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Stormy clouds in seventh heaven

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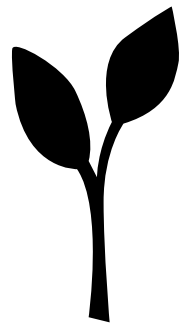
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summary

Approximately 10-15% of all women experience symptoms of anxiety or depression during the antenatal or postpartum period. It has been known that having elevated stress levels in the antenatal period is associated with adverse outcomes in the child, but the mechanism behind this observation has not been found yet. Amongst the main risk factors for anxiety or depression in the antenatal or postpartum period are having a history of previous symptoms, traumatic events during childhood, recent major life events and specific personality traits. Literature is still inconclusive on the associations with traumatic events specifically during pregnancy, delivery or in the immediate postpartum period. Chapters 2 and 3 of this thesis focus on the influence of such events on the course of anxiety and depression in the antenatal and postpartum period.

Screening for anxiety and depression during pregnancy is generally recommended by guidelines on antenatal and postpartum anxiety or depression, although antenatal screening tools that accurately predict an individual risk on symptoms in the postpartum period are not available yet. Chapters 4 and 5 of this thesis investigate whether two commonly used tools in screening for current symptomatology can be used in predicting later symptomatology.

Treatment options for symptoms of anxiety or depression can be divided into pharmacological and non-pharmacological treatment. During the antenatal and breastfeeding period, women generally prefer non-pharmacological treatment, such as cognitive behavioral therapy. Outside pregnancy, this therapy has been proven to be successful in treating anxiety and depression. Chapter 6 focuses on a randomized controlled trial investigating the effect of cognitive behavioral therapy on pregnant women and their babies.

Chapter 2 investigates the association between specific types of life events during pregnancy and change in symptoms of antenatal anxiety and depression between the first and the third trimester ($n=1,603$). Life events were divided into pregnancy related and non-pregnancy related events. We hypothesized that experiencing an event that was related to the pregnancy, such as hearing that there might be something wrong with the baby or that the partner does not want the child, would have a larger effect on maternal symptomatology than non-pregnancy related events. Both types of events were statistically significantly associated with an increase in symptoms of anxiety and depression. In contrast to our hypothesis however, effect sizes for non-pregnancy related events were larger than for pregnancy related events: 1.17 versus 0.75 for anxiety, and 1.31 versus 0.59 for depression. We subsequently tested whether the type of event would be associated with specific anxiety by adjusting for depression levels at the third trimester of pregnancy and vice versa, and found that non-pregnancy related events were specifically associated with an increase in symptoms

of depression (Bo.62, 95%CI 0.37-0.86), whereas pregnancy related events were merely associated with increasing symptoms of anxiety (Bo.4, 95%CI 0.10-0.58).

We further investigated associations with and potential moderation by levels of neuroticism or extraversion, or the experience of a childhood trauma. Personality traits were associated with increasing symptoms of both anxiety and depression, but no moderating effects were found. Childhood trauma did neither predict changes in anxiety and depression levels, nor did it moderate the associations between life events and symptomatology.

In chapter 3, the transition of symptoms from the antenatal into the postpartum period is studied (n=3,842). More specifically, to what extent specific life events during pregnancy or delivery contributed to the risk of having symptoms of anxiety or depression at six months postpartum when they already experienced symptoms in their first trimester of pregnancy. We found that experiencing life events during pregnancy that were related to the pregnancy, the mode of delivery or the newborn were found not to be associated with an increase in levels of anxiety and depression. This is not different for women with and without antenatal anxiety or depression.

Chapter 4 investigated the predictive accuracy of the ten-item Edinburgh Postnatal Depression Scale (EPDS) (n=1,620). This tool is commonly used in identifying symptoms of depression in the antenatal and postpartum period. The main objective was to investigate whether antenatal scores above cut-off accurately predict postpartum scores above cut-off. Although the overall discriminatory power was reasonable in all trimesters (AUC \geq 0.74), the EPDS was not sufficiently accurate in predicting an individual risk of symptoms of depression in the postpartum period. We first tested the prevailing cut-offs, i.e. \geq 13 for antenatal scores, and \geq 10 for postpartum scores and subsequently lowered the cut-off gradually. Lowering the antenatal cut-off to \geq 5 somewhat improved the prediction, though not sufficiently. Women scoring $<$ 5 can however be reassured that it is very unlikely that they will experience symptoms of depression in the postpartum period, as the negative predictive value was exceedingly high (96%). Lastly, we found that the predictive accuracy of a two-item screening including only items that are key symptoms in depression was not sufficiently accurate.

Although using only the antenatal scores of the ten-item EPDS may not be accurate in predicting an individual risk, they may be adequate in a two-stage screening of which the first step would be the EPDS screening in the first trimester. Women with a score \geq 5 can subsequently be screened more elaborately on other risk factors, such as a history of depressive episodes, recent life events and social support. Future studies should focus on

developing and testing such a screening model.

In chapter 5, the six-item State and Trait Anxiety Inventory (STAI) was investigated on its predictive accuracy ($n=4,856$). This tool is also commonly used, and validated in samples of pregnant and postpartum women. Using the prevailing cut-off (≥ 42), the odds ratio was >3.49 in all three trimesters. Adding the antenatal EPDS-scores decreased the odds ratios.

The overall discriminatory power was reasonable (AUC 0.73) in the second and third trimesters only. Irrespective of cut-off, the predictive performance was poor; with cut-off ≥ 42 in the first trimester, sensitivity and positive predictive value were approximately 30%, specificity and negative predictive value were around 90%. Using cut-off ≥ 36 in the second trimester, sensitivity and specificity were both approximately 67%, the positive predictive value was 23%, while the negative predictive value increased to 93%.

As negative predictive values were high at all times, women with low anxiety levels can be reassured that it is very unlikely that they will experience symptoms of anxiety in the postpartum period. A two-stage screening as proposed in chapter 4 cannot be recommended here, as there are still many uncertainties about specific risk factors for antenatal postpartum anxiety. Future studies should therefore focus on specific anxiety in the antenatal and postpartum period, rather than considering anxiety to be a comorbidity of depression.

Chapter 6 presents the design of a randomized controlled trial (RCT). We included 7,275 women in the cohort in order to include 300 women with mild to moderate levels of anxiety or depression in the trial. Women who are randomized into the intervention arm are offered 10-14 individual cognitive behavioral therapy (CBT) sessions, of which 6-10 will be received during pregnancy. Women in the control group receive care as usual (CAU). After baseline screening in the first trimester, there are 7 follow-up measurements. The final measurement at 18 months postpartum includes maternal anxiety and depression and testing the child on cognitive, psychomotor and behavioral development. Besides anxiety and depression, the follow-up questionnaires include the experience of life events, personality traits, lifestyle, attitudes, coping style, health care consumption and quality of life.

The thesis concludes with a general discussion in chapter 7 on whether or not to screen on antenatal symptomatology in order to prevent postpartum symptoms. The criteria listed by Wilson and Jungner and the WHO are applied. Although it is a recognized health problem with a high burden, there are too many uncertainties for a heartfelt 'yes' on whether an antenatal screening program for postpartum symptomatology would be beneficial.

