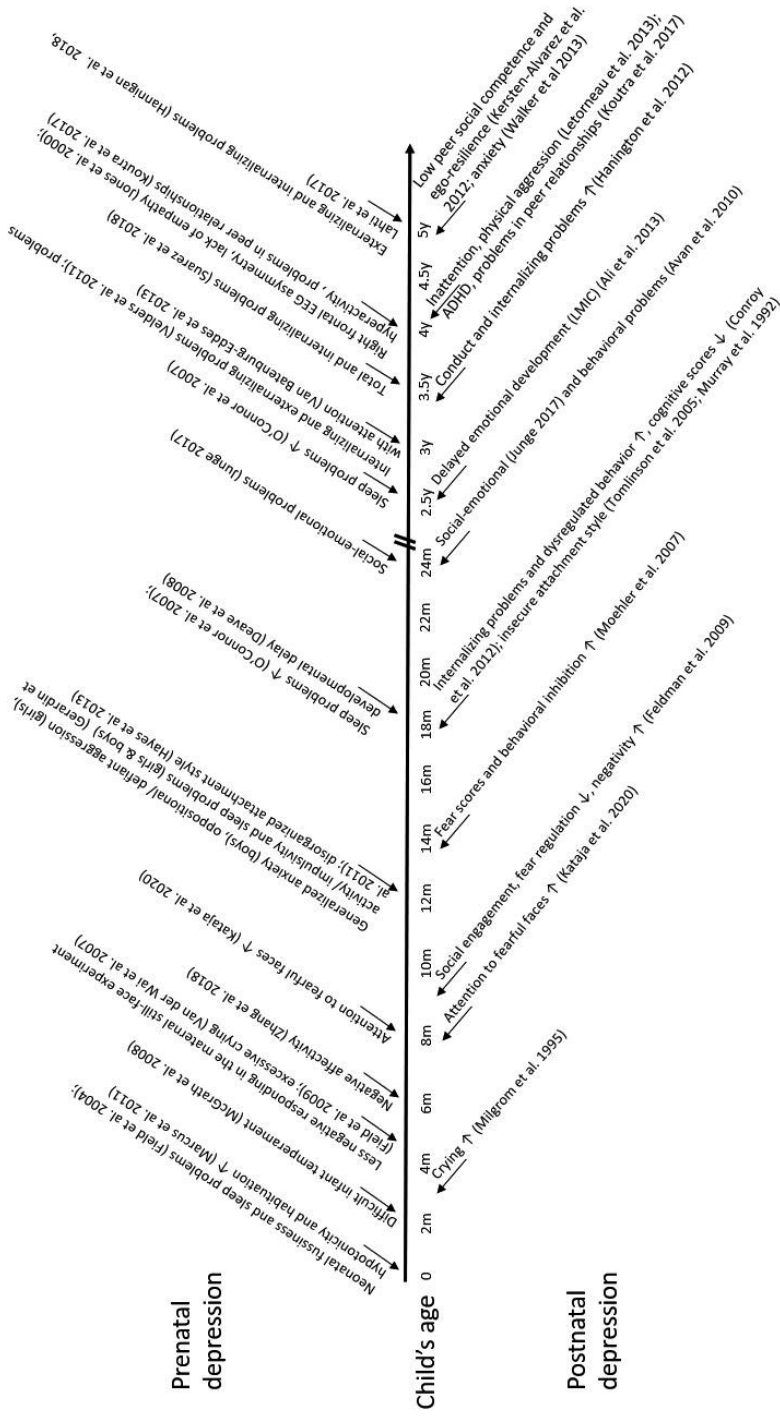
The main modifiable mechanism between parental depression and children’s poor outcomes, however, is thought to be the influence of parental depression on **parenting**. Lovejoy et al. (2000), in their meta-analysis of maternal depression and parenting behaviour, reported moderate effect sizes for the association between maternal depressive symptoms/disorder and negative, hostile parenting (mean  $d = 0.40$ ) and disengaged (withdrawn) parenting (mean  $d = 0.29$ ). In the same meta-analysis, a small but significant association was also found between depression and less frequent use of positive parenting practices ( $d = 0.16$ ). Unfortunately, these adverse parenting qualities may not improve to a level that is comparable with a never-depressed parent, even if depression remits (England and Sim, 2009b). Based on another meta-analysis, key components of successful parenting programmes are positive reinforcement and nonviolent discipline techniques (Leijten et al., 2019). Concerning parents having severe mental health disorders, evidence of community-based parenting programmes in improving the quality of life in the offspring is lacking: children’s emotional symptoms (ES 0.06, 95% CI -0.20 to -0.33) and social functioning (ES 0.23, 95% CI 0.00–0.46) did not improve (Bee et al., 2014). Medium to large effect sizes were, however, found concerning parental depressive symptoms (ES 0.73, 95% CI 0.51–0.94) and parenting behaviours (ES 0.67, 95% CI 0.32–1.02). Thus, offspring of parents with severe mental disorders might need an earlier, longer and more comprehensive approach to overcome the adverse effect of years of exposure to parental disorder and stressors commonly

accompanying such conditions (e.g. poverty, exposure to violence, lack of one parent).

Recently, the importance of parental predictable behaviour vs unpredictable and fragmented care has received attention (Davis et al., 2019; Glynn and Baram, 2019). Glynn et al. reported how unpredictable and fragmented maternal care can cause aberrant maturation of certain brain circuits in the child's developing brain. Thus, changing the pattern of maternal care to a more predictable style can offer a strategy for future interventions. Davis et al. found such an unpredictable pattern of maternal care to have a lasting effect on the child; executive function was still poorer at the age of 9 years.

Importantly, Meaney (2018) noted how subclinical levels of maternal depressive symptoms can have as harmful an effect on maternal psychosocial functioning and parenting as clinical depression. Furthermore, neurodevelopmental changes (such as cortical thinning) in the offspring appear to respond in a dose-dependent manner to increasing maternal mental health symptoms, in contrast to the traditional view, according to which only mothers scoring above a certain cut-off threshold in depression questionnaires indicating clinical depression are offered treatment. The treatment of maternal depressive symptoms has been shown to reduce the risk of children's behavioural problems (Weissman et al. 2015; Herba et al. 2013).

In **Figure 1**, the key findings and studies concerning maternal pre- and postnatal depression vs children's emotional problems are presented.



Note: ↑Higher level, ↓lower level

**Figure 1.** Key findings concerning maternal pre-/postnatal depression and children emotional problems, when compared to children with non-depressed mothers.

### **2.3.2 EFFECTS OF PATERNAL DEPRESSION ON OFFSPRING**

The effect of paternal depression on the socioemotional development of the offspring has gained interest in recent years. Paternal depression has been associated with at least poorer obstetric outcomes in the offspring (Liu et al., 2016), impaired language development (Paulson et al., 2009), an increased risk of child neglect (Lee et al., 2012), and in some studies with an increased risk of asthma and injuries (reviewed by Pierce et al., 2019). Based on a recent review and meta-analysis (Ayano et al., 2019), paternal depression does not increase autism spectrum disorders in the offspring.

Several reviews (Gentile and Fusco, 2017; Ramchandani and Psychogiou, 2009; Sweeney and MacBeth, 2016) have investigated associations between paternal perinatal depression and children's emotional outcomes. Gentile found paternal depression to predict developmental and behavioural problems from very early on; even 8-week-old babies had excessive crying and impaired father-child bonding if fathers had perinatal depressive symptoms. In infants and toddlers, paternal depression associated with a range of symptoms including hyperactivity, conduct problems, developmental delays and social problems, whereas school-aged children had a doubled risk of developing specific psychiatric disorders when compared to the offspring of non-depressed fathers. Ramchandani and Psychogiou concluded in their review that some studies have found boys to be more susceptible to adverse effects than girls, and paternal mental disorders appear to be associated more with behavioural than emotional problems in children. Sweeney and MacBeth confirmed in their review the negative effect of paternal depression prenatally, postnatally and during adolescence on offspring development, as well as internalizing and externalizing problems; the associations were stronger during early childhood, matching the hypotheses concerning sensitive periods in child development. Sweeney and MacBeth also noted several important mediators: paternal involvement, negative expressiveness, hostility and marital conflict.

Barker et al. (2017) focused their review on paternal involvement and separated it into distinct domains: positive engagement in activities, warmth-responsiveness, control, indirect care and process responsibility. This theoretical concept is also clinically interesting, because different domains of paternal involvement can also influence children's psychosocial development in different ways. Moreover, Barker et al. suggested that in father-child interactions, engagement and withdrawal may be more important than sensitivity; in a video-recorded and coded father-child interaction, 3-month-old babies were shown to have an increased risk of early externalizing behaviour at the age of 1 year if their fathers were disengaged (OR 5.3) or remote (OR 3.3) (Ramchandani et al., 2013).

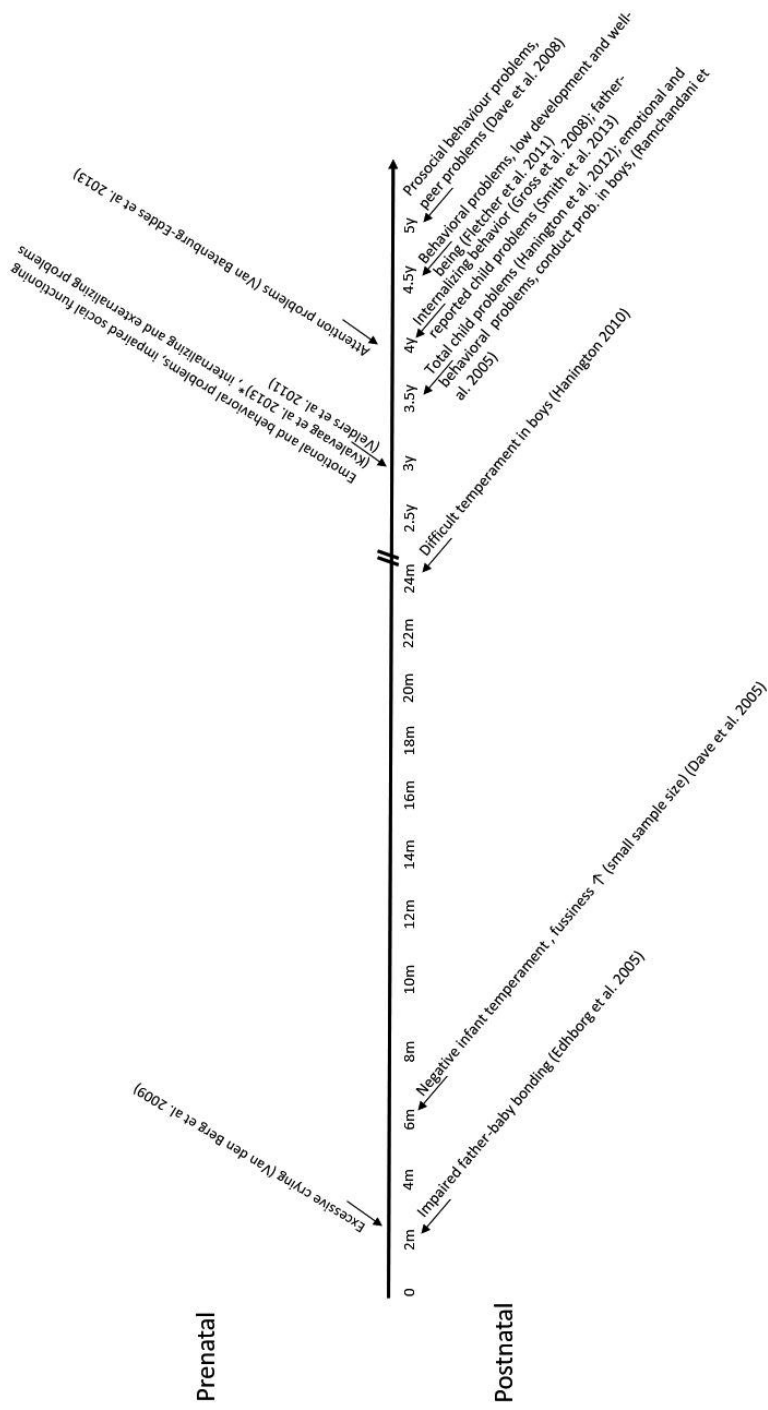
In meta-analyses on the subject (Cheung and Theule, 2019; Connell and Goodman, 2002; Kane and Garber, 2004), and most recently that by Cui et al. (2020) researchers have consistently found associations between paternal depression and children's internalizing and externalizing problems. Cheung and Theule (2019) studied the relationship between paternal depression and children's externalizing problems and found a weak relationship ( $r = .15$ ; 95% CI 0.13–0.18). Cui et al. compared the offspring of fathers with and without perinatal depression and reported children's behavioural problems (meta-estimate of OR 1.2; 95% CI 1.1–1.3), emotional problems (1.3; 95% CI 1.2–1.4) and social problems (1.3; 95% CI 1.0–1.74) to increase in relation to paternal perinatal depression. However, the meta-analysis of Cui et al. was based on only 9 studies, of which 4 were from different birth cohorts (ALSPAC/UK; LSAC/Australia; MoBa/Norway and Generation-R/Netherlands), and only LSAC and most of the ALSPAC studies were adjusted for maternal depression. In an older meta-analysis, Connell & Goodman (2002) reported that externalizing problems in the offspring were equally related to maternal and paternal psychopathology, whereas internalizing problems were more associated with maternal psychopathology; all average effect sizes were small. Kane and Garber (2004) reported in their meta-analysis mean effect sizes of 0.24 (95% CI .15–0.34) for internalizing, 0.19 (95% CI 0.11–0.28) for externalizing and 0.20 (95% CI 0.09–0.30) for father–child conflict. In meta-analyses of Kane and Garber, the ages of children varied from 3 to 14 years, which makes the results more difficult to interpret.

Studies from the ALSPAC cohort have reported that children whose fathers were depressed both pre- and postnatally had the highest risk of psychopathology at the age of 3.5 years (OR 3.6; 95% CI 2.1–6.1) and of total problems and a psychiatric diagnosis at the age of 7 (OR 2.5; 95% CI 1.2–5.4) (Ramchandani et al., 2008a). Sons were particularly affected; boys had an increased risk of conduct disorder at the age of 3.5 years (OR 2.1) if their father had postnatal depression, whereas the group with prenatally depressed fathers was not at increased risk. The effect can be long-lasting; Gutierrez-Galve et al. (2019) reported offspring of postnatally depressed fathers to be at risk of depression at the age of 18, even after adjusting for paternal age and education. This effect was seen in girls. The authors noted that paternal depression seemed to influence late emotional problems in girls at least partly via maternal depression. Maternal depression at 8 months explained 20% of the association between paternal depression postnatally and offspring depression, and furthermore, conduct problems at the age of 3.5 years explained 10% of this association.

Mechanisms by which paternal depression influences the offspring include direct genetic as well as epigenetic mechanisms (O'Donnell and Meaney, 2020). Paternal stress exposure has been shown to alter the sperm

microRNA content and thus reprogramme the HPA axis in the offspring (Rodgers et al., 2013). Based on animal studies, paternal stress prior to conception also influences DNA methylation patterns in the offspring, resulting in behaviour changes (Mychasiuk et al., 2013). While genetic influences are difficult to overcome, impaired parenting behaviour (reviewed by S. Wilson & Durbin, 2010) and paternal involvement (reviewed by Sarkadi, Kristiansson, Oberklaid, & Bremberg, 2008) offer a modifiable target for interventions.

In **Figure 2**, we present the key outcomes in the offspring of fathers with perinatal depression.

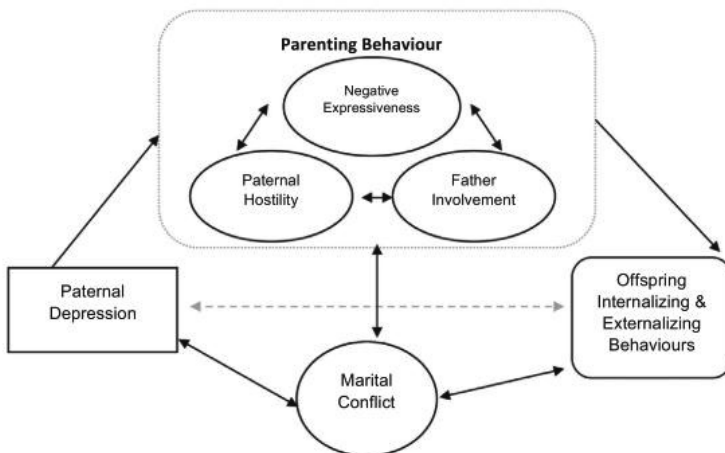


Note: ↑Higher level, ↓lower level

**Figure 2.** Key findings concerning paternal pre/postnatal depression and child emotional problems (0–5 years) when compared to children with non-depressed fathers. \*Kvaleaag et al. (2013) used SCL-5 to assess paternal mental health; two of the items of the questionnaire measure depression and three anxiety.

Several mediators and moderators (**Figure 3**) for the association between paternal depression and emotional and behavioural problems in children have been proposed. Gutierrez-Galve et al. (2019) measured maternal and paternal depressive symptoms 8 weeks postnatally and child outcomes at the ages of 3.5 and 7 years ( $n > 13\ 000$ ). They found family factors such as maternal depression and couple conflict to mediate two-thirds of the association between paternal depression and child outcomes at both ages. In contrast, in the case of maternal depression, family factors mediated less than 20% of the association. In the Gutierrez-Galve (ALSPAC) study, parental education and antisocial traits did not have a mediating role. Other suggested moderators include the child's age, gender, year of publication of the study (levels of paternal involvement with children have risen) and the composition of families (two caregivers vs divorced/widowed/single parent) (Connell and Goodman, 2002).

Finally, the treatment of paternal depressive symptoms is important: Tichovolsky, Griffith, Rolon-Arroyo, Arnold, & Harvey, (2018) demonstrated that reducing paternal depressive symptoms also ameliorated children's depressive symptoms, whereas increasing paternal depression resulted in an increase in children's symptoms during a 3-year follow-up.



**Figure 3.** Mediation model of risk. Reprinted from The effects on paternal depression on child and adolescent outcomes: A systematic review, Sweeney & MacBeth, *Journal of Affective Disorders* 205 (2016) 44-59, with permission from Elsevier.

### **2.3.3 COMBINED EFFECT OF PARENTAL DEPRESSION ON OFFSPRING**

Exposure to two depressed parents has been repeatedly reported to increase the risk of adverse outcomes in children (Goodman & Gotlib 1999; Mezulis et al. 2004; Foley et al. 2001; Goodman et al. 1993; Dierker et al. 1999; Reich 1993). Goodman and Gotlib (1999) found in their review of empirical evidence that fathers may either exacerbate the risk of psychopathology in children or protect them from the hazardous results of maternal depression. Mezulis et al. (2004) emphasized that the amount of time fathers spent with their infants had a key role: paternal depression indeed exacerbated the effect of maternal depression, increasing children's internalizing symptoms, but this moderation was limited to fathers whose spent considerable (from medium to high amounts) time with their infants. The authors noted that if the mother is the primary caregiver, the adverse effects of maternal depression may not be compensated by small amounts of positive paternal involvement.

Dierker et al. (1999) investigated parental mating types and the risk of psychopathology in children aged 7 to 17 years in a setting where parents had anxiety and/or substance use disorder. They reported a direct relationship between affected parents and the amount of psychopathology in children, particularly concerning anxiety disorders. However, the risk of conduct disorders was only elevated if both parents were affected. Foley et al. (2001) studied concordance in parental and offspring mental disorders in 850 twin families. Of note is that they personally interviewed the twins (aged 8 to 17 years) and both parents. They found an association between parental depression, that was not comorbid or associated with a different spousal disorder, and depression and overanxious symptoms/disorder in the offspring. Maternal depression posed a higher risk than paternal depression for these symptoms in the offspring, but the risk was highest if both parents were affected. The risks were also higher for girls than boys, particularly concerning overanxious disorder. Foley et al. also stated that maternal depression was associated with an increased risk of conduct disorder and symptoms of oppositional-defiant symptoms if the father also had a history of alcoholism. This underlines the need for broader diagnostic evaluations in the family system if one family member presents with a mental disorder.

Weismann et al. (2016) followed families (n = 91 in the first generation) for 30 years and studied whether parental depression can have affects lasting to the third generation. Grandchildren (n = 38) with both a depressed parent and grandparent were at highest (3-fold) risk of major depression. Recently, Pearson et al. (2019) investigated three generations in a Brazilian birth cohort. Psychiatric symptoms in grandmothers increased behavioural and emotional problems in their grandchildren as much as emotional symptoms in the mothers. Curiously, there was no evidence for associations with

paternal symptoms. Furthermore, the effects were substantially larger for maternal grandmothers when compared to paternal grandmothers. While the findings of Pearson et al. might relate to cultural differences (the maternal grandmother providing childcare during working hours, for example), it is unfortunate that families that might need and benefit most from warm and caring grandparental attendance in the children's lives are also the ones at greatest risk of lacking such support. In the future, broadening the family context further from fathers to the inclusion of grandparents and their mental well-being would be fruitful areas for further investigations.

Different parental disorders can lead to the same outcome in the children (equifinality), whereas the same parental mental disorder can lead to different psychiatric disorders in the offspring (multifinality); most studies have found evidence for the latter (reviewed by van Santvoort, Koesum, & Reupert, 2015). Thus, the offspring of depressed parents may develop a wide range of mental disorders. However, parental anxiety disorders seem to be an exception to the rule of multifinality, as the offspring of anxious parents tend to particularly develop anxiety disorders themselves, but not other disorders (transgenerational concordance) (Floor van Santvoort et al., 2015).

Reuben et al. (2015) reviewed the concept of resilience and possible protecting factors that help children survive despite parental depression. They concluded that the duration and timing of child exposure varies, and not all interventions appear to work for the children at highest risk. They also concluded that children are rarely able to escape without adversities in any life areas, and that resilience changes dynamically over time. Furthermore, we should separately evaluate different areas (social competence, school performance, emotional disturbances) and offer a wide range of protecting factors, particularly during sensitive development periods.

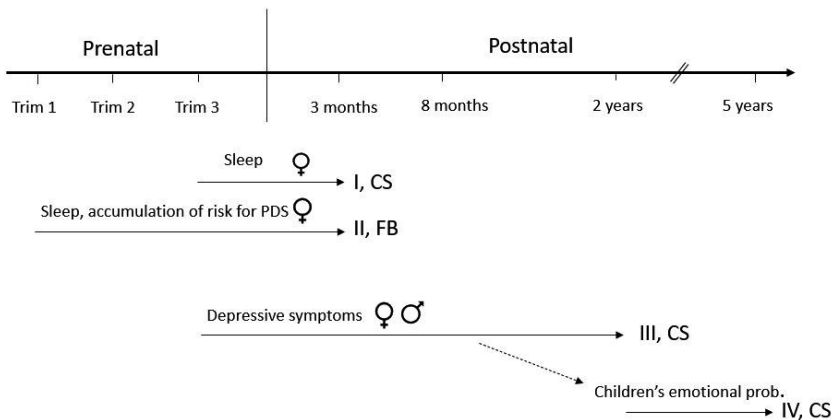
Lastly, it should be noted that many parents continue to parent their children well despite having mental disorders. For example, how a parent manages to function despite suffering from depression has an influence. In a study by Rutton & Quinton (1984), approximately 1/3 of children of psychiatric patients showed transient problems, 1/3 long-lasting problems and 1/3 did not show emotional problems in a four-year follow-up. The severity and duration of parental depression, the level of social support, psychiatric symptoms in the other parent and the child's temperament and characteristics all influence the outcome (Stein, 2014).

### 3 AIMS OF THE STUDY

This doctoral study investigated parental depressive symptoms from pregnancy until two years postnatally, and the association of various risk factors such as prenatal sleeping problems with maternal depressive symptoms postnatally. In addition, the association of parental depressive symptoms with children’s emotional problems was investigated.

Specific aims were as follows:

1. To examine the associations of pre- and postnatal sleeping problems with postnatal depressive symptoms (Study I).
2. To investigate a) whether insomnia symptoms across pregnancy predict postnatal depressive symptoms and b) the cumulative risk of postnatal depressive symptoms (Study II).
3. To study a) maternal and paternal depressive symptom trajectories from late pregnancy until 2 years postnatally, and b) risk factors associating with a higher level of parental depressive symptoms (Study III).
4. To assess how maternal and paternal depressive symptom trajectories associate with children’s emotional problems at the ages of two and five years (Study IV).



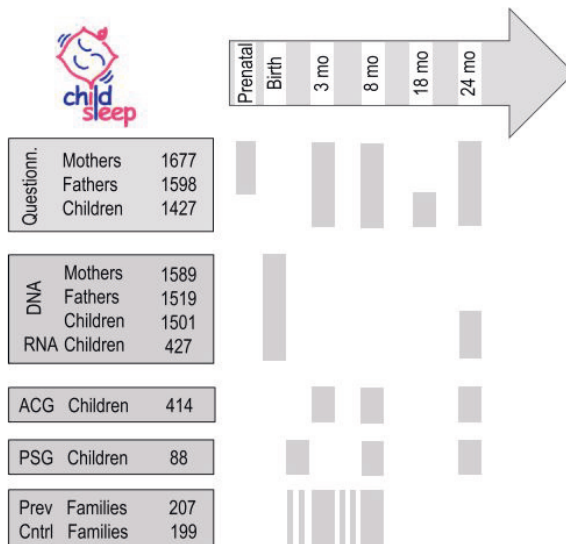
**Figure 4.** Timescales, themes and birth cohorts in Studies I–IV.

## 4 MATERIALS AND METHODS

### 4.1 THE CHILD-SLEEP COHORT (I, III, IV)

Studies I, III and IV were conducted as part of the CHILD-SLEEP study (Figure 5), which is a population-based birth cohort recruited from Pirkanmaa Hospital District. The CHILD-SLEEP study is a collaborative research project between Tampere University Hospital and the University of Tampere, Helsinki University Hospital and the University of Helsinki, the National Institute for Health and Welfare and the University of Eastern Finland. The ethics committee of Pirkanmaa Hospital District approved the study protocol (9.3.2011, ethical research permission code R11032).

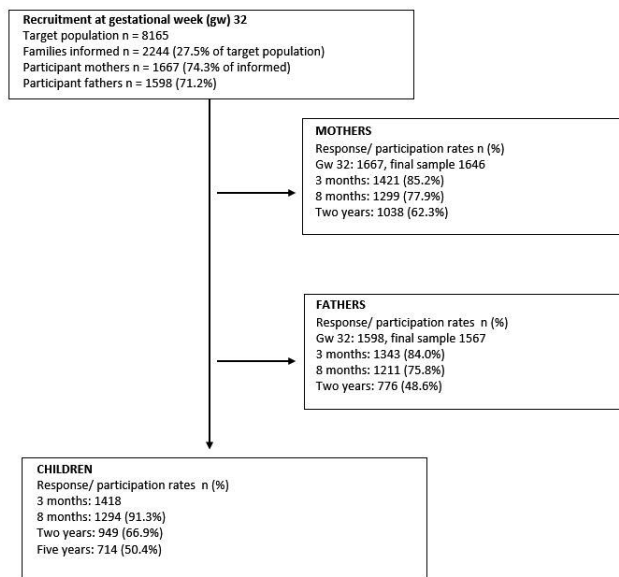
The study protocol and recruitment are described in detail elsewhere (Paavonen et al., 2017). Recruitment took place between April 2011 and December 2012 at the local maternity clinics. The inclusion criterion was delivery at Tampere University Hospital, where approximately 5000 infants are born per year. As an exclusion criterion, only Finnish-speaking families were included in the study. In 2014, about 5% of the families in the target area spoke another language as their mother language. As a total of 8165 infants were born in the target area during the recruitment process, the sample coverage was around 29% (Figure 6).



**Figure 5.** The study design of the CHILD-SLEEP cohort. From Paavonen et al. (2017). Figure reproduced with permission from the authors and Elsevier. DNA = deoxyribonucleic acid, RNA = ribonucleic acid, ACG = actigraphy, PSG = polysomnography, Prev = prevention group, Cntrl = control group.

### 4.1.1 PARTICIPANTS

CS



**Figure 6.** Flow chart of the participants in the CS cohort

In Study I, data were used from all the mothers who had completed both the prenatal (gw 32) and 3-month postnatal questionnaires, after excluding 21 women who had completed the prenatal questionnaire after delivery. In Study III, we used all available data for mothers and fathers from gw 32 and 3 months, 8 months and 24 months after delivery. In Study IV, we excluded five children with developmental disability/severe disorder and five twins, leaving a final sample of 939 children at age two. At age five, we excluded eight twins and six children with developmental disability or severe disorder, leaving a final sample of 700 children (128 of whom had not participated at age two). The characteristics of the participants are presented in **Table 7** (adults) and **Table 8** (children).

**Table 7.** Sociodemographic and clinical characteristics of the participants in the CHILD-SLEEP cohort.

Measure		Mothers		Fathers	
		N=1670	Mean (SD) / %	N=1604	Mean (SD) / %
Age		1626	30.7 (4.6)	1436	32.5 (5.3)
Previous children	At least one	1527	52.7%	1386	54.4%
Relationship status	Lives with a partner	1397	98.6%		
Educational level	None or some vocational training	1607	7.3%	1531	11.0%
	Vocational degree or polytechnic		58.4%		59.3%
	University		34.2%		29.7%
Income level	Low personal net income	1609	23.1%	1543	6.9%
Smoking	During pregnancy/ currently	1640	5.8%	1555	18.1%
Psychiatric disorders (lifetime)	Depression	1474	14.4%	1349	7.1%
	Panic disorder	1456	6.3%	1338	3.4%
	Schizophrenia	1443	0.4%	1330	0.4%
	ADHD/ADD	1444	0.7%	1332	1.0%
	Other psych. diagnoses	1444	2.8%	1330	2.1%
Antidep. medication (SSRI/SNRI)	Previous six months (asked at gw 32)	1635	3.2%	1557	4.6%
	3 months	1398	2.3%		
Sleep medication (daily/ almost daily)	Gw 32	1646	0.3%	1567	1.7%
Depressive symptoms (CES-D)	Gw 32	1640	5.11 (3.50)	1557	3.76 (3.14)
	3 months	1415	4.63 (3.78)	1316	3.75 (3.23)
	8 months	1291	5.47 (4.08)	1196	4.10 (3.56)
	24 months	1038	5.51 (3.96)	774	4.73 (3.48)
CES-D ≥ 10	Gw 32	1640	11.0%	1557	5.1%
	3 months	1415	10.5%	1316	5.2%
	8 months	1291	14.7%	1196	6.9%
	24 months	1038	14.5%	774	10.2%

ADHD = Attention Deficit/Hyperactivity Disorder; CES-D = Center for Epidemiological Studies Depression Scale; Gw = gestational week; SSRI = Selective serotonin reuptake inhibitors; SNRI = Selective serotonin and norepinephrine reuptake inhibitors

At age two, 68% (645) of the child questionnaires were completed by the mother, 0.9% (9) by the father and 30% (286) by both parents. At age five,

69% (490) of the child questionnaires were completed by the mother, 1% (8) by the father and 25% (74) by both parents.

**Table 8.** Children's characteristics in the CHILD-SLEEP cohort

Measure	Girls		Boys		
	2 years N=939 5 years N=700	2 years n= 442 5 years n= 332	Mean (SD) / % (N)	2 years n= 497 5 years n= 368	Mean (SD) / % (N)
Birth weight (g)		431	3507.7 (437.4)	485	3635.0 (455.8)
Gestational age (gw)		431	39.63 (1.22)	484	39.53 (1.32)
Mean age when completed BITSEA (years)		423	2.04 (0.11)	460	2.05 (0.12)
Emotional problems at 2 years/ BITSEA	Total	441	9.06 (5.34)	494	9.27 (5.15)
	Externalizing	442	2.81 (2.13)	496	3.33 (2.18)
	Internalizing	441	3.91 (2.87)	493	3.56 (2.83)
Mean age when completed FTF		317	5.68 (0.56)	353	5.68 (0.53)
Emotional problems at 5 years/ SDQ	Total	313	7.62 (4.04)	354	8.39 (4.68)
	Conduct	313	1.87 (1.50)	354	2.04 (1.65)
	Internalizing	313	1.50 (1.50)	354	1.28 (1.46)
Emotional problems at 5 years/ FTF	Total	317	4.08 (4.03)	354	4.53 (4.67)
	Externalizing	317	2.56 (2.94)	354	3.03 (3.45)
	Internalizing	317	1.52 (1.71)	354	1.50 (1.85)

BITSEA = Brief Infant Toddler Social Emotional Assessment; SDQ = Strengths and Difficulties Questionnaire; FTF = Five to Fifteen Questionnaire

## 4.1.2 MEASURES

### 4.1.2.1 Parental questionnaires (Studies I, III and IV)

The Center for Epidemiological Studies Depression Scale (CES-D) (short version, 10 items) is a brief self-report questionnaire for measuring depressive symptoms derived from the original scale (Irwin et al., 1999; Radloff, 1977). The items are rated on a four-point Likert scale. Three of the items were reverse scored, after which the items were summed, a higher score indicating a higher level of depressive symptoms (range 0–30). A cut-off point of  $\geq 10$  was used to indicate increased depressive symptoms (Grzywacz et al., 2006). Cronbach's alpha for the sum score was 0.78 for mothers and 0.77 for fathers.

The Basic Nordic Sleep Questionnaire (BNSQ) (21 items) is a self-report scale of sleep latency, nocturnal sleep duration, sleep quality, night awakenings and other insomnia symptoms during the previous three months (Partinen and Gislason, 1995). Most of the questions are rated on a five-point Likert scale rated from 1 (never or less than once per month) to 5 (daily or almost daily). Sleep quality (“How well have you been sleeping?”) is rated as follows: 1 = well, 2 = rather well, 3 = neither well nor badly, 4 = rather badly and 5 = badly. The items were dichotomized to two times per week or less vs three times per week or more; sleep latency was dichotomized at a cut-off of  $\geq 20$  minutes, and sleep duration to  $\leq 6$  hours and  $\leq 7$  hours. Sleep loss was defined as the difference between sleep need and average sleep duration. If the difference between these was more than two hours, sleep loss was considered to be clinically relevant. Daytime tiredness was measured with a separate question: “Do you consider yourself more tired than other people of your age during the daytime?” The answers were dichotomized to “yes, almost always” and “often” vs “no” and “I don’t know”. The BNSQ sum score (range 0–5) comprised the dichotomized five items, including difficulty falling asleep, night awakenings per week, night awakenings per night, too early awakenings and poor sleep quality. A score of four or more indicated several frequent sleep problems and was used as a cut-off.

The Epworth Sleepiness Scale (ESS) (8 items) is a self-report questionnaire for sleepiness (Johns M. W., 1991). The questions were rated on a four-point Likert scale (from 0 = would never doze to 3 = high chance of dozing) and the sum score of items (range 0–24) was dichotomized at the cut-off level of  $\geq 11$  to indicate increased sleepiness. Cronbach’s alpha for the sum score was 0.65 for mothers and 0.69 for fathers.

The Spielberg Trait Anxiety Scale (STAI) (short version of STAI-T, 6 items) is a self-report questionnaire for anxiety (Bieling et al., 1998). The items on the four-point Likert scale were summed (range 4–24), and a cut-off level of  $\geq 12$  (90<sup>th</sup> percentile) was used to indicate an increased level of anxiousness. Cronbach’s alpha for the sum score was 0.78 for mothers and 0.77 for fathers.

The Perceived Stress Scale (PSS) (5 items) is self-report five-point Likert scale for measuring stress (Cohen et al., 1983). In this study we used a 5-item version of the original scale. Two of the items we reverse scored, after which the items were summed (range 0–20). A cut-off level of  $\geq 10$  was used to indicate increased stress levels. Cronbach’s alpha for the sum score was 0.69 for mothers and 0.63 for fathers.

The List of Threatening Experiences Scale (LTE) is a self-report of 11 adverse life events (such as a financial crisis, the death of a relative, separation due to marital difficulties) (Brugha and Cragg, 1990). We calculated a dichotomized variable of  $\geq 2$  distressing events (range 0–11).

Family atmosphere was measured using a Likert-type seven-point scale (Paavonen et al., 2017) (e.g. safe (1)–unsafe (7); tense (1) – cosy (7)). Three of the items were reverse scored. A sum score of the items was calculated (range

7–49) and dichotomized at  $\leq 35$  points (10<sup>th</sup> percentile) to indicate a poor family atmosphere. Cronbach's alpha was 0.86 for women and 0.84 for men. As part of the gw 32 prenatal questionnaires, we obtained sociodemographic background information from the parents. The parental education level was divided into three categories: 1 = none or some vocational training, 2 = vocational degree or polytechnic/ university of applied sciences and 3 = university. Income level was rated as "low" if the personal net income was below 1000 euros per month. Maternal smoking was rated "yes" if the mother had smoked at least once during the previous six months and rated "yes" for fathers if they were current smokers. Parents were also asked about their current somatic disorders/disabilities (yes/no), lifetime psychiatric diagnoses (yes/no) and usage of SSRI/SNRI medication during the previous six months (yes/no). The number of previous children was divided into three categories: 0 vs 1 vs 2 or more previous children. Psychiatric disorders diagnosed by a physician were categorized as 1 = never, 2 = earlier and 3 = current.

#### **4.1.2.2 Children's questionnaires (Study IV)**

The Brief Infant Toddler Social Emotional Assessment (BITSEA) (42 items) is a questionnaire for assessing children's social and emotional problems and competence (Briggs-Gowan et al., 2004). The items are rated on a three-point Likert scale, a higher score indicating a higher risk of emotional/behavioural problems. In study IV, we used the subscales of total emotional problems (31 items, scale range 0–62), which comprises externalizing problems (7 items) such as overactivity, aggression and defiance, and internalizing problems (14 items) such as anxiety and depressive behaviour. Sum scores for all the subscales were calculated, a higher score indicating a higher level of problems. Cronbach's alpha was 0.752 for total problems, 0.62 for externalizing problems and 0.66 for internalizing problems.

The Strengths and Difficulties Questionnaire (SDQ) (25 items) is a screening tool for children's social and emotional problems (Goodman, 1997). The total difficulties score (20 items, scale range 0–40, a higher score indicating a higher level of problems) comprises subscales for hyperactivity/inattention (5 items), conduct (5 items), emotional (5 items) and peer-relationship (5 items) problems. Parents rated the items on a three-point Likert scale, and five of the items were reverse scored. Cronbach's alpha was 0.77 for the hyperactivity/inattention subscale, 0.58 for conduct problems, 0.55 for emotional problems, 0.47 for peer relationship problems and 0.74 for the 20-item total difficulties score.

The Five to Fifteen questionnaire (FTF) (181 items) is a parent-reported screening tool for the risk of children's motor, cognitive and emotional problems (Kadesjö et al., 2004). In Study IV, we used the subscale of

emotional/behavioural problems total score (25 items, scale range 0–50, a higher score indicating a higher level of problems), which can be further divided into externalizing (13 items) and internalizing problems (12 items), with three response alternatives for each item. Cronbach’s alpha was 0.84 for externalizing problems, 0.59 for internalizing problems and 0.83 for the total emotional/behavioural problems subscale.

Birth weight was obtained from hospital registries.

## 4.2 THE FINNBRAIN COHORT (II)

Study II was conducted as part of the FinnBrain birth cohort study ([www.finnbrain.fi](http://www.finnbrain.fi)) (Karlsson et al., 2018). The FinnBrain cohort (**Figure 7**) is a general population-based cohort recruited in the area of Turku University Hospital District and the Åland Islands in Finland between December 2011 and April 2015. Research nurses recruited the families from three maternity welfare clinics after the pregnancy ultrasound visit. As inclusion criteria, sufficient knowledge of Finnish or Swedish and normal results in pregnancy ultrasound screening were required. Approximately 70% of the informed families agreed to participate in the study.

The Ethics Committee of the Hospital District of Southwest Finland approved the study design (ETMK 57/180/2011, 14.6.2011 § 168) and parents also gave their written informed consent on behalf of their unborn child.

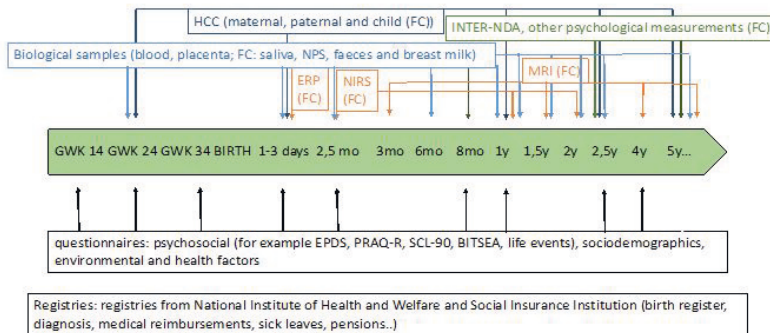


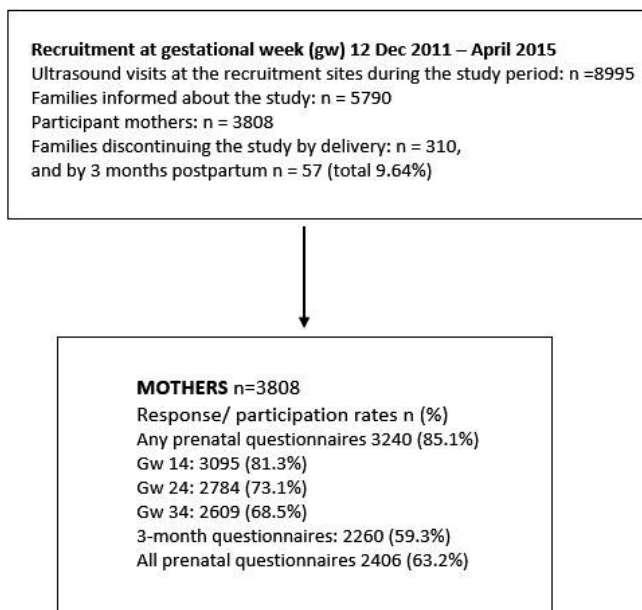
Figure 1. FinnBrain Cohort Study Research Schedule. Families are recruited at gwk 12 at maternity clinics in South-Western Finland. FC = studies targeted for Focus Cohort, HCC = hair cortisol concentration, NPS = nasopharyngeal sample, ERP = event related potential, NIRS = near-infra-red spectroscopy, MRI = magnetic resonance imaging, INTER-NDA = a tool for measuring neurocognitive development

**Figure 7.** Study design of the FinnBrain cohort. Printed with permission from Linnea and Hasse Karlsson.

#### 4.2.1 PARTICIPANTS

A total of 3808 women decided to participate in the birth cohort. In Study IV, we used maternal prenatal questionnaires completed in gw 14, 24 and 34 and a questionnaire completed 3 months postnatally. Responses to the three-month postnatal questionnaire were required for all the included participants, leaving a final sample size of 2157 women at gw 14, 2169 at gw 24, 2136 at gw 34 and 2271 women 3 months postpartum. Registry data on social and medical issues and benefits (for example, [www.kela.fi](http://www.kela.fi), [www.tilastokeskus.fi](http://www.tilastokeskus.fi), [www.thl.fi](http://www.thl.fi)) were available for the baseline participants.

The flow of the study and the sociodemographic and clinical characteristics of the participants are presented in **Figure 8** and **Table 9**.



**Figure 8.** Flow chart adapted from Karlsson et al. 2018 Cohort Profile: The FinnBrain Birth Cohort Study (Karlsson et al., 2018).

**Table 9.** Sociodemographic and clinical characteristics of the participant mothers in the FinnBrain cohort

Measure		N	Mean (SD)/ %
Age	At delivery	2271	30.64 (4.48)
Previous children	At least one	2146	46.8%
Relationship status	Married	2271	55.7%
	Lives with a partner (gw 34)		97.2%
Educational level <sup>a</sup>	Mid/low	2151	33.7%
	High/voc		30.2%
	High		36.2%
Monthly income level	≤€1000	2150	21.0%
	€1001-2000		50.2%
	≥€2001		28.8%
Smoking during pregnancy	Early pregnancy	2270	8.5%
	Late pregnancy		5.3%
Psychiatric disorders (life-time)	Depression	2152	12.4%
	Anxiety disorder		5.6%
	Eating disorder		5.0%
	Psychotic disorder		0.2%
	ADHD/ADD		0.1%
	Alcohol dependency		0%
Antidep. medication (SSRI/SNRI or other)	Gw 14	2129	3.0 + 0.2%
	Gw 34	2097	2.9 + 0.2%
Sleep medication	Gw 14	2115	0.8%
	Gw 24	2160	0.5%
	Gw 34	2126	0.9%
Depressive symptoms (EPDS)	Gw 14		4.97 (3.90)
	Gw 24		4.74 (3.98)
	Gw 34		4.74 (4.01)
	3 months postpartum		4.26 (3.82)
EPDS ≥ 11	Gw 14	2126	8.9 %
	Gw 24	2163	9.2%
	Gw 34	2129	9.3%
	3 months postpartum	2244	7.0%

<sup>a</sup> 1 = mid/low (vocational school/matriculation examination or less), 2 = high/voc (college/university of applied sciences) and 3 = university; EPDS = Edinburgh Postnatal Depression scale; ADHD = Attention Deficit/ Hyperactivity Disorder; SSRI/SNRI = Selective serotonin and norepinephrine reuptake inhibitors

#### 4.2.2 MEASURES

The Edinburgh Postnatal Depression Scale (EPDS) (10 items) is a self-report 4-point Likert scale for assessing depressive symptoms during the previous two weeks (Cox et al., 1987). Seven of the items were reverse scored. A cut-off level of ≥11 for the sum score (range 0–30) was used to indicate increased depressive symptoms. The EPDS has been widely used and

validated for both ante- and postnatal depression (Eberhard-Gran et al., 2001; Kozinszky and Dudas, 2015). In this study, Cronbach's alpha for the sum score was 0.81.

The anxiety subscale of the Symptom Checklist 90 (SCL-90) (10 items) is a five-point Likert scale for anxiety symptoms (Derogatis et al., 1973). After summing the items, the sum score was dichotomized at  $\geq 10$  points, a higher score indicating a higher level of anxiousness. The scale has also been validated in Finland (Holi et al., 1998). Anxiety was measured at each pregnancy time point (gw 14, gw 24 and gw 34). In this study, Cronbach's alpha for the sum score was 0.83.

The Basic Nordic Sleep Questionnaire (BNSQ) (21 items) (Partinen and Gislason, 1995) was also used to measure sleep in the FinnBrain cohort. The items were dichotomized as described above (Chapter 4.1.2.1). BNSQ items were measured at each pregnancy time point (gw 14, gw 24 and gw 34). The Athens Insomnia Scale (AIS) (8 items) is a self-assessment scale for sleep difficulties based on the ICD-10 criteria (Soldatos et al., 2000). We dichotomized the items "sense of well-being during the day" and "functioning (physical and mental) during the day" as follows: 0 = normal, 1 = slightly decreased vs 2 = markedly decreased and 3 = highly decreased. Women's subjective well-being and functioning were assessed at gw 14, gw 24 and gw 34. A question concerning the amount of sleep was dichotomized as 0 and 1 (= 'sufficient' and 'slightly insufficient') or 1 and 2 (= 'markedly insufficient' and 'very insufficient or did not sleep at all').

Educational level was divided into three categories as follows: 1 = mid/low (vocational school/matriculation examination or less), 2 = high/voc (college/ university of applied sciences) and 3 = university.

Income level was asked about as part of the gw 14 questionnaire and categorized as follows: personal net monthly income  $\leq$  €1000 vs €1001–2000 vs  $\geq$  €2001. Smoking during pregnancy (early/late) was dichotomized to "yes" if women had reported smoking in either the national registry or prenatal questionnaires.

Physical illnesses/disabilities and the lifetime history of depression and other psychiatric disorders (yes/no) were asked about as a part of the baseline questionnaire. Registry data concerning medical and social issues were available for the baseline participants ([www.thl.fi](http://www.thl.fi), [www.kela.fi](http://www.kela.fi), [www.tilastokeskus.fi](http://www.tilastokeskus.fi)).

## 4.3 STATISTICAL METHODS

In all the analyses, two-tailed p-values  $<0.05$  were considered statistically significant. We calculated 95% confidence intervals (CI) for odds ratios (OR) and adjusted odds ratios (AOR).

### 4.3.1 STUDY (I)

In Study I, we first compared sleep latency, sleep duration, sleep need, several insomnia symptom variables, the BNSQ sum score and ESS score (11 or more) between women with/without postnatal depressive symptoms (CES-D  $</\geq 10$  three months after delivery). We used either the independent samples t-test or chi-squared test for independence (with Yates' continuity correction), depending on whether the measure of interest was continuous or not. McNemar's test or the paired-samples t-test was used to study differences in sleep variables between two time points. As a measure of the effect size, we used either Cohen's d or Cramer's V, depending on the variable type.

Next, we conducted logistic regression analyses using CES-D  $\geq 10$  three months postpartum as the dependent variable and dichotomized prenatal (gw 32) sleeping variables as independent variables. Each prenatal insomnia symptom variable was investigated separately in the model. We controlled for background variables (maternal age, education, number of children living in the family, smoking during pregnancy, general health), depressive symptoms during pregnancy (CES-D  $\geq 10$  at gw 32) and a lifetime history of depression. Separately, we investigated cross-sectionally the associations of postnatal sleeping problems with postnatal depressive symptoms (both 3 months after delivery). As a sensitivity test, we repeated the analyses with linear regression models and the postnatal CES-D score without the sleep item ("my sleep was restless"). IBM Statistical Package for Social Sciences (SPSS) (IBM Corp., 2017) 24 and a two-tailed alpha level of 0.05 was used for the analyses.

### 4.3.2 STUDY (II)

In Study II, we first conducted logistic regression analyses separately for each time point (T1–T3) and each explanatory dichotomized sleep variable, similarly to Study I, to assess whether different manifestations of insomnia increased the risk of postnatal (T4) depressive symptoms. The models were adjusted for mother's age, parity, education and income levels, as well as

somatic illnesses/conditions. IBM Statistical Package for Social Sciences SPSS (version 25) and a two-tailed alpha level of 0.05 was used for the analyses.

Next, using the statistical software tool R (version 3.6.1, DescTools package, R Core Team, 2019), we constructed predictive models (a second series of logistic regression) to assess the risk of postnatal depressive symptoms (EPDS  $\geq$  11 at T4). First, the best predictive models for each time point (T1, T2 and T3) were formulated (Table 2 in Study II). We used the dichotomized sleep variables, depression (EPDS score  $\geq$  11) and anxiety (SCL  $\geq$  10) scores at the concurrent time point as the explanatory variables. The background factors (mother's age, parity, education, income and somatic illnesses/conditions) were also included in the model at time point T1. The complete case data ( $n = 1504$ ) for participants were used in these analyses. The best model for each time point was selected based on the smallest Akaike information criterion (AIC) (Akaike, 1973). Nagelkerke (Nagelkerke, 1991) and McFadden (McFadden, 1974) were used to assess how well the models predicted the risk of increased postnatal depressive symptoms.

Next, cumulative models combining the best predictive models for each time point were constructed. We aimed to explore how much the follow-up data from time points T2 and T3 improved the model fit and its predictive value compared to the original model at time point T1. The three best-fitting models from time points T1, T2 and T3 were combined to construct models T1+T2 and T1+T2+T3. The logic was to simulate the clinic situation where, at the first pregnancy assessment, only information concerning the psychiatric and clinical history, as well as measures from early pregnancy, would be available. As the pregnancy progresses, more measurement information becomes available from later pregnancy time points.

Finally, we constructed heat maps to demonstrate the accumulation of risk for postnatal depressive symptoms. Odds ratios (OR) relative to the lowest risk category were calculated for various risk groups. In the first heat map (T1), we report the best predictive model for T1, in the second heat map the best combined model for T1+T2 and in the third heat map the best combined model for T1+T2+T3.

Attrition analysis was performed to compare women who participated at T4 and at least once at T1, T2 or T3 ( $n = 2224$ ) versus women who dropped out ( $n = 1004$ ). The drop-out rate was higher for women with higher depressive symptoms (EPDS  $>$  10), anxiety (SCL  $>$  10) and lower educational and income levels ( $p <$  0.05), whereas concerning a lifetime history of depression, no difference was seen between the groups.

### 4.3.3 STUDY (III)

Latent profile analysis (LPA) (Gibson, 1959) was applied to parental depressive symptom scores (CESD-D) from gw 32 until 24 months postpartum to identify different longitudinal pathways in time for parental perinatal depressive symptoms. The criteria to determine the best number of trajectories were Bayesian Information Criteria (BIC), sample-size adjusted BIC (A-BIC), the Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR), Lo-Mendell-Rubin Adjusted likelihood ratio test (LMR-A) and bootstrapped likelihood ratio test (BLRT). As an inclusion criterion, we required at least one CES-D sum score from the four assessment points (1670 mothers and 1604 fathers). We handled attrition using full information maximum likelihood (FIML) estimation (Allison, 2003).

Using logistic regression models, we assessed whether prenatal risk factors/parental characteristics were associated with higher parental depressive symptom trajectories (increased depressive symptoms). Univariate analyses were first run and multivariate analyses were then conducted using backward stepwise selection. We used IBM SPSS Statistics 25 and Mplus 7.1 software (Muthen and Muthen, 1998) for analyses.

### 4.3.4 STUDY (IV)

In Study IV, we combined the stable three-class maternal and paternal depressive symptom trajectories constructed in Study III into four combined parental groups: in Group 1, neither parent was depressive; in Group 2, only mothers were persistently depressive, while fathers were not; in Group 3, only fathers were persistently depressive and mothers not; and in Group 4, both parents were persistently depressive. Individuals belonging to stable intermediate and stable high depression trajectory groups in separate three-class solutions were considered as “depressive”, whereas parents belonging to stable low trajectories were considered as “non-depressive”.

Next, we constructed general linear models using children’s emotional symptoms (BITSEA total/externalizing and internalizing problems scores at age 2 and SDQ total/conduct/internalizing and FTF total/ externalizing/internalizing problem scores at age 5) as dependent variables and parental depressive symptom groups (1–4) as explanatory variables. Tests were performed separately for the two-year and five-year time points. Either the Tamhane or Bonferroni test was used in *post hoc* comparisons, depending on the homogeneity of variances in the parental groups. Interaction effects between parental depression and child gender were examined. In sensitivity testing, we also repeated the analyses using non-parametric (Kruskal-Wallis) models and transformed (square root/log10 transformation) the dependent

variables to obtain more normally distributed dependent variables. The main results remained unchanged.

Then, we adjusted the models for background variables: maternal age, education, income and the number of previous children, as well as paternal age, education and income, and in the second step additionally for the child's gestational age, birth age, gender and age when the BITSEA/FTF questionnaires were completed. We used either the Bonferroni or Tamhane T2 test for *post hoc* comparisons in the adjusted models.

Finally, general linear models were constructed to study the associations of separate maternal and paternal three-class trajectories with child emotional problems (at age 2 and age 5), with child emotional problems serving as the dependent variables and child gender and parental three-class depressive symptom trajectories as explanatory variables. IBM SPSS 25 was used in all analyses.

## 5 RESULTS

### 5.1 SLEEPING PROBLEMS AS A RISK FACTOR FOR POSTNATAL DEPRESSIVE SYMPTOMS (I, II)

#### 5.1.1 EARLY PREGNANCY (II)

For the FinnBrain birth cohort, the occurrence of different sleep problems during pregnancy is reported in detail elsewhere (Aukia et al. 2020). Only 3.6% (n = 107) of women had a BNSQ sum score of 4 or more, indicating several sleeping problems occurring over three times per week during the previous three months. Altogether, 76.8% (n = 2317) of women reported waking up at least 3–5 nights per week, while 13.6% (n = 410) reported waking up three or more times per night. Sleep latency was reported by 25.8% (n = 775) of women to be 20 minutes or more. When women were given an opportunity to freely describe their sleeping difficulties, many reported being repeatedly woken by their first-born or other children, sometimes their husband snored, many reported thoughts spinning in their minds and having difficulties falling asleep at night because of this. Many needed to urinate repeatedly during the night and had difficulties falling asleep after going to the lavatory. Nightmares were the main reason for sleep difficulties for 12 women, and many also reported job-related or other types of stress. Of all mothers, 7.3% (n = 216) reported snoring over three times/week in early pregnancy, whereas only 10 mothers (0.3%) reported sleep apnoea more than 3 times per week. In total, 6.8% (n = 205) of mothers reported sensations of restless legs more than three times per week, and six mothers reported restless legs to be the main cause of sleep difficulties. There was a statistically significant correlation (Pearson's chi-squared 16.7, likelihood ratio 15.3,  $p < 0.001$ ) between sleep latency of over 20 minutes and restless legs over 3 times/week.

The following sleep variables in early pregnancy associated with postnatal depressive symptoms after adjusting for background characteristics and simultaneous depressive symptoms: long sleep latency, frequent night awakenings, subjectively insufficient total sleep time, decreased well-being and decreased functional ability (**Table 10**). All data were included in the analyses (n = 2224).

**Table 10.** Logistic regression analysis of sleep-related variables in early pregnancy (T1, gw 14) vs postnatal depressive symptoms (EPDS  $\geq 11$  points three months postpartum as the dependent variable) in the FinnBrain birth cohort.

<b>Sleep variables at gw 14</b>		<b>OR</b>	<b>95% CI</b>	<b>p</b>	<b>AOR</b>	<b>95% CI</b>	<b>p</b>
Sleep latency	$\geq 20$ min	2.33	1.65–3.29	<0.001	1.87	1.29–2.71	0.001
Night awakenings	$\geq 3$ x/night	2.22	1.47–3.35	<0.001	1.86	1.20–2.87	0.005
Early morning awakenings	$\geq 3$ x/week	1.77	1.04–3.02	0.037	1.46	0.83–2.57	0.194
Sleep quality	rather poor/poor	2.07	1.37–3.11	0.001	1.50	0.96–2.34	0.073
Short sleep	$\leq 6$ h	2.21	1.20–4.07	0.011	1.32	0.68–2.58	0.412
Short sleep	$\leq 7$ h	1.31	0.91–1.89	0.145	1.13	0.77–1.66	0.539
Insuff. total sleep time	Yes	2.51	1.58–4.01	<0.001	1.86	1.13–3.06	0.015
Decreased well-being	Yes	3.11	2.03–4.75	<0.001	1.93	1.21–3.09	0.006
Decreased functioning	Yes	2.99	1.90–4.72	<0.001	1.91	1.17–3.17	0.011

AOR: adjusted for background variables (mother's age when the child was born; primi/multipara; education, three classes; income, three classes; somatic disease/disability) and simultaneous depressive symptoms (EPDS  $\geq 11$  at gw14)

### 5.1.2 MIDDLE PREGNANCY (II)

In middle pregnancy, 4.1% (n = 110) of the women had a BNSQ sum score of 4 or over. Altogether, 77.4 % (n = 2121) of women reported waking up at least 3–5 nights per week, while 15.5% (n = 423) woke four or more times per night. In middle pregnancy, 27.2% (n = 744) of women had a sleep latency of 20 minutes or more. Snoring was reported to occur daily in 5.2% (n = 142) of women. Sensations of restless legs were reported by 11.0% (n = 300) of women three or more times per week.

In middle pregnancy, only the following variables associated with postnatal depressive symptoms (EPDS  $\geq 11$  points three months postpartum) after adjustments: insufficient total sleep time, decreased well-being and a decreased functional ability (**Table 11**).

**Table 11.** Sleep-related variables in middle pregnancy (T2) vs postnatal depressive symptoms in the FinnBrain birth cohort.

<b>Sleep variables at gw 24</b>		<b>OR</b>	<b>95% CI</b>	<b>p</b>	<b>AOR</b>	<b>95% CI</b>	<b>p</b>
Sleep latency	≥20 min	1.77	1.24–2.52	0.002	1.26	0.85–1.86	0.258
Night awakenings	≥3x/night	1.70	1.12–2.58	0.013	1.35	0.86–2.12	0.199
Early morning awakenings	≥3x/week	1.42	0.81–2.48	0.221	0.89	0.48–1.66	0.714
Sleep quality	rather poor/poor	2.16	1.46–3.21	<0.001	1.43	0.92–2.22	0.115
Short sleep	≤6 h	1.68	0.90–3.13	0.105	0.91	0.45–1.83	0.781
Short sleep	≤7 h	1.49	1.05–2.12	0.024	1.33	0.91–1.94	0.136
Insuff. total sleep time	Yes	3.27	2.11–5.07	<0.001	1.99	1.21–3.28	0.007
Decreased well-being	Yes	4.40	2.81–6.89	<0.001	2.23	1.31–3.79	0.003
Decreased functioning	Yes	3.25	2.11–5.01	<0.001	2.02	1.24–3.29	0.005

AOR: adjusted for background variables (mother's age when the child was born; primi/multiparity; education, three classes; income, three classes; somatic disease/disability) and simultaneous depressive symptoms (EPDS ≥ 11 at gw 24).

### 5.1.3 LATE PREGNANCY (I, II)

Sleeping problems increased in late pregnancy, as 11.2% (n = 283) of the women in the FB cohort and 9.8% (n = 161) in the CS cohort reported a BNSQ sum score of 4 or over. Moreover, 92.3% (n = 2348) (FB)/94.9% (n = 1581) (CS) of women reported waking up at least 3–5 nights per week, and 36.0% (n = 889) (FB)/36.2% (n = 602) (CS) woke three times or more per night. Sleep latency was more than 20 minutes for 36.0% (n = 910) (FB)/22.1% (n = 362) (CS) of women. Snoring increased and was reported daily by 8.5% (n = 212) (FB)/8.8% (n = 142) (CS) of women. Sensations of restless legs were reported by 17.3% (n = 438) (FB) of women more than three times per week.

Logistic regression analysis was performed utilizing postnatal depressive symptoms as the dependent variable (EPDS ≥11 (FB)/CES-D ≥10 (CS)) and individual sleep variables as the independent variables.

In late pregnancy, at gw 32 (CS)/34 (FB), sleep latency of >20 min, poor sleep quality and short sleep of less than 7 hours associated with postnatal depressive symptoms in both birth cohorts (**Table 12**, Table 3 in the Study I and Online Resource 1, Table c in the Study II). Moreover, an insufficient total sleep time in the FB cohort, and tiredness during the day, sleep loss of ≥2 hours and short sleep of ≤6 hours in the CS cohort also had a similar association.

**Table 12.** Sleeping problems during late pregnancy in the FinnBrain (FB) and CHILD-SLEEP (CS) birth cohorts versus postnatal (3 months) depressive symptoms (EPDS  $\geq 11$  (FB)/ CES-D  $\geq 10$  (CS)): logistic regression analysis

Sleep variables at gw 34/32	FB				CS							
	OR	95% CI	p	AOR1	95% CI	p	OR	95% CI	p	AOR2	95% CI	p
Sleep latency $\geq >20$ min	2.28	1.61–3.23	<0.001	1.73	1.18–2.55	0.005	2.18	1.50–3.16	<0.001	1.63	1.03–2.59	0.037
Night awakenings $\geq 3 \times$ /night	1.51	1.07–2.13	0.019	1.20	0.81–1.73	0.347	1.66	1.17–2.35	0.006	1.10	0.72–1.69	0.666
Early morning awakenings $\geq 3 \times$ /week	2.29	1.51–3.49	<0.001	1.54	0.95–2.51	0.079	2.17	1.36–3.46	0.001	1.17	0.64–2.15	0.618
Sleep quality rather poor/poor	2.93	2.08–4.14	<0.001	2.15	1.45–3.18	<0.001	2.83	1.99–4.02	<0.001	1.87	1.21–2.88	0.005
Short sleep $\leq 6$ h	1.66	0.96–2.63	0.051	1.33	0.76–2.34	0.314	3.13	1.66–5.88	<0.001	2.36	1.03–5.40	0.042
Short sleep $\leq 7$ h	1.75	1.23–2.49	0.002	1.74	1.18–2.57	0.006	1.78	1.20–2.65	0.006	1.92	1.18–3.14	0.009
Insuff. total sleep time	3.97	2.68–5.90	<0.001	2.76	1.73–4.40	<0.001	–	–	–	–	–	–
Decreased well-being	3.18	2.07–4.90	<0.001	1.50	0.90–2.50	0.123	–	–	–	–	–	–
Decreased functioning	2.52	1.68–3.77	<0.001	1.52	0.96–2.40	0.075	–	–	–	–	–	–
Tiredness during the day	–	–	–	–	–	–	3.38	2.37–4.81	<0.001	2.19	1.41–3.38	<0.001
ESS $\geq 11$	–	–	–	–	–	–	1.43	0.69–2.96	0.334	1.63	0.69–3.83	0.264
Sleep loss $\geq 2$ hours	–	–	–	–	–	–	2.49	1.45–4.26	0.001	2.07	1.06–4.05	0.034

AOR<sub>1</sub> = adjusted for mother's age; parity (primi/multiparity); education in three classes; income in three classes; somatic disease/disability, simultaneous depressive symptoms (EPDS  $\geq 11$  at gw 34).

AOR<sub>2</sub> = adjusted for age, education level in three classes, number of children living in the family, smoking during pregnancy, general health and with prenatal depressiveness (CES-D  $\geq 10$ )  
 ESS = Epworth Sleepiness Scale, a higher score indicating increased sleepiness

### 5.1.4 THREE MONTHS POSTNATALLY (I)

Three months postnatally, 6.4% (n = 84) of all women had a BNSQ sum score of over 4, and the difference between non-depressed and depressed women was clear: 4.4% (n = 51) of women without depressive symptoms versus 24.1% (n = 33) of women with concurrent depressive symptoms (Study I, Table 2). Of the women showing depressive symptoms postnatally, 30.1% (n = 43) reported difficulty falling asleep more than three times per week, whereas only 5% (n = 62) of the non-depressive mothers had the same complaint.

Postnatally, 44% (n = 579) reported waking up at least once every or almost every night, and 44% (n = 579) of women woke three times or more per night. Sleep latency was more than 20 minutes for 15.1% (208) of women.

Three months postnatally, almost all investigated sleep variables associated with concurrent depressive symptoms in the CS cohort (**Table 13** and Table 4 in the Study I).

**Table 13.** Sleep variables three months postnatally vs postnatal depressive symptoms in the CS birth cohort.

Sleep variables 3 months postnatally		OR	95% CI	p	AOR	95% CI	p
Difficulty falling asleep	Yes	8.19	5.28–12.71	<0.001	7.93	4.76–13.20	<0.001
Sleep latency	>20 min	4.78	3.27–6.97	<0.001	4.93	3.20–7.59	<0.001
Night awakenings	≥3x/night	1.92	1.34–2.74	<0.001	2.09	1.41–3.09	<0.001
Early morning awakenings	≥3x/week	3.25	2.02–5.23	<0.001	3.68	2.19–6.20	<0.001
Sleep quality	rather poor/poor	5.26	3.68–7.54	<0.001	5.28	3.56–7.82	<0.001
Short sleep	≤6 h	3.53	2.38–5.24	<0.001	4.09	2.62–6.39	<0.001
Short sleep	≤7 h	2.23	1.56–3.18	<0.001	2.74	1.83–4.10	<0.001
Tiredness during the day	Yes	5.45	3.70–8.01	<0.001	5.49	3.59–8.37	<0.001
ESS	≥ 11	1.61	0.87–2.98	0.132	1.68	0.87–3.24	0.123
Sleep loss	≥ 2 h	3.71	2.50–5.51	<0.001	3.71	2.39–5.75	<0.001

AOR: adjusted models controlled for age, educational level in three classes, number of children living in the family, smoking during pregnancy, and general health.

### 5.1.5 ACCUMULATION OF RISK FOR POSTNATAL DEPRESSIVE SYMPTOMS (II)

The cumulative risk models for time points T1, T1+T2 and T1+T2+T3 are presented in **Table 14** and Table 2 in the Study II. The best model was selected by assessing the best predictive value and the smallest Akaike information criterion (AIC), with the variables being removed from the model until no further reduction could be achieved. In early pregnancy (T1), multiparity, a low income level, a history of depression, sleep latency over 20 minutes and over 3 awakenings per night, as well as decreased functioning, anxiety and depressive symptoms in early pregnancy best predicted postnatal depressive symptoms. In middle pregnancy, anxiety and depressive symptoms at T2 were included. In addition, in the most comprehensive model for late pregnancy, insufficient sleep at T3 as well as depressive symptoms in late pregnancy were included in the best-fitting model.

**Table 14.** Cumulative model predicting postnatal depressive symptoms in the FB cohort.

Measure	T1		T1+T2		T1 +T2 +T3	
AIC	<b>675.549</b>		<b>660.136</b>		<b>633.878</b>	
Variable	Beta (SE)	p	Beta (SE)	p	Beta (SE)	p
Intercept	-5.237 (0.537)	<2E <sup>-16</sup>	-6.023 (0.575)	<2E <sup>-16</sup>	-6.231 (0.515)	<2E <sup>-16</sup>
Parity	0.677 (0.226)	0.003	0.605 (0.228)	0.008	0.355 (0.237)	0.134
Income 1	0.495 (0.281)	0.080	0.398 (0.286)	0.164	-	-
Income 2	-0.085 (0.341)	0.804	-0.091 (0.344)	0.790	-	-
History of depression	0.937 (0.257)	<0.001	0.906 (0.257)	<0.001	0.801 (0.265)	0.003
Sleep latency ≥20 min T1	0.440 (0.235)	0.062	0.504 (0.235)	0.032	0.425 (0.239)	0.075
Night awakenings >3x/ night T1	0.423 (0.276)	0.126	-	-	-	-
Decreased funct. T1	0.603 (0.296)	0.042	-	-	-	-
Anxiety T1	0.775 (0.340)	0.023	0.576 (0.341)	0.090	0.633 (0.314)	0.044
EPDS ≥ 11 T1	0.851 (0.311)	0.006	0.649 (0.320)	0.043	-	-
Decreased funct. T2	-	-	0.773 (0.279)	0.006	0.688 (0.286)	0.016
EPDS ≥11 T2	-	-	0.938 (0.284)	<0.001	0.671 (0.292)	0.021
Insuff. sleep T3	-	-	-	-	0.650 (0.275)	0.018
EPDS ≥ 11 T3	-	-	-	-	1.363 (0.270)	<0.001

AIC = Akaike information criterion; EPDS = Edinburgh Postnatal Depression scale. Income = personal net monthly income ≤€1000 vs €1001–2000 vs ≥€2001.

Figures 1A and 1B and 1C in Study II display heat maps of the cumulative models in early, middle and late pregnancy. The accumulation of risk rather

than individual risk factors increase the risk of developing postnatal depressive symptoms.

The cumulative models were able to explain increased postnatal depressive symptoms as follows: Model T1, 14.9% (Nagelkerke 0.149); Model T1+T2, 17.4% (Nagelkerke 0.174); and Model T1+T2+T3, 21.2% (Nagelkerke 0.212).

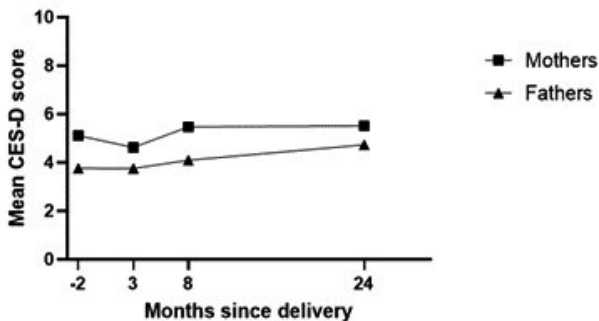
In sensitivity analysis, we repeated the predictive model analyses after removing the sleep item “I have been so unhappy that I have had difficulty sleeping” from EPDS sum score. The main result remained the same (Online Resource 2 in the Study II), with some small changes (for example, frequent night awakenings at T1 were no longer associated with postnatal depressive symptoms).

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## 5.2 PARENTAL PERINATAL DEPRESSIVE SYMPTOMS (III, IV)

Maternal depression scores were higher than paternal scores at all time points. Interestingly, mean maternal depressive symptoms decreased slightly from late pregnancy until three months postnatally, but increased above the prenatal level at both 8 months and 24 months. Mean paternal depression scores continued to increase throughout the measurement period from late pregnancy until 24 months postnatally. Altogether, 11.0% of mothers prenatally and 14.5% at 24 months postpartum had a CESD depression score above the cut-off level of  $\geq 10$ , whereas the paternal prevalence of depressive symptoms doubled from 5.1% (late pregnancy) to 10.2%.

Mean maternal and paternal depression scores from late pregnancy until 2 years after delivery in the CS cohort are presented in **Figure 9**.

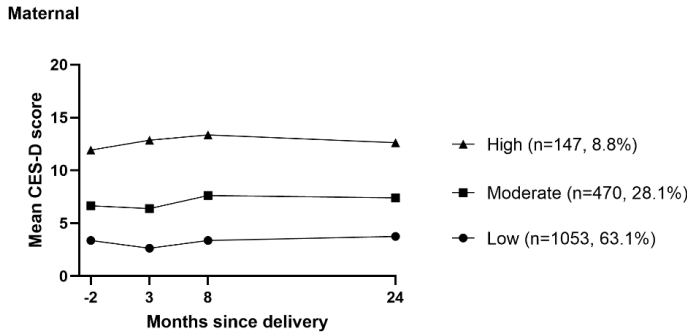


**Figure 9.** Mean maternal and paternal depression (CES-D) score in the CHILD-SLEEP birth cohort. Adapted from Kiviruusu et al. (2020) (Kiviruusu et al., 2020).

### 5.2.1 MATERNAL DEPRESSIVE SYMPTOMS (III)

#### 5.2.1.1 Maternal depressive symptom trajectories

Latent profile analysis (LPA) was applied to maternal depression scores to examine the longitudinal pattern of depressive symptoms. As described in the Study III, we found a three-profile solution of maternal depressive symptom trajectories to best fit the data and clinical situation (**Figure 10** and Figure 1 of the Study III).



**Figure 10.** Maternal depressive symptom (CES-D) trajectories.

We found three relatively stable maternal depressive symptom trajectories: stable low (63.1%), stable moderate (28.1%) and stable high (8.8%). The stable low (mean CES-D < 4) and moderate (mean CES-D above 6 and below 9 points) groups had a subclinical level of depressive symptoms from late pregnancy until 24 months postpartum, while the stable high group constantly reported depressive symptoms above the threshold level, CES-D  $\geq 10$ .

### 5.2.1.2 Risk factors associating with maternal moderate and high depressive symptom trajectories

Prenatal risk factors for being assigned to the moderate or high maternal depressive symptom trajectory group were investigated using the backward stepwise selection method in multinomial logistic regression (Study III, Table 3 and **Table 15**).

**Table 15.** Prenatal predictors of maternal moderate and high depressive symptom trajectory groups in the CS cohort. Multivariate relative risk ratios (RRR) for the logistic regression model, backward stepwise selection method used.

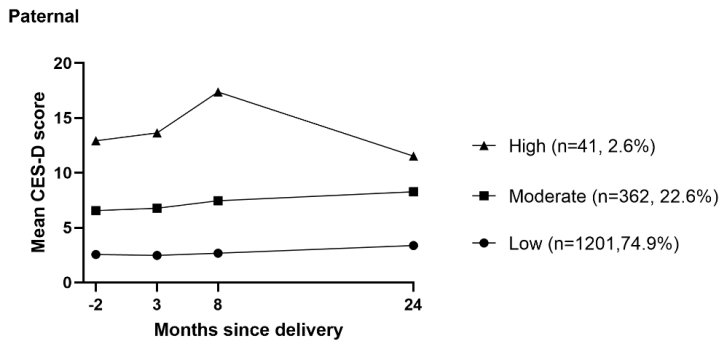
Predictor variable	Moderate depressive symptom trajectory			High depressive symptom trajectory		
	RRR	95% CI	p	RRR	95% CI	p
Insomnia BNSQ $\geq 2$	1.55	1.18–2.04	0.002	2.23	1.27–3.92	0.005
Previous depression, lifetime	2.48	1.66–3.70	<0.001	5.12	2.78–9.44	<0.001
Anxiousness (STAI $\geq 12$ )	3.66	2.24–5.96	<0.001	10.75	5.60–20.64	<0.001
Stressfulness (PSS $\geq 10$ )	3.29	1.67–6.49	0.001	11.03	5.02–24.22	<0.001
Poor family atmosphere	5.26	3.09–8.98	<0.001	14.34	7.22–28.49	<0.001

BNSQ = Basic Nordic Sleep Questionnaire (five items); ESS = Epworth Sleepiness Scale; STAI = State-Trait Anxiety Inventory (six items); PSS = Perceived Stress Scale (five items). a Stable low depressive symptom trajectory (N = 1053) as a base category.

## 5.2.2 PATERNAL DEPRESSIVE SYMPTOMS (III)

### 5.2.2.1 Paternal depressive symptom trajectories

Similarly to mothers, latent profile analysis was run for fathers in order to study the longitudinal pattern of paternal depressive symptoms. For fathers, a three-profile solution also best fitted the data (**Figure 11** and Figure 1 of the Study III).



**Figure 11.** Paternal depressive symptom (CES-D) trajectories in the CS cohort

The fathers were assigned to the stable low (74.9%), stable moderate (22.6%) or stable high (2.6%) depressive symptom group based on their longitudinal pattern of depressive symptoms. The stable high trajectory group constantly reported depressive symptoms above the cut-off level of 10, whereas the stable moderate group constantly reported a subclinical level of depressive symptoms throughout the study period.

### 5.2.2.2 Risk factors associating with paternal moderate and high depressive symptom trajectories

In **Table 16** and Table 4 of the Study III, we present how different prenatal risk factors predict paternal stable moderate and stable high depressive symptom trajectories.

**Table 16.** Prenatal predictors of paternal moderate and high depressive symptom trajectory groups in the CS cohort. Multivariate relative risk ratios (RRR) for the logistic regression model, backward stepwise selection method used.

Predictor variable	Moderate depressive symptom trajectory			High depressive symptom trajectory		
	RRR	95% CI	p	RRR	95% CI	p
Insomnia BNSQ $\geq 2$	4.01	2.47–6.51	<0.001	6.94	2.60–18.50	<0.001
Previous depression, lifetime	2.34	1.18–4.62	0.015	10.76	3.82–30.30	<0.001
Anxiousness (STAI $\geq 12$ )	8.82	4.98–15.64	<0.001	20.45	7.13–58.69	<0.001
Stressfulness (PSS $\geq 10$ )	5.66	2.76–11.65	<0.001	15.29	5.01–46.65	<0.001
Two or more distressing life events	2.06	1.24–3.44	0.006	2.07	0.73–5.90	0.171
Poor family atmosphere	2.84	1.68–4.79	<0.001	10.20	3.93–26.46	<0.001

BNSQ = Basic Nordic Sleep Questionnaire (five items); ESS = Epworth Sleepiness Scale; STAI = State-Trait Anxiety Inventory (six items); PSS = Perceived Stress Scale (five items). a Stable low depressive symptom trajectory as a base category.

A moderate or high depressive symptom trajectory in the mother also increased the risk that the father belonged to the higher depressive symptom trajectory groups (OR = 2.7,  $p < .001$ ;  $\chi^2 = 104.6$ ,  $df = 4$ ,  $p < 0.001$ ) (Study III, Table 5).

### 5.2.3 COMBINED PARENTAL DEPRESSIVE SYMPTOM TRAJECTORIES (IV)

The maternal and paternal depressive symptoms trajectories were combined to form four groups according the parental depressive symptom status (Study IV, Table 2). In Group 1 (Mat-, Pat-), neither parent had depressive symptoms, in Group 2 (Mat+, Pat-) only mothers had, in Group 3 (Mat-, Pat+) only fathers had, while in Group 4 (Mat+, Pat+), both parents had depressive symptoms.

### 5.3 ASSOCIATION OF PARENTAL DEPRESSIVE SYMPTOMS WITH CHILDREN’S EMOTIONAL PROBLEMS (IV)

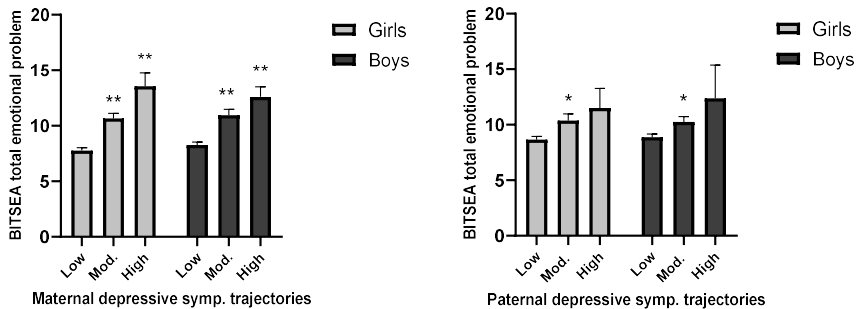
The descriptive statistics for the sample and the BITSEA, SDQ and FTF questionnaires are presented in **Table 8** and in Table 1 of the Study IV.

#### 5.3.1 CHILDREN’S EMOTIONAL PROBLEMS AT AGE 2

##### 5.3.1.1 Maternal and paternal three-class trajectories

In the Study IV, supplemental Figure 1S, supplemental Table 1S and **Figure 12**, we illustrate how maternal and paternal three-class trajectories associated with children’s emotional problems at the age of two.

Maternal stable moderate and high depressive symptoms associated with a higher level of emotional problems in children, while a higher level of paternal depressive symptoms did not show a similar gradually increasing pattern of children’s emotional problems.

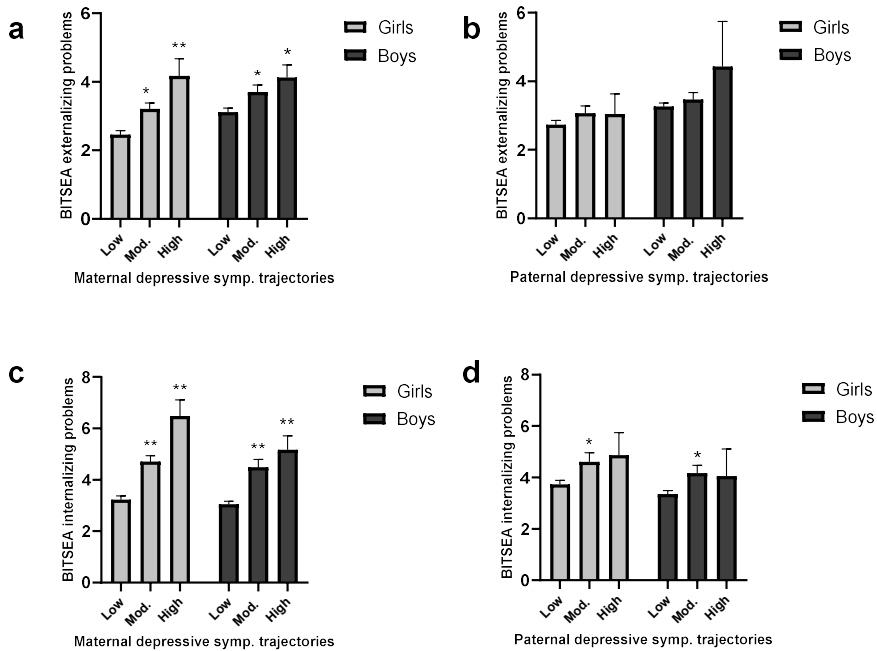


Note: BITSEA = Brief Infant Toddler Social Emotional Assessment. Asterisks indicate a difference between the mean scores when compared with the non-depressive 'stable low' group. \*\*p < 0.001, \*p < 0.05. Error bars indicate standard errors.

**Figure 12.** Maternal and paternal three-class trajectories (CESD) and total emotional problems (BITSEA) in girls and boys at the age of two. Previously unpublished figure.

When children’s externalizing and internalizing problems were examined separately among girls and boys (**Figure 13**), it was shown that boys had more externalizing problems and girls had more internalizing problems. When the level of maternal depressive symptoms was higher, so too were externalizing and internalizing problems among both girls and boys.

Interestingly, paternal depressive symptom trajectories did not associate with externalizing problems in either girls or boys. The adjusted effect sizes were moderate for maternal three-class depressive symptom trajectories and total problems (0.101), as well as internalizing problems (0.095), and were otherwise small (Study IV, supplemental table S1).

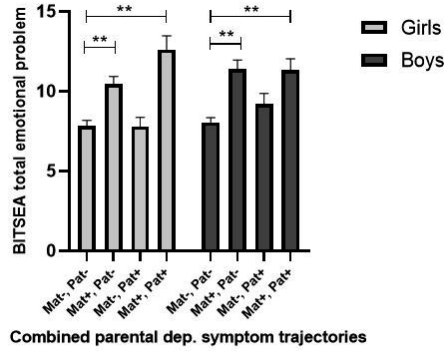


Note: BITSEA = Brief Infant Toddler Social Emotional Assessment. Asterisks indicate a difference between the mean scores when compared with the non-depressive 'stable low' group. \*\*p < 0.001, \*p < 0.05. Error bars indicate standard errors.

**Figure 13.** Maternal and paternal three-class depressive symptom trajectories and externalizing and internalizing emotional problems in girls and boys at the age of two. Previously unpublished figure.

### 5.3.1.2 Combined parental trajectories

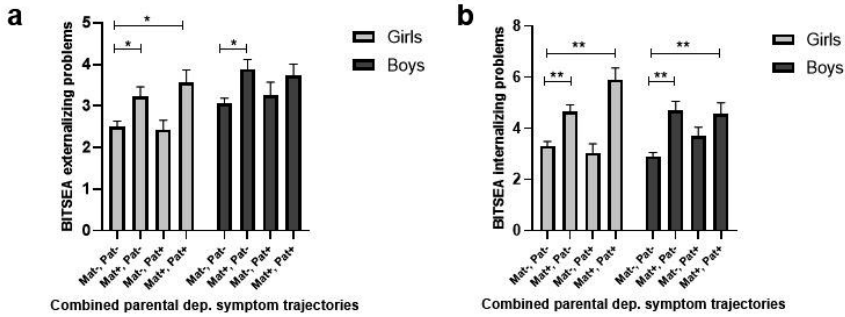
As illustrated in **Figure 14**, 15 as well as Figure 1 and Table 3 in the Study IV, maternal depressive symptoms were associated with a higher level of emotional problems in both girls and boys, whereas paternal depressive symptom alone did not increase children's externalizing or internalizing problems. Girls with two depressive parents had a higher level of internalizing problems than other groups.



Note. Asterisks indicate a difference between the mean scores when compared with the 'Mat-, Pat-' group, \*\*p < 0.001, \*p < 0.05. Error bars indicate standard errors.

**Figure 14.** Combined parental depressive symptom trajectories (CESD) and total emotional problems in girls and boys (BITSEA) at the age of two. Previously unpublished figure.

The adjusted effect sizes were medium for total (0.105) and internalizing (0.081) problems and small (0.035) for externalizing problems (Table 3 in the Study IV).



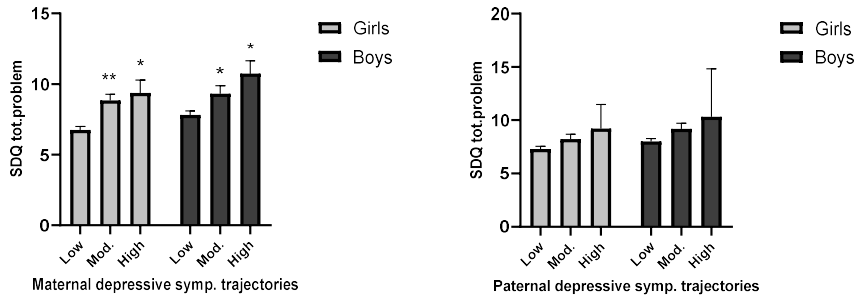
Note: Asterisks indicate a difference between the mean scores when compared with the 'Mat-, Pat-' group, \*\*p < 0.001, \*p < 0.05. Error bars indicate standard errors.

**Figure 15.** Combined parental depressive symptom trajectories and externalizing and internalizing problems (BITSEA) in girls and boys at the age of two. Previously unpublished figure.

## 5.3.2 CHILDREN'S EMOTIONAL PROBLEMS AT AGE 5

### 5.3.2.1 Maternal and paternal three-class trajectories

In **Figure 16** and the Study IV, supplemental Figure 2S and 3S we show how maternal and paternal three-class trajectories associate with children's emotional problems at the age 5.



Note: Asterisks indicate a difference between the mean scores when compared with the non-depressive 'stable low' group. \*\* $p < 0.001$ , \* $p < 0.05$ . Error bars indicate standard errors.

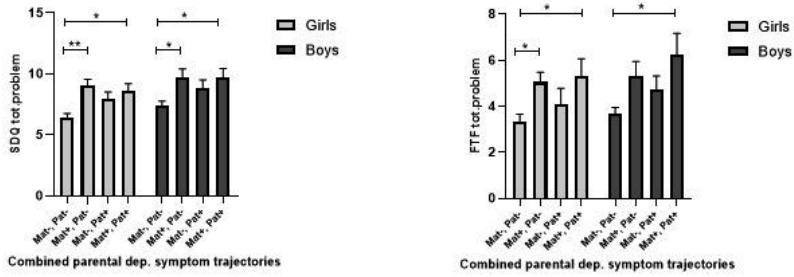
**Figure 16.** Maternal and paternal three-class trajectories versus girls and boys emotional problems at the age of five (SDQ). Previously unpublished figure.

The emotional problems in girls and boys were at a higher level when the mother's depressive symptoms were higher. Paternal depressive symptom trajectories did not associate with children's conduct or internalizing problems measured by the SDQ questionnaire or FTF internalizing problems. Other associations with paternal trajectories had small effect sizes.

### 5.3.2.2 Combined trajectories

In **Figure 17** and Figure 2 of Study IV, we present how combined parental depressive symptom groups associated with children's emotional problems at the age of five.

Results



**Figure 17.** Combined parental depressive symptom trajectories and emotional problems in girls and boys at the age of five (SDQ and FTF). Previously unpublished figure.

Similarly to what was seen at the age of two, maternal depressive symptoms associated with a higher level of emotional problems in both girls and boys, measured by the SDQ and FTF questionnaires. The effect sizes for the SDQ total problem and FTF internalizing problems were medium, but otherwise small.

## 6 DISCUSSION

### 6.1 MAIN FINDINGS

This study investigated the risk factors for parental postnatal depressive symptoms and how parental depressiveness affected the offspring. In Studies I and II, our main objective was to investigate whether the different types of sleeping problems during pregnancy predicted postnatal depressive symptoms (I, II) and how the accumulation of various types of risk factors increased the risk of postnatal depressiveness (II). In Study III, our objective was to investigate how parental depressive symptoms evolved from late pregnancy until two years after delivery and which prenatal risk factors associated with higher parental depressiveness. Finally, in Study IV, our objective was to investigate how parental depressive symptoms associated with children's emotional problems at the ages of two and five years. Studies I, III and IV followed the Finnish CHILD-SLEEP birth cohort (n = 1667 mothers) from late pregnancy until five years after delivery, while Study II followed pregnant women (n = 3808) in the FinnBrain birth cohort from early pregnancy until three months after delivery.

In Study I, we found that both pre- and postnatal insomnia symptoms were related to postnatal depressive symptoms in mothers. After adjusting for background characteristics and prenatal depressiveness, the following insomnia symptoms in late pregnancy (gw 32) predicted depressive symptoms 3 months postnatally: long sleep latency (>20 min), poor general sleep quality, short sleep of  $\leq 6$  h and  $\leq 7$  h, sleep loss of  $\geq 2$  h and tiredness during the day. The best predictors were short sleep of  $\leq 6$  h (AOR 2.4, 95% CI 1.0–5.4) and tiredness during the day (AOR 2.2, 95% CI 1.4–3.4). Almost every investigated postnatal sleep variable was associated with concurrent depressive symptomatology, for example difficulty falling asleep (AOR 7.9, 95% CI 4.8–13.2).

In Study II, we explored insomnia-related symptoms further in the FinnBrain birth cohort, in which prenatal sleep was studied in early, middle and late pregnancy. We examined their associations with postnatal depressive symptoms 3 months postnatally. In adjusted simple logistic regression models, long sleep latency ( $\geq 20$  min), frequent night awakenings during early pregnancy and insufficient sleep time decreased well-being and functioning associated with postnatal depressive symptoms, whereas in middle pregnancy, only subjectively insufficient sleep, decreased well-being and functioning predicted postnatal depressiveness. In late pregnancy, long sleep latency ( $\geq 20$  min), poor sleep quality, short sleep of  $\leq 7$  hours and insufficient sleep time predicted postnatal depressiveness. In the cumulative models, we found long sleep latency ( $\geq 20$  min) in early pregnancy, decreased functioning in middle pregnancy and insufficient sleep time during late

pregnancy to be the most important sleep-related predictors of PDS. The accumulation of various risk factors, such as a history of depression, anxiety, multiparity, sleep-related problems and prenatal depressive symptoms in early pregnancy, rather than any single risk factor increased the risk.

In Study III, latent profile analysis was conducted to examine the longitudinal pattern of maternal and paternal depressive symptoms from late pregnancy until two years postnatally. We found three relatively stable trajectory groups among both mothers and fathers: stable low (63.1% of mothers, 74.9% of fathers), stable moderate (28.1% of mothers, 22.6% of fathers) and a stable high level of symptoms (8.8% of mothers, 2.6% of fathers). The prenatal risk factors predicting caseness in higher depressive group trajectories were similar for mothers and fathers: insomnia, anxiousness, stressfulness, a poor family atmosphere and lifetime depression. Furthermore, parental depressive symptom trajectories were correlated, as depressiveness in one parent was a risk factor for depressiveness in the other parent.

In Study IV, we found that even mild maternal depressive symptoms associated with a higher level of emotional problems in the child at the ages of both two and five, whereas paternal depressive symptoms did not show such an association. If both parents were depressive, the offspring had a similar level of emotional problems as in the group with only a depressed mother. In the following sections, I further discuss the findings from Studies I–IV.

## **6.2 PRENATAL SLEEPING PROBLEMS AS A RISK FACTOR FOR POSTNATAL DEPRESSIVE SYMPTOMS (I, II)**

In Studies I and II, our main objective was to examine whether prenatal sleeping problems associate with postnatal depressive symptoms. In Study I, we found a clear association between several insomnia symptoms during late pregnancy and postnatal depressive symptoms, even after adjusting for prenatal depressive symptoms. Our finding confirms a previously described connection (summarized in Okun, 2016) between poor sleep during (late) pregnancy and episodes of postpartum depression (Bei et al., 2010; Dorheim et al., 2014; Tomfohr et al., 2015; Wolfson et al., 2003).

Pregnancy changes sleep; for example, most women wake up several times per night during late pregnancy because of the need to urinate or other reasons. Therefore, the use of the same insomnia summary scores as during other phases of life might not be as informative. For example, frequent night awakenings during late pregnancy are not a pathological sign of insomnia, as almost all women wake up several times in the late stages of pregnancy due

to the frequent need to urinate and physical discomfort. Probably due to this reason, in the Study I, the BNSQ summary score did not associate with postnatal depressive symptoms after adjusting for prenatal depressiveness, while such an association was observed with individual insomnia symptoms. This leaves us with the need to identify which insomnia symptoms associate with disadvantageous outcomes such as postnatal depressive symptoms and at which stage of pregnancy. Furthermore, screening during early pregnancy could give more time for preventive interventions before the birth of the baby.

Insomnia and depression can be thought of as different clinical syndromes with comorbidity and overlap (Paunio et al., 2020). However, the relationship between these entities is complex and disputed, as insomnia is also part of depression and one of its diagnostic criteria (Table 1). Nevertheless, it must be acknowledged that not all individuals suffering from insomnia symptoms show symptoms of depression. Some mothers can have brief pregnancy-related insomnia symptoms that do not fulfil either insomnia or depression diagnostic criteria. We sought to distinguish physiological pregnancy-related insomnia symptoms (such as frequent night awakenings during late pregnancy) from insomnia symptoms predicting postnatal depressive symptoms. In Study I, as a sensitivity analysis, we repeated the analysis after removing the sleep item from the depression scale and adjusted for prenatal depressive symptoms. The main findings remained unchanged. Long sleep latency during early (Study II) and late pregnancy, decreased functioning in middle pregnancy, as well as poor sleep quality, short sleep of  $\leq 7$  h, tiredness during the day (Study I) and insufficient sleep (Study II) during late pregnancy represent insomnia-related symptoms that associate with postnatal depressive symptoms and should be noted in maternity clinic settings. Some of these insomnia symptoms might in fact indicate ongoing depressive symptomatology if mood symptoms were not recognized. However, from the perspective of treating individuals with insomnia and/or depressive symptoms, these conceptual definitions are not essential; patients benefit from treatment for insomnia whenever it is detected.

Our sample was representative and the occurrence of postpartum depression in CS and FB cohorts (late pregnancy 11% (CS)/9.3% (FB); postnatally 10.5% (CS)/7.1% (FB)) fell within the range of previously reported values in Europe (Shorey et al., 2018). In the FB cohort, we used EPDS  $\geq 11$  as the cut-off level, which is lower than the commonly used cut-off of  $\geq 13$  for clinically probable depression. However, Australian researchers (Austin et al., 2017) have argued in their clinical guidelines that, in other languages besides English, a culturally relevant approach and a lower cut-off score should be used: an EPDS score of  $\geq 9$  might indicate that the probability of depression is relatively high.

In our Study I, we used a 10-item CES-D scale with a cut-off level of 10 points to indicate increased depressive symptoms (Grzywacz et al., 2006).

However, the use of this CES-D cut-off level may also underestimate the prevalence of depression. Tandon et al. (2012) stated that lower cut-off scores than those recommended by screening tool developers for non-pregnant populations should be considered when working with perinatal women. They compared three depression screening tools, the EPDS, CES-D and BDI-II, with a structured clinical interview in a population of pregnant or recently delivered women and reported that all three scales accurately detected both major and minor depression in the perinatal population.

In Study I, 26.6% and 22.5% of mothers reported poor or quite poor sleep quality pre- or postnatally, respectively. Varying rates have previously been reported from Finland and elsewhere, ranging from 15% to 54% (Facco et al., 2010b; Hedman et al., 2002; Polo-Kantola et al., 2017). While these rates are typical in other samples of pregnant women, Mindell et al. (2015) reported a much higher prevalence of poor sleep quality (76%). However, this high figure is probably explained by their Internet-based data collection, which might have resulted in participant bias. While their sample was large (2427 pregnant women), the data were collected online and the questionnaire was set as a pop-up screen on a popular pregnancy website, which might particularly attract women with sleeping problems. In the FB cohort, our finding that long sleep latency already predicts postnatal depressive symptoms in early pregnancy is novel. Interestingly, in line with our finding, Blanken et al. (2020) recently reported that in a non-pregnant sample of 768 participants, difficulty initiating sleep (DIS) was the only insomnia symptom that predicted first-onset MDD. Two Japanese studies have also highlighted the importance of DIS as a predictor of depression: Ikeda et al. (2017), in a study on daytime workers ( $n = 1184$ ), and Yokoyama et al. (2010), in an elderly population ( $n = 4997$ ). Goyal et al. (2007) have reported DIS in late pregnancy to predict postnatal depression in a sample of primiparous women ( $n = 124$ ).

Literature is scarce concerning insomnia symptoms during early pregnancy and their association with postnatal depression/depressive symptoms. Jomeen and Martin (2007) conducted one of the few studies investigating insomnia symptoms during *early* pregnancy, but their study design was cross-sectional and the number of participants was relatively low ( $n = 184$ ). Jomeen and Martin examined several early insomnia symptoms associated with concurrent depressive symptoms.

In *mid-pregnancy*, only subjectively insufficient sleep predicted postnatal depressive symptoms in our sample. Previous literature on the subject is scarce. In a recent study by Osnes et al. (2020) ( $n = 530$ ), however, mid-pregnancy insomnia was associated with concurrent and postpartum maternal anxiety and obsessive-compulsive symptoms. Osnes and colleagues used the sum score of the Bergen insomnia scale and concluded that mid-pregnancy insomnia can be considered as a marker for concurrent insomnia and a predictor of postnatal OCD symptoms.

Most studies have evaluated insomnia symptoms during late pregnancy and their association with postnatal depressive symptoms. Based on our findings in the CS cohort, in late pregnancy, at least the following items should be used for insomnia screening purposes: sleep latency of >20 min, poor sleep quality, short sleep of  $\leq 7$  hours and tiredness during the day. We replicated this finding in the FB cohort in late pregnancy: again, sleep latency of >20 min, poor sleep quality and short sleep of  $\leq 7$  hours stood out as potential screening items.

Which insomnia symptoms should we use for screening purposes during early pregnancy then? Based on our findings in the Study II, during early pregnancy, long sleep latency (AOR 1.87,  $p = 0.001$ ) and frequent night awakenings (1.86,  $p = 0.005$ ) predicted depressive symptoms three months postnatally. Moreover, anxiety and a decreased functional ability, together with a history of depression, further increased the risk. Importantly, Barger et al. (2013) concluded in their clinical recommendations that initiation insomnia during pregnancy is rare and should be further evaluated for underlying causes. In our study, we demonstrated that initiation insomnia is indeed a risk factor for increased postnatal depressive symptoms in early and late pregnancy, but curiously, not in middle pregnancy.

What could be the potential mechanism connecting long sleep latency in early pregnancy and a higher level of postnatal depressive symptoms? Palagini et al. investigated stress-related sleep reactivity (the degree to which sleep is disrupted in response to stress exposure) in middle pregnancy and found that it was associated with depression, anxiety and suicidality in pregnant women in their mid-pregnancy. They used the Ford Insomnia Response to Stress Test (FIRST) questionnaire to assess how easily the sleep of participants was influenced by stress. It seems that our finding of an association between sleep-onset difficulties in early pregnancy and postpartum depressive symptoms is in line with their finding, and both implicate the importance of stress-coping mechanisms and emotional dysregulation. If women typically sleep long during early pregnancy (Hedman et al., 2002), difficulties in this stage with sleep onset could already be a sign of more troubles to come. Usually, sleep continues to deteriorate as pregnancy continues, and these women could be the ones at particularly increased risk if other risk factors are present. Difficulty initiating sleep in early pregnancy, when biological pregnancy-related factors do not yet cause severe sleep disruption, might be a sign of reactivity to stress or sensitivity to hormones and thus **a vulnerability marker**, as similarly described concerning adolescents (Tesler et al., 2013), perhaps indicating difficulty in adaptation. Interestingly, Kalmbach et al. 2020, in a recent cross-sectional study from mid- to late pregnancy, found in that sleep onset insomnia together with a tendency for negative rumination was a strong risk factor for depression (35% of women with both sleep onset insomnia and rumination), whereas insomnia symptoms or rumination alone did not associate strongly with concurrent depressive symptoms. They connected sleep onset

symptoms with concurrent stress and sleep maintenance problems with pregnancy-related discomfort.

Our findings provide a new alternative to target the prevention of depression, as treatment for insomnia is well established and effective. Several treatment alternatives exist (ranging from Internet-based, individual and group CBT to medication). Indeed, it has previously been reported that women who received sleep medication for insomnia during the third trimester reported fewer depressive symptoms postnatally than those who did not receive treatment (Khazaie et al., 2013). Moreover, it has been reported that the presence of sleep problems reduces the efficacy of depression treatment, and targeted sleep interventions such as cognitive-behavioural therapy for insomnia (CBT-I) enhance the depression outcome (Manber et al., 2008; Pigeon et al., 2008). In line with this, it has been reported that postnatally, worsening sleep may predict PPD symptom severity (Posmontier, 2008).

International and national guidelines for the treatment of sleep disorders should be followed (Riemann et al., 2017; Working group set up by the Finnish Medical Society Duodecim and the Finnish Sleep Research Society, 2020). It is clear that sleep medications should not be used during pregnancy and, importantly, that alternative treatment options exist (Carroll et al., 2019). For example, according to a meta-analysis, exercise and massage can enhance maternal sleep quality postnatally (Owais et al., 2018). CBT-I is, however, the most important treatment modality; it has been shown to be efficient during pregnancy (Manber et al., 2019) and is also the method of choice of expecting couples rather than medication (Sedov et al., 2019). Recently, studies have demonstrated the effectiveness of digital CBT-I (Zachariae et al., 2016) for pregnant women (Felder et al., 2020). This approach can increase the availability of CBT-I to pregnant women on a large scale.

### **6.3 ACCUMULATION OF THE RISK OF POSTNATAL DEPRESSIVE SYMPTOMS (II)**

In the FinnBrain cohort study (II), we investigated how the accumulation of risk factors from early pregnancy onwards associated with the risk of postnatal depressive symptoms. We created heat maps illustrating the calculated risk for each combination of risks. These heat maps are a way of demonstrating the accumulation of risk and starting a conversation with a client concerning the need for possible preventive interventions. Sleep patterns have typically been neglected in predictive models for postnatal depression. One of our main conclusions from these predictive models was that one or two risk factors increased the risk of postnatal depressive symptoms only slightly, whereas the accumulation of risk factors (up to eight) strikingly increased the risk.

Heat maps have long been used in somatic medicine to demonstrate the risk, for example, of cardiovascular disease (Vartiainen et al., 2016). To our knowledge, however, this is the first time that heat maps have been used to demonstrate the risk of postnatal depression. Furthermore, our study used data from early, middle and late pregnancy to examine whether the accumulating information would enhance the predictive model, and how an early pregnancy predictive risk model would compare with models also including data from middle and late pregnancy.

The risk factors used in our models were as follows: multiparity, a low educational and income level, a history of depression, anxiety and depressive symptoms in early, middle and late pregnancy, a lower functional ability, and various sleep variables at all pregnancy time points. Of the sleep variables, sleep latency of  $\geq 20$  min in early pregnancy and night awakenings  $> 3x/night$  were included in the best predictive model with a lower AIC. In the cumulative model comprising background information and all the measures from early and middle pregnancy, none of the sleep variables from middle pregnancy were included in the best T1+T2 predictive model, whereas long sleep latency in early pregnancy remained in the model. In late pregnancy, subjectively insufficient sleep in this stage of pregnancy was included in the best cumulative model comprising data from early, middle and late pregnancy.

The ability of the models to predict increased depressive symptoms increased as more data accumulated, demonstrated by decreasing AIC values and an increasing predictive ability (Nagelkerke/McFadden). The best cumulative model (early + middle + late pregnancy) was able to predict 21.2% of postnatal depressiveness, which is an acceptable rate for a model in social sciences. Comparison with previous literature is challenging, as we are not aware of the use of a similar approach to model postnatal depressive symptoms in the literature. In the future, the antenatal risk questionnaire (ANRQ) by Austin et al. (2013), for example, could take even more psychosocial risk factors into account, such as life-time traumatization, the relationship with the women's own mother or tendencies for perfectionism.

## **6.4 MATERNAL AND PATERNAL DEPRESSIVE SYMPTOM TRAJECTORIES (III)**

Consistently with previous literature (**Table 2** in the literature review and Santos et al., 2017), we found three relatively stable maternal depressive symptom trajectories from late pregnancy until two years postnatally. Most of the studies included in the review by Santos and co-authors described at least three stable maternal trajectories.

From our data, we cannot be certain whether the mothers were already experiencing depressive symptoms during earlier stages of pregnancy or pre-pregnancy. Wilcox et al. (2020) reported nearly 10% of mothers to enter

pregnancy already depressed and, importantly, Patton et al. (2015) reported an 8.4-fold higher risk (95% CI 3.3–20.9) of perinatal depressive symptoms if the mother had had mental health problems in both adolescence and young adulthood prior to pregnancy. We also found a history of diagnosed depression to be a risk factor for stable moderate and high depressive symptoms. However, the level of depressive symptoms immediately pre-conception or in early/middle pregnancy is not known in our data. The most important observation from the clinical point of view is, however, that if maternal or paternal depressive symptoms are found during pregnancy, evidence-based treatment efforts should be started, because the risk of depression will otherwise continue.

Our finding concerning the relative stability of maternal depressive symptoms from pregnancy until 24 months postpartum is in line with previous literature. In a review by Vliegen et al. (2014) concerning the longitudinal pattern of maternal PPD, four studies from community samples (Blabey et al., 2009; Campbell and Cohn, 1997; Horowitz and Goodman, 2004; Viinamäki et al., 1997) reported that 13% to 46% of mothers diagnosed with PPD still met the criteria for major depression 24 months postnatally. In clinical samples, the figure was even higher, being up to 50%. Vliegen also summarized five studies that identified a group of mothers whose depression remitted (51% to 64% of initially depressed mothers) and another subgroup of mothers who were chronically depressed (36% to 49% of the sample).

In a more recent study comprising 9848 mothers from the ALSPAC cohort (Netsi et al., 2018), maternal depression was defined as chronic if depression scores were elevated (EPDS  $\geq 13$ ) both two and eight months after delivery. For those with persistent depression (up to 2.9% of all mothers), the mean depression scores remained relatively stable from 21 months until 11 years. The authors concluded that maternal depression should be screened both early during the postnatal years and again later during the first years after delivery in order to find mothers at risk of developing chronic postnatal depression. Also, similarly to our findings, Campbell et al. (2007; 2009) described a subgroup of mothers showing stable subclinical depressive symptoms throughout the study period from an offspring age of 1 month until 12 years of age. Importantly, Meaney (2018) highlighted these subclinical levels of maternal depressive symptoms as an issue of concern for population health, as mothers with a high subclinical level of depressive symptoms in the general population have a similar level of impairment in their psychosocial functioning to clinically depressed mothers. It would be of interest to know whether such mothers were in fact suffering from dysthymia (persistent depressive disorder/DSM.5), a condition where mild depressive symptoms continue for at least two years without full remission.

The offspring of depressed mothers appear to be affected in a dose-dependent manner (Cents et al., 2013; Meaney, 2018) concerning an increasing severity of maternal depression symptoms. Thus, it is also

clinically important to take notice of the subclinically depressed population of mothers.

Recently, the US Preventive Services Task Force recommended in its statement (2019) counselling interventions, either CBT or interpersonal psychotherapy, for mothers showing subclinical levels of depressive symptoms or having certain psychosocial risk factors to prevent PPD. This makes sense, since Holden et al. (1989) reported as early as in 1989 that mothers who had been given counselling by health visitors showed a significant decrease in depression scores, whereas mothers without treatment had a more stable level of depression (32% difference between treatment and control groups in remission). In addition, Blom et al. (2017) followed patients for three years who at baseline reported both depression and insomnia symptoms. The patients ( $n = 43$ ) were randomized to either a CBT-I group or CBT group. After three years, the depression scores had remitted similarly in both groups, but in the CBT-I group, the patients had fewer insomnia symptoms ( $d = .066$ ,  $p < 0.05$ ). The authors concluded that CBT-I was more beneficial in long-term follow-up for patients with comorbid depression and insomnia symptoms. Considering pregnant and delivered women, CBT-I might thus be an even wiser option than CBT for depressed perinatal women with disturbing insomnia symptoms.

Paternal depression is attracting increasing interest, but when compared to depression in mothers, the literature is limited. From some longitudinal studies with relatively small sample sizes, we have learned that paternal depressive symptoms appear relatively stable prenatally until 12 months postpartum (Matthey et al., 2000; Paulson et al., 2016), a finding that was confirmed in our study. In the ALSPAC cohort ( $n = 10\,975$ ), paternal depressive symptoms were measured at gw 18 and 8 weeks, 8 months and 21 months postnatally (Ramchandani et al., 2008b), with 37% of fathers responding at all time points. Paternal depressive symptoms exceeded the cut-off point of EPDS  $> 12$  in 2.3–3.5% of fathers, but with imputed data the prevalence rose to 3.4–3.8%. Interestingly, depressive symptoms were lowest 8 months postpartum, whereas prenatally and 21 months postpartum the prevalence was approximately the same, and higher than at other measurement points. In a meta-analysis by Paulson and Bazemore (2010), the meta-estimate of paternal depression was 10.4%, with higher depression rates being reported 3 to 6 months postpartum. Recently, Rao et al. (2020) reported a meta-estimate of 10.1% in the third trimester and 8.8% during the first year. However, in European countries, the meta-estimate of postnatal depression was significantly lower (5.5%). Our level of paternal depressive symptoms was within the limits of these meta-analyses and European levels, from 5.1% prenatally to 10.2% 24 months postnatally (when CES-D  $\geq 10$  was used as the cut-off level), but in contrast to the ALSPAC group findings and the meta-analysis of Paulson & Bazemore, paternal depressive symptoms increased throughout our study period, similarly to Areias et al. (1996).

For paternal depressive symptom trajectories, the literature is scarce (**Table 4** in the literature review). We found that both the number and pattern of paternal depressive symptoms resembled those of mothers. Similarly to us, Molgora et al. (2017) reported three groups of fathers showing stable low (“resilient”, 52%), moderate depressive symptomatology (“distress”, 37%) and a group with emergent clinical depression (“emergent depression”, 11%). Their time span did not, however, exceed the first postnatal year, and the sample size was relatively small ( $n = 126$ ). It is of interest to note the similar pattern of increasing paternal symptoms both in our fathers and in the study by Molgora et al.; in the emergent depression group, fathers reached the EPDS cut-off level of 12.5 twelve months postnatally.

Paternal ( $n = 2076$ ) depressive and anxiety symptom trajectories during the prenatal period in the Finnish FinnBrain cohort have been described by Korja et al. (2018). Comparison with our findings is difficult because of the different time points used in the analyses, but in late pregnancy, three levels of depressive symptoms in fathers could be seen: “constantly low (71%) + moderate and decreasing (9%)”, “moderate (15%)” and “constantly high (3%) + moderate and increasing (2%)”. In our study, the “stable high” paternal depressive symptom group (2.6% of fathers) was about same size as in the FinnBrain cohort. It seems that during pregnancy, depressive symptoms in a small sub-group of fathers increased as the pregnancy progressed and reached the “constantly high” group in late pregnancy. Fathers in the two subgroups with the highest depressive symptoms at the end of pregnancy in the FinnBrain cohort might be similar to those fathers in our sample whose depressive symptoms continued two years postnatally.

In a recent study by Hughes et al. (2020), trajectories were constructed taking into account both depressive and anxiety symptoms from the third trimester until 24 months postpartum among mothers and fathers ( $n = 438$  expectant couples). Maternal problems were found to be stable, but similarly to us, paternal problems worsened during the study period.

#### **6.4.1 RISK FACTORS**

We found maternal and paternal prenatal risk factors for depressive symptoms to be remarkably similar: previous depression, anxiousness, stressfulness, insomnia, a poor family atmosphere and, among fathers, also two or more distressing life events. These risk factors are consistent with previous literature (Howard et al., 2014; Lawson et al., 2015; Vliegen et al., 2014; Wee et al., 2011). Previously, some studies have noted paternal risk factors to be more situational than maternal ones (Bielawska-Batorowicz and Kossakowska-Petrycka, 2006). Our results indicated more similarities between parental risk factors, similarly to Davé et al. (2010) and Matthey et al. (2000). In a review by Beck (2001), a significant factor in the duration of PPD was also the length of delay in receiving adequate treatment.

Neither maternal nor paternal age was a risk factor in our sample. This is in line with most previous studies: in a review by Vliegen et al. (2014) assessing maternal risk factors for persistent depression, only three out of the nine studies reported a younger maternal or child's age as a risk factor for PPD. It should be noted, however, that our sample consisted almost exclusively of couples, and there were only a few single mothers and no single fathers, which might be due to the recruitment protocol (via maternity clinics). In the ALSPAC cohort with over 10 000 participants, paternal risk factors for PPD included a history of severe depression, prenatal depression, prenatal anxiety, a lower educational level, having other children and maternal prenatal depression; of these, paternal prenatal anxiety showed the highest adjusted odds ratio (5.0, 95% CI 3.6–6.9). Paternal prenatal anxiety was also the best predictor of stable moderate or stable high depressive symptoms in our sample of fathers. Interestingly, among mothers, a poor prenatal family atmosphere was an even better predictor of both moderate and stable high maternal depressive symptoms.

#### **6.4.2 CORRELATION BETWEEN MATERNAL AND PATERNAL DEPRESSION**

Maternal and paternal depression have been shown to correlate strongly (Paulson and Bazemore, 2010; Wee et al., 2011), with an increase in depression in one parent placing the other parent at increased risk. In particular, paternal depression has been argued to depend on maternal depression, and Goodman et al. (2004) highlighted maternal depression as the most important risk factor for paternal depression: in their meta-analysis, the incidence of paternal depression varied from 1.2% to 25.5% in community samples and from 24% to 50% among fathers whose partners were depressed. In a meta-analysis by Paulson & Bazemore (2010), the correlation between maternal and paternal depression was found to be moderate in size ( $r = 0.31$ , 95% CI 0.23–0.38). However, in their study ( $n = 80$  couples), prenatal depression in fathers predicted worsening depressive symptoms in mothers across the first six months postpartum, but not vice versa. In our sample, we also found maternal and paternal depressive symptom trajectories to be highly correlated, but without additional modelling we cannot make any statements concerning the direction of the correlation.

Marital dissatisfaction could be one possible mechanism explaining the correlation between parental depressive symptoms (Bruno et al., 2020; Wee et al., 2011). In line with this, a poor prenatal family atmosphere was the strongest predictor in our mothers and also an important predictor for fathers in our sample. Assortative mating is another possible mechanism: individuals with similar characteristics are more likely to couple than would be expected randomly (Dierker et al., 1999; Van Grootheest et al., 2008).

This can mean that individuals more prone to depression might choose a partner who would also be more prone to it. Household chores and childcare responsibilities may also increase the workload of the non-affected parent if the other parent is depressed. This might particularly increase paternal responsibilities at home and thus paternal stress levels, possibly leading to depression.

Interestingly, Saxbe et al. (2016) found maternal and paternal poor sleep quality at six months to predict depressive symptoms at both 6 and 12 months postnatally. Furthermore, poor maternal sleep quality at 6 months postnatally predicted paternal depressive symptoms at 6 and 12 months. Both sleep and depressive symptoms were strongly associated in couples in the study of Saxbe et al. This is understandable, as poor maternal sleep is also likely to influence paternal sleep and set the stage for depressive symptoms.

## **6.5 ASSOCIATION OF PARENTAL DEPRESSIVE SYMPTOMS TO CHILDREN'S EMOTIONAL PROBLEMS (IV)**

In Study IV, we used for the first time both maternal and paternal depressive symptom trajectories in the risk analysis of emotional problems in the offspring. We found that maternal depressive symptoms were associated with children's emotional problems at the ages of both 2 and 5 years, whereas paternal depressiveness did not increase emotional symptoms in the offspring if the mother was nondepressive. Quite surprisingly, having two parents with depressive symptoms did not increase the risk of emotional problems in the offspring when compared to the group in which only the mother was affected. When we investigated maternal and paternal three-class depressive symptom trajectories separately, we discovered a gradual increase in children's internalizing and externalizing problems at the ages of both two and five years as the maternal depressive symptoms increased. Paternal depressive symptoms did not show such a dose-responsive association with the risk of emotional problems in their offspring. We found boys to have more externalizing symptoms and girls more internalizing symptoms. However, there were no significant interaction effects between parental depressive symptom trajectories and the child's gender. In previous literature, the findings have been mixed concerning whether parental depression differently affects girls and boys (Goodman et al., 2011).

Our finding concerning the importance of subclinical levels of maternal depression is in line with those from the Generation R cohort (Cents et al., 2013; Meaney, 2018); in this cohort, a dose-responsive increase in the offspring's emotional problems as maternal depressive symptoms increased was also described. Importantly, fathers also evaluated their children's

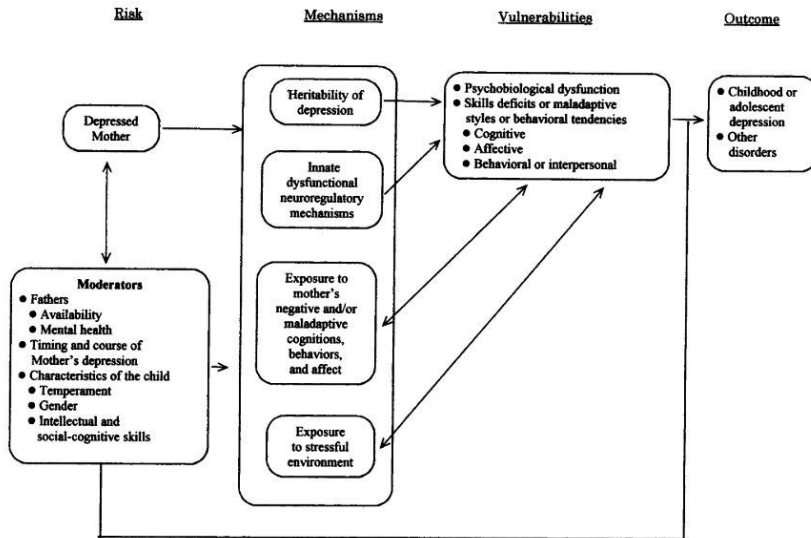
problems in the study of Cents and co-authors, and the evaluations of depressive mothers and their spouses appeared to be very similar. Conners-Burrows and colleagues (2016) investigated 1844 mother–child pairs from multiple sites, beginning when the children were 14 months of age and continuing until the age of 11 years. They found both sub-clinical levels and clinically significant levels of maternal depressive symptoms to increase internalizing and externalizing problems in the children at the age of 11. For example, the offspring of mothers with sub-clinical levels of depressive symptoms had double the risk of internalizing problems when compared to offspring whose mothers had never had depression. These mothers and children were categorized as “screen negative” and were thus unlikely to receive any support from mental health or other services. Impairments in the psychosocial functioning of sub-clinically depressed women can, however, be as severe as in mothers with clinical depression (Weinberg et al., 2001).

In addition to describing associations between maternal depressive symptom trajectories and children’s emotional problems, we were able to assess paternal and combined parental depressive symptom trajectories in terms of how they influence children’s emotional symptoms. Knowledge concerning the significance of paternal depression for offspring emotional well-being is rapidly increasing (recently reviewed by Chunying et al. 2020). In the meta-analysis of Chunying and co-authors, paternal perinatal depression increased behavioural problems (pooled OR 1.2, 95%CI 1.1–1.3) and emotional problems (OR 1.3, 95% CI 1.2–1.4) in the offspring, whereas concerning social functioning in the children, no such effect was found (OR 1.3, 95% CI 1.0–1.7). We observed the paternal “stable moderate” depressive symptom trajectory to associate with internalizing problems in boys and girls at the age of two, but the high depressive symptom trajectory did not associate with internalizing or externalizing problems in the offspring, and at the age of five, we found only a slight association with offspring externalizing symptoms measured by the FTF questionnaire. The number of fathers in the “stable high” depressive symptom trajectory group was small at the offspring age of two ( $n = 19$ ), and even smaller at the age of five ( $n = 11$ ) when compared to the maternal “stable high” depressive symptom trajectory group ( $n = 74$  at the age of two and  $n = 50$  at the age of five). It has previously been suggested that traditional depression questionnaires do not capture mental ill-being in fathers; men tend to have more avoidant, numbing and escape behaviours, which can lead to aggressive behaviour (Brownhill et al., 2005). Brownhill et al. noted that the experience of depression seems not to differ between genders per se, but the expression of it does differ.

We hypothesized that having two parents with a depressive disorder would double the risk for their offspring. However, in our Study IV, we did not find paternal depression to increase children’s emotional problems. Previously, for example, Goodman & Gotlib (1999) stated in their review that a supportive adult is generally considered to increase resilience in children (Reuben and Shaw, 2015). Fathers could serve as a positive role model,

provide care to children and support their depressed spouses or constitute an additional risk through both genetic and environmental mechanisms. Fathers may thus moderate the effect by which maternal depression affects their children. More recently, Gutierrez-Galve et al. (2015) estimated that two-thirds of the association between paternal depressive symptoms and children's risk of emotional problems is mediated by the family atmosphere and maternal depression, whereas maternal depression appears to influence the children via direct mother-child contact. Furthermore, Connell and Goodman (2002) concluded in their meta-analysis that the younger the children were, the smaller was the influence of paternal depression. It might thus be that we did not see a direct effect of paternal depression on children because of the young age of the children and the moderating role of paternal depression.

Goodman & Gotlib (1999) outlined four possible mechanisms by which maternal depression confers a risk of emotional disturbance in their offspring (**Figure 18**): a) genetic heritability, b) innate dysfunctional neuroregulatory mechanisms, c) exposure to maternal negative behaviour and affect and d) the context and other risk factors in the lives of these families. While new information concerning genetic mechanisms (Hannigan et al., 2018) and innate dysfunctional neuroregulatory mechanisms (Meaney, 2018; O'Donnell and Meaney, 2017) is emerging, parenting is still considered to be the main modifiable mechanism mediating the effect of parental depression on the offspring (Goodman and Gotlib, 1999). It should be noted that the connection is reciprocal: children's behavioural and other emotional problems may worsen parental depressive symptomatology. To avoid the formation of a vicious cycle, the treatment of maternal depression in particular during pregnancy, including subclinical levels, would be wise.

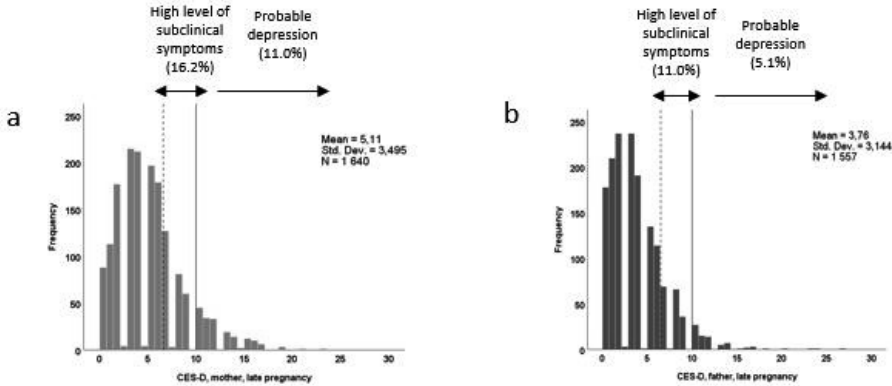


**Figure 18.** Mechanisms by which maternal depression affects the offspring from Goodman & Gotlib (1999). Risk for Psychopathology in the Children of Depressed Mothers: A Developmental Model for Understanding Mechanisms of Transmission, Psychological Review, 1999: vol 106, No. 3, 458-490. Published by APA, reprinted with permission.

From another perspective, approximately 79% of children referred to mental health services in an Australian study had parents with mental health disturbances (Naughton et al., 2018). Meanwhile, most parents suffering from mental health problems do not receive any treatment for it (Swartz et al., 2005). Moreover, as Naughton et al. pointed out, many of these families have issues with domestic violence and limited social support. Adverse childhood experiences have a cumulative effect; in a study by Burke et al. (2011), children with four or more ACEs had a 32-fold increased risk of learning or behavioural problems and 2-fold increased risk of obesity when compared to children without ACEs. Wertz (2019) suggested in her editorial that adult and child psychiatric services should be better linked: treating the child could offer an opportunity to also treat the parental disorder, thus reducing medical and mental disorders in children (Bagner et al., 2010; Lyngsøe et al., 2019).

Concerning the clinical implications of Study IV, the current cut-off value used for detecting perinatal depression in Finland (EPDS  $\geq 13$ ) is probably too high. Matthey et al. (2006) have pointed out that cut-offs used in English-speaking countries might not be applicable for other populations. Thus, in Study II we chose to use the EPDS cut-off level of 11 or more. In **Figure 19**, we present maternal and paternal depression scores in late pregnancy, as well as cut-off levels (high subclinical symptoms/probable clinical depression) for mothers and fathers in the CS birth cohort, and in

**Figure 20**, we present maternal depression scores at three pregnancy time points in the FB cohort.



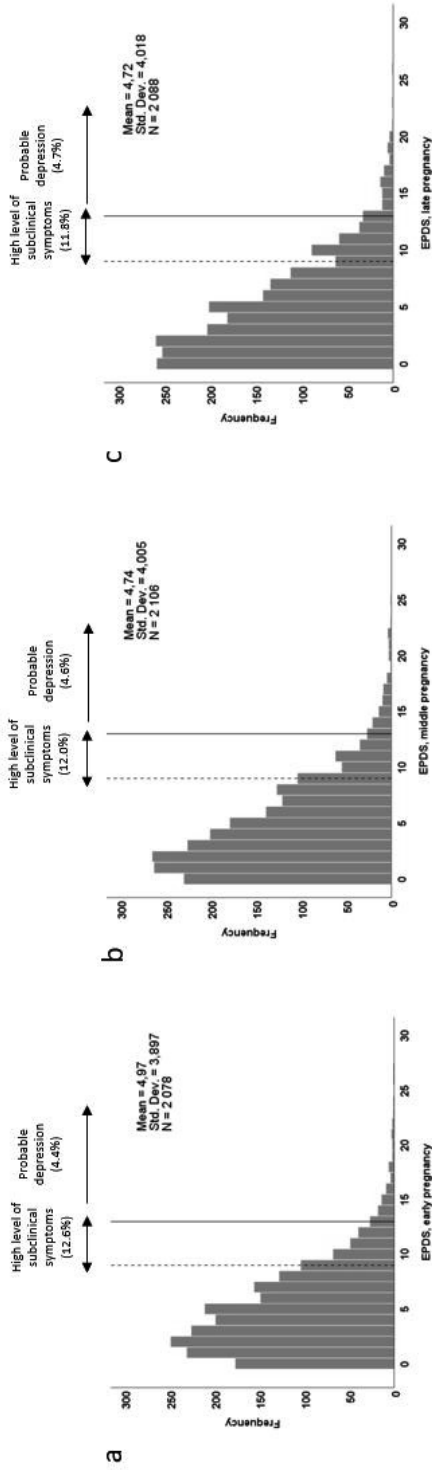
**Figure 19.** Maternal and paternal depression scores in late pregnancy in the CS cohort, with high subclinical ( $\geq 6.5$ ) and probable clinical ( $\geq 10$ ) cut-off lines presented. Previously unpublished figure.

Usually, a lower cut-off threshold of EPDS is used to detect depression in fathers compared to that for mothers. This is understandable based on the reluctance of fathers to report and recognize depressive symptoms and their different symptom pattern. However, based on current knowledge concerning the consequences of early foetal stress, epigenetic changes, and lasting neurodevelopmental effects (Lautarescu et al., 2020; Zou et al., 2019), as well as our results from Study IV, I would argue that the use of relatively lower cut-off values for mothers compared to fathers would be justifiable, at least in terms of offering counselling and psychotherapeutic interventions. Based on strong evidence from the US Preventive Services Task Force (Curry et al., 2019; O’Connor et al., 2019), counselling interventions should also be offered to mothers with subclinical depressive symptoms, a history of depression or other risk factors for perinatal depression. Paternal depression is often connected to maternal depression and marital conflicts; in these cases, therapeutic approaches for couples could be fruitful.

From the psychodynamic perspective, Joan Raphale-Leff (1991/2005; 1993/2001) and Margareta Brodén (2013) have written about the psychological maturation process of becoming a mother and distinguished several phases: fusion, differentiation and separation. Each of these phases has its own developmental goals as a woman mirrors the care she herself received from her caregivers, the dreams and fantasies concerning the imaginary baby developing in the womb and the physical reality of actually carrying the real baby inside her. Mental work is done on the level of representations and ideas in the mother’s mind (Raphael-Leff, 2010). This

developmental crisis and transformation prepares the mother for the role shift and the first contact with the child. To simplify these complex processes, depression and anxiety can obstruct and hinder the maturation process and thus leave the mother unprepared to meet the newborn. Parent–infant psychotherapy is preferably already started during pregnancy so that the mother can meet the newborn mentally more prepared. The experience of being a good or a bad mother/parent goes deep into the core self, and in the treatment of perinatal mental disorders, this should be taken account. Using, for example, cognitive behavioural techniques without addressing the core pain and its developmental background might thus not be sufficient for the healing process to start. Despite the technique used, mothers would benefit from strengthening the good they see in their own past caregivers and their own motherhood.

Fathers go through their own psychological maturation process, which differs from the one mothers go through (Raphael-Leff, 1993/2001). On a mental level, expectant fathers may re-evaluate their relationship with their own fathers and how it was to be a child of their own parents. One could speculate that the spouse's pregnancy is usually a positive experience for men if the pregnancy is not unwanted, and serves to strengthen manhood. After the child is born, fathers might be at risk of feeling left out as mothers concentrate on newborns. Together with the combination of work-related duties, this could lead to an increase in paternal depressive symptoms, which can be seen in our results. However, these interpretations need confirmation from further research. If problems emerge, expectant and new fathers might, however, benefit from a different approach compared to mothers and separate groups for dads and dad programmes have been developed (Fletcher et al., 2015).



**Figure 20.** Maternal depression scores (EPDS) in the FB cohort in early, middle and late pregnancy, with high subclinical ( $\geq 9$ ) and probable clinical ( $\geq 13$ ) cut-off lines based on international recommendations. Mothers in Finland should be offered counselling interventions at a lower threshold level (high subclinical symptoms/history of depression) than the EPDS cut-off of  $\geq 13$  currently in clinical usage. Adapted and modified from (Meaney, 2018). Previously unpublished figure.

## **6.6 STUDY STRENGTHS**

### **6.6.1 STUDIES I, II, III AND IV**

One of the main strengths of our studies is our representative, relatively large population-based study samples of Finnish expecting families. The inclusion of almost 1600 fathers in the CHILD-SLEEP cohort is exceptional, and longitudinal data from both parents from late pregnancy until five years postnatally is rare. In Study IV, the assessment of children's emotional problems at the ages of both two and five and the use of two different questionnaires in the evaluation of children's risk of emotional problems is also a major strength. The use of the BNSQ sleep questionnaire in both the CS (Study I) and FB (Study II) cohorts enabled us to investigate various insomnia problems and also to compare findings in two different samples. The study designs were constructed while keeping the clinical implications in mind.

## **6.7 LIMITATIONS**

### **6.7.1 STUDIES I, III AND IV**

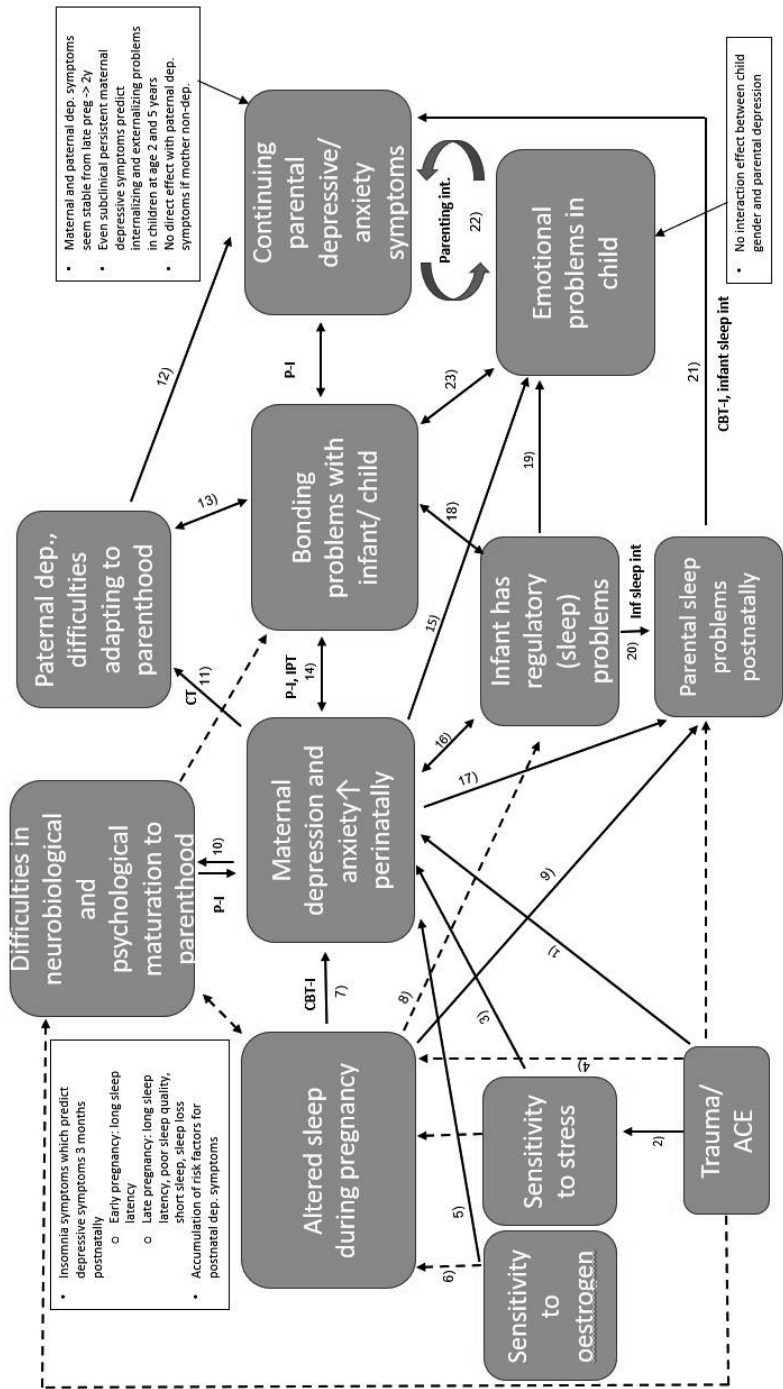
Our studies also had certain limitations. The mothers in both of our study populations smoked less (5.8 % in CS; 5.3% in FB cohort) than other Finnish pregnant women (15%) (Official Statistics of Finland (OSF), 2015) and the number of single mothers was very small (1.8% in CS/2.8% in FB vs 9.2% mothers non-married or not cohabiting according to Official Statistics Finland). This makes the results more difficult to generalize to risk groups. We did not use standardized interviews to evaluate the level of depressive symptoms (Studies I, II, III, IV) or objective measures (actigraphy or polysomnography) to evaluate sleep (I, II). Moreover, we did not have information concerning the severity of earlier depression in either study population. Depression rarely exists in isolation, but we did not take into account psychiatric comorbidities (anxiety disorders, PTSD, personality disorders), the parental trauma history or the effect of obstetric complications on the development of postnatal depressive symptoms. Many other prenatal factors that could influence children's internalizing and externalizing symptoms also exist, including maternal overweight/obesity, substance use, environmental exposures, maternal inflammation/infection and psychosocial risk factors such as intimate partner violence (Tien et al., 2019). Our drop-out rate in both study samples was non-negligible, and the

attrition rate of fathers was higher than that of mothers. In Study III, the trajectories were constructed using full information maximum likelihood estimation in order to deal with missing values due to attrition. Thus, we were able to construct trajectories for all fathers and mothers who had participated at least once at the four measurement points. In Study IV, we did not have an informant outside the family to rate children's emotional problems. According to Goodman et al. (2011), the relationship between child outcomes and maternal depression was strongest in studies where mothers rated their children's emotional/conduct problems in relation to studies using teacher, laboratory assistant or mother-child dyad reports. Depressed mothers may either be sensitive to accurately noticing true disorders in their children (Richters, 1992) or their perception might be negatively biased (Goodman et al., 2011). In Study IV, approximately 68% of the children's questionnaires were completed by the mothers at 2 and 5 years, 1% by the fathers and 24–30% by both parents.

### 6.7.2 STUDY I, II

In Studies I and II, both depression scales (CES-D and EPDS) used included one question concerning sleep. We repeated the analyses with the EPDS and CES-D after removing the sleep question; the results were practically unaffected. We did not take into account the effect of sleep disordered breathing (SDB) or restless legs syndrome (RSL) when evaluating insomnia symptoms (I, II). The inclusion of BMI as a covariate could have been beneficial in terms of catching SDB cases, as overweight can associate with apnoea during sleep. However, the amount of reported apnoea was very low in our sample. Restless legs syndrome is important to take notice of, because the treatment differs from that for other insomnia symptoms, as it is associated with iron deficiency. Transferritin and other iron metabolism-related laboratory tests should be checked and, depending on the results, the starting of iron supplementation should be considered (Lee et al., 2001; Manconi et al., 2004). Long sleep latency in early pregnancy (Study II) was partly associated with restless legs syndrome in early pregnancy, but according to most of the mothers, the reason for being unable to fall asleep was due to thoughts spinning in their heads or stress-related reasons, and only a very small fraction of mothers described unpleasant sensations in their legs or RLS to be their main sleep problem.

Finally, in **Figure 21**, possible pathways and intervention opportunities between altered sleep during pregnancy, maternal perinatal depression and anxiety, bonding problems with the child, continuing parental depressive symptoms and children's emotional problems are described.



Note: CBT-I = Cognitive behavioural therapy for insomnia; P-I = parent-infant psychotherapy (may be started during pregnancy); IPT = Interpersonal psychotherapy; CBT = Cognitive behavioural therapy; CT = Cognitive therapy/intervention; Inf. sleep int. = Infant sleep intervention/ Parental guidance with baby sleep  
**Figure 21.** Suggested pathways between altered sleep during pregnancy, continuing parental depressive symptoms and children's emotional problems and some possible intervention strategies.

## Discussion

1) Choi et al. 2019; Heim and Binder 2012; Onoye et al. 2009; Grekin et al. 2017; Faisal-Cury et al. 2013; Silverman and Loudon 2010; Seng et al. 2010; Guintivano et al. 2018, reviews ; Howard et al. 2013; Ross and Dennis 2009; 2) Heim and Binder 2012; 3) O'Donnell and Meaney 2020; Heim and Binder 2012; 4) Seng et al. 2010; Miller-Graff and Cheng 2017; 5) Mehta et al. 2019; O'Donnell and Meaney 2020; Guintivano et al. 2014; 6) Lee et al. 2000a; Franco et al. 2020; 7) Lawson et al. 2015; Okun 2016 ; González-Mesa et al. 2019; Emamian et al. 2019; 8) Aswathy et al. 2018; Field 2017; Field et al. 2007; 9) Sivertsen et al. 2015; 10) Broden 2013; Barba-Muller et al. 2019; Pawluwski et al. 2017 ; 11) Dudley et al. 2001; Cameron et al. 2016; Goodman et al. 2004; Fredriksen et al. 2019; Wee et al. 2011; 12) Paulson et al. 2016; 13) Edhborg et al. 2005 ; Nishigori et al. 2019; 14) Brockington 2004; Atkinson et al 2000 ; Badovinac et al. 2018; 15) Field 2011; Gentile 2017; Tien et al. 2019; Waters et al. 2014; Stein et al. 2014; Goodman et al. 2011; Slomian et al. 2019; 16) O'Connor et al. 2007 ; Gress-Smith et al. 2012; Netsi 2015; Armitage et al. 2009; Conroy et al. 2012 ; Morales-Muñoz et al. 2018: review by Korja 2017; 17) Lawson et al. 2015 ; 18) Brockington 2004; 19) Morales-Muñoz et al., 2020; Huidanpää et al. 2019 ; Gregory and O'Connor 2002; Gregory and Sadeh, 2012 ; 20) McDaniel & Teti 2012 ; Sadeh et al. 2010; 21) McDaniel & Teti 2012; Saxbe et al 2016; Sadeh et al. 2010 ; 22) Naughton et al. 2018; Swartz et al. 2005; 23) Spruit et al. 2020

## 7 CONCLUSIONS AND CLINICAL IMPLICATIONS

Pregnancy has been called the final frontier in mental health research (Pawluski and Dickens, 2019). Almost 20% of pregnant women suffer from perinatal mood and/or anxiety disorders (PMAD) (Dennis et al., 2017; Shorey et al., 2018) and over 23% of children live with mothers who have a mental disorder (Abel et al., 2019), the proportion peaking in the first postnatal months, which is particularly harmful for infants. Despite this, we are only starting to understand how the brain changes and matures during normal pregnancy and postpartum (Barba-Müller et al., 2019; Glynn et al., 2018), let alone in situations when normal maturation is disrupted. The situation is also complex in terms of selecting an appropriate treatment.

Our epidemiological research in this study stems from this background. Maternal and paternal depression were relatively stable from late pregnancy until two years postnatally, and even subclinical levels of maternal persistent depression associated with children's emotional problems at the ages of two and five years. If these parents could already be identified and targeted with appropriate treatment protocols during pregnancy, much harm and suffering might be avoidable at the family, parent and the infant level. Pregnancy is a window of opportunity to get in touch with families at risk. Mothers and families are also willing to accept help and take part in psychological interventions during pregnancy. Later on, these families tend to be more difficult to reach, yet most of the families referred to child mental health units have parents suffering from mental disorders, most of them untreated (Swartz et al., 2005).

The costs of not treating PMADs are becoming evident from Australian (PwC Consulting Australia, 2019), British (Bauer et al., 2014) and US (Luca et al., 2019) reports. Screening is the first step in the chain towards recovery. However, it is crucial to understand that screening alone without local treatment pathways will not lead to a change (Camacho and Shields, 2018). Alongside the EPDS, the Antenatal Risk Questionnaire (ANRQ) (Austin et al., 2013) for screening psychosocial risk factors would be wise to take into clinical practice, as in Australia (Austin et al., 2017). As the results from our study show, depression in one parent increases the risk of the spouse developing depression. The screening of both parents would also be recommendable based on our study.

We should not only seek to treat the most severely affected parents, but also consider how postnatal depression and other mental health disorders can be prevented. In our study, sleep onset problems during early and late pregnancy predicted postnatal depressive symptoms, in addition to poor sleep quality and short sleep in late pregnancy. Intensive treatment of insomnia symptoms is needed, both during pregnancy and postnatally, as

almost all perinatal mental health disorders are linked to disrupted sleep (Lawson et al., 2015).

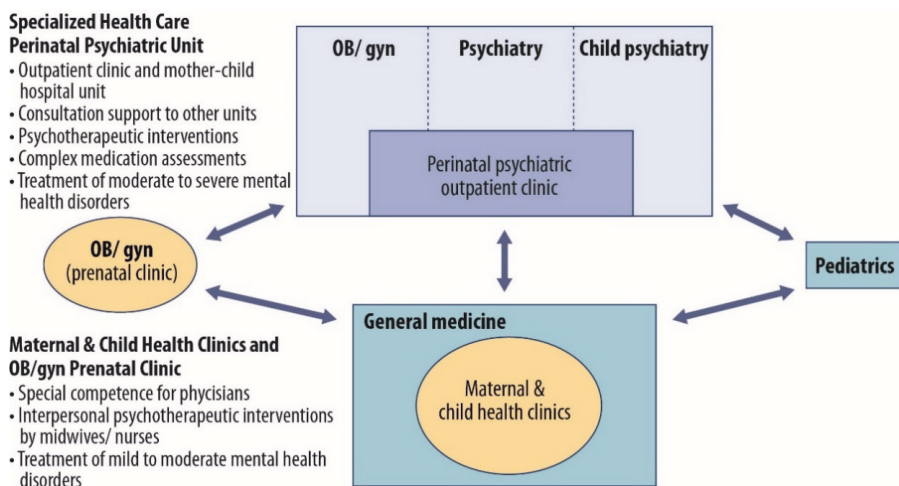
Interpersonal therapy (IPT) is better validated than antidepressant medication for the treatment of perinatal depression and, together with CBT, is in the first line of treatment options for PMADS (Sockol, 2018; Sockol et al., 2011; Stuart and Koleva, 2014). From the foetal perspective, non-pharmacological treatments should also be preferred if available. The US Preventive Task Force (Curry et al., 2019) also recommended counselling interventions, particularly IPT and CBT, for the treatment of sub-clinical depressive symptoms and prevention of postnatal depression for mothers with risk factors. Reproductive mental health clinics, for example in Toronto (Women's College Hospital Toronto, n.d.) and Vancouver, offer various group psychotherapeutic, couple, individual and mother–baby psychological interventions. Moreover, treatment programmes such as the Mother to Baby CBT programme are now also available in an online format ([www.eMB.health](http://www.eMB.health)). Based on the US Task Force recommendations (Curry et al., 2019; O'Connor et al., 2019), such programmes and counselling should be offered with a low threshold in primary care, as well as in more specialized units. This would benefit not only the mother but also the child: the treatment of maternal mental disorder has been consistently shown to improve child outcomes (Gunlicks and Weissman, 2008; Howard and Challacombe, 2018; Weissman et al., 2015; Wickramaratne et al., 2011).

This study was strongly focused on parental perinatal depression, as has most previous literature on perinatal mental health, but anxiety disorders might be even more prevalent (Dennis et al., 2017; Rees et al., 2019). In practice, postpartum depression seems to be an umbrella term for depressive disorders (including bipolar depression), PTSD and other trauma disorders, anxiety disorders such as perinatal obsessive–compulsive disorder, personality disorders including borderline personality disorders, adjustment disorders, psychotic disorders, and so on, yet the EPDS only screens depression and partly anxiousness. It is rare for a mental health disorder to exist in isolation, and as our cumulative model showed, the risk of mental disorder increases strikingly with the accumulation of risk factors. More knowledge concerning the duration, timing and content of effective parenting interventions for families with severe parental mental health disorders is needed (Bee et al., 2014; Stein et al., 2018).

In Finland, we have one of the few 4-year training programmes for mother–infant psychotherapy in the world, but more clinical research is needed on the subject. Furthermore, despite evidence concerning the efficacy of IPT and CBT, local implementations and adaptations to the Finnish system are lacking. This dissertation sets the ground for future implementation trials.

The public health service in Finland needs to adapt to the growing need for perinatal mental health services, and psychotherapeutic interventions, in particular, need to be constructed at both the primary care and specialized

health care levels (**Figure 22**). National treatment guidelines concerning perinatal mental health disorders need to be published, mothers should be able to attend counselling interventions with a lower threshold, and the evaluation and treatment of mother–child bonding disorders should be an integral part of the treatment of perinatal mental health disorders at all levels (Pietikäinen, Hakulinen and Holopainen 2020; Murray, Fearon, and Cooper 2015). Specialized perinatal mental health outpatient clinics, as well as psychiatric mother–baby wards/beds, should be set up; they would also serve staff educational purposes. We need to start taking better care of our young families, and as a position statement by 33 nationalities (Brockington et al., 2017) indicates, perinatal psychiatry is a much needed and vital novel area of specialization.



**Figure 22.** Suggestion for a Finnish perinatal mental health service. From Pietikäinen J, Taka-Eilola T, Paunio T. Suomeen tarvitaan perinataalipsykiatria. Duodecim 2019; 135: 1809–1120. Reproduced with permission from the publisher Duodecim.

## 8 REFERENCES

- Abbott, S.M., Attarian, H., Zee, P.C., 2014. Sleep disorders in perinatal women. *Best Pract. Res. Clin. Obstet. Gynaecol.* 28, 159–168. <https://doi.org/10.1016/j.bpobgyn.2013.09.003>
- Abel, K.M., Hope, H., Swift, E., Parisi, R., Ashcroft, D.M., Kosidou, K., Osam, C.S., Dalman, C., Pierce, M., 2019. Prevalence of maternal mental illness among children and adolescents in the UK between 2005 and 2017: a national retrospective cohort analysis. *Lancet Public Heal.* 4, e291–300. [https://doi.org/10.1016/S2468-2667\(19\)30059-3](https://doi.org/10.1016/S2468-2667(19)30059-3)
- Accortt, E., Wong, M., 2017. It Is Time for Routine Screening for Perinatal Mood and Anxiety Disorders in Obstetrics and Gynecology Settings. *Obstet. Gynecol. Surv.* 72, 553–568.
- Agebjörn, J., Linder, H., 2015. *Postpartum Depression in Fathers*. University of Lund.
- 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. *Arch. Womens. Ment. Health* 21, 689–698. <https://doi.org/10.1007/s00737-018-0845-y>
- Akaike, H., 1973. Information theory and an extension of the maximum likelihood principle, in: Petrov, B.N., Csáki, F. (Eds.), *2nd International Symposium on Information Theory*. Akadémiai Kiadó, Tsahkadsor, Armenia, USSR, pp. 267–281.
- Alipour, Z., Lamyian, M., 2012. Sleep quality in late pregnancy and postpartum depression. *Iran. J. Obstet. Gynecol. Infertil.* 14, 39–47.
- Allison, P.D., 2003. Missing Data Techniques for Structural Equation Modeling. *J. Abnorm. Psychol.* 112, 545–557. <https://doi.org/10.1037/0021-843X.112.4.545>
- American Psychiatric Association, 2013. *Diagnostic and statistical manual of mental disorders*, 5th editio. ed. American Psychiatric Publishing, Washington, DC.
- Areias, M.E.G., Kumar, R., Barros, H., Figueiredo, E., 1996. Correlates of postnatal depression in mothers and fathers. *Br. J. Psychiatry* 169, 36–41. <https://doi.org/10.1192/bjp.169.1.36>
- Armitage, R., Flynn, H., Hoffmann, R., Vazquez, D., Lopez, J., Marcus, S., 2009. Early developmental changes in sleep in infants: The impact of maternal depression. *Sleep* 32, 693–696. <https://doi.org/10.1093/sleep/32.5.693>
- Aswathy, B.S., Kumar, V.M., Gulia, K.K., 2018. The effects of rapid eye movement sleep deprivation during late pregnancy on newborns' sleep. *J. Sleep Res.* 27, 197–205. <https://doi.org/10.1111/jsr.12564>
- Atkinson, L., Paglia, A., Coolbear, J., Niccols, A., Parker, K.C.H., Guger, S., 2000. Attachment security: A meta-analysis of maternal mental health correlates. *Clin. Psychol. Rev.* 20, 1019–1040. [https://doi.org/10.1016/S0272-7358\(99\)00023-9](https://doi.org/10.1016/S0272-7358(99)00023-9)
- Atzil, S., Hendler, T., Zagoory-Sharon, O., Winetraub, Y., Feldman, R., 2012. Synchrony and specificity in the maternal and the paternal brain: Relations to oxytocin and vasopressin. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 798–811. <https://doi.org/10.1016/j.jaac.2012.06.008>
- Austin, M.P., Colton, J., Priest, S., Reilly, N., Hadzi-Pavlovic, D., 2013. The

- antenatal risk questionnaire (ANRQ): Acceptability and use for psychosocial risk assessment in the maternity setting. *Women and Birth* 26, 17–25. <https://doi.org/10.1016/j.wombi.2011.06.002>
- Austin, M.P., Highet, N., Group, E.W., 2017. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline [WWW Document]. URL <https://cope.org.au/wp-content/uploads/2017/10/Final-COPE-Perinatal-Mental-Health-Guideline.pdf>
- Avan, B., Richter, L.M., Ramchandani, P.G., Norris, S.A., Stein, A., 2010. Maternal postnatal depression and children’s growth and behaviour during the early years of life: Exploring the interaction between physical and mental health. *Arch. Dis. Child.* 95, 690–695. <https://doi.org/10.1136/adc.2009.164848>
- Ayano, G., Maravilla, J.C., Alati, R., 2019. Risk of autistic spectrum disorder in offspring with parental mood disorders: A systematic review and meta-analysis. *J. Affect. Disord.* 248, 185–197. <https://doi.org/10.1016/j.jad.2019.01.038>
- Badovinac, S., Martin, J., Guerin-Marion, C., O’Neill, M., Riddell, R.P., Bureau, J.F., Spiegel, R., 2018. Associations between mother-preschooler attachment and maternal depression symptoms: A systematic review and metaanalysis. *PLoS One* 13, e0204374. <https://doi.org/10.1371/journal.pone.0204374>
- Baglioni, C., Spiegelhalder, K., Nissen, C., Riemann, D., 2011. Clinical implications of the causal relationship between insomnia and depression: How individually tailored treatment of sleeping difficulties could prevent the onset of depression. *EPMA J.* 2, 287–293. <https://doi.org/10.1007/s13167-011-0079-9>
- Bagner, D.M., Pettit, J.W., Lewinsohn, P.M., Seeley, J.R., 2010. Effect of maternal depression on child behavior: A sensitive period? *J. Am. Acad. Child Adolesc. Psychiatry* 49, 699–707. <https://doi.org/10.1097/00004583-201007000-00010>
- Baratte-Beebe, K.R., 1999. Sources of midsleep awakenings in childbearing women. *Clin. Nurs. Res.* 8, 386–397.
- Barba-Müller, E., Craddock, S., Carmona, S., Hoekzema, E., 2019. Brain plasticity in pregnancy and the postpartum period: links to maternal caregiving and mental health. *Arch. Womens. Ment. Health* 22, 289–299. <https://doi.org/10.1007/s00737-018-0889-z>
- Barger, M.K., Caughey, A.B., Lee, K.A., 2013. Evaluating Insomnia During Pregnancy and Postpartum, in: Attarian, H.P., Viola-Saltzman, M. (Eds.), *Sleep Disorders in Women*. Humana Press, Totowa, NJ, New York, pp. 225–242.
- Barker, B., Iles, J.E., Ramchandani, P.G., 2017. Fathers, fathering and child psychopathology. *Curr. Opin. Psychol.* 15, 87–92. <https://doi.org/10.1016/j.copsyc.2017.02.015>
- Barker, E.D., 2013. The duration and timing of maternal depression as a moderator of the relationship between dependent interpersonal stress, contextual risk and early child dysregulation. *Psychol. Med.* 43, 1587–1596. <https://doi.org/10.1017/S0033291712002450>
- Barker, E.D., Copeland, W., Maughan, B., Jaffee, S.R., Uher, R., 2012. Relative impact of maternal depression and associated risk factors on offspring psychopathology. *Br. J. Psychiatry* 200, 124–129. <https://doi.org/10.1192/bjp.bp.111.092346>
- Barnes, J., Theule, J., 2019. Maternal depression and infant attachment security: A meta-analysis. *Infant Ment. Health J.* 40, 817–834. <https://doi.org/10.1002/imhj.21812>
- 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. *J. Affect. Disord.* 223, 194–208. <https://doi.org/10.1016/j.jad.2017.07.046>
- Barthel, D., Kriston, L., Fordjour, D., Mohammed, Y., Kra-Yao, E.D., Bony Kotchi, C.E., Koffi Armel, E.J., Eberhardt, K.A., Feldt, T., Hinz, R., Mathurin, K., Schoppen, S., Bindt, C., Ehrhardt, S., 2017. Trajectories of maternal ante- and postpartum depressive symptoms and their association with child- and mother-related characteristics in a West African birth cohort study. *PLoS One* 12, e0187267. <https://doi.org/10.1371/journal.pone.0187267>
- Bastien, C.H., Vallières, A., Morin, C.M., 2001. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med.* 2, 297–307. [https://doi.org/10.1016/S1389-9457\(00\)00065-4](https://doi.org/10.1016/S1389-9457(00)00065-4)
- Bauer, A., Parsonage, M., Knapp, M., Iemmi, V., Adelaja, B., Hogg, S., 2014. The costs of perinatal mental health problems, LSE; PSSRU; Centre for Mental Health. <https://doi.org/10.13140/2.1.4731.6169>
- Bayrampour, H., Tomfohr, L., Tough, S., 2016. Trajectories of perinatal depressive and anxiety symptoms in a community cohort. *J. Clin. Psychiatry* 77, e1467-1473. <https://doi.org/10.4088/JCP.15m10176>
- Beardslee, W.R., 2019. Master Clinician Review: Parental Depression and Family Health and Wellness: What Clinicians Can Do and Reflections on Opportunities for the Future. *J. Am. Acad. Child Adolesc. Psychiatry* 58, 759–767. <https://doi.org/10.1016/j.jaac.2019.02.008>
- Beardslee, W.R., Wright, E., Rothberg, P.C., Salt, P., Versage, E., 1996. Response of families to two preventive intervention strategies: Long-term differences in behavior and attitude change. *J. Am. Acad. Child Adolesc. Psychiatry* 35, 774–782. <https://doi.org/10.1097/00004583-199606000-00017>
- Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., Erbaugh, J., 1961. An Inventory for Measuring Depression. *Arch. Gen. Psychiatry* 4, 561–571. <https://doi.org/10.1001/archpsyc.1961.01710120031004>
- Beck, C.T., 2001. Predictors of postpartum depression: An update. *Nurs. Res.* 50, 275–285. <https://doi.org/10.1097/00006199-200109000-00004>
- Bee, P., Bower, P., Byford, S., Churchill, R., Calam, R., Stallard, P., Prymachuk, S., Berzins, K., Cary, M., Wan, M., Abel, K., 2014. The clinical effectiveness, cost-effectiveness and acceptability of community-based interventions aimed at improving or maintaining quality of life in children of parents with serious mental illness: A systematic review. *Health Technol. Assess. (Rockv)*. 18, 1–249. <https://doi.org/10.3310/hta18080>
- Bei, B., Milgrom, J., Erickson, J., Trinder, J., 2010. Subjective perception of sleep, but not its objective quality, is associated with immediate postpartum mood disturbances in healthy women. *Sleep* 33, 531–538. <https://doi.org/10.1093/sleep/33.4.531>
- Bennett, I.M., Schott, W., Krutikova, S., Behrman, J.R., 2015. Maternal mental health, and child growth and development, in four low-income and middle-income countries. *J. Epidemiol. Community Health* 70, 168–173. <https://doi.org/10.1136/jech-2014-205311>
- Bianchi, D.W., Zickwolf, G.K., Weil, G.J., Sylvester, S., Demaria, M.A., 1996. Male fetal progenitor cells persist in maternal blood for as long as 27 years postpartum. *Proc. Natl. Acad. Sci. U. S. A.* 93, 705–708. <https://doi.org/10.1073/pnas.93.2.705>

- Bielawska-Batorowicz, E., Kossakowska-Petrycka, K., 2006. Depressive mood in men after the birth of their offspring in relation to a partner's depression, social support, fathers' personality and prenatal expectations. *J. Reprod. Infant Psychol.* 24, 21–29. <https://doi.org/10.1080/02646830500475179>
- Bieling, P.J., Antony, M.M., Swinson, R.P., 1998. The state-trait anxiety inventory, trait version: Structure and content re-examined. *Behav. Res. Ther.* 36, 777–788. [https://doi.org/10.1016/S0005-7967\(98\)00023-0](https://doi.org/10.1016/S0005-7967(98)00023-0)
- Blabey, M.H., Locke, E.R., Goldsmith, Y.W., Perham-Hester, K.A., 2009. Experience of a controlling or threatening partner among mothers with persistent symptoms of depression. *Am. J. Obstet. Gynecol.* 201, e1-9. <https://doi.org/10.1016/j.ajog.2009.04.025>
- Blair, L.M., Porter, K., Leblebicioglu, B., Christian, L.M., 2015. Poor Sleep Quality and Associated Inflammation Predict Preterm Birth: Heightened Risk among African Americans. *Sleep* 38, 1259–1267. <https://doi.org/10.5665/sleep.4904>
- Blanken, T.F., Borsboom, D., Penninx, B.W., Van Someren, E.J., 2020. Network outcome analysis identifies difficulty initiating sleep as a primary target for prevention of depression: a 6-year prospective study. *Sleep* 43(5), 1-6. <https://doi.org/10.1093/sleep/zsz288>
- Blom, K., Jernelöv, S., Rück, C., Lindefors, N., Kaldo, V., 2017. Three-Year Follow-Up Comparing Cognitive Behavioral Therapy for Depression to Cognitive Behavioral Therapy for Insomnia, for Patients With Both Diagnoses. *Sleep* 40, 1–5. <https://doi.org/10.1093/sleep/zsx108>
- Börjesson, K., Ruppert, S., Bågedahl-Strindlund, M., 2005. A longitudinal study of psychiatric symptoms in primiparous women: Relation to personality disorders and sociodemographic factors. *Arch. Womens. Ment. Health* 8, 232–242. <https://doi.org/10.1007/s00737-005-0086-8>
- Brennan, P.A., Hammen, C., Andersen, M.J., Bor, W., Najman, J.M., Williams, G.M., 2000. Chronicity, severity, and timing of maternal depressive symptoms: relationships with child outcomes at age 5. *Dev. Psychol.* 36, 759–766. <https://doi.org/10.1037/0012-1649.36.6.759>
- Briggs-Gowan, M.J., Carter, A.S., Irwin, J.R., Wachtel, K., Cicchetti, D. V., 2004. The Brief Infant-Toddler Social and Emotional Assessment: Screening for Social-Emotional Problems and Delays in Competence. *J. Pediatr. Psychol.* 28, 143–155. <https://doi.org/10.1093/jpepsy/jsh017>
- Briggs-Gowan, M.J., Carter, A.S., Skuban, E.M., Horwitz, S.M.C., 2001. Prevalence of social-emotional and behavioral problems in a community sample of 1- and 2-year-old children. *J. Am. Acad. Child Adolesc. Psychiatry* 40, 811–819. <https://doi.org/10.1097/00004583-200107000-00016>
- Brockington, I., 2004. Postpartum psychiatric disorders. *Lancet* 363, 303–10. [https://doi.org/10.1016/S0140-6736\(03\)15390-1](https://doi.org/10.1016/S0140-6736(03)15390-1)
- Brockington, I., Butterworth, R., Glangeaud-Freudenthal, N., 2017. An international position paper on mother-infant (perinatal) mental health, with guidelines for clinical practice. *Arch. Womens. Ment. Health* 20, 113–120. <https://doi.org/10.1007/s00737-016-0684-7>
- Broden, M., 2013. *Raskausajan mahdollisuudet*, 4th ed. Therapeia and Margareta Broden, Helsinki.
- Brownhill, S., Wilhelm, K., Barclay, L., Schmied, V., 2005. “Big build”: Hidden depression in men. *Aust. N. Z. J. Psychiatry* 39, 921–931. <https://doi.org/10.1111/j.1440-1614.2005.01665.x>

## References

- Brugha, T.S., Cragg, D., 1990. The List of Threatening Experiences: the reliability and validity of a brief life events questionnaire. *Acta Psychiatr. Scand.* 82, 77–81. <https://doi.org/10.1111/j.1600-0447.1990.tb01360.x>
- Bruno, A., Celebre, L., Mento, C., Rizzo, A., Silvestri, M.C., De Stefano, R., Zoccali, R.A., Muscatello, M.R.A., 2020. When fathers begin to falter: A comprehensive review on paternal perinatal depression. *Int. J. Environ. Res. Public Health* 17. <https://doi.org/10.3390/ijerph17041139>
- Burke, N.J., Hellman, J.L., Scott, B.G., Weems, C.F., Carrion, V.G., 2011. The impact of adverse childhood experiences on an urban pediatric population. *Child Abus. Negl.* 35, 408–413. <https://doi.org/10.1016/j.chiabu.2011.02.006>
- Buysse, D.J., Reynolds, C.F., Monk, T.H., Berman, S.R., Kupfer, D.J., 1989. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res.* 28, 193–213. [https://doi.org/10.1016/0165-1781\(89\)90047-4](https://doi.org/10.1016/0165-1781(89)90047-4)
- Calhoun, S.L., Fernandez-Mendoza, J., Vgontzas, A.N., Liao, D., Bixler, E.O., 2014. Prevalence of insomnia symptoms in a general population sample of young children and preadolescents: Gender effects. *Sleep Med.* 15, 91–95. <https://doi.org/10.1016/j.sleep.2013.08.787>
- Camacho, E.M., Shields, G.E., 2018. Cost-effectiveness of interventions for perinatal anxiety and/or depression: A systematic review. *BMJ Open* 8, e022022. <https://doi.org/10.1136/bmjopen-2018-022022>
- Cameron, E.E., Sedov, I.D., Tomfohr-Madsen, L.M., 2016. Prevalence of paternal depression in pregnancy and the postpartum: An updated meta-analysis. *J. Affect. Disord.* <https://doi.org/10.1016/j.jad.2016.07.044>
- Campbell, S., Cohn, J., 1997. The timing and chronicity of postpartum depression: implications for infant development, in: *Postpartum Depression and Child Development*. Guilford, New York, pp. 165–97.
- Campbell, S.B., Matestic, P., von Stauffenberg, C., Mohan, R., Kirchner, T., 2007. Trajectories of Maternal Depressive Symptoms, Maternal Sensitivity, and Children's Functioning at School Entry. *Dev. Psychol.* 43, 1202–1215. <https://doi.org/10.1037/0012-1649.43.5.1202>
- Campbell, S.B., Morgan-Lopez, A.A., Cox, M.J., McLoyd, V.C., 2009. A Latent Class Analysis of Maternal Depressive Symptoms Over 12 Years and Offspring Adjustment in Adolescence. *J. Abnorm. Psychol.* 118, 479–193. <https://doi.org/10.1037/a0015923>
- Cantwell, R., Clutton-Brock, T., Cooper, G., Dawson, A., Drife, J., Garrod, D., 2011. Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006–08. The Eighth Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG* 118, 132–142. <https://doi.org/10.1111/j.1471-0528.2010.02847.x>
- Carlberg, M., Edhborg, M., Lindberg, L., 2018. Paternal Perinatal Depression Assessed by the Edinburgh Postnatal Depression Scale and the Gotland Male Depression Scale: Prevalence and Possible Risk Factors. *Am. J. Mens. Health* 12, 720–729. <https://doi.org/10.1177/1557988317749071>
- Carroll, J.E., Teti, D.M., Hall, M.H., Christian, L.M., 2019. Maternal Sleep in Pregnancy and Postpartum Part II: Biomechanisms and Intervention Strategies. *Curr. Psychiatry Rep.* 21:19. <https://doi.org/10.1007/s11920-019-1000-9>
- Cents, R.A.M., Diamantopoulou, S., Hudziak, J.J., Jaddoe, V.W. V, Hofman, A., Verhulst, F.C., Lambregtse-Van Den Berg, M.P., Tiemeier, H., 2013.

- Trajectories of maternal depressive symptoms predict child problem behaviour: The Generation R Study. *Psychol. Med.* 43, 13–25. <https://doi.org/10.1017/S0033291712000657>
- Chan, W.F.N., Gurnot, C., Montine, T.J., Sonnen, J.A., Guthrie, K.A., Nelson, J.L., 2012. Male Microchimerism in the Human Female Brain. *PLoS One* 7, e45592. <https://doi.org/10.1371/journal.pone.0045592>
- Charrois, J., Côté, S.M., Japel, C., Séguin, J.R., Paquin, S., Tremblay, R.E., Herba, C.M., 2017. Child-care quality moderates the association between maternal depression and children’s behavioural outcome. *J. Child Psychol. Psychiatry Allied Discip.* 58, 1210–1218. <https://doi.org/10.1111/jcpp.12764>
- Cheung, K., Theule, J., 2019. Paternal depression and child externalizing behaviors: A meta-analysis. *J. Fam. Psychol.* 33, 98–108. <https://doi.org/10.1037/fam0000473>
- Choi, K.W., Houts, R., Arseneault, L., Pariante, C., Sikkema, K.J., Moffitt, T.E., 2019. Maternal depression in the intergenerational transmission of childhood maltreatment and its sequelae: Testing postpartum effects in a longitudinal birth cohort. *Dev. Psychopathol.* 31, 143–156. <https://doi.org/10.1017/S0954579418000032>
- Christian, L.M., Carroll, J.E., Porter, K., Hall, M.H., 2019a. Sleep quality across pregnancy and postpartum: effects of parity and race. *Sleep Heal.* 5, 327–334. <https://doi.org/10.1016/j.sleh.2019.03.005>
- Christian, L.M., Carroll, J.E., Teti, D.M., Hall, M.H., 2019b. Maternal Sleep in Pregnancy and Postpartum Part I: Mental, Physical, and Interpersonal Consequences. *Curr. Psychiatry Rep.* 21:20. <https://doi.org/10.1007/s11920-019-0999-y>
- Chung, T.-C., Chung, C.-H., Peng, H.-J., Tsao, C.-H., Chien, W.-C., Sun, H.-F., 2018. An analysis of whether sleep disorder will result in postpartum depression. *Oncotarget* 9, 25304–25314. <https://doi.org/10.18632/oncotarget.25219>
- Cohen, S., Kamarck, T., Mermelstein, R., 1983. A Global Measure of Perceived Stress. *J. Health Soc. Behav.* 24, 385–396. <https://doi.org/10.2307/2136404>
- Collins, C.H., Zimmerman, C., Howard, L.M., 2011. Refugee, asylum seeker, immigrant women and postnatal depression: Rates and risk factors. *Arch. Womens. Ment. Health* 14, 3–11. <https://doi.org/10.1007/s00737-010-0198-7>
- Connell, A.M., Goodman, S.H., 2002. The association between psychopathology in fathers versus mothers and children’s internalizing and externalizing behavior problems: A meta-analysis. *Psychol. Bull.* 18, 746–773. <https://doi.org/10.1037//0033-2909.128.5.746>
- Connors-Burrow, N.A., McKelvey, L., Perry, D., Whiteside-Mansell, L., Kraleti, S., Mesman, G., Holmes, K., Kyzer, A., 2016. Low-Level Symptoms of Depression in Mothers of Young Children are Associated with Behavior Problems in Middle Childhood. *Matern. Child Health J.* 20, 516–524. <https://doi.org/10.1007/s10995-015-1849-0>
- Conroy, S., Pariante, C.M., Marks, M.N., Davies, H.A., Farrelly, S., Schacht, R., Moran, P., 2012. Maternal psychopathology and infant development at 18 months: The impact of maternal personality disorder and depression. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 51–61. <https://doi.org/10.1016/j.jaac.2011.10.007>
- Coo Calcagni, S., Bei, B., Milgrom, J., Trinder, J., 2012. The Relationship Between

## References

- Sleep and Mood in First-Time and Experienced Mothers. *Behav. Sleep Med.* 10, 167–179. <https://doi.org/10.1080/15402002.2012.668147>
- Coo, S., Milgrom, J., Kuppens, P., Cox, P., Trinder, J., 2014. Exploring the association between maternal mood and self-reports of sleep during the perinatal period. *JOGNN - J. Obstet. Gynecol. Neonatal Nurs.* 43, 465–477. <https://doi.org/10.1111/1552-6909.12464>
- Cooper, P.J., Murray, L., 1995. Course and recurrence of postnatal depression evidence for the specificity of the diagnostic concept. *Br. J. Psychiatry* 166, 191–195. <https://doi.org/10.1192/bjp.166.2.191>
- Cox, E.Q., Sowa, N.A., Meltzer-Brody, S.E., Gaynes, B.N., 2016. The perinatal depression treatment cascade: Baby steps toward improving outcomes. *J. Clin. Psychiatry* 77, 1189–1200. <https://doi.org/10.4088/JCP.15r10174>
- Cox, J., 2019. Thirty years with the Edinburgh Postnatal Depression Scale: Voices from the past and recommendations for the future. *Br. J. Psychiatry* 214, 127–129. <https://doi.org/10.1192/bjp.2018.245>
- Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of Postnatal Depression: Development of the 10-item Edinburgh Postnatal Depression scale. *Br. J. Psychiatry* 150, 782–786.
- Crittenden, P.M., Landini, A., Kozłowska, K., 2015. The effect of parents' psychiatric disorder on children's attachment: theory and cases, in: Reupert, A., Maybery, D., Nicholson, J., Göpfert, M., Seeman, M. V. (Eds.), *Parental Psychiatric Disorder: Distressed Parents and Their Families*. Cambridge University Press, pp. 29–41.
- Crowley, G., Molyneaux, E., Nath, S., Trevillion, K., Moran, P., Howard, L.M., 2020. Disordered personality traits and psychiatric morbidity in pregnancy: a population-based study. *Arch. Womens. Ment. Health* 23, 43–52. <https://doi.org/10.1007/s00737-018-0937-8>
- Cui, C., Li, M., Yang, Y., Liu, C., Cao, P., Wang, L., 2020. The effects of paternal perinatal depression on socioemotional and behavioral development of children: A meta-analysis of prospective studies. *Psychiatry Res.* 284. <https://doi.org/10.1016/j.psychres.2020.112775>
- Cummings, E.M., Keller, P.S., Davies, P.T., 2005. Towards a family process model of maternal and paternal depressive symptoms: Exploring multiple relations with child and family functioning. *J. Child Psychol. Psychiatry Allied Discip.* 46, 479–489. <https://doi.org/10.1111/j.1469-7610.2004.00368.x>
- Curry, S.J., Krist, A.H., Owens, D.K., Barry, M.J., Caughey, A.B., Davidson, K.W., Doubeni, C.A., Epling, J.W., Grossman, D.C., Kemper, A.R., Kubik, M., Landefeld, C.S., Mangione, C.M., Silverstein, M., Simon, M.A., Tseng, C.W., Wong, J.B., 2019. Interventions to Prevent Perinatal Depression: US Preventive Services Task Force Recommendation Statement. *JAMA - J. Am. Med. Assoc.* 321, 580–587. <https://doi.org/10.1001/jama.2019.0007>
- Davé, S., Nazareth, I., Sherr, L., Senior, R., 2005. The association of paternal mood and infant temperament: A pilot study. *Br. J. Dev. Psychol.* 609–621. <https://doi.org/10.1348/026151004X22962>
- Davé, S., Petersen, I., Sherr, L., Nazareth, I., 2010. Incidence of maternal and paternal depression in primary care: A cohort study using a primary care database. *Arch. Pediatr. Adolesc. Med.* 164, 1038–1044. <https://doi.org/10.1001/archpediatrics.2010.184>
- Davé, S., Sherr, L., Senior, R., Nazareth, I., 2008. Associations between paternal

- depression and behaviour problems in children of 4-6 years. *Eur. Child Adolesc. Psychiatry* 17, 306–15. <https://doi.org/10.1007/s00787-007-0672-6>
- Davis, E.P., Korja, R., Karlsson, L., Glynn, L.M., Sandman, C.A., Vegetabile, B., Kataja, E.L., Nolvi, S., Sinervä, E., Pelto, J., Karlsson, H., Stern, H.S., Baram, T.Z., 2019. Across continents and demographics, unpredictable maternal signals are associated with children's cognitive function. *EBioMedicine* 46, 256–263. <https://doi.org/10.1016/j.ebiom.2019.07.025>
- de Bruijn, A.T.C.E., van Bakel, H.J.A., van Baar, A.L., 2009. Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Hum. Dev.* 85, 319–324. <https://doi.org/10.1016/j.earlhumdev.2008.12.009>
- Deater-Deckard, K., Pickering, K., Dunn, J.F., Golding, J., 1998. Family structure and depressive symptoms in men preceding and following the birth of a child. The Avon Longitudinal Study of Pregnancy and Childhood Study Team. *Am. J. Psychiatry* 155, 818–823. <https://doi.org/10.1176/ajp.155.6.818>
- Deave, T., Heron, J., Evans, J., Emond, A., 2008. The impact of maternal depression in pregnancy on early child development. *BJOG An Int. J. Obstet. Gynaecol.* 115, 1043–1051. <https://doi.org/10.1111/j.1471-0528.2008.01752.x>
- Denckla, C.A., Mancini, A.D., Consedine, N.S., Milanovic, S.M., Basu, A., Seedat, S., Spies, G., Henderson, D.C., Bonanno, G.A., Koenen, K.C., 2018. Distinguishing postpartum and antepartum depressive trajectories in a large population-based cohort: The impact of exposure to adversity and offspring gender. *Psychol. Med.* 48, 1139–1147. <https://doi.org/10.1017/S0033291717002549>
- Dennis, C.L., Falah-Hassani, K., Shiri, R., 2017. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *Br. J. Psychiatry* 210, 315–323. <https://doi.org/10.1192/bjp.bp.116.187179>
- Derogatis, L.R., Lipman, R.S., Covi, L., 1973. The SCL-90: An outpatient psychiatric rating scale. *Psychopharmacol. Bull.* 9, 13–28.
- Di Florio, A., Forty, L., Gordon-Smith, K., Heron, J., Jones, L., Craddock, N., Jones, I., 2013. Perinatal episodes across the mood disorder spectrum. *JAMA Psychiatry* 70, 168–175. <https://doi.org/10.1001/jamapsychiatry.2013.279>
- Dierker, L.C., Merikangas, K.R., Szatmari, P., 1999. Influence of parental concordance for psychiatric disorders on psychopathology in offspring. *J. Am. Acad. Child Adolesc. Psychiatry* 38, 280–288. <https://doi.org/10.1097/00004583-199903000-00015>
- Dørheim, S.K., Bjorvatn, B., Eberhard-Gran, M., 2014. Can insomnia in pregnancy predict postpartum depression? A longitudinal, population-based study. *PLoS One* 9, e94674. <https://doi.org/10.1371/journal.pone.0094674>
- Dørheim, S.K., Bjorvatn, B., Eberhard-Gran, M., 2012. Insomnia and Depressive Symptoms in Late Pregnancy: A Population-Based Study. *Behav. Sleep Med.* 10, 152–166. <https://doi.org/10.1080/15402002.2012.660588>
- Drozdz, F., Haga, S.M., Valla, L., Slinning, K., 2018. Latent trajectory classes of postpartum depressive symptoms: A regional population-based longitudinal study. *J. Affect. Disord.* 241, 29–36. <https://doi.org/10.1016/j.jad.2018.07.081>
- Dudley, M., Roy, K., Kelk, N., Bernard, D., 2001. Psychological correlates of depression in fathers and mothers in the first postnatal year. *J. Reprod. Infant Psychol.* 19, 187–202. <https://doi.org/10.1080/02646830124397>
- Eberhard-Gran, M., Eskild, A., Tambs, K., Opjordsmoen, S., Samuelsen, S.O., 2001.

- Review of validation studies of the Edinburgh postnatal depression scale. *Acta Psychiatr. Scand.* 104, 243–249. <https://doi.org/10.1034/j.1600-0447.2001.00187.x>
- Edhborg, M., Matthiesen, A.S., Lundh, W., Widström, A.M., 2005. Some early indicators for depressive symptoms and bonding 2 months postpartum - A study of new mothers and fathers. *Arch. Womens. Ment. Health* 8, 221–231. <https://doi.org/10.1007/s00737-005-0097-5>
- Edward, K. leigh, Castle, D., Mills, C., Davis, L., Casey, J., 2015. An Integrative Review of Paternal Depression. *Am. J. Mens. Health* 9, 26–34. <https://doi.org/10.1177/1557988314526614>
- Emamian, F., Khazaie, H., Okun, M.L., Tahmasian, M., Sepehry, A.A., 2019. Link between insomnia and perinatal depressive symptoms: A meta-analysis. *J. Sleep Res.* e12858. <https://doi.org/10.1111/jsr.12858>
- England, M., Sim, L., 2009a. Introduction and magnitude of the problem, in: England, M.J., Sim, L.J. (Eds.), *Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention*. National Academies Press, Washington, DC, pp. 15–42. <https://doi.org/10.17226/12565>
- England, M., Sim, L., 2009b. Association between depression in parents and parenting, child health, and child psychological functioning, in: England, M., Sim, L. (Eds.), *Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention*. National Academies Press, Washington, DC, pp. 119–182.
- Facco, F.L., Grobman, W.A., Kramer, J., Ho, K.H., Zee, P.C., 2010a. Self-reported short sleep duration and frequent snoring in pregnancy: Impact on glucose metabolism. *Am. J. Obstet. Gynecol.* 203, e1-5. <https://doi.org/10.1016/j.ajog.2010.03.041>
- Facco, F.L., Kramer, J., Ho, K.H., Zee, P.C., Grobman, W.A., 2010b. Sleep disturbances in pregnancy. *Obstet. Gynecol.* <https://doi.org/10.1097/AOG.0b013e3181c4f8ec>
- Faisal-Cury, A., Menezes, P.R., D'Oliveira, A.F.P.L., Schraiber, L.B., Lopes, C.S., 2013. Temporal relationship between intimate partner violence and postpartum depression in a sample of low income women. *Matern. Child Health J.* 17, 1297–1303. <https://doi.org/10.1007/s10995-012-1127-3>
- Felder, J.N., Epel, E.S., Neuhaus, J., Krystal, A.D., Prather, A.A., 2020. Efficacy of Digital Cognitive Behavioral Therapy for the Treatment of Insomnia Symptoms among Pregnant Women: A Randomized Clinical Trial. *JAMA Psychiatry.* <https://doi.org/10.1001/jamapsychiatry.2019.4491>
- Feldman, R., Gordon, I., Influx, M., Gutbir, T., Ebstein, R.P., 2013. Parental oxytocin and early caregiving jointly shape children's oxytocin response and social reciprocity. *Neuropsychopharmacology* 38, 1154–1162. <https://doi.org/10.1038/npp.2013.22>
- Feldman, R., Granat, A., Pariente, C., Kanety, H., Kuint, J., Gilboa-Schechtman, E., 2009. Maternal Depression and Anxiety Across the Postpartum Year and Infant Social Engagement, Fear Regulation, and Stress Reactivity. *J. Am. Acad. Child Adolesc. Psychiatry* 48, 919–927. <https://doi.org/10.1097/CHI.0b013e3181b21651>
- Fellmeth, G., Fazel, M., Plugge, E., 2017. Migration and perinatal mental health in women from low- and middle-income countries: a systematic review and meta-analysis. *BJOG An Int. J. Obstet. Gynaecol.* 124, 742–752.

- <https://doi.org/10.1111/1471-0528.14184>
- Field, T., 2017. Infant sleep problems and interventions: A review. *Infant Behav. Dev.* 47, 40–53. <https://doi.org/10.1016/j.infbeh.2017.02.002>
- Field, T., 2011. Prenatal depression effects on early development: A review. *Infant Behav. Dev.* 34, 1–14. <https://doi.org/10.1016/j.infbeh.2010.09.008>
- Field, T., Diego, M., Dieter, J., Hernandez-Reif, M., Schanberg, S., Kuhn, C., Yando, R., Bendell, D., 2004. Prenatal depression effects on the fetus and the newborn. *Infant Behav. Dev.* 27, 216–229. <https://doi.org/10.1016/j.infbeh.2003.09.010>
- Field, T., Diego, M., Hernandez-Reif, M., 2009. Depressed mothers' infants are less responsive to faces and voices. *Infant Behav. Dev.* 32, 239–244. <https://doi.org/10.1016/j.infbeh.2009.03.005>
- Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Schanberg, S., Kuhn, C., 2007. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav. Dev.* 30, 127–133. <https://doi.org/10.1016/j.infbeh.2006.08.002>
- Fisher, J., de Mello, M.C., Patel, V., Rahman, A., Tran, T., Holton, S., Holmes, W., 2012. Prevalence and determinants of common perinatal mental disorders in women in low-and lower-middle-income countries: A systematic review. *Bull. World Health Organ.* 90, 139–149G. <https://doi.org/10.2471/BLT.11.091850>
- Fisher, S.D., Sit, D.K., Yang, A., Ciolino, J.D., Gollan, J.K., Wisner, K.L., 2019. Four maternal characteristics determine the 12-month course of chronic severe postpartum depressive symptoms. *Depress. Anxiety* 36, 375–383. <https://doi.org/10.1002/da.22879>
- Fleming, A.S., Corter, C., Stallings, J., Steiner, M., 2002. Testosterone and prolactin are associated with emotional responses to infant cries in new fathers. *Horm. Behav.* 42, 399–413. <https://doi.org/10.1006/hbeh.2002.1840>
- Fletcher, R., Garfield, C.F., Matthey, S., 2015. Fathers' Perinatal Mental Health, in: Milgrom, J., Gemmill, A., W. (Eds.), *Identifying Perinatal Depression and Anxiety: Evidence-Based Practice in Screening, Psychosocial Assessment and Management*. John Wiley & Sons, Incorporated, pp. 228–241.
- Fletcher, R.J., Feeman, E., Garfield, C., Vimpani, G., 2011. The effects of early paternal depression on children's development. *Med. J. Aust.* 195, 685–9. <https://doi.org/10.5694/mja11.10192>
- Flynn, H.A., Blow, F.C., Marcus, S.M., 2006. Rates and predictors of depression treatment among pregnant women in hospital-affiliated obstetrics practices. *Gen. Hosp. Psychiatry* 28, 289–295. <https://doi.org/10.1016/j.genhosppsych.2006.04.002>
- Foley, D.L., Pickles, A., Simonoff, E., Maes, H.H., Silberg, J.L., Hewitt, J.K., Eaves, L.J., 2001. Parental concordance and comorbidity for psychiatric disorder and associate risks for current psychiatric symptoms and disorders in a community sample of juvenile twins. *J. Child Psychol. Psychiatry Allied Discip.* 42, 381–394. <https://doi.org/10.1017/S0021963001007077>
- Forder, P.M., Rich, J., Harris, S., Chojenta, C., Reilly, N., Austin, M.P., Loxton, D., 2020. Honesty and comfort levels in mothers when screened for perinatal depression and anxiety. *Women and Birth* 33, e142–e150. <https://doi.org/10.1016/j.wombi.2019.04.001>
- Franco, P., Putois, B., Guyon, A., Raoux, A., Papadopoulou, M., Guignard-Perret, A., Bat-Pitault, F., Hartley, S., Plancoulaine, S., 2020. Sleep during development: Sex and gender differences. *Sleep Med. Rev.* 51.

- <https://doi.org/10.1016/j.smr.2020.101276>
- Fredriksen, E., von Soest, T., Smith, L., Moe, V., 2017. Patterns of pregnancy and postpartum depressive symptoms: Latent class trajectories and predictors. *J. Abnorm. Psychol.* 126, 173–183. <https://doi.org/10.1037/abn0000246>
- Fredriksen, E., Von Soest, T., Smith, L., Moe, V., 2019. Depressive symptom contagion in the transition to parenthood: Interparental processes and the role of partner-related attachment. *J. Abnorm. Psychol.* 128, 397–403. <https://doi.org/10.1037/abn0000429>
- Gao, M., Hu, J., Yang, L., Ding, N., Wei, X., Li, L., Liu, L., Ma, Y., Wen, D., 2019. Association of sleep quality during pregnancy with stress and depression: A prospective birth cohort study in China. *BMC Pregnancy Childbirth* 19. <https://doi.org/10.1186/s12884-019-2583-1>
- Garbaza, C., Hacketh, S., Riccardi, S., Cajochen, C., Cicolin, A., D’Agostino, A., Cirignotta, F., Manconi, M., 2020. Polysomnographic features of pregnancy: A systematic review. *Sleep Med. Rev.* 50, 101249. <https://doi.org/10.1016/j.smr.2019.101249>
- Gardner, F., Leijten, P., 2017. Incredible Years parenting interventions: current effectiveness research and future directions. *Curr. Opin. Psychol.* 15, 99–104. <https://doi.org/10.1016/j.copsyc.2017.02.023>
- Garfield, C.F., Duncan, G., Rutsohn, J., McDade, T.W., Adam, E.K., Coley, R.L., Chase-Lansdale, P.L., 2014. A longitudinal study of paternal mental health during transition to fatherhood as young adults. *Pediatrics* 133, 836–843. <https://doi.org/10.1542/peds.2013-3262>
- Garman, E.C., Cois, A., Tomlinson, M., Rotheram-Borus, M.J., Lund, C., 2019. Course of perinatal depressive symptoms among South African women: associations with child outcomes at 18 and 36 months. *Soc. Psychiatry Psychiatr. Epidemiol.* 54, 1111–1123. <https://doi.org/10.1007/s00127-019-01665-2>
- Gavin, N., Gaynes, B.N., Lohr, K.N., Meltzer-Brody, S., Gartlehner, G., Swinson, T., 2005. Perinatal depression: A systematic review of prevalence and incidence. *Obstet. Gynecol.* 106, 1071–1083. <https://doi.org/10.1097/01.AOG.0000183597.31630.db>
- Gavin, N.I., Meltzer-Brody, S., Glover, V., Gaynes, B., 2015. Is population-based identification of perinatal depression and anxiety desirable? A public health perspective on the perinatal depression care continuum, in: J. Milgrom & A. W. Gemmill (Ed.), *Identifying Perinatal Depression and Anxiety: Evidence-Based Practice in Screening, Psychosocial Assessment, and Management*. Wiley-Blackwell., pp. 11–31.
- GBD 2016 Disease and Injury Incidence and Prevalence Collaborators, 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 390, 1211–59. [https://doi.org/10.1016/S0140-6736\(17\)32154-2](https://doi.org/10.1016/S0140-6736(17)32154-2)
- Gehrman, P.R., Thase, M.E., Riemann, D., Perlis, M., 2010. Depressive disorders (Chapter 15), in: Winkelman, J.W., Plante, D.T. (Eds.), *Foundations of Psychiatric Sleep Medicine*. Cambridge University Press, Madison, pp. 247–265.
- Gentile, S., 2017. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. *Neuroscience* 342, 154–166.

- <https://doi.org/10.1016/j.neuroscience.2015.09.001>
- Gentile, S., Fusco, M.L., 2017. Untreated perinatal paternal depression: Effects on offspring. *Psychiatry Res.* 252, 325–332. <https://doi.org/10.1016/j.psychres.2017.02.064>
- Gerardin, P., Wendland, J., Bodeau, N., Galin, A., Bialobos, S., Tordjman, S., Mazet, P., Darbois, Y., Nizard, J., Dommergues, M., Cohen, D., 2011. Depression during pregnancy: Is the developmental impact earlier in boys? A prospective case-control study. *J. Clin. Psychiatry* 72, 378–387. <https://doi.org/10.4088/JCP.09m05724blu>
- Gettler, L.T., McDade, T.W., Feranil, A.B., Kuzawa, C.W., 2011. Longitudinal evidence that fatherhood decreases testosterone in human males. *Proc. Natl. Acad. Sci. U. S. A.* 108, 16194–16199. <https://doi.org/10.1073/pnas.1105403108>
- Giallo, R., Bahreinian, S., Brown, S., Cooklin, A., Kingston, D., Kozyrskyj, A., 2015a. Maternal depressive symptoms across early childhood and asthma in school children: Findings from a longitudinal Australian population based study. *PLoS One* 10, e0121459. <https://doi.org/10.1371/journal.pone.0121459>
- Giallo, R., Cooklin, A., Nicholson, J.M., 2014. Risk factors associated with trajectories of mothers' depressive symptoms across the early parenting period: An Australian population-based longitudinal study. *Arch. Womens. Ment. Health* 17, 115–125. <https://doi.org/10.1007/s00737-014-0411-1>
- Giallo, R., D'Esposito, F., Cooklin, A., Mensah, F., Lucas, N., Wade, C., Nicholson, J.M., 2013. Psychosocial risk factors associated with fathers' mental health in the postnatal period: Results from a population-based study. *Soc. Psychiatry Psychiatr. Epidemiol.* 48, 563–573. <https://doi.org/10.1007/s00127-012-0568-8>
- Giallo, R., Woolhouse, H., Gartland, D., Hiscock, H., Brown, S., 2015b. The emotional-behavioural functioning of children exposed to maternal depressive symptoms across pregnancy and early childhood: a prospective Australian pregnancy cohort study. *Eur. Child Adolesc. Psychiatry* 24, 1233–1244. <https://doi.org/10.1007/s00787-014-0672-2>
- Gibson, W.A., 1959. Three multivariate models: Factor analysis, latent structure analysis, and latent profile analysis. *Psychometrika* 24, 229–251. <https://doi.org/10.1007/BF02289845>
- Girchenko, P., Lahti, M., Tuovinen, S., Savolainen, K., Lahti, J., Binder, E.B., Reynolds, R.M., Entringer, S., Buss, C., Wadhwa, P.D., Hämäläinen, E., Kajantie, E., Pesonen, A.K., Villa, P.M., Laivuori, H., Räikkönen, K., 2017. Cohort Profile: Prediction and prevention of preeclampsia and intrauterine growth restriction (PREDO) study. *Int. J. Epidemiol.* 5, 1380–1381g. <https://doi.org/10.1093/ije/dyw154>
- Glasheen, C., Richardson, G.A., Kim, K.H., Larkby, C.A., Swartz, H.A., Day, N.L., 2013. Exposure to maternal pre- and postnatal depression and anxiety symptoms: Risk for major depression, anxiety disorders, and conduct disorder in adolescent offspring. *Dev. Psychopathol.* 25, 1045–1063. <https://doi.org/10.1017/S0954579413000369>
- Glover, V., 2014. Maternal depression, anxiety and stress during pregnancy and child outcome; What needs to be done. *Best Pract. Res. Clin. Obstet. Gynaecol.* 28, 25–35. <https://doi.org/10.1016/j.bpobgyn.2013.08.017>
- Glynn, L.M., Baram, T.Z., 2019. The influence of unpredictable, fragmented parental signals on the developing brain. *Front. Neuroendocrinol.* 53, 100736.

- <https://doi.org/10.1016/j.yfrne.2019.01.002>
- Glynn, L.M., Howland, M.A., Fox, M., 2018. Maternal programming: Application of a developmental psychopathology perspective. *Dev. Psychopathol.* 30, 905–919. <https://doi.org/10.1017/S0954579418000524>
- González-Mesa, E., Cuenca-Marín, C., Suarez-Arana, M., Tripliana-Serrano, B., Ibrahim-Díez, N., Gonzalez-Cazorla, A., Blasco-Alonso, M., 2019. Poor sleep quality is associated with perinatal depression. A systematic review of last decade scientific literature and meta-analysis. *J. Perinat. Med.* 47, 689–703. <https://doi.org/https://doi.org/10.1515/jpm-2019-0214>
- Goodman, J.H., 2004. Paternal postpartum depression, its relationship to maternal postpartum depression, and implications for family health. *J. Adv. Nurs.* 45, 26–35. <https://doi.org/10.1046/j.1365-2648.2003.02857.x>
- Goodman, J.H., Tyer-Viola, L., 2010. Detection, treatment, and referral of perinatal depression and anxiety by obstetrical providers. *J. Women's Heal.* 19, 477–490. <https://doi.org/10.1089/jwh.2008.1352>
- Goodman, R., 1997. The strengths and difficulties questionnaire: A research note. *J. Child Psychol. Psychiatry Allied Discip.* 38, 581–586. <https://doi.org/10.1111/j.1469-7610.1997.tb01545.x>
- Goodman, S.H., Gotlib, I.H., 1999. Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychol. Rev.* 106, 458–490. <https://doi.org/10.1037/0033-295X.106.3.458>
- Goodman, S.H., Rouse, M.H., Connell, A.M., Broth, M.R., Hall, C.M., Heyward, D., 2011. Maternal Depression and Child Psychopathology: A Meta-Analytic Review. *Clin. Child Fam. Psychol. Rev.* 14, 1–27. <https://doi.org/10.1007/s10567-010-0080-1>
- Goyal, D., Gay, C.L., Lee, K.A., 2007. Patterns of sleep disruption and depressive symptoms in new mothers. *J. Perinat. Neonatal Nurs.* 21, 123–129. <https://doi.org/10.1097/01.JPN.0000270629.58746.96>
- Greenwood, K.M., Hazendonk, K.M., 2004. Self-reported sleep during the third trimester of pregnancy. *Behav. Sleep Med.* 2, 191–204. [https://doi.org/10.1207/s15402010bsm0204\\_2](https://doi.org/10.1207/s15402010bsm0204_2)
- Gregory, A.M., O'Connor, T.G., 2002. Sleep Problems in Childhood: A Longitudinal Study of Developmental Change and Association with Behavioral Problems. *J. Am. Acad. Child Adolesc. Psychiatry* 41, 964–971. <https://doi.org/10.1097/00004583-200208000-00015>
- Gregory, A.M., Sadeh, A., 2012. Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Med. Rev.* 16, 129–136. <https://doi.org/10.1016/j.smrv.2011.03.007>
- Grekin, R., Brock, R.L., O'Hara, M.W., 2017. The effects of trauma on perinatal depression: Examining trajectories of depression from pregnancy through 24 months postpartum in an at-risk population. *J. Affect. Disord.* 218, 296–276. <https://doi.org/10.1016/j.jad.2017.04.051>
- Gress-Smith, J.L., Luecken, L.J., Lemery-Chalfant, K., Howe, R., 2012. Postpartum depression prevalence and impact on infant health, weight, and sleep in low-income and ethnic minority women and infants. *Matern. Child Health J.* 16, 887–893. <https://doi.org/10.1007/s10995-011-0812-y>
- Grigoriadis, S., VonderPorten, E.H., Mamisashvili, L., Tomlinson, G., Dennis, C.L., Koren, G., Steiner, M., Mousmanis, P., Cheung, A., Radford, K., Martinovic, J.,

- Ross, L.E., 2013. The impact of maternal depression during pregnancy on perinatal outcomes: A systematic review and meta-analysis. *J. Clin. Psychiatry* 74, e321-41. <https://doi.org/10.4088/JCP.12r07968>
- Gross, H.E., Shaw, D.S., Moilanen, K.L., Dishion, T.J., Wilson, M.N., 2008. Reciprocal Models of Child Behavior and Depressive Symptoms in Mothers and Fathers in a Sample of Children at Risk for Early Conduct Problems. *J. Fam. Psychol.* 22, 742–751. <https://doi.org/10.1037/a0013514>
- Grzywacz, J.G., Hovey, J.D., Seligman, L.D., Arcury, T.A., Quandt, S.A., 2006. Evaluating short-form versions of the CES-D for measuring depressive symptoms among immigrants from Mexico. *Hisp. J. Behav. Sci.* 28, 404–424. <https://doi.org/10.1177/0739986306290645>
- Guintivano, J., Arad, M., Gould, T.D., Payne, J.L., Kaminsky, Z.A., 2014. Antenatal prediction of postpartum depression with blood DNA methylation biomarkers. *Mol. Psychiatry* 19, 560–567. <https://doi.org/10.1038/mp.2013.62>
- Guintivano, J., Putnam, K.T., Sullivan, P.F., Meltzer-Brody, S., 2019. The international postpartum depression: action towards causes and treatment (PACT) consortium. *Int. Rev. Psychiatry* 31, 229–236. <https://doi.org/10.1080/09540261.2018.1551191>
- Guintivano, J., Sullivan, P.F., Stuebe, A.M., Penders, T., Thorp, J., Rubinow, D.R., Meltzer-Brody, S., 2018. Adverse life events, psychiatric history, and biological predictors of postpartum depression in an ethnically diverse sample of postpartum women. *Psychol. Med.* 48, 1190–1200. <https://doi.org/10.1017/S0033291717002641>
- Gunlicks, M.L., Weissman, M.M., 2008. Change in child psychopathology with improvement in parental depression: A systematic review. *J. Am. Acad. Child Adolesc. Psychiatry* 47, 379–389. <https://doi.org/10.1097/CHI.0b013e3181640805>
- Gutierrez-Galve, L., Stein, A., Hanington, L., Heron, J., Lewis, G., O'Farrelly, C., Ramchandani, P.G., 2019. Association of Maternal and Paternal Depression in the Postnatal Period with Offspring Depression at Age 18 Years. *JAMA Psychiatry* 76, 290–296. <https://doi.org/10.1001/jamapsychiatry.2018.3667>
- Gutierrez-Galve, L., Stein, A., Hanington, L., Heron, J., Ramchandani, P., 2015. Paternal Depression in the Postnatal Period and Child Development: Mediators and Moderators. *Pediatrics* 135, e399–e347. <https://doi.org/10.1542/peds.2014-2411>
- Hadjimarkou, M.M., Benham, R., Schwarz, J.M., Holder, M.K., Mong, J.A., 2008. Estradiol suppresses rapid eye movement sleep and activation of sleep-active neurons in the ventrolateral preoptic area. *Eur. J. Neurosci.* 27, 1780–1792. <https://doi.org/10.1111/j.1460-9568.2008.06142.x>
- Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry* 23, 56–62. <https://doi.org/10.1136/jnnp.23.1.56>
- Hammerton, G., Mahedy, L., Mars, B., Harold, G.T., Thapar, A., Zammit, S., Collishaw, S., 2015. Association between Maternal Depression Symptoms across the First Eleven Years of Their Child's Life and Subsequent Offspring Suicidal Ideation. *PLoS One* 10, e0131885. <https://doi.org/10.1371/journal.pone.0131885>
- Hanington, L., Heron, J., Stein, A., Ramchandani, P., 2012. Parental depression and child outcomes - is marital conflict the missing link? *Child. Care. Health Dev.* 38, 520–529. <https://doi.org/10.1111/j.1365-2214.2011.01270.x>

- Hanington, L., Ramchandani, P., Stein, A., 2010. Parental depression and child temperament: Assessing child to parent effects in a longitudinal population study. *Infant Behav. Dev.* 33, 88–95. <https://doi.org/10.1016/j.infbeh.2009.11.004>
- Hannigan, L.J., Eilertsen, E.M., Gjerde, L.C., Reichborn-Kjennerud, T., Eley, T.C., Rijdsdijk, F. V., Ystrom, E., McAdams, T.A., 2018. Maternal prenatal depressive symptoms and risk for early-life psychopathology in offspring: genetic analyses in the Norwegian Mother and Child Birth Cohort Study. *The Lancet Psychiatry* 5, 808–15. [https://doi.org/10.1016/S2215-0366\(18\)30225-6](https://doi.org/10.1016/S2215-0366(18)30225-6)
- Hayes, L.J., Goodman, S.H., Carlson, E., 2013. Maternal antenatal depression and infant disorganized attachment at 12 months. *Attach. Hum. Dev.* 15, 133–153. <https://doi.org/10.1080/14616734.2013.743256>
- Hedman, C., Pohjasvaara, T., Tolonen, U., Suhonen-Malm, A.S., Myllylä, V. V., 2002. Effects of pregnancy on mothers' sleep. *Sleep Med.* 3, 37–42. [https://doi.org/10.1016/S1389-9457\(01\)00130-7](https://doi.org/10.1016/S1389-9457(01)00130-7)
- Heim, C., Binder, E.B., 2012. Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene-environment interactions, and epigenetics. *Exp. Neurol.* 233, 102–111. <https://doi.org/10.1016/j.expneurol.2011.10.032>
- Heiss, C.N., Olofsson, L.E., 2019. The role of the gut microbiota in development, function and disorders of the central nervous system and the enteric nervous system. *J. Neuroendocrinol.* 31, e12684. <https://doi.org/10.1111/jne.12684>
- Hertenstein, E., Feige, B., Gmeiner, T., Kienzler, C., Spiegelhalder, K., Johann, A., Jansson-Fröjmark, M., Palagini, L., Rücker, G., Riemann, D., Baglioni, C., 2019. 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>
- Herzenberg, L.A., Bianchi, D.W., Schröder, J., Cann, H.M., Iverson, G.M., 1979. Fetal cells in the blood of pregnant women: Detection and enrichment by fluorescence-activated cell sorting. *Proc. Natl. Acad. Sci. U. S. A.* 76, 1453–1455. <https://doi.org/10.1073/pnas.76.3.1453>
- Holi, M.M., Sammallahti, P.R., Aalberg, V.A., 1998. A Finnish validation study of the SCL-90. *Acta Psychiatr. Scand.* 97, 42–46. <https://doi.org/10.1111/j.1600-0447.1998.tb09961.x>
- Horowitz, J.A., Goodman, J., 2004. A longitudinal study of maternal postpartum depression symptoms. *Res. Theory Nurs. Pract.* 18, 149–163. <https://doi.org/10.1891/rtnp.18.2.149.61285>
- Howard, L.M., Challacombe, F., 2018. Effective treatment of postnatal depression is associated with normal child development. *The Lancet Psychiatry* 5, 95–97. [https://doi.org/10.1016/S2215-0366\(18\)30008-7](https://doi.org/10.1016/S2215-0366(18)30008-7)
- Howard, L.M., Molyneaux, E., Dennis, C.L., Rochat, T., Stein, A., Milgrom, J., 2014. Non-psychotic mental disorders in the perinatal period. *Lancet* 384, 1775–88. [https://doi.org/10.1016/S0140-6736\(14\)61276-9](https://doi.org/10.1016/S0140-6736(14)61276-9)
- Howard, L.M., Oram, S., Galley, H., Trevillion, K., Feder, G., 2013. Domestic Violence and Perinatal Mental Disorders: A Systematic Review and Meta-Analysis. *PLoS Med.* 10, e1001452. <https://doi.org/10.1371/journal.pmed.1001452>
- Howard, L.M., Ryan, E.G., Trevillion, K., Anderson, F., Bick, D., Bye, A., Byford, S., O'Connor, S., Sands, P., Demilew, J., Milgrom, J., Pickles, A., 2018.

- Accuracy of the Whooley questions and the Edinburgh Postnatal Depression Scale in identifying depression and other mental disorders in early pregnancy. *Br. J. Psychiatry* 212, 50–56. <https://doi.org/10.1192/bjp.2017.9>
- Hughes, C., T. Devine, R., Foley, S., D. Ribner, A., Mesman, J., Blair, C., 2020. Couples becoming parents: Trajectories for psychological distress and buffering effects of social support. *J. Affect. Disord.* 265, 372–380. <https://doi.org/10.1016/j.jad.2020.01.133>
- Huhdanpää, H., Morales-Muñoz, I., Aronen, E.T., Pölkki, P., Saarenpää-Heikkilä, O., Paunio, T., Kylliäinen, A., Paavonen, E.J., 2019. Sleep Difficulties in Infancy Are Associated with Symptoms of Inattention and Hyperactivity at the Age of 5 Years: A Longitudinal Study. *J. Dev. Behav. Pediatr.* 40, 432–440. <https://doi.org/10.1097/DBP.0000000000000684>
- IBM Corp., 2017. IBM SPSS Statistics for Windows.
- Ikeda, H., Kayashima, K., Sasaki, T., Kashima, S., Koyama, F., 2017. The relationship between sleep disturbances and depression in daytime workers: A cross-sectional structured interview survey. *Ind. Health* 55, 455–459. <https://doi.org/10.2486/indhealth.2017-0055>
- Irwin, M., Artin, K.H., Oxman, M.N., 1999. Screening for depression in the older adult: Criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Arch. Intern. Med.* 159, 1701–1704. <https://doi.org/10.1001/archinte.159.15.1701>
- Jarde, A., Morais, M., Kingston, D., Giallo, R., MacQueen, G.M., Giglia, L., Beyene, J., Wang, Y., McDonald, S.D., 2016. Neonatal outcomes in women with untreated antenatal depression compared with women without depression: A systematic review and meta-analysis. *JAMA Psychiatry* 73, 826–837. <https://doi.org/10.1001/jamapsychiatry.2016.0934>
- Johns M. W., 1991. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 14, 540–545. <https://doi.org/10.1016/j.sleep.2007.08.004>
- Johnson, S.M., 2004. *The Practice of Emotionally Focused Couple Therapy. Creating connection.* Taylor & Francis Books, Inc.
- Jomeen, J., Martin, C., 2007. Assessment and relationship of sleep quality to depression in early pregnancy. *J. Reprod. Infant Psychol.* 25, 87–99. <https://doi.org/10.1080/02646830601117308>
- Jones, A., 2019. Help Seeking in the Perinatal Period: A Review of Barriers and Facilitators. *Soc. Work Public Health* 34, 596–605. <https://doi.org/10.1080/19371918.2019.1635947>
- Jones, N.A., Field, T., Davalos, M., 2000. Right frontal EEG asymmetry and lack of empathy in preschool children of depressed mothers. *Child Psychiatry Hum. Dev.* 30, 189–204. <https://doi.org/10.1023/A:1021399605526>
- Kadesjö, B., Janols, L.O., Korkman, M., Mickelsson, K., Strand, G., Trillingsgaard, A., Gillberg, C., 2004. The FTF (Five to Fifteen): The development of a parent questionnaire for the assessment of ADHD and comorbid conditions. *Eur. Child Adolesc. Psychiatry, Suppl.* 3, III/3-III/13. <https://doi.org/10.1007/s00787-004-3002-2>
- Kalmbach, D.A., Cheng, P., Ong, J.C., Ciesla, J.A., Kingsberg, S.A., Sangha, R., Swanson, L.M., O'Brien, L.M., Roth, T., Drake, C.L., 2020. Depression and suicidal ideation in pregnancy: exploring relationships with insomnia, short sleep, and nocturnal rumination. *Sleep Med.* 65, 62–73. <https://doi.org/10.1016/j.sleep.2019.07.010>

- Kane, P., Garber, J., 2004. The relations among depression in fathers, children's psychopathology, and father-child conflict: A meta-analysis. *Clin. Psychol. Rev.* 24, 339–360. <https://doi.org/10.1016/j.cpr.2004.03.004>
- Karlsson, L., Nousiainen, N., Scheinin, N.M., Maksimow, M., Salmi, M., Lehto, S.M., Tolvanen, M., Lukkarinen, H., Karlsson, H., 2017. Cytokine profile and maternal depression and anxiety symptoms in mid-pregnancy—the FinnBrain Birth Cohort Study. *Arch. Womens. Ment. Health* 20, 39–48. <https://doi.org/10.1007/s00737-016-0672-y>
- Karlsson, L., Tolvanen, M., Scheinin, N.M., Uusitupa, H.-M., Korja, R., Ekholm, E., Tuulari, J.J., Pajulo, M., Huotilainen, M., Paunio, T., Karlsson, H., FinnBrain Birth Cohort Study Group, 2018. Cohort Profile: The FinnBrain Birth Cohort Study (FinnBrain). *Int. J. Epidemiol.* 47, 15–16j. <https://doi.org/10.1093/ije/dyx173>
- Kataja, E.L., Karlsson, L., Leppänen, J.M., Pelto, J., Häikiö, T., Nolvi, S., Pesonen, H., Parsons, C.E., Hyönä, J., Karlsson, H., 2020. Maternal Depressive Symptoms During the Pre- and Postnatal Periods and Infant Attention to Emotional Faces. *Child Dev.* 91, e475–e490. <https://doi.org/10.1111/cdev.13152>
- Kendler, K.S., Gatz, M., Gardner, C.O., Pedersen, N.L., 2006. A Swedish national twin study of lifetime major depression. *Am. J. Psychiatry* 163, 109–114. <https://doi.org/10.1176/appi.ajp.163.1.109>
- Kersten-Alvarez, L.E., Hosman, C.M.H., Riksen-Walraven, J.M., Van Doesum, K.T.M., Smeekens, S., Hoefnagels, C., 2012. Early school outcomes for children of postpartum depressed mothers: Comparison with a community sample. *Child Psychiatry Hum. Dev.* 43, 201–218. <https://doi.org/10.1007/s10578-011-0257-y>
- Khazaie, H., Ghadami, M.R., Knight, D.C., Emamian, F., Tahmasian, M., 2013. Insomnia treatment in the third trimester of pregnancy reduces postpartum depression symptoms: A randomized clinical trial. *Psychiatry Res.* 210, 901–905.
- Kim, P., Swain, J.E., 2007. Sad dads: paternal postpartum depression. *Psychiatry (Edgmont)*. 4, 35–47.
- Kingsbury, A.M., Plotnikova, M., Clavarino, A., Mamun, A., Najman, J.M., 2018. Social adversity in pregnancy and trajectories of women's depressive symptoms: A longitudinal study. *Women and Birth* 31, 52–58. <https://doi.org/10.1016/j.wombi.2017.06.016>
- Kingston, D., Kehler, H., Austin, M.P., Mughal, M.K., Wajid, A., Vermeyden, L., Benzies, K., Brown, S., Stuart, S., Giallo, R., 2018. Trajectories of maternal depressive symptoms during pregnancy and the first 12 months postpartum and child externalizing and internalizing behavior at three years. *PLoS One* 13, e0195365. <https://doi.org/10.1371/journal.pone.0195365>
- Kiviruusu, O., Pietikäinen, J.T., Kylliäinen, A., Pölkki, P., Saarenpää-Heikkilä, O., Marttunen, M., Paunio, T., Paavonen, E.J., 2020. Trajectories of mothers' and fathers' depressive symptoms from pregnancy to 24 months postpartum. *J. Affect. Disord.* 629–637. <https://doi.org/10.1016/j.jad.2019.09.038>
- Ko, J.Y., Farr, S.L., Dietz, P.M., Robbins, C.L., 2012. Depression and treatment among U.S. pregnant and nonpregnant women of reproductive age, 2005–2009. *J. Women's Heal.* 21, 830–836. <https://doi.org/10.1089/jwh.2011.3466>
- Korja, R., Nolvi, S., Grant, K.A., McMahon, C., 2017. The Relations Between

- Maternal Prenatal Anxiety or Stress and Child's Early Negative Reactivity or Self-Regulation: A Systematic Review. *Child Psychiatry Hum. Dev.* 48, 851–869. <https://doi.org/10.1007/s10578-017-0709-0>
- 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. <https://doi.org/10.1371/journal.pone.0207856>
- Koutra, K., Roumeliotaki, T., Kyriklaki, A., Kampouri, M., Sarri, K., Vassilaki, M., Bitsios, P., Kogevinas, M., Chatzi, L., 2017. Maternal depression and personality traits in association with child neuropsychological and behavioral development in preschool years: Mother-child cohort (Rhea Study) in Crete, Greece. *J. Affect. Disord.* 217, 89–98. <https://doi.org/10.1016/j.jad.2017.04.002>
- Kozinszky, Z., Dudas, R.B., 2015. Validation studies of the Edinburgh Postnatal Depression Scale for the antenatal period. *J. Affect. Disord.* 176, 95–105. <https://doi.org/10.1016/j.jad.2015.01.044>
- Kroenke, K., Spitzer, R.L., Williams, J.B.W., 2001. The PHQ-9: Validity of a brief depression severity measure. *J. Gen. Intern. Med.* 16, 606–613. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
- Kvalevaag, A.L., Ramchandani, P.G., Hove, O., Assmus, J., Eberhard-Gran, M., Biringer, E., 2013. Paternal mental health and socioemotional and behavioral development in their children. *Pediatrics* 131, e463–e469. <https://doi.org/10.1542/peds.2012-0804>
- Labonte, B., Yerko, V., Gross, J., Mechawar, N., Meaney, M.J., Szyf, M., Turecki, G., 2012. Differential glucocorticoid receptor exon 1 B, 1 C, and 1 H expression and methylation in suicide completers with a history of childhood abuse. *Biol. Psychiatry* 72, 41–48. <https://doi.org/10.1016/j.biopsych.2012.01.034>
- Lahti, M., Savolainen, K., Tuovinen, S., Pesonen, A.K., Lahti, J., Heinonen, K., Hämäläinen, E., Laivuori, H., Villa, P.M., Reynolds, R.M., Kajantie, E., Räikkönen, K., 2017. Maternal Depressive Symptoms During and After Pregnancy and Psychiatric Problems in Children. *J. Am. Acad. Child Adolesc. Psychiatry* 56, 30–39. <https://doi.org/10.1016/j.jaac.2016.10.007>
- Lautarescu, A., Craig, M.C., Glover, V., 2020. Prenatal stress: Effects on fetal and child brain development, in: *International Review of Neurobiology*. pp. 17–40. <https://doi.org/10.1016/bs.irn.2019.11.002>
- Lawson, A., Murphy, K.E., Sloan, E., Uleryk, E., Dalfen, A., 2015. The relationship between sleep and postpartum mental disorders: A systematic review. *J. Affect. Disord.* 176, 65–77. <https://doi.org/10.1016/j.jad.2015.01.017>
- Leathers, S.J., Kelley, M.A., 2000. Unintended pregnancy and depressive symptoms among first-time mothers and fathers. *Am. J. Orthopsychiatry* 70, 523–531. <https://doi.org/10.1037/h0087671>
- Lee, C.T., Stroo, M., Fuemmeler, B., Malhotra, R., Østbye, T., 2014. Trajectories of Depressive Symptoms Over 2 Years Postpartum Among Overweight or Obese Women. *Women's Heal. Issues* 559–566. <https://doi.org/10.1016/j.whi.2014.05.008>
- Lee, K.A., 1998. Alterations in sleep during pregnancy and postpartum: A review of 30 years of research. *Sleep Med. Rev.* 2, 231–242. [https://doi.org/10.1016/S1087-0792\(98\)90010-7](https://doi.org/10.1016/S1087-0792(98)90010-7)

## References

- Lee, K.A., Gay, C.L., 2004. Sleep in late pregnancy predicts length of labor and type of delivery. *Am. J. Obstet. Gynecol.* 191, 2041–6. <https://doi.org/10.1016/j.ajog.2004.05.086>
- Lee, K.A., McEnany, G., Zaffke, M.E., 2000a. REM Sleep and Mood State in Childbearing Women: Sleepy or Weepy? *Sleep* 23, 1–9. <https://doi.org/10.1093/sleep/23.7.1b>
- Lee, K.A., Zaffke, M.E., Baratte-Beebe, K., 2001. Restless legs syndrome and sleep disturbance during pregnancy: The role of folate and iron. *J. Women's Heal. Gender-Based Med.* 10, 335–341. <https://doi.org/10.1089/152460901750269652>
- Lee, K.A., Zaffke, M.E., McEnany, G., 2000b. Parity and sleep patterns during and after pregnancy. *Obstet. Gynecol.* 95, 14–8. [https://doi.org/10.1016/S0029-7844\(99\)00486-X](https://doi.org/10.1016/S0029-7844(99)00486-X)
- Lee, S.J., Taylor, C.A., Bellamy, J.L., 2012. Paternal depression and risk for child neglect in father-involved families of young children. *Child Abus. Negl.* 36, 461–469. <https://doi.org/10.1016/j.chiabu.2012.04.002>
- Leijten, P., Gardner, F., Melendez-Torres, G.J., van Aar, J., Hutchings, J., Schulz, S., Knerr, W., Overbeek, G., 2019. Meta-Analyses: Key Parenting Program Components for Disruptive Child Behavior. *J. Am. Acad. Child Adolesc. Psychiatry* 58, 180–190. <https://doi.org/10.1016/j.jaac.2018.07.900>
- Letourneau, N.L., Tramonte, L., Willms, J.D., 2013. Maternal depression, family functioning and children's longitudinal development. *J. Pediatr. Nurs.* 28, 223–234. <https://doi.org/10.1016/j.pedn.2012.07.014>
- Leung, B.M.Y., Letourneau, N.L., Giesbrecht, G.F., Ntanda, H., Hart, M., 2017. Predictors of Postpartum Depression in Partnered Mothers and Fathers from a Longitudinal Cohort. *Community Ment. Health J.* 53, 420–431. <https://doi.org/10.1007/s10597-016-0060-0>
- Li, H., Bowen, A., Bowen, R., Balbuena, L., Feng, C., Bally, J., Muhajarine, N., 2020. Mood instability during pregnancy and postpartum: a systematic review. *Arch. Womens. Ment. Health* 23, 29–41. <https://doi.org/10.1007/s00737-019-00956-6>
- Liu, C., Cnattingius, S., Bergström, M., Östberg, V., Hjern, A., 2016. Prenatal parental depression and preterm birth: a national cohort study. *BJOG An Int. J. Obstet. Gynaecol.* 123, 1973–1982. <https://doi.org/10.1111/1471-0528.13891>
- Liu, Y., Kaaya, S., Chai, J., McCoy, D.C., Surkan, P.J., Black, M.M., Sutter-Dallay, A.L., Verdoux, H., Smith-Fawzi, M.C., 2017. Maternal depressive symptoms and early childhood cognitive development: A meta-analysis. *Psychol. Med.* 47, 680–689. <https://doi.org/10.1017/S003329171600283X>
- Lockwood Estrin, G., Ryan, E.G., Trevillion, K., Demilew, J., Bick, D., Pickles, A., Howard, L.M., 2019. Young pregnant women and risk for mental disorders: findings from an early pregnancy cohort. *BJPsych Open* 5, 1–7. <https://doi.org/10.1192/bjo.2019.6>
- Lovejoy, M.C., Graczyk, P.A., O'Hare, E., Neuman, G., 2000. Maternal depression and parenting behavior: A meta-analytic review. *Clin. Psychol. Rev.* 20, 561–592. [https://doi.org/10.1016/S0272-7358\(98\)00100-7](https://doi.org/10.1016/S0272-7358(98)00100-7)
- Luca, D.L., Garlow, N., Staats, C., Margiotta, C., Zivin, K., 2019. Societal Costs of Untreated Perinatal Mood and Anxiety Disorders in the United States. Cambridge, MA: Mathematica Policy Research.
- Lyngsøe, B.K., Rytter, D., Munk-Olsen, T., Vestergaard, C.H., Christensen, K.S.,

- Bech, B.H., 2019. Maternal depression and primary healthcare use for children: A population-based cohort study in Denmark. *Br. J. Gen. Pract.* 69, e182–e189. <https://doi.org/10.3399/bjgp18X700733>
- Madigan, S., Oatley, H., Racine, N., Fearon, R.M.P., Schumacher, L., Akbari, E., Cooke, J.E., Tarabulsky, G.M., 2018. A Meta-Analysis of Maternal Prenatal Depression and Anxiety on Child Socioemotional Development. *J. Am. Acad. Child Adolesc. Psychiatry* 57, 645–657. <https://doi.org/10.1016/j.jaac.2018.06.012>
- Maguire, J., Mody, I., 2008. GABAAR Plasticity during Pregnancy: Relevance to Postpartum Depression. *Neuron* 59, 207–213. <https://doi.org/10.1016/j.neuron.2008.06.019>
- Manber, R., Bei, B., Simpson, N., Asarnow, L., Rangel, E., Sit, A., Lyell, D., 2019. Cognitive Behavioral Therapy for Prenatal Insomnia. *Obstet. Gynecol.* 133, 911–919. <https://doi.org/10.1097/AOG.0000000000003216>
- Manber, R., Edinger, J.D., Gress, J.L., San Pedro-Salcedo, M.G., Kuo, T.F., Kalista, T., 2008. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep* 31, 489–495. <https://doi.org/10.1093/sleep/31.4.489>
- Manconi, M., Govoni, V., De Vito, A., Tiberio Economou, N., Cesnik, E., Mollica, G., Granieri, E., 2004. Pregnancy as a risk factor for restless legs syndrome. *Sleep Med.* 5, 305–308. <https://doi.org/10.1016/j.sleep.2004.01.013>
- Marcus, S., Lopez, J.F., McDonough, S., MacKenzie, M.J., Flynn, H., Neal, C.R., Gahagan, S., Volling, B., Kaciroti, N., Vazquez, D.M., 2011. Depressive symptoms during pregnancy: Impact on neuroendocrine and neonatal outcomes. *Infant Behav. Dev.* 34, 26–34. <https://doi.org/10.1016/j.infbeh.2010.07.002>
- Marcus, S.M., 2009. Depression during pregnancy: rates, risks and consequences--Motherisk Update 2008. *Can. J. Clin. Pharmacol.* 16, e15–e22.
- Markkula, N., Suvisaari, J., Saarni, S.I., Pirkola, S., Peña, S., Saarni, S., Ahola, K., Mattila, A.K., Viertiö, S., Strehle, J., Koskinen, S., Härkänen, T., 2015. Prevalence and correlates of major depressive disorder and dysthymia in an eleven-year follow-up - Results from the Finnish Health 2011 Survey. *J. Affect. Disord.* 173, 73–80. <https://doi.org/10.1016/j.jad.2014.10.015>
- Marques, M., Bos, S., Soares, M.J., Maia, B., Pereira, A.T., Valente, J., Gomes, A.A., Macedo, A., Azevedo, M.H., 2011. Is insomnia in late pregnancy a risk factor for postpartum depression/depressive symptomatology? *Psychiatry Res.* 186, 272–280. <https://doi.org/10.1016/j.psychres.2010.06.029>
- Martins, C., Gaffan, E.A., 2000. Effects of early maternal depression on patterns of infant-mother attachment: A meta-analytic investigation. *J. Child Psychol. Psychiatry Allied Discip.* 41, 737–746. <https://doi.org/10.1017/S0021963099005958>
- Mascaro, J.S., Hackett, P.D., Rilling, J.K., 2014. Differential neural responses to child and sexual stimuli in human fathers and non-fathers and their hormonal correlates. *Psychoneuroendocrinology* 46, 153–163. <https://doi.org/10.1016/j.psyneuen.2014.04.014>
- Matijasevich, A., Anselmi, L., Barros, A.J.D., Barros, F.C., Santos, I.S., Murray, J., Cooper, P.J., 2015. Trajectories of maternal depression and offspring psychopathology at 6 years: 2004 Pelotas cohort study. *J. Affect. Disord.* 174, 424–431.
- Matthey, S., Barnett, B., Kavanagh, D.J., Howie, P., 2001. Validation of the

- Edinburgh Postnatal Depression Scale for men, and comparison of item endorsement with their partners. *J. Affect. Disord.* 64, 175–184. [https://doi.org/10.1016/S0165-0327\(00\)00236-6](https://doi.org/10.1016/S0165-0327(00)00236-6)
- Matthey, S., Barnett, B., Ungerer, J., Waters, B., 2000. Paternal and maternal depressed mood during the transition to parenthood. *J. Affect. Disord.* 60, 75–85. [https://doi.org/10.1016/S0165-0327\(99\)00159-7](https://doi.org/10.1016/S0165-0327(99)00159-7)
- Matthey S, Henshaw C, Elliott S, Barnett B. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale - Implications for clinical and research practice. *Arch Womens Ment Health.* 2006;9:309–15.
- McCall-Hosenfeld, J.S., Phiri, K., Schaefer, E., Zhu, J., Kjerulff, K., 2016. Trajectories of Depressive Symptoms Throughout the Peri-and Postpartum Period: Results from the First Baby Study. *J. Women’s Heal.* 25, 1112–1121. <https://doi.org/10.1089/jwh.2015.5310>
- McDaniel, B.T., Teti, D.M., 2012. Coparenting quality during the first three months after birth: The role of infant sleep quality. *J. Fam. Psychol.* 26, 886895. <https://doi.org/10.1037/a0030707>
- McFadden, D., 1974. Conditional logit analysis of qualitative choice behaviour, in: Zarembka, P. (Ed.), *Frontiers in Econometrics*. Wiley, New York.
- McGrath, J.M., Records, K., Rice, M., 2008. Maternal depression and infant temperament characteristics. *Infant Behav. Dev.* 31, 71–80. <https://doi.org/10.1016/j.infbeh.2007.07.001>
- Meaney, M.J., 2018. Perinatal maternal depressive symptoms as an issue for population health. *Am. J. Psychiatry* 185, 297–317. <https://doi.org/10.1176/appi.ajp.2018.17091031>
- Mehta, D., Rex-Haffner, M., Sondergaard, H.B., Pinborg, A., Binder, E.B., Frokjaer, V.G., 2019. Evidence for oestrogen sensitivity in perinatal depression: Pharmacological sex hormone manipulation study. *Br. J. Psychiatry* 215, 519–527. <https://doi.org/10.1192/bjp.2018.234>
- Meltzer-Brody, S., Colquhoun, H., Riesenber, R., Epperson, C.N., Deligiannidis, K.M., Rubinow, D.R., Li, H., Sankoh, A.J., Clemson, C., Schacterle, A., Jonas, J., Kaner, S., 2018a. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet* 392, 1058–70. [https://doi.org/10.1016/S0140-6736\(18\)31551-4](https://doi.org/10.1016/S0140-6736(18)31551-4)
- Meltzer-Brody, S., Howard, L.M., Bergink, V., Vigod, S., Jones, I., Munk-Olsen, T., Honikman, S., Milgrom, J., 2018b. Postpartum psychiatric disorders. *Nat. Rev. Dis. Prim.* 4, 1–18. <https://doi.org/10.1038/nrdp.2018.22>
- Menting, A.T.A., Orobio de Castro, B., Matthys, W., 2013. Effectiveness of the Incredible Years parent training to modify disruptive and prosocial child behavior: A meta-analytic review. *Clin. Psychol. Rev.* 33, 901–913. <https://doi.org/10.1016/j.cpr.2013.07.006>
- Mezulis, A.H., Hyde, J.S., Clark, R., 2004. Father involvement moderates the effect of maternal depression during a child’s infancy on child behavior problems in kindergarten. *J. Fam. Psychol.* 18, 575–588. <https://doi.org/10.1037/0893-3200.18.4.575>
- Milgrom, J., Westley, D.T., McCloud, P.I., 1995. Do infants of depressed mothers cry more than other infants? *J. Paediatr. Child Health* 31, 218–221. <https://doi.org/10.1111/j.1440-1754.1995.tb00789.x>
- Miller-Graff, L.E., Cheng, P., 2017. Consequences of violence across the lifespan: Mental health and sleep quality in pregnant women. *Psychol. Trauma Theory,*

- Res. Pract. Policy 9, 587–595. <https://doi.org/10.1037/tra0000252>
- Mindell, J.A., Cook, R.A., Nikolovski, J., 2015. Sleep patterns and sleep disturbances across pregnancy. *Sleep Med.* 16, 483–488. <https://doi.org/10.1016/j.sleep.2014.12.006>
- Moehler, E., Kagan, J., Parzer, P., Brunner, R., Reck, C., Wiebel, A., Poustka, L., Resch, F., 2007. Childhood behavioral inhibition and maternal symptoms of depression. *Psychopathology* 40, 446–452. <https://doi.org/10.1159/000107429>
- Molgora, S., Fenaroli, V., Malgaroli, M., Saita, E., 2017. Trajectories of Postpartum Depression in Italian First-Time Fathers. *Am. J. Mens. Health* 11, 880–887. <https://doi.org/10.1177/1557988316677692>
- Mong, J.A., Cusmano, D.M., 2016. Sex differences in sleep: Impact of biological sex and sex steroids. *Philos. Trans. R. Soc. B Biol. Sci.* 371, 20150110. <https://doi.org/10.1098/rstb.2015.0110>
- Montgomery-Downs, H.E., Insana, S.P., Clegg-Kraynok, M.M., Mancini, L.M., 2010. Normative longitudinal maternal sleep: The first 4 postpartum months. *Am. J. Obstet. Gynecol.* 203, e1-7. <https://doi.org/10.1016/j.ajog.2010.06.057>
- Mora, P.A., Bennett, I.M., Elo, I.T., Mathew, L., Coyne, J.C., Culhane, J.F., 2009. Distinct trajectories of perinatal depressive symptomatology: Evidence from growth mixture modeling. *Am. J. Epidemiol.* 169, 24–32. <https://doi.org/10.1093/aje/kwn283>
- Morales-Muñoz, I., Lemola, S., Saarenpää-Heikkilä, O., Kylliäinen, A., Pölkki, P., Paunio, T., Broome, M.R., Paavonen, E.J., 2020. Parent-reported early sleep problems and internalising, externalising and dysregulation symptoms in toddlers. *BMJ Paediatr. Open* 4, e000622. <https://doi.org/10.1136/bmjpo-2019-000622>
- Morales-Muñoz, I., Saarenpää-Heikkilä, O., Kylliäinen, A., Pölkki, P., Porkka-Heiskanen, T., Paunio, T., Paavonen, E.J., 2018. The effects of maternal risk factors during pregnancy on the onset of sleep difficulties in infants at 3 months old. *J. Sleep Res.* 27, e12696. <https://doi.org/10.1111/jsr.12696>
- Murray, L., Fearon, P., Cooper, P., 2015. Postnatal Depression, Mother–Infant Interactions, and Child Development Prospects for Screening and Treatment, in: Milgrom, J., Gemmill, A.W. (Eds.), *Identifying Perinatal Depression and Anxiety: Evidence-Based Practice in Screening, Psychosocial Assessment and Management*. John Wiley & Sons, Incorporated, pp. 195–227.
- Murray, L., Sinclair, D., Cooper, P., Ducournau, P., Turner, P., Stein, A., 1999. The socioemotional development of 5-year-old children of postnatally depressed mothers. *J. Child Psychol. Psychiatry Allied Discip.* 40, 1259–1271. <https://doi.org/10.1017/S002196309900476X>
- Muthen, L.K., Muthen, B.O., 1998. *MPlus User's Guide*.
- Mychasiuk, R., Harker, A., Ilnytsky, S., Gibb, R., 2013. Paternal stress prior to conception alters DNA methylation and behaviour of developing rat offspring. *Neuroscience* 241, 100–105. <https://doi.org/10.1016/j.neuroscience.2013.03.025>
- Nagelkerke, N.J.D., 1991. A note on a general definition of the coefficient of determination. *Biometrika* 78, 691–692. <https://doi.org/10.1093/biomet/78.3.691>
- Nath, S., Psychogiou, L., Kuyken, W., Ford, T., Ryan, E., Russell, G., 2016. The prevalence of depressive symptoms among fathers and associated risk factors during the first seven years of their child's life: Findings from the Millennium Cohort Study. *BMC Public Health* 16, 509. <https://doi.org/10.1186/s12889-016->

3168-9

- National Institute for Health and Care Excellence, 2014. Antenatal and postnatal mental health: clinical management and service guidance. CG192.
- National Sleep Foundation, 2007. NSF 2007 Sleep in America Poll.
- Naughton, M.F.A., Maybery, D.J., Goodyear, M., 2018. Prevalence of mental illness within families in a regional child-focused mental health service. *Int. J. Ment. Health Nurs.* 27, 901–910. <https://doi.org/10.1111/inm.12386>
- Nemoda, Z., Szyf, M., 2017. Epigenetic Alterations and Prenatal Maternal Depression. *Birth Defects Res.* 109, 888–897. <https://doi.org/10.1002/bdr2.1081>
- Netsi, E., Pearson, R.M., Murray, L., Cooper, P., Craske, M.G., Stein, A., 2018. Association of persistent and severe postnatal depression with child outcomes. *JAMA Psychiatry* 75, 247–253. <https://doi.org/10.1001/jamapsychiatry.2017.4363>
- Netsi, E., Van Ijzendoorn, M.H., Bakermans-Kranenburg, M.J., Wulff, K., Jansen, P.W., Jaddoe, V.W.V., Verhulst, F.C., Tiemeier, H., Ramchandani, P.G., 2015. Does Infant Reactivity Moderate the Association between Antenatal Maternal Depression and Infant Sleep? *J. Dev. Behav. Pediatr.* 36, 440–449. <https://doi.org/10.1097/DBP.0000000000000181>
- NHS England, 2018. NHS long term plan [WWW Document]. URL <https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf> (accessed 3.30.20).
- Nilsen, A.B.V., Waldenström, U., Rasmussen, S., Hjelmstedt, A., Schytt, E., 2013. Characteristics of first-time fathers of advanced age: A Norwegian population-based study. *BMC Pregnancy Childbirth* 13. <https://doi.org/10.1186/1471-2393-13-29>
- Nishigori, H., Obara, T., Nishigori, T., Metoki, H., Mizuno, S., Ishikuro, M., Sakurai, K., Hamada, H., Watanabe, Z., Hoshiai, T., Arima, T., Nakai, K., Kuriyama, S., Yaegashi, N., 2019. Mother-to-infant bonding failure and intimate partner violence during pregnancy as risk factors for father-to-infant bonding failure at 1 month postpartum: an adjunct study of the Japan Environment and Children's Study. *J. Matern. Neonatal Med.* 15, 1–8. <https://doi.org/10.1080/14767058.2018.1560414>
- Nofzinger, E.A., Boisse, D.J., Germain, A., Price, J.C., Miewald, J.M., Kopfer, D.J., 2004. Functional neuroimaging evidence for hyperarousal in insomnia. *Am. J. Psychiatry* 161, 2126–2129. <https://doi.org/10.1176/appi.ajp.161.11.2126>
- Norhayati, M.N., Nik Hazlina, N.H., Asrenee, A.R., Wan Emilin, W.M.A., 2015. Magnitude and risk factors for postpartum symptoms: A literature review. *J. Affect. Disord.* 175, 34–52. <https://doi.org/10.1016/j.jad.2014.12.041>
- O'Connor, E., Senger, C.A., Henninger, M.L., Coppola, E., Gaynes, B.N., 2019. Interventions to Prevent Perinatal Depression: Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA - J. Am. Med. Assoc.* 321, 588–601. <https://doi.org/10.1001/jama.2018.20865>
- O'Connor, T.G., Caprariello, P., Blackmore, E.R., Gregory, A.M., Glover, V., Fleming, P., 2007. Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Hum. Dev.* 83, 451–458. <https://doi.org/10.1016/j.earlhumdev.2006.08.006>
- O'Donnell, K.J., Glover, V., Barker, E.D., O'Connor, T.G., 2014. The persisting effect of maternal mood in pregnancy on childhood psychopathology. *Dev.*

- Psychopathol. 26, 393–403. <https://doi.org/10.1017/S0954579414000029>
- O'Donnell, K.J., Meaney, M.J., 2020. Epigenetics, Development, and Psychopathology. *Annu. Rev. Clin. Psychol.* 16, 17.1-17.24. <https://doi.org/10.1146/annurev-clinpsy-050718-095530>
- O'Donnell, K.J., Meaney, M.J., 2017. Fetal origins of mental health: The developmental origins of health and disease hypothesis. *Am. J. Psychiatry* 174, 319–328. <https://doi.org/10.1176/appi.ajp.2016.16020138>
- O'Hara, M.W., McCabe, J.E., 2013. Postpartum Depression: Current Status and Future Directions. *Annu. Rev. Clin. Psychol.* 9, 379–407. <https://doi.org/10.1146/annurev-clinpsy-050212-185612>
- O'Hara, M.W., Swain, A.M., 1996. Rates and risk of postpartum depression - A meta-analysis. *Int. Rev. Psychiatry* 8, 37. <https://doi.org/10.3109/09540269609037816>
- O'Hara, M.W., Zekoski, E.M., Philipps, L.H., Wright, E.J., 1990. Controlled prospective study of postpartum mood disorders: Comparison of childbearing and nonchildbearing women. *J. Abnorm. Psychol.* 99, 3–15. <https://doi.org/10.1037/0021-843x.99.1.3>
- Official Statistics of Finland (OSF), 2015. Perinatal statistics - parturients, deliveries and newborns [e-publication]. Helsinki.
- Ohayon, M.M., 2002. Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Med. Rev.* 6, 97–111. <https://doi.org/10.1053/smr.2002.0186>
- Ohayon, M.M., Roth, T., 2003. Place of chronic insomnia in the course of depressive and anxiety disorders. *J. Psychiatr. Res.* 37, 9–15. [https://doi.org/10.1016/S0022-3956\(02\)00052-3](https://doi.org/10.1016/S0022-3956(02)00052-3)
- Okun, M.L., 2016. Disturbed Sleep and Postpartum Depression. *Curr Psychiatry Rep* 18, 66. <https://doi.org/10.1007/s11920-016-0705-2>
- Okun, M.L., 2015. Sleep and postpartum depression. *Curr. Opin. Psychiatry* 28, 490–496. <https://doi.org/10.1097/YCO.0000000000000206>
- Okun, M.L., Hanusa, B.H., Hall, M., Wisner, K.L., 2009. Sleep complaints in late pregnancy and the recurrence of postpartum depression. *Behav. Sleep Med.* 7, 106–117. <https://doi.org/10.1080/15402000902762394>
- Onoye, J.M., Goebert, D., Morland, L., Matsu, C., Wright, T., 2009. PTSD and postpartum mental health in a sample of Caucasian, Asian, and Pacific Islander women. *Arch. Womens. Ment. Health* 12, 393–400. <https://doi.org/10.1007/s00737-009-0087-0>
- Osborne, L., Clive, M., Kimmel, M., Gispén, F., Guintivano, J., Brown, T., Cox, O., Judy, J., Meilman, S., Braier, A., Beckmann, M.W., Kornhuber, J., Fasching, P.A., Goes, F., Payne, J.L., Binder, E.B., Kaminsky, Z., 2016. Replication of epigenetic postpartum depression biomarkers and variation with hormone levels. *Neuropsychopharmacology* 41, 1648–1658. <https://doi.org/10.1038/npp.2015.333>
- Osnes, R.S., Eberhard-Gran, M., Follstad, T., Kallestad, H., Morken, G., Roaldset, J.O., 2020. Mid-pregnancy insomnia is associated with concurrent and postpartum maternal anxiety and obsessive-compulsive symptoms: A prospective cohort study. *J. Affect. Disord.* 266, 319–326. <https://doi.org/10.1016/j.jad.2020.01.140>
- Owais, S., Chow, C.H.T., Furtado, M., Frey, B.N., Van Lieshout, R.J., 2018. Non-pharmacological interventions for improving postpartum maternal sleep: A

- systematic review and meta-analysis. *Sleep Med. Rev.* 41, 87–100. <https://doi.org/10.1016/j.smrv.2018.01.005>
- Paavonen, E.J., Saarenpää-Heikkilä, O., Pölkki, P., Kylliäinen, A., Porkka-Heiskanen, T., Paunio, T., 2017. Maternal and paternal sleep during pregnancy in the Child-sleep birth cohort. *Sleep Med.* 29, 47–56. <https://doi.org/10.1016/j.sleep.2016.09.011>
- Palagini, L., Baglioni, C., Ciapparelli, A., Gemignani, A., Riemann, D., 2013. REM sleep dysregulation in depression: State of the art. *Sleep Med. Rev.* 17, 377–390. <https://doi.org/10.1016/j.smrv.2012.11.001>
- Palagini, L., Cipollone, G., Masci, I., Novi, M., Caruso, D., Kalmbach, D.A., Drake, C.L., 2019. Stress-related sleep reactivity is associated with insomnia, psychopathology and suicidality in pregnant women: preliminary results. *Sleep Med.* 56, 145–150. <https://doi.org/10.1016/j.sleep.2019.01.009>
- Palladino, C.L., Singh, V., Campbell, J., Flynn, H., Gold, K.J., 2011. Homicide and suicide during the perinatal period: Findings from the national violent death reporting system. *Obstet. Gynecol.* 118, 1056–1063. <https://doi.org/10.1097/AOG.0b013e31823294da>
- 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. Skills* 107, 691–706. <https://doi.org/10.2466/PMS.107.3.691-706>
- Palmer, C.A., Alfano, C.A., 2017. Sleep and emotion regulation: An organizing, integrative review. *Sleep Med. Rev.* 31, 6–16. <https://doi.org/10.1016/j.smrv.2015.12.006>
- Pamidi, S., Pinto, L.M., Marc, I., Benedetti, A., Schwartzman, K., Kimoff, R.J., 2014. Maternal sleep-disordered breathing and adverse pregnancy outcomes: A systematic review and metaanalysis. *Am. J. Obstet. Gynecol.* 210, e1-14. <https://doi.org/10.1016/j.ajog.2013.07.033>
- Partinen, M., Gislason, T., 1995. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J. Sleep Res.* 4, 150–155. <https://doi.org/10.1111/j.1365-2869.1995.tb00205.x>
- Patton, G.C., Romaniuk, H., Spry, E., Coffey, C., Olsson, C., Doyle, L.W., Oats, J., Hearps, S., Carlin, J.B., Brown, S., 2015. Prediction of perinatal depression from adolescence and before conception (VIHCS): 20-year prospective cohort study. *Lancet* 386, 875–83. [https://doi.org/10.1016/S0140-6736\(14\)62248-0](https://doi.org/10.1016/S0140-6736(14)62248-0)
- Paulson, J.F., Bazemore, S.D., 2010. Prenatal and postpartum depression in fathers and its association with maternal depression: A meta-analysis. *JAMA - J. Am. Med. Assoc.* 303, 1961–1969. <https://doi.org/10.1001/jama.2010.605>
- Paulson, J.F., Bazemore, S.D., Goodman, J.H., Leiferman, J.A., 2016. The course and interrelationship of maternal and paternal perinatal depression. *Arch. Womens. Ment. Health* 19, 655–663. <https://doi.org/10.1007/s00737-016-0598-4>
- Paulson, J.F., Dauber, S., Leiferman, J.A., 2006. Individual and combined effects of postpartum depression in mothers and fathers on parenting behavior. *Pediatrics* 118, 659–668. <https://doi.org/10.1542/peds.2005-2948>
- Paulson, J.F., Keefe, H.A., Leiferman, J.A., 2009. Early parental depression and child language development. *J. Child Psychol. Psychiatry Allied Discip.* 50, 254–262. <https://doi.org/10.1111/j.1469-7610.2008.01973.x>
- Paulson, J.L., Miller-Graff, L., 2019. Prenatal sleep quality and mental health symptoms across the perinatal period: A longitudinal study of high-risk women.

- J. Psychosom. Res. 116, 31–36.  
<https://doi.org/10.1016/j.jpsychores.2018.11.011>
- Paunio, T. 2020. A specific complaint of insomnia—trouble falling asleep—a target for preventing depression SLEEPJ, 2020, 1–3. doi: 10.1093/sleep/zsaa081
- Pawluski, J., Dickens, M., 2019. Pregnancy: a final frontier in mental health research. Arch. Womens. Ment. Health 22, 831–832.  
<https://doi.org/10.1007/s00737-019-00988-y>
- Pawluski, J.L., Lonstein, J.S., Fleming, A.S., 2017. The Neurobiology of Postpartum Anxiety and Depression. Trends Neurosci. 40, 106–120.  
<https://doi.org/10.1016/j.tins.2016.11.009>
- Payne, J.L., 2019. Reproductive psychiatry: giving birth to a new subspecialty. Int. Rev. Psychiatry 31, 207–209. <https://doi.org/10.1080/09540261.2018.1579991>
- Payne, J.L., Maguire, J., 2019. Pathophysiological mechanisms implicated in postpartum depression. Front. Neuroendocrinol. 52, 165–180.  
<https://doi.org/10.1016/j.yfrne.2018.12.001>
- Payne, J.L., Palmer, J.T., Joffe, H., 2009. A reproductive subtype of depression: Conceptualizing models and moving toward etiology. Harv. Rev. Psychiatry 17, 72–86. <https://doi.org/10.1080/10673220902899706>
- Pearson, N.J., 2006. Insomnia, Trouble Sleeping, and Complementary and Alternative Medicine. Arch. Intern. Med. 166, 1775–1782.  
<https://doi.org/10.1001/archinte.166.16.1775>
- Pearson, R.M., Carnegie, R.E., Cree, C., Rollings, C., Rena-Jones, L., Evans, J., Stein, A., Tilling, K., Lewcock, M., Lawlor, D.A., 2018. Prevalence of Prenatal Depression Symptoms Among 2 Generations of Pregnant Mothers: The Avon Longitudinal Study of Parents and Children. JAMA Netw. open 1, e180725.  
<https://doi.org/10.1001/jamanetworkopen.2018.0725>
- Pearson, R.M., Culpin, I., Loret De Mola, C., Matijasevich, A., Santos, I.S., Horta, B.L., Barros, F.C., Stein, A., 2019. Grandmothers' mental health is associated with grandchildren's emotional and behavioral development: A three-generation prospective study in Brazil. BMC Psychiatry 19.  
<https://doi.org/10.1186/s12888-019-2166-8>
- Pérez C., F., Brahm, P., Riquelme, S., Rivera, C., Jaramillo, K., Eickhorst, A., 2017. Paternal post-partum depression: How has it been assessed? A literature review. Ment. Heal. Prev. 7, 28–36. <https://doi.org/10.1016/j.mhp.2017.07.001>
- Perlis, M.L., Giles, D.E., Buysse, D.J., Thase, M.E., Tu, X., Kupfer, D.J., 1997. Which depressive symptoms are related to which sleep electroencephalographic variables? Biol. Psychiatry 42, 904–913. [https://doi.org/10.1016/S0006-3223\(96\)00439-8](https://doi.org/10.1016/S0006-3223(96)00439-8)
- Pierce, M., Hope, H.F., Kolade, A., Gellatly, J., Osam, C.S., Perchard, R., Kosidou, K., Dalman, C., Morgan, V., Di Prinzio, P., Abel, K.M., 2019. Effects of parental mental illness on children's physical health: systematic review and meta-analysis. Br. J. Psychiatry Oct, 1–10. <https://doi.org/10.1192/bjp.2019.216>
- Pietikäinen, J.T., Hakulinen, T., Holopainen, A., 2020. Raskausajan ja synnytyksen jälkeisen masennuksen ja ahdistuneisuuden varhaista hoitoa tulee tehostaa. Sos. Aikakausl. 57, 192–194.
- Pietikäinen, J.T., Taka-Eilola, T., Paunio, T., 2019. Suomeen tarvitaan perinataalipsykiatriaa. Duodecim 135, 1809–11.
- Pigeon, W.R., Hegel, M., Unützer, J., Fan, M.Y., Sateia, M.J., Lyness, J.M., Phillips, C., Perlis, M.L., 2008. Is insomnia a perpetuating factor for late-life depression

- in the IMPACT cohort? *Sleep* 31, 481–488. <https://doi.org/10.1093/sleep/31.4.481>
- 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>
- Posmontier, B., 2008. Sleep quality in women with and without postpartum depression. *JOGNN - J. Obstet. Gynecol. Neonatal Nurs.* 37, 722–737. <https://doi.org/10.1111/j.1552-6909.2008.00298.x>
- Powell, J.G., Garland, S., Preston, K., Piszczatoski, C., 2020. Brexanolone (Zulresso): Finally, an FDA-Approved Treatment for Postpartum Depression. *Ann. Pharmacother.* 54, 157–163. <https://doi.org/10.1177/1060028019873320>
- Pryor, J., Morton, S., Bandara, D., Robinson, E., Grant, C., 2014. Pregnant partners: Fathers of the Growing Up in New Zealand children. *J. Fam. Stud.* 20, 5–18. <https://doi.org/10.5172/jfs.2014.20.1.5>
- Psouni, E., Agebjörn, J., Linder, H., 2017. Symptoms of depression in Swedish fathers in the postnatal period and development of a screening tool. *Scand. J. Psychol.* 58, 485–496. <https://doi.org/10.1111/sjop.12396>
- Putnam, K., Robertson-Blackmore, E., Sharkey, K., Payne, J., Bergink, V., Munk-Olsen, T., Deligiannidis, K., Altemus, M., Newport, J., Apter, G., Devouche, E., Viktorin, A., Magnusson, P., Lichtenstein, P., Penninx, B., Buist, A., Bilszta, J., O'Hara, M., Stuart, S., Brock, R., Roza, S., Tiemeier, H., Guille, C., Neill Epperson, C., Kim, D., Schmidt, P., Martinez, P., Wisner, K.L., Stowe, Z., Jones, I., Rubinow, D., Sullivan, P., Meltzer-Brody, S., 2015. Heterogeneity of postpartum depression: A latent class analysis. *The Lancet Psychiatry* 2, 59–67. [https://doi.org/10.1016/S2215-0366\(14\)00055-8](https://doi.org/10.1016/S2215-0366(14)00055-8)
- Putnam, K.T., Wilcox, M., Robertson-Blackmore, E., Sharkey, K., Bergink, V., Munk-Olsen, T., Deligiannidis, K.M., Payne, J., Altemus, M., Newport, J., Apter, G., Devouche, E., Viktorin, A., Magnusson, P., Penninx, B., Buist, A., Bilszta, J., O'Hara, M., Stuart, S., Brock, R., Roza, S., Tiemeier, H., Guille, C., Epperson, C.N., Kim, D., Schmidt, P., Martinez, P., Di Florio, A., Wisner, K.L., Stowe, Z., Jones, I., Sullivan, P.F., Rubinow, D., Wildenhaus, K., Meltzer-Brody, S., 2017. Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an international consortium. *The Lancet Psychiatry* 4, 477–85. [https://doi.org/10.1016/S2215-0366\(17\)30136-0](https://doi.org/10.1016/S2215-0366(17)30136-0)
- PwC Consulting Australia, 2019. The cost of perinatal depression and anxiety in Australia.
- R Core Team, 2019. R: A language and environment for statistical computing.
- Rackers, H.S., Thomas, S., Williamson, K., Posey, R., Kimmel, M.C., 2018. Emerging literature in the Microbiota-Brain Axis and Perinatal Mood and Anxiety Disorders. *Psychoneuroendocrinology* 95, 86–96. <https://doi.org/10.1016/j.psyneuen.2018.05.020>
- Radloff, L.S., 1977. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Appl. Psychol. Meas.* 1, 385–401. <https://doi.org/10.1177/014662167700100306>
- Räisänen, S., Lehto, S.M., Nielsen, H.S., Gissler, M., Kramer, M.R., Heinonen, S., 2013. Fear of childbirth predicts postpartum depression: A population-based analysis of 511 422 singleton births in Finland. *BMJ Open* 3, e004047. <https://doi.org/10.1136/bmjopen-2013-004047>
- Rajhans, P., Goin-Kochel, R.P., Strathearn, L., Kim, S., 2019. It takes two!

- Exploring sex differences in parenting neurobiology and behaviour. *J. Neuroendocrinol.* 31, e12721. <https://doi.org/10.1111/jne.12721>
- Ramchandani, P., Psychogiou, L., 2009. Paternal psychiatric disorders and children's psychosocial development. *Lancet* 374, 646–53. [https://doi.org/10.1016/S0140-6736\(09\)60238-5](https://doi.org/10.1016/S0140-6736(09)60238-5)
- Ramchandani, P., Stein, A., Evans, J., O'Connor, T.G., 2005. Paternal depression in the postnatal period and child development: A prospective population study. *Lancet* 365, 2201–05. [https://doi.org/10.1016/S0140-6736\(05\)66778-5](https://doi.org/10.1016/S0140-6736(05)66778-5)
- Ramchandani, P.G., Domoney, J., Sethna, V., Psychogiou, L., Vlachos, H., Murray, L., 2013. Do early father-infant interactions predict the onset of externalising behaviours in young children? Findings from a longitudinal cohort study. *J. Child Psychol. Psychiatry Allied Discip.* 54, 55–64. <https://doi.org/10.1111/j.1469-7610.2012.02583.x>
- Ramchandani, P.G., O'Connor, T.G., Evans, J., Heron, J., Murray, L., Stein, A., 2008a. The effects of pre- and postnatal depression in fathers: A natural experiment comparing the effects of exposure to depression on offspring. *J. Child Psychol. Psychiatry Allied Discip.* 49, 1069–1078. <https://doi.org/10.1111/j.1469-7610.2008.02000.x>
- Ramchandani, P.G., Stein, A., O'Connor, T.G., Heron, J., Murray, L., Evans, J., 2008b. Depression in men in the postnatal period and later child psychopathology: A population cohort study. *J. Am. Acad. Child Adolesc. Psychiatry* 47, 390–398. <https://doi.org/10.1097/CHI.0b013e31816429c2>
- Rao, W.W., Zhu, X.M., Zong, Q.Q., Zhang, Q., Hall, B.J., Ungvari, G.S., Xiang, Y.T., 2020. Prevalence of prenatal and postpartum depression in fathers: A comprehensive meta-analysis of observational surveys. *J. Affect. Disord.* 263, 491–499. <https://doi.org/10.1016/j.jad.2019.10.030>
- Raphael-Leff, J. 2010. Chapter 1 - Mothers' and fathers' orientations: patterns of pregnancy, parenting and the bonding process. In S., Tyano, K., Keren, H., Herrman & J., Cox Ó. (Eds.) *Parenthood and Mental Health: A Bridge between Infant and Adult Psychiatry*. Chichester, Wiley-Blackwell, pp.9-22
- Raphael-Leff, J. (1993/2001). *Pregnancy: the inside story*. London and New York: Karnac Books
- Rathgeber, M., Bürkner, P.C., Schiller, E.M., Holling, H., 2019. The Efficacy of Emotionally Focused Couples Therapy and Behavioral Couples Therapy: A Meta-Analysis. *J. Marital Fam. Ther.* 45, 447–463. <https://doi.org/10.1111/jmft.12336>
- Redpath, N., Rackers, H.S., Kimmel, M.C., 2019. The Relationship Between Perinatal Mental Health and Stress: a Review of the Microbiome. *Curr. Psychiatry Rep.* 21, 1–9. <https://doi.org/10.1007/s11920-019-0998-z>
- Rees, S., Channon, S., Waters, C.S., 2019. The impact of maternal prenatal and postnatal anxiety on children's emotional problems: a systematic review. *Eur. Child Adolesc. Psychiatry* 28, 257–280. <https://doi.org/10.1007/s00787-018-1173-5>
- Reuben, J.D., Shaw, D.S., 2015. Resilience in the Offspring of Depressed Mothers: Variation Across Risk, Domains, and Time. *Clin. Child Fam. Psychol. Rev.* 18, 300–327. <https://doi.org/10.1007/s10567-015-0195-5>
- Richters, J.E., 1992. Depressed mothers as informants about their children: A critical review of the evidence for distortion. *Psychol. Bull.* 112, 485–499. <https://doi.org/10.1037/0033-2909.112.3.485>

- 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., Weeß, H.G., Wichniak, A., Zavalko, I., Arnardottir, E.S., Deleanu, O.C., Strazisar, B., Zoetmulder, M., Spiegelhalder, K., 2017. European guideline for the diagnosis and treatment of insomnia. *J. Sleep Res.* 26, 675–700. <https://doi.org/10.1111/jsr.12594>
- Rodgers, A.B., Morgan, C.P., Bronson, S.L., Revello, S., Bale, T.L., 2013. Paternal stress exposure alters sperm MicroRNA content and reprograms offspring HPA stress axis regulation. *J. Neurosci.* 33, 9003–9012. <https://doi.org/10.1523/JNEUROSCI.0914-13.2013>
- Rogathi, J.J., Manongi, R., Mushi, D., Rasch, V., Sigalla, G.N., Gammeltoft, T., Meyrowitsch, D.W., 2017. Postpartum depression among women who have experienced intimate partner violence: A prospective cohort study at Moshi, Tanzania. *J. Affect. Disord.* 218, 238–245. <https://doi.org/10.1016/j.jad.2017.04.063>
- Ross, L.E., Dennis, C.L., 2009. The prevalence of postpartum depression among women with substance use, an abuse history, or chronic illness: A systematic review. *J. Women's Heal.* 18, 475–486. <https://doi.org/10.1089/jwh.2008.0953>
- Ross, L.E., Murray, B.J., Steiner, M., 2005. Sleep and perinatal mood disorders: A critical review. *J. Psychiatry Neurosci.* 30, 247–256.
- Ruohomäki, A., Toffol, E., Upadhyaya, S., Keski-Nisula, L., Pekkanen, J., Lampi, J., Voutilainen, S., Tuomainen, T.P., Heinonen, S., Kumpulainen, K., Pasanen, M., Lehto, S.M., 2018. The association between gestational diabetes mellitus and postpartum depressive symptomatology: A prospective cohort study. *J. Affect. Disord.* 241, 263–268. <https://doi.org/10.1016/j.jad.2018.08.070>
- Rutter, M., Quinton, D., 1984. Parental psychiatric disorder: Effects on children. *Psychol. Med.* 14, 853–80.
- Sadeh, A., Tikotzky, L., Scher, A., 2010. Parenting and infant sleep. *Sleep Med. Rev.* 14, 89–96. <https://doi.org/10.1016/j.smr.2009.05.003>
- Salo, S.J., Flykt, M., Mäkelä, J., Biringen, Z., Kalland, M., Pajulo, M., Punamäki, R.L., 2019. The effectiveness of Nurture and Play: A mentalisation-based parenting group intervention for prenatally depressed mothers. *Prim. Heal. Care Res. Dev.* 20, 1–11. <https://doi.org/10.1017/S1463423619000914>
- Sandman, C.A., Buss, C., Head, K., Davis, E.P., 2015. Fetal exposure to maternal depressive symptoms is associated with cortical thickness in late childhood. *Biol. Psychiatry* 15, 324–334. <https://doi.org/10.1016/j.biopsych.2014.06.025>
- Sandman, C.A., Glynn, L.M., Davis, E.P., 2013. Is there a viability-vulnerability tradeoff? Sex differences in fetal programming. *J. Psychosom. Res.* 75, 327–335. <https://doi.org/10.1016/j.jpsychores.2013.07.009>
- Santiago, J.R., Nolleto, M.S., Kinzler, W., Santiago, T. V., 2001. Sleep and sleep disorders in pregnancy. *Ann. Intern. Med.* 134, 396–408. <https://doi.org/10.7326/0003-4819-134-5-200103060-00012>
- Santos, H., Tan, X., Salomon, R., 2017. Heterogeneity in perinatal depression: how far have we come? A systematic review. *Arch. Womens. Ment. Health* 20, 11–23. <https://doi.org/10.1007/s00737-016-0691-8>
- Sarkadi, A., Kristiansson, R., Oberklaid, F., Bremberg, S., 2008. Fathers' involvement and children's developmental outcomes: A systematic review of longitudinal studies. *Acta Paediatr. Int. J. Paediatr.* 97, 153–158.

- <https://doi.org/10.1111/j.1651-2227.2007.00572.x>
- Saxbe, D.E., Schetter, C.D., Guardino, C.M., Ramey, S.L., Shalowitz, M.U., Thorp, J., Vance, M., 2016. Sleep Quality Predicts Persistence of Parental Postpartum Depressive Symptoms and Transmission of Depressive Symptoms from Mothers to Fathers. *Ann. Behav. Med.* 50, 862–875. <https://doi.org/10.1007/s12160-016-9815-7>
- Saxbe, D.E., Schetter, C.D., Simon, C.D., Adam, E.K., Shalowitz, M.U., 2017. High paternal testosterone may protect against postpartum depressive symptoms in fathers, but confer risk to mothers and children. *Horm. Behav.* 95, 103–112. <https://doi.org/10.1016/j.yhbeh.2017.07.014>
- Sedov, I., Madsen, J.W., Goodman, S.H., Tomfohr-Madsen, L.M., 2019. Couples' treatment preferences for insomnia experienced during pregnancy. *Fam. Syst. Heal.* 37, 46–55. <https://doi.org/10.1037/fsh0000391>
- Sedov, I.D., Cameron, E.E., Madigan, S., Tomfohr-Madsen, L.M., 2018. Sleep quality during pregnancy: A meta-analysis. *Sleep Med. Rev.* 38, 168–176. <https://doi.org/10.1016/j.smrv.2017.06.005>
- Seng, J.S., Rauch, S.A.M., Resnick, H., Reed, C.D., King, A., Low, L.K., McPherson, M., Muzik, M., Abelson, J., Liberzon, I., 2010. Exploring posttraumatic stress disorder symptom profile among pregnant women. *J. Psychosom. Obstet. Gynecol.* 31, 176–187. <https://doi.org/10.3109/0167482X.2010.486453>
- Shadrina, M., Bondarenko, E.A., Slominsky, P.A., 2018. Genetics factors in major depression disease. *Front. Psychiatry* 9, 1–18. <https://doi.org/10.3389/fpsy.2018.00334>
- Shorey, S., Chee, C.Y.I., Ng, E.D., Chan, Y.H., Tam, W.W.S., Chong, Y.S., 2018. Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. *J. Psychiatr. Res.* 104, 235–248. <https://doi.org/10.1016/j.jpsychires.2018.08.001>
- Silverman, M.E., Loudon, H., 2010. Antenatal reports of pre-pregnancy abuse is associated with symptoms of depression in the postpartum period. *Arch. Womens. Ment. Health* 13, 411–415. <https://doi.org/10.1007/s00737-010-0161-7>
- Silvestri, R., Aricò, I., 2019. Sleep disorders in pregnancy. *Sleep Sci.* 12, 232–239. <https://doi.org/10.5935/1984-0063.20190098>
- Sivertsen, B., Hysing, M., Dørheim, S.K., Eberhard-Gran, M., 2015. Trajectories of maternal sleep problems before and after childbirth: A longitudinal population-based study. *BMC Pregnancy Childbirth* 15, 129. <https://doi.org/10.1186/s12884-015-0577-1>
- Slomian, J., Honvo, G., Emonts, P., Reginster, J.Y., Bruyère, O., 2019. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Women's Heal.* 15, 1–55. <https://doi.org/10.1177/1745506519844044>
- Slopen, N., Loucks, E.B., Appleton, A.A., Kawachi, I., Kubzansky, L.D., Non, A.L., Buka, S., Gilman, S.E., 2015. Early origins of inflammation: An examination of prenatal and childhood social adversity in a prospective cohort study. *Psychoneuroendocrinology* 51, 403–413. <https://doi.org/10.1016/j.psyneuen.2014.10.016>
- Smith, H.R., Eryigit-Madzwamuse, S., Barnes, J., 2013. Paternal postnatal and subsequent mental health symptoms and child socio-emotional and behavioural

- problems at school entry. *Infant Child Dev.* 22, 335–348. <https://doi.org/10.1002/icd.1800>
- Sokol, L.E., 2018. A systematic review and meta-analysis of interpersonal psychotherapy for perinatal women. *J. Affect. Disord.* 232, 316–328. <https://doi.org/10.1016/j.jad.2018.01.018>
- Sokol, L.E., Epperson, C.N., Barber, J.P., 2011. A meta-analysis of treatments for perinatal depression. *Clin. Psychol. Rev.* 31, 839–849. <https://doi.org/10.1016/j.cpr.2011.03.009>
- Soe, N.N., Wen, D.J., Poh, J.S., Chong, Y.S., Broekman, B.F., Chen, H., Shek, L.P., Tan, K.H., Gluckman, P.D., Fortier, M. V., Meaney, M.J., Qiu, A., 2018. Perinatal maternal depressive symptoms alter amygdala functional connectivity in girls. *Hum. Brain Mapp.* 39, 680–690. <https://doi.org/10.1002/hbm.23873>
- Solantaus, T., Paavonen, E.J., Toikka, S., Punamäki, R.L., 2010. Preventive interventions in families with parental depression: children’s psychosocial symptoms and prosocial behaviour. *Eur. Child Adolesc. Psychiatry* 19, 883–892. <https://doi.org/10.1007/s00787-010-0135-3>
- Soldatos, C.R., Dikeos, D.G., Paparrigopoulos, T.J., 2000. Athens Insomnia Scale: Validation of an instrument based on ICD-10 criteria. *J. Psychosom. Res.* 48, 555–560. [https://doi.org/10.1016/S0022-3999\(00\)00095-7](https://doi.org/10.1016/S0022-3999(00)00095-7)
- Sourander, A., McGrath, P.J., Ristkari, T., Cunningham, C., Huttunen, J., Hinkka-Yli-Salomäki, S., Kurki, M., Lingley-Pottie, P., 2018. Two-Year Follow-Up of Internet and Telephone Assisted Parent Training for Disruptive Behavior at Age 4. *J. Am. Acad. Child Adolesc. Psychiatry* 57, 658–668. <https://doi.org/10.1016/j.jaac.2018.07.001>
- Sourander, A., McGrath, P.J., Ristkari, T., Cunningham, C., Huttunen, J., Lingley-Pottie, P., Hinkka-Yli-Salomäki, S., Kinnunen, M., Vuorio, J., Sinokki, A., Fossum, S., Unruh, A., 2016. Internet-assisted parent training intervention for disruptive behavior in 4-year-old children: A randomized clinical trial. *JAMA Psychiatry* 73, 378–387. <https://doi.org/10.1001/jamapsychiatry.2015.3411>
- Spitzer R, Williams J, Kroenke K et al. . Utility of a new procedure for diagnosing mental disorders in primary care: the PRIME-MD 1000 study. *JAMA* 1994;272:1749–56. [10.1001/jama.1994.03520220043029](https://doi.org/10.1001/jama.1994.03520220043029)
- Spruit, A., Goos, L., Weenink, N., Rodenburg, R., Niemeyer, H., Stams, G.J., Colonesi, C., 2020. The Relation Between Attachment and Depression in Children and Adolescents: A Multilevel Meta-Analysis. *Clin. Child Fam. Psychol. Rev.* 23, 54–69. <https://doi.org/10.1007/s10567-019-00299-9>
- Stein, A., Netsi, E., Lawrence, P.J., Granger, C., Kempton, C., Craske, M.G., Nickless, A., Mollison, J., Stewart, D.A., Rapa, E., West, V., Scerif, G., Cooper, P.J., Murray, L., 2018. Mitigating the effect of persistent postnatal depression on child outcomes through an intervention to treat depression and improve parenting: a randomised controlled trial. *The Lancet Psychiatry* 5, 134–44. [https://doi.org/10.1016/S2215-0366\(18\)30006-3](https://doi.org/10.1016/S2215-0366(18)30006-3)
- Stein, A., Pearson, R.M., Goodman, S.H., Rapa, E., Rahman, A., McCallum, M., Howard, L.M., Pariante, C.M., 2014. Effects of perinatal mental disorders on the fetus and child. *Lancet* 384, 1800–19. [https://doi.org/10.1016/S0140-6736\(14\)61277-0](https://doi.org/10.1016/S0140-6736(14)61277-0)
- Stewart, D.E., Vigod, S.N., 2019. Postpartum Depression: Pathophysiology, Treatment, and Emerging Therapeutics. *Annu. Rev. Med.* 70, 183–96. <https://doi.org/10.1146/annurev-med-041217-011106>

- Storey, A.E., Walsh, C.J., Quinton, R.L., Wynne-Edwards, K.E., 2000. Hormonal correlates of paternal responsiveness in new and expectant fathers. *Evol. Hum. Behav.* 21, 9–95. [https://doi.org/10.1016/S1090-5138\(99\)00042-2](https://doi.org/10.1016/S1090-5138(99)00042-2)
- Stuart, S., Koleva, H., 2014. Psychological treatments for perinatal depression. *Best Pract. Res. Clin. Obstet. Gynaecol.* 28, 61–70. <https://doi.org/10.1016/j.bpobgyn.2013.09.004>
- Suarez, A., Lahti, J., Czamara, D., Lahti-Pulkkinen, M., Knight, A.K., Girchenko, P., Hämäläinen, E., Kajantie, E., Lipsanen, J., Laivuori, H., Villa, P.M., Reynolds, R.M., Smith, A.K., Binder, E.B., Räikkönen, K., 2018. The Epigenetic Clock at Birth: Associations With Maternal Antenatal Depression and Child Psychiatric Problems. *J. Am. Acad. Child Adolesc. Psychiatry* 57, 321–328. <https://doi.org/10.1016/j.jaac.2018.02.011>
- Sullivan, P.F., Neale, M.C., Kendler, K.S., 2000. Genetic epidemiology of major depression: Review and meta-analysis. *Am. J. Psychiatry* 157, 1552–1562. <https://doi.org/10.1176/appi.ajp.157.10.1552>
- Suri, R., Stowe, Z.N., Cohen, L.S., Newport, D.J., Burt, V.K., Aquino-Elias, A.R., Knight, B.T., Mintz, J., Altshuler, L.L., 2017. Prospective longitudinal study of predictors of postpartum-onset depression in women with a history of major depressive disorder. *J. Clin. Psychiatry* 78, 1110–1116. <https://doi.org/10.4088/JCP.15m10427>
- Sutter-Dallay, A.L., Cosnefroy, O., Glatigny-Dallay, E., Verdoux, H., Rasclé, N., 2012. Evolution of perinatal depressive symptoms from pregnancy to two years postpartum in a low-risk sample: The MATQUID cohort. *J. Affect. Disord.* 139, 23–29. <https://doi.org/10.1016/j.jad.2011.08.018>
- Svenlin, N., 2015. Validation of the Edinburgh Gotland Depression Scale for Swedish fathers. University of Umeå. <https://doi.org/diva2:897483>
- Swartz, H.A., Shear, M.K., Wren, F.J., Greeno, C.G., Sales, E., Sullivan, B.K., Ludewig, D.P., 2005. Depression and anxiety among mothers who bring their children to a pediatric mental health clinic. *Psychiatr. Serv.* 9, 1077–1083. <https://doi.org/10.1176/appi.ps.56.9.1077>
- Sweeney, S., MacBeth, A., 2016. The effects of paternal depression on child and adolescent outcomes: A systematic review. *J. Affect. Disord.* 205, 44–59. <https://doi.org/10.1016/j.jad.2016.05.073>
- Tandon, S.D., Cluxton-Keller, F., Leis, J., Le, H.N., Perry, D.F., 2012. A comparison of three screening tools to identify perinatal depression among low-income African American women. *J. Affect. Disord.* 136, 155–162. <https://doi.org/10.1016/j.jad.2011.07.014>
- Tesler, N., Gerstenberg, M., Huber, R., 2013. Developmental changes in sleep and their relationships to psychiatric illnesses. *Curr. Opin. Psychiatry* 26, 572–579. <https://doi.org/10.1097/YCO.0b013e328365a335>
- Tham, E.K.H., Tan, J., Chong, Y.S., Kwek, K., Saw, S.M., Teoh, O.H., Goh, D.Y.T., Meaney, M.J., Brockman, B.F.P., 2016. Associations between poor subjective prenatal sleep quality and postnatal depression and anxiety symptoms. *J. Affect. Disord.* 202, 91–94. <https://doi.org/10.1016/j.jad.2016.05.028>
- Tichovolsky, M.H., Griffith, S.F., Rolon-Arroyo, B., Arnold, D.H., Harvey, E.A., 2018. A Longitudinal Study of Fathers' and Young Children's Depressive Symptoms. *J. Clin. Child Adolesc. Psychol.* 47, S190–S204. <https://doi.org/10.1080/15374416.2016.1212357>
- Tien, J., Lewis, G.D., Liu, J., 2019. Prenatal risk factors for internalizing and

- externalizing problems in childhood. *World J. Pediatr.* <https://doi.org/10.1007/s12519-019-00319-2>
- Tomfohr, L.M., Buliga, E., Letourneau, N.L., Campbell, T.S., Giesbrecht, G.F., 2015. Trajectories of Sleep Quality and Associations with Mood during the Perinatal Period. *Sleep* 38, 1237–1245. <https://doi.org/10.5665/sleep.4900>
- Tomlinson, M., Cooper, P., Murray, L., 2005. The mother - Infant relationship and infant attachment in a South African peri-urban settlement. *Child Dev.* 76, 1044–1054. <https://doi.org/10.1111/j.1467-8624.2005.00896.x>
- Troxel, W.M., Buysse, D.J., 2010. Chapter 12 - Principles of insomnia, in: Winkelmann, J.W., Plante, D.T. (Eds.), *Foundations of Psychiatric Sleep Medicine*. Cambridge University Press, Madison, pp. 203–215.
- Tuovinen, S., Lahti-Pulkkinen, M., Girchenko, P., Lipsanen, J., Lahti, J., Heinonen, K., Reynolds, R.M., Hämäläinen, E., Kajantie, E., Laivuori, H., Pesonen, A.K., Villa, P.M., Räikkönen, K., 2018. Maternal depressive symptoms during and after pregnancy and child developmental milestones. *Depress. Anxiety* 35, 732–741. <https://doi.org/10.1002/da.22756>
- Underwood, L., Waldie, K., D’Souza, S., Peterson, E.R., Morton, S., 2016. A review of longitudinal studies on antenatal and postnatal depression. *Arch. Womens. Ment. Health* 19, 711–720. <https://doi.org/10.1007/s00737-016-0629-1>
- Underwood, L., Waldie, K.E., D’Souza, S., Peterson, E.R., Morton, S.M.B., 2017a. A Longitudinal Study of Pre-pregnancy and Pregnancy Risk Factors Associated with Antenatal and Postnatal Symptoms of Depression: Evidence from Growing Up in New Zealand. *Matern. Child Health J.* 21, 915–931. <https://doi.org/10.1007/s10995-016-2191-x>
- Underwood, L., Waldie, K.E., Peterson, E., D’Souza, S., Verbiest, M., McDaid, F., Morton, S., 2017b. Paternal depression symptoms during pregnancy and after childbirth among participants in the growing up in New Zealand study. *JAMA Psychiatry* 74, 360–369. <https://doi.org/10.1001/jamapsychiatry.2016.4234>
- Van Batenburg-Eddes, T., Brion, M.J., Henrichs, J., Jaddoe, V.W.V., Hofman, A., Verhulst, F.C., Lawlor, D.A., Davey Smith, G., Tiemeier, H., 2013. Parental depressive and anxiety symptoms during pregnancy and attention problems in children: A cross-cohort consistency study. *J. Child Psychol. Psychiatry Allied Discip.* 54, 591–600. <https://doi.org/10.1111/jcpp.12023>
- Van Den Berg, M.P., Van Der Ende, J., Crijnen, A.A.M., Jaddoe, V.W.V., Moll, H.A., Mackenbach, J.P., Hofman, A., Hengeveld, M.W., Tiemeier, H., Verhulst, F.C., 2009. Paternal depressive symptoms during pregnancy are related to excessive infant crying. *Pediatrics.* <https://doi.org/10.1542/peds.2008-3100>
- Van Der Waerden, J., Galéra, C., Larroque, B., Saurel-Cubizolles, M.J., Sutter-Dallay, A.L., Melchior, M., 2015. Maternal depression trajectories and children’s behavior at age 5 years. *J. Pediatr.* 166, 1440–8. <https://doi.org/10.1016/j.jpeds.2015.03.002>
- Van Grootheest, D.S., Van Den Berg, S.M., Cath, D.C., Willemsen, G., Boomsma, D.I., 2008. Marital resemblance for obsessive-compulsive, anxious and depressive symptoms in a population-based sample. *Psychol. Med.* 38, 1731–1740. <https://doi.org/10.1017/S0033291708003024>
- van Santvoort, F., Doesum, K.T.M., Reupert, A., 2015. Parental diagnosis and children’s outcomes, in: Reupert, A., Maybery, D., Nicholson, J., Göpfert, M., Seeman, M., V. (Eds.), *Parental Psychiatric Disorder; Distressed Parents and*

- Their Families. Cambridge University Press, pp. 96–106.
- van Santvoort, Floor, Hosman, C.M.H., Janssens, J.M.A.M., van Doesum, K.T.M., Reupert, A., van Loon, L.M.A., 2015. The Impact of Various Parental Mental Disorders on Children's Diagnoses: A Systematic Review. *Clin. Child Fam. Psychol. Rev.* 18, 281–299. <https://doi.org/10.1007/s10567-015-0191-9>
- Vänskä, M., Punamäki, R.-L., Tolvanen, A., Lindblom, J., Flykt, M., Unkila-Kallio, L., Tulppala, M., Tiitinen, A., 2017. Paternal mental health trajectory classes and early fathering experiences: Prospective study on a normative and formerly infertile sample. *Int. J. Behav. Dev.* 41, 570–580. <https://doi.org/10.1177/0165025416654301>
- Vänskä, M., Punamäki, R.L., Tolvanen, A., Lindblom, J., Flykt, M., Unkila-Kallio, L., Tiitinen, A., Repokari, L., Sinkkonen, J., Tulppala, M., 2011. Maternal pre- and postnatal mental health trajectories and child mental health and development: Prospective study in a normative and formerly infertile sample. *Int. J. Behav. Dev.* 35, 517–531. <https://doi.org/10.1177/0165025411417505>
- Vartiainen, E., Laatikainen, T., Peltonen, M., Puska, P., 2016. Predicting Coronary Heart Disease and Stroke: The FINRISK Calculator. *Glob. Heart* 11, 213–216. <https://doi.org/10.1016/j.ghheart.2016.04.007>
- Velders, F.P., Dieleman, G., Henrichs, J., Jaddoe, V.W.V., Hofman, A., Verhulst, F.C., Hudziak, J.J., Tiemeier, H., 2011. Prenatal and postnatal psychological symptoms of parents and family functioning: The impact on child emotional and behavioural problems. *Eur. Child Adolesc. Psychiatry* 20, 341–350. <https://doi.org/10.1007/s00787-011-0178-0>
- Viinamäki, H., Niskanen, L., Pesonen, P., Saarikoski, S., 1997. Evolution of postpartum mental health. *J. Psychosom. Obstet. Gynaecol.* 18, 213–19. <https://doi.org/10.3109/01674829709080690>
- Viktorin, A., Meltzer-Brody, S., Kuja-Halkola, R., Sullivan, P.F., Landén, M., Lichtenstein, P., Magnusson, P.K.E., 2016. Heritability of perinatal depression and genetic overlap with nonperinatal depression. *Am. J. Psychiatry* 173, 158–165. <https://doi.org/10.1176/appi.ajp.2015.15010085>
- Vliegen, N., Casalin, S., Luyten, P., 2014. The course of postpartum depression: a review of longitudinal studies. *Harv. Rev. Psychiatry* 22, 1–22. <https://doi.org/10.1097/HRP.0000000000000013>
- Walinder, J., Rutz, W., 2001. Male depression and suicide. *Int. Clin. Psychopharmacol.* 16, S21–S24.
- Walker, M.J., Davis, C., Al-Sahab, B., Tamim, H., 2013. Reported maternal postpartum depression and risk of childhood psychopathology. *Matern. Child Health J.* 17, 907–917. <https://doi.org/10.1007/s10995-012-1071-2>
- Warland, J., Dorrian, J., Morrison, J.L., O'Brien, L.M., 2018. Maternal sleep during pregnancy and poor fetal outcomes: A scoping review of the literature with meta-analysis. *Sleep Med. Rev.* 41, 197–219. <https://doi.org/10.1016/j.smrv.2018.03.004>
- Warren, J.R., Luo, L., Halpern-Manners, A., Raymo, J.M., Palloni, A., 2015. Do different methods for modeling age-graded trajectories yield consistent and valid results? *Am. J. Sociol.* 120, 1809–1856. <https://doi.org/10.1086/681962>
- Wassing, R., Benjamins, J.S., Dekker, K., Moens, S., Spiegelhalter, K., Feige, B., Riemann, D., Van Der Sluis, S., Van Der Werf, Y.D., Talamini, L.M., Walker, M.P., Schalkwijk, F., Van Someren, E.J.W., 2016. Slow dissolving of emotional distress contributes to hyperarousal. *Proc. Natl. Acad. Sci. U. S. A.*

- 113, 2538–2543. <https://doi.org/10.1073/pnas.1522520113>
- Waters, C.S., Hay, D.F., Simmonds, J.R., van Goozen, S.H.M., 2014. Antenatal depression and children’s developmental outcomes: potential mechanisms and treatment options. *Eur. Child Adolesc. Psychiatry* 23, 957–971. <https://doi.org/10.1007/s00787-014-0582-3>
- Wee, K.Y., Skouteris, H., Pier, C., Richardson, B., Milgrom, J., 2011. Correlates of ante- and postnatal depression in fathers: A systematic review. *J. Affect. Disord.* 130, 358–377. <https://doi.org/10.1016/j.jad.2010.06.019>
- Weinberg, M.K., Tronick, E.Z., Beeghly, M., Olson, K.L., Kernan, H., Riley, J.M., 2001. Subsyndromal depressive symptoms and major depression in postpartum women. *Am. J. Orthopsychiatry* 71, 87–97. <https://doi.org/10.1037/0002-9432.71.1.87>
- Weissman, M.M., Berry, O.O., Warner, V., Gameroff, M.J., Skipper, J., Talati, A., Pilowsky, D.J., Wickramaratne, P., 2016. A 30-year study of 3 generations at high risk and low risk for depression. *JAMA Psychiatry* 73, 970–977. <https://doi.org/10.1001/jamapsychiatry.2016.1586>
- Weissman, M.M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., Verdelli, H., 2006. Offspring of depressed parents: 20 Years later. *Am. J. Psychiatry* 163, 1001–1008. <https://doi.org/10.1176/ajp.2006.163.6.1001>
- Weissman, M.M., Wickramaratne, P., Pilowsky, D.J., Poh, E., Batten, L.A., Hernandez, M., Flament, M.F., Stewart, J.A., McGrath, P., Blier, P., Stewart, J.W., 2015. Treatment of maternal depression in a medication clinical trial and its effect on children. *Am. J. Psychiatry* 172, 450–459. <https://doi.org/10.1176/appi.ajp.2014.13121679>
- Wertz, J., 2019. Editorial: Using Parents’ Past to Predict Children’s Future: Parental History of Mental Disorders as a Predictor of Outcomes in Children With Disruptive Behavior. *J. Am. Acad. Child Adolesc. Psychiatry* 58, 756–758. <https://doi.org/10.1016/j.jaac.2019.03.011>
- Whiffen, V.E., Johnson, S.M., 1998. An attachment theory framework for the treatment of childbearing depression. *Clin. Psychol. Sci. Pract.* 5, 478–493. <https://doi.org/10.1111/j.1468-2850.1998.tb00168.x>
- Whooley, M.A., Avins, A.L., Miranda, J., Browner, W.S., 1997. Case-finding instruments for depression: Two questions are as good as many. *J. Gen. Intern. Med.* 12, 439–445. <https://doi.org/10.1046/j.1525-1497.1997.00076.x>
- Wickramaratne, P., Gameroff, M.J., Pilowsky, D.J., Hughes, C.W., Garber, J., Malloy, E., King, C., Cerda, G., Sood, A.B., Alpert, J.E., Trivedi, M.H., Fava, M., Rush, A.J., Wisniewski, S., Weissman, M.M., 2011. Children of depressed mothers 1 year after remission of maternal depression: Findings from the STAR\*D-child study. *Am. J. Psychiatry* 168, 593–602. <https://doi.org/10.1176/appi.ajp.2010.10010032>
- Wiebe, S.A., Johnson, S.M., 2016. A Review of the Research in Emotionally Focused Therapy for Couples. *Fam. Process* 55, 390–407. <https://doi.org/10.1111/famp.12229>
- Wilcox, M., McGee, B.A., Ionescu, D.F., Leonte, M., LaCross, L., Reys, J., Wildenhaus, K., 2020. Perinatal depressive symptoms often start in the prenatal rather than postpartum period: results from a longitudinal study. *Arch. Womens. Ment. Health.* <https://doi.org/10.1007/s00737-020-01017-z>
- Wilkie, G., Shapiro, C.M., 1992. Sleep deprivation and the postnatal blues. *J. Psychosom. Res.* 36, 309–316. [https://doi.org/10.1016/0022-3999\(92\)90067-C](https://doi.org/10.1016/0022-3999(92)90067-C)

- Willis, S.K., Hatch, E.E., Wise, L.A., 2019. Sleep and female reproduction. *Curr. Opin. Obstet. Gynecol.* 31, 222–227. <https://doi.org/10.1097/gco.0000000000000554>
- Wilson, D.L., Barnes, M., Ellett, L., Permezel, M., Jackson, M., Crowe, S.F., 2011. Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy. *Aust. New Zeal. J. Obstet. Gynaecol.* 51, 38–46. <https://doi.org/10.1111/j.1479-828X.2010.01252.x>
- Wilson, S., Durbin, C.E., 2010. Effects of paternal depression on fathers' parenting behaviors: A meta-analytic review. *Clin. Psychol. Rev.* 30, 167–180. <https://doi.org/10.1016/j.cpr.2009.10.007>
- Wisner, K.L., Perel, J.M., Peindl, K.S., Hanusa, B.H., 2004. Timing of depression recurrence in the first year after birth. *J. Affect. Disord.* 78, 249–252. [https://doi.org/10.1016/S0165-0327\(02\)00305-1](https://doi.org/10.1016/S0165-0327(02)00305-1)
- Wisner, K.L., Sit, D.K.Y., McShea, M.C., Rizzo, D.M., Zoretich, R.A., Hughes, C.L., Eng, H.F., Luther, J.F., Wisniewski, S.R., Costantino, M.L., Confer, A.L., Moses-Kolko, E.L., Famy, C.S., Hanusa, B.H., 2013. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry* 70, 490–498. <https://doi.org/10.1001/jamapsychiatry.2013.87>
- Wolford, E., Lahti, M., Tuovinen, S., Lahti, J., Lipsanen, J., Savolainen, K., Heinonen, K., Hämäläinen, E., Kajantie, E., Pesonen, A.K., Villa, P.M., Laivuori, H., Reynolds, R.M., Räikkönen, K., 2017. Maternal depressive symptoms during and after pregnancy are associated with attention-deficit/hyperactivity disorder symptoms in their 3- to 6-year-old children. *PLoS One* 12, e0190248. <https://doi.org/10.1371/journal.pone.0190248>
- Women's College Hospital Toronto, n.d. Reproductive Life Stages Program (RLS) [WWW Document]. URL <https://www.womenscollegehospital.ca/care-programs/mental-health/rls/> (accessed 4.20.20).
- Woolhouse, H., Brown, S., Krastev, A., Perlen, S., Gunn, J., 2009. Seeking help for anxiety and depression after childbirth: Results of the Maternal Health Study. *Arch. Womens. Ment. Health* 12, 75–83. <https://doi.org/10.1007/s00737-009-0049-6>
- Working group set up by the Finnish Medical Society Duodecim and the Finnish Sleep Research Society, 2020. Insomnia. Current Care Summary. Suomalainen Lääkäriseura Duodecim, Helsinki.
- World Health Organization, 2018. International Classification of Disease. [WWW Document]. URL <https://icd.who.int/browse11/1-m/en> (accessed 5.6.20).
- World Health Organization (WHO), 1992. International classification of disease, 10th ed. ed. Geneva.
- Wu, M., Li, X., Feng, B., Wu, H., Qiu, C., Zhang, W., 2014. Poor sleep quality of third-trimester pregnancy is a risk factor for postpartum depression. *Med. Sci. Monit.* 20, 2740–2745. <https://doi.org/10.12659/MSM.891222>
- Yan, L., Silver, R., 2016. Neuroendocrine underpinnings of sex differences in circadian timing systems. *J. Steroid Biochem. Mol. Biol.* 160, 118–126. <https://doi.org/10.1016/j.jsbmb.2015.10.007>
- Yokoyama, E., Kaneita, Y., Saito, Y., Uchiyama, M., Matsuzaki, Y., Tamaki, T., Munezawa, T., Ohida, T., 2010. Association between depression and insomnia subtypes: A longitudinal study on the elderly in Japan. *Sleep* 33, 1693–1702. <https://doi.org/10.1093/sleep/33.12.1693>

## References

- Zachariae, R., Lyby, M.S., Ritterband, L.M., O'Toole, M.S., 2016. Efficacy of internet-delivered cognitive-behavioral therapy for insomnia - A systematic review and meta-analysis of randomized controlled trials. *Sleep Med. Rev.* 30, 1–10. <https://doi.org/10.1016/j.smr.2015.10.004>
- Zeng, X.X., Tan, K.H., Yeo, A., Sasajala, P., Tan, X., Xiao, Z.C., Dawe, G., Udolph, G., 2010. Pregnancy-associated progenitor cells differentiate and mature into neurons in the maternal brain. *Stem Cells Dev.* 19, 1819–1830. <https://doi.org/10.1089/scd.2010.0046>
- Zhang, W., Finik, J., Dana, K., Glover, V., Ham, J., Nomura, Y., 2018. Prenatal Depression and Infant Temperament: The Moderating Role of Placental Gene Expression. *Infancy* 23, 211–231. <https://doi.org/10.1111/infa.12215>
- Zhou, H., Li, W., Ren, Y., 2018. Poor sleep quality of third trimester exacerbates the risk of experiencing postnatal depression. *Psychol. Heal. Med.* 25, 229–238. <https://doi.org/10.1080/13548506.2018.1549738>
- Zhu, B., Calvo, R.S., Wu, L., Simon, L., Shah, K., Piano, M., Khain, U., Izci-Balserak, B., 2018. Objective sleep in pregnant women: a comparison of actigraphy and polysomnography. *Sleep Heal.* 4, 390–396. <https://doi.org/10.1016/j.sleh.2018.07.011>
- Zierau, F., Bille, A., Rutz, W., Bech, P., 2002. The Gotland Male Depression Scale: A validity study in patients with alcohol use disorder. *Nord. J. Psychiatry* 56, 265–271. <https://doi.org/10.1080/08039480260242750>
- Zou, R., Tiemeier, H., Van Der Ende, J., Verhulst, F.C., Muetzel, R.L., White, T., Hillegers, M., El Marroun, H., 2019. Exposure to maternal depressive symptoms in fetal life or childhood and offspring brain development: A population-based imaging study. *Am. J. Psychiatry* 176, 702–710. <https://doi.org/10.1176/appi.ajp.2019.18080970>
- Zouk, H., Tousignant, M., Seguin, M., Lesage, A., Turecki, G., 2006. Characterization of impulsivity in suicide completers: Clinical, behavioral and psychosocial dimensions. *J. Affect. Disord.* 92, 195–204. <https://doi.org/10.1016/j.jad.2006.01.016>