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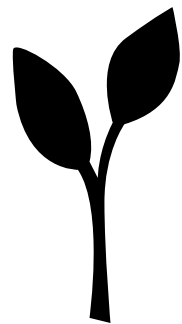
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Associations of life events during pregnancy with longitudinal change in symptoms of antenatal anxiety and depression.

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chapter 2

Abstract

Objective

To investigate the association of life events during pregnancy with change in antenatal anxiety and depression symptoms. We distinguished pregnancy related and non-pregnancy related events and assessed specificity of these associations for depressive or anxious symptoms. In addition, we investigated whether the associations were affected by personality or childhood adversities.

Measurements and findings

1,603 women during their first trimester of pregnancy were included between May 2010 and May 2012. We associated pregnancy related and non-pregnancy related life events, childhood adversities and the personality traits neuroticism and extraversion with the change in symptoms of anxiety (State Trait Anxiety Inventory) and depression (Edinburgh Postnatal Depression Scale) from week 12 to week 36.

Life events during pregnancy were associated with increasing antenatal symptoms of anxiety and depression. Effect sizes associated with the highest numbers of events observed ranged from 0.59 to 1.31. Pregnancy related events were specifically associated with increasing symptoms of anxiety, whereas non-pregnancy related events were merely associated with an increase in symptoms of depression. Neither personality traits nor childhood trauma influenced the associations under study.

Key conclusions

Compared to pregnancy related events, non-pregnancy related events show stronger associations with increases in symptoms of anxiety or depression. Pregnancy related life events during pregnancy increase levels of antenatal anxiety, whereas depression levels increase when women experience life events that are unrelated to pregnancy. There was no evidence of modification of these associations by neuroticism, extraversion or childhood trauma.

Implications for practice

Our findings may help midwives to tailor psychosocial care to the specific risks of the pregnant woman which may eventually have a positive impact on the health of mother and child.

Background

During pregnancy, 10-15% of all women experience mild to moderate symptoms of anxiety or depression^{1,2}. In addition to the burden to women themselves, these symptoms are associated with unfavorable obstetric outcomes, as well as with an adverse cognitive, motor and psychosocial development of the child^{3,4}.

The most consistent predictor of depression in both the general population^{5,6} and pregnant women⁷, is having experienced life events. However, studies among pregnant women mostly considered events that happened before pregnancy, ignoring life events experienced during pregnancy. Recency of a life event, however, has shown to be associated with particularly high levels of anxiety or depression⁸. Therefore, stressors that occur during pregnancy, e.g. physical problems⁹, are likely to have a higher impact on antenatal symptoms of anxiety or depression than those occurring before pregnancy. Moreover, we hypothesize that in particular life events that are specifically related to pregnancy might trigger anxious or depressive feelings. As far as we know, neither life events during pregnancy as a separate category nor specific pregnancy related life events have been investigated in relation to change in levels of antenatal anxiety or depression to date.

Besides the experience of life events, personality traits are known to be closely linked to psychopathology^{10,11}. High levels of neuroticism and low extraversion are not only directly associated with depression and anxiety. They have also shown to modify the promoting effects of life events on the onset and maintenance of psychopathology in such a way that being high neurotic or low extraverted makes people more vulnerable to become anxious or depressed when experiencing negative life events⁶.

In addition to personality traits, a history of traumatic childhood events such as physical or sexual abuse or loss of a parent have been suggested as modifiers of the association of adult life events with psychopathology. Indeed, having experienced childhood trauma makes people more vulnerable to depression in adult life^{5,12}.

It is presently unknown whether the aforementioned relationships are any different during pregnancy. Animal studies have shown that female brains change during the transition to motherhood and that these changes might lead to a change in their behavior¹³. Women may therefore respond differently to an event during pregnancy than outside pregnancy, and personality traits as well as childhood events may play a disparate role herein.

The present study is the first to investigate the change in symptoms of antenatal anxiety or depression associated with life events during pregnancy making a distinction between pregnancy and non-pregnancy events. The specificity of these associations for depressive

symptoms and symptoms of anxiety is investigated as well as their potential modification by neuroticism, extraversion and childhood trauma.

Methods

Subjects

The present study was carried out within the ongoing Pregnancy, Anxiety and Depression (PAD) Study. This is a prospective cohort study that was set up to investigate symptoms of and risk factors for anxiety or depression during pregnancy and the first year postpartum. All pregnant women visiting primary and secondary obstetric care centers in the Netherlands during their first trimester are invited, and those who participate are followed up until 12 months postnatal. The study protocol was approved by the medical ethical committee of the University Medical Centre Groningen.

For the present study we included 3,358 women that were screened at a pregnancy duration of around 12 weeks from May 2010 to May 2012. By the end of that period, 101 primary and 7 secondary obstetric care centers were participating. Follow-up in the current study was collected at a pregnancy duration of approximately 36 weeks.

Response, follow-up and missing data

Out of 3,358 women responding to the baseline screening questionnaire, 1,603 (48%) also filled out the follow-up questionnaires and formed the study population for the present analysis. The majority of women who did not respond to the follow-up questionnaire had pregnancy durations of less than 36 weeks or gave birth before even reaching this duration and was therefore not eligible to be included in the present study. Women with pregnancy durations of 36 weeks or more who had not responded to the follow-up questionnaire, 453 in number (26%), showed no marked differences with those who did complete the follow-up assessment, with respect to mean baseline anxiety and depression, personality scores, number of life events, parity, age, educational level or income.

The percentage of missing data in the present study ranged from 3.5 to 37.1 for the variables of main interest; anxiety (3.7%), depression (4.2%), childhood trauma (3.5%), non-pregnancy related events during pregnancy (37.3%), pregnancy related events during pregnancy (35.1%), neuroticism (5.2%) and extraversion (4.4%). The percentage of missing data of the potential confounders ranged from 5.9 (maternal age) to 40.7 (total family income).

Complete case analysis can give biased results and exclusion of patients with missing data will decrease the statistical power of a study¹⁴. Missing values for all variables except for the outcome variables were imputed because it has been shown that when outcome measures are not imputed, the precision of a study is generally larger¹⁴.

Missing data was imputed using multiple imputation by chained equations under the assumption that missing values were missing at random or missing completely at random. Multiple data sets (N=5) were generated to account for the uncertainty in imputed data. The regression coefficients and standard errors were pooled using Rubin's method for multiple imputation inference¹⁵.

Imputation and all analyses were carried out using STATA MP 11.0.

Instruments

Anxiety, depression were measured at both baseline and follow-up. Personality traits, childhood trauma and measures on all potential confounders were assessed at baseline, and life events during pregnancy were assessed at follow-up.

The 6-item State Trait Anxiety Inventory (STAI) was used for the measurement of anxiety. This shortened version has demonstrated to be as valid as the original 20-item STAI¹⁶. Scores ≥ 42 indicate moderate to high levels of anxiety.

The Edinburgh Postnatal Depression Scale (EPDS) was used to measure state of depressive symptoms and has shown to be valid for both pregnant and postnatal women¹⁷. A cut-off score ≥ 12 indicates a moderate to high level of depression.

Data on life events during pregnancy was collected using a 50-item questionnaire developed in the Avon Longitudinal Study of Parents And Children (ALSPAC)¹⁸. This questionnaire measures life events regarding employment, marital problems, illness or death of loved ones, abuse of either the mother or one of her children and substance misuse in her family. In addition, it contains questions on life events that relate to pregnancy, i.e. testing for congenital anomalies, test results indicating that the baby might have abnormalities, being told that it is a twin pregnancy, finding out that the partner does not want to have the baby, bleeding and being afraid to miscarry, trying to get an abortion, and finding out that something that happened might be harmful to the baby. For the analyses, we used the number of life events during pregnancy categorized as general life events or life events related to pregnancy.

We defined childhood trauma as the occurrence of an event before the age of 16 that is generally considered relevant for developing emotional symptoms¹². It was analyzed as the

number of positive responses to the following items from the Life Events Scale (CERQ)¹⁹: loss of a parent due to divorce or death, severe mental illness of a parent, substance misuse in family of origin, violence in family of origin, physical abuse and sexual abuse.

The Dutch version²⁰ of the NEO Five Factor Inventory (NEO-FFI) was used to assess personality traits. The NEO-FFI is a shortened version of the NEO-Personality Inventory-Revised (NEO-PI-R), has proved to be valid and has an internal consistency ranging from 0.68 to 0.86²¹. This instrument consists of 60 items covering the five major dimensions of personality; neuroticism, extraversion, openness, agreeableness and conscientiousness. A 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) was used for the responses. In the present study, the dimensions neuroticism and extraversion were considered only because of their established relation with psychopathology^{10,11}.

Potential Confounders

Several a priori potential confounders were considered: marital status (married yes/no), maternal age at baseline, social support assessed by asking a rank for the satisfaction of the perceived support in specific situations on a scale from 1 to 6, primiparity (yes/no) and socio-economic position. Socio-economic position was calculated as the equally weighted average of the educational attainment level of the respondent, her partner, and their total income.

Statistical Analysis

To compare effect sizes between the associations studied, we started by creating Z-scores for personality traits, depression and anxiety. Numbers of life events were standardized to a continuous number between 0 and 1. This was done by dividing the number of events for each woman by the maximum number of events that had occurred within each category of life events, and then analyzed as continuous variables. Consequently, coefficients from subsequent regression analyses indicated the effect size (Cohen's d) of a difference between no life events and the maximum number of life events per category.

A paired t-test was performed to evaluate whether changes in levels of anxiety and depression between baseline and follow-up were statistically significant.

The associations of life events, childhood trauma and personality traits with the mean change of symptoms of anxiety and depression from baseline to follow-up were analyzed using linear regression models. Mean change of symptoms was analyzed as the follow-up level adjusted for its baseline value. First, the two distinct categories of life events, childhood trauma and both personality traits were entered separately as predictor variables.

As depression and anxiety are often comorbid, we additionally investigated specificity of the associations for either anxiety or depression by adjusting the analysis of anxiety for baseline and follow-up depressive symptoms, and vice versa. Second, we analyzed whether the associations of life events with symptom levels were modified by personality traits and childhood trauma. This was done by entering interaction terms for these variables and each of the life event variables, next to their main effects, and assessing their statistical significance.

In each regression analysis, potential confounders were added as independent variables and the amount of change in the coefficients of the variables of interest was assessed. The change was considered a measure of the extent of confounding. Confounders with substantial effects (>10%) were retained in all regression analyses.

Findings

At both baseline and follow-up, symptoms of antenatal anxiety were more prevalent than those of depression. Slightly more women experienced symptoms of anxiety at follow-up (N=219, 14%) compared to baseline (N=199, 12%). The prevalence of depression did not change during follow-up (N=98, 6%).

Table 1 shows that most women were medium to highly educated, and their total family income was generally modal. An ample half of all women experienced specific pregnancy related events during pregnancy (57%), whereas non-pregnancy related events were more common (78%). Childhood trauma was experienced by 26% of women. Mean levels of anxiety and depression slightly increased from baseline to follow-up in a statistically significant way ($p < 0.001$). Subsequent regression analyses indicated that none of the confounders considered had a substantial influence on the associations. Therefore, they were not included in the final models.

Table 1 Characteristics of the study population (N=1,603)

Maternal age in years, mean (min-max)	30 (17-46)
Primiparae, N (%)	655 (41%)
Education, N (%)	
Elementary education	5 (0,3%)
Lower tracts of secondary education	71 (4%)
Higher tracts of secondary education	609 (38%)
Higher vocational education	640 (40%)
University education	278 (17%)
Total family income N (%)	
0 – 30.999 euros	294 (18%)
31.000 – 59.999 euros	823 (51%)
60.000 euros or more	486 (30%)
Pregnancy related life events ^a	
One or more, N (%)	914 (57%)
Median number (min-max)	1 (0-4)
Non-pregnancy related life events ^a	
One or more, N (%)	1250 (78%)
Median number (min-max)	2 (0-20)
Childhood adversities ^b	
One or more, N (%)	417 (26%)
Median number (min-max)	0 (0-6)
Anxiety (STAI) baseline level ^c, mean (SD)	32.35 (8,41)
Anxiety (STAI) follow-up level ^d, mean (SD)	32.96 (9,20)
Depression (EPDS) baseline level ^c, mean (SD)	4.32 (3,52)
Depression (EPDS) follow-up level ^d, mean (SD)	4.93 (3,68)

STAI – Spielberger State Trait Anxiety Inventory (min-max 20-80)

EPDS – Edinburgh Postnatal Depression Scale (min-max 0-30)

^a experienced during pregnancy

^b before age of 16

^c pregnancy duration of 12 weeks

^d pregnancy duration of 36 weeks

Table 2 shows the associations of the two categories of life events, childhood trauma, and both personality traits with the change in symptoms of anxiety and depression from baseline to follow-up.

Both types of life events, non-pregnancy related and pregnancy related, showed a statistically significant association with increasing levels of antenatal symptoms of anxiety and depression. These associations were monotonous and approximately linear. Effect sizes associated with the maximum number of events compared to no events were moderate to very large, i.e. ranged from 0.59 to 1.31. Compared to pregnancy related events, non-pregnancy related events showed stronger associations with increases in these symptoms. Life events that were related to pregnancy were still associated with the change in anxiety when correcting for depression, which indicates specificity of the association for anxious symptoms. Conversely, non-pregnancy related events merely had a statistically significant influence on change in depression when corrected for anxiety.

Childhood trauma was not associated with change in antenatal symptoms of anxiety or depression. Personality traits did show a statistically significant association; higher levels of neuroticism as well as lower levels of extraversion were associated with increasing levels of antenatal symptoms of anxiety and depression.

There was no statistically significant modification by the personality traits or childhood trauma of the associations between life events during pregnancy and change in anxious or depressive symptom levels (data not shown).

Table 2 Associations of life events during pregnancy, childhood adversities and personality with changes in antenatal symptoms of depression and anxiety

	Anxiety (STAI)		Depression (EPDS)	
	Mean change (95% CI)	Mean change (95% CI) ^c	Mean change (95% CI)	Mean change (95% CI) ^d
Non-pregnancy related life events ^a	1.166 (.598 ; 1.735)	.009 (-.008 ; .025)	1.312 (.807 ; 1.817)	.031 (.019 ; .043)
Pregnancy related life events ^a	.746 (.470 ; 1.022)	.085 (.024 ; .145)	.586 (.349 ; .823)	.025 (-.029 ; .078)
Childhood adversities ^b	.129 (-.369 ; .627)	-	-.222 (-.716 ; .273)	-
Neuroticism (NEO-FFI)	.260 (.207 ; .313)	-	.245 (.188 ; .302)	-
Extraversion (NEO-FFI)	-.172 (-.217 ; -.127)	-	-.096 (-.140 ; -.0521)	-

Mean changes are follow-up (week 36) values adjusted for baseline (week 12) values

Levels of depression, anxiety and personality traits were standardized by calculating Z-scores.

Number of life events and childhood adversities were standardized to values ranging from 0 to 1

STAI – Spielberger State Trait Anxiety Inventory (min-max 20-80)

EPDS – Edinburgh Postnatal Depression Scale (min-max 0-30)

a number per woman

b number per woman before the age of 16, standardized to values ranging from 0 to 1

c additionally corrected for depression level at baseline and follow-up

d additionally corrected for anxiety level at baseline and at follow-up

NEO-FFI NEO Five Factor Inventory

Discussion

In the present prospective cohort study, we investigated associations of pregnancy related and non-pregnancy related life events during pregnancy with longitudinal change in symptoms of antenatal anxiety or depression. We studied the specificity of the associations for anxiety or depression, and the potential modification of the associations by specific personality traits and childhood trauma.

We demonstrated that in general higher numbers of life events that had occurred during pregnancy were associated with increasing antenatal symptoms of anxiety or depression from 12 to 36 weeks of pregnancy. Non-pregnancy related events showed stronger associations than pregnancy related events. Pregnancy related events were specifically associated with increasing symptoms of anxiety, whereas non-pregnancy related events were merely associated with an increase in symptoms of depression. Further, we observed that higher levels of neuroticism and lower levels of extraversion were associated with increasing symptoms of both anxiety and depression, and that childhood trauma did not predict changes in symptoms of anxiety or depression. Neither neuroticism, nor extraversion, nor having experienced childhood trauma moderated the associations between life events and symptoms of anxiety or depression.

Contrary to our hypothesis pregnancy related events were less strongly associated with antenatal increases of anxiety or depression than non-pregnancy related events. Interestingly however, pregnancy related events were differentially associated with type of symptomatology, i.e. especially increases in anxiety were explained by these events. Conversely, non-pregnancy related events associated with development of depressive symptoms. This makes sense, as it is very likely that a woman's first response to an event such as hearing that prenatal screening results indicate that something might be wrong with the baby is worrying about the future of her child, whereas an event like the loss of a loved one is more likely to trigger feelings of depression. It is important to note that antenatal anxiety might have a larger impact on the child's neuromotor development than depression during pregnancy²².

A limited number of studies have been conducted on psychological outcomes after experiencing specific pregnancy related events during pregnancy. Most studies addressed prenatal testing and diagnosis. Kowalcek (2003) found that women had higher anxiety levels both before and after prenatal testing, especially when they had a positive test result²³. In addition, at the time of prenatal screening²⁴ or shortly after the diagnosis of an anomaly²⁵,

the majority of women in their respective samples had higher stress levels. In line with our finding is that a prenatal diagnosis of congenital heart disease was associated more with anxiety than with depression²⁶. Nevertheless, results of the only randomized controlled trial on this topic conducted by Kleinveld et al. (2006) demonstrated that offering prenatal screening did not increase subsequent anxiety levels²⁷. Our findings largely corroborate those obtained in a large cohort study showing that various pregnancy related and non-pregnancy related stressors went with increases in both antenatal anxiety and depression²⁸. They did not demonstrate that specifically pregnancy related factors were associated with anxiety rather than depression. However, this study was cross-sectional with data collected at varying pregnancy durations. Another cross-sectional study showed that several pregnancy and non-pregnancy related events were associated with emotional and somatic distress but in the analyses no distinction between the two types of events was made²⁹.

As to the associations between personality traits and anxiety or depression, research has mostly been conducted in men and non-pregnant women^{10,11}. We observed in our study that both high neuroticism and low extraversion are associated with increasing levels of both antenatal anxiety and depression, not contradicting our hypothesis that during pregnancy the associations of these traits with antenatal anxiety and depression are different³³.

We further hypothesized that the association between life events during pregnancy and the change in symptoms of antenatal anxiety or depression is modified by personality traits or childhood trauma. However, none of the pertaining interactions were substantial or significant. This is contrary to our expectation. Spinhoven et al. (2010) considered neuroticism as a modifier³⁰; however, they studied this personality trait as a modifier in the association between childhood trauma and anxiety or depressive disorders, whereas we considered childhood trauma to be an effect modifier itself. In addition, our study did not consider disorders but subsyndromal symptoms.

Our findings did not identify childhood trauma as an effect modifier; which may indicate that having experienced childhood trauma does not make women more vulnerable to an adverse impact of life events during pregnancy. These findings are supported as well as contradicted by previous studies. For example, Comijs (2007) did not find evidence for moderation of the association between life events and depression or anxiety by childhood trauma³¹. However, this study consisted of an elderly population in which most reported childhood traumas were related to the Second World War. On the other hand, Brown and Harris (1978) found a moderating effect of a specific traumatic event⁵, i.e. loss of the mother during childhood, on the association of recent stressful life events and ongoing difficulties.

Further, Bifulco et al. (2000) found that in particular the combination of childhood trauma and negative life events in adulthood predicted recurrent depressive episodes in women³². A possible explanation for the discrepancy of the findings in these studies with our observations is that they included people with anxiety or depressive disorders, not subsyndromal symptoms.

A few limitations of this study need to be considered. First, all assessments on life events were done using retrospective self-report checklists, which may be prone to recall bias. People with mental health problems tend to over-report the number and severity of stressors that they have experienced³³. We used the number of life events and not the perceived severity to minimize this potential bias. Second, current affective state might influence the assessment of personality²⁰. However, when we excluded women with moderate to high levels of anxiety or depression at baseline, results were similar. Third, the items measuring neuroticism in the NEO-FFI and the items of the EPDS are alike, which might have inflated the associations between depression and personality traits²⁰. However, the time frames of both measurements differ; EPDS measures state ('how do you feel at this moment'), whereas NEO-FFI measures trait ('how do you usually feel'). Finally, although we observed increasing anxiety and depression associated with life events, mean scores remained below the cut-off value for subclinical and clinical disorders. Therefore our results are not necessarily applicable to pregnant women with anxiety or depressive disorders. Nevertheless, having subthreshold symptoms of depression is a risk factor for developing a clinical disorder as convincingly shown in a systematic literature review³⁴.

These limitations are potentially offset by strengths of this study. First, the sample size was considerable and as far as we know one of the largest in this field. Further, the present study is the first to investigate specific pregnancy related events compared to general types of events, and interactions between these categories and personality traits as well as childhood trauma. Finally, this study was the first to consider longitudinally assessed change in symptoms of antenatal anxiety or depression in relation to events during pregnancy. This approach makes reverse causality, i.e. the events were induced by declining mental health unlikely. Furthermore, symptoms measured at a single time point in pregnancy may be the result of enduring depression or anxiety that started before pregnancy.

In conclusion, the present study shows that women do not essentially respond differently to a life event during pregnancy than outside pregnancy. Compared to pregnancy related events, non-pregnancy related events have more substantial associations with increases in symptoms of anxiety and depression. The study also shows that during pregnancy, events

that are related to pregnancy go with increases in anxiety, whereas levels of depression increase in association with non-pregnancy related events. We found no evidence of modification of these associations by neuroticism, extraversion or childhood trauma. Our findings may help midwives to tailor psychosocial care to the specific risks of a woman and thereby to contribute to the health of mother and child.

References

1. Evans J, Heron J, Francomb H, Oke S, Golding J. Cohort study of depressed mood during pregnancy and after childbirth. *BMJ* 2001 323, 257-260
2. Dayan J, Creveuil C, Marks MN, et al. Prenatal depression, prenatal anxiety, and spontaneous preterm birth: a prospective cohort study among women with early and regular care. *Psychosom Med* 2006 68, 938-46.
3. Van den Bergh BR, Mulder EJ, Mennes M, Glover V. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neurosci Biobehav Rev* 2005 29, 237-258.
4. Talge NM, Neal C, Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *J Child Psychol Psychiatry* 2007 48, 245-261.
5. Brown GW, Harris T. Social origins of depression: a study of psychiatric disorder in women. Taylor & Francis 1978.
6. Ormel J, Oldehinkel AJ, Brilman EI. The interplay and etiological continuity of neuroticism, difficulties, and life events in the etiology of major and subsyndromal, first and recurrent depressive episodes in later life. *Am J Psychiatry* 2001 158, 885-891.
7. Leigh B, Milgrom J. Risk factors for antenatal depression, postnatal depression and parenting stress. *BMC Psychiatry* 2008 8, 24.
8. Surtees PG, Miller PM, Ingham JG, Kreitman NB, Rennie D, Sashidharan SP. Life events and the onset of affective disorder. A longitudinal general population study. *J Affect Disord* 1986 10, 37-50.
9. Perlen S, Woolhouse H, Gartland D, Brown SJ. Maternal depression and physical health problems in early pregnancy: findings of an Australian nulliparous pregnancy cohort study. *Midwifery* 2013 Mar;29(3):233-239.
10. Klein DN, Kotov R, Bufferd SJ. Personality and depression: explanatory models and review of the evidence. *Annu Rev Clin Psychol* 2010 7, 5.1-5.27.
11. Kotov R, Gamez W, Schmidt F, Watson D. Linking "big" personality traits to anxiety, depressive and substance use disorders: a meta-analysis. *Psychol Bull* 2010 136, 768-821.
12. Hovens JG, Giltay EJ, Wiersma JE, Spinhoven P, Penninx BW, Zitman FG. Impact of childhood life events and trauma on the course of depressive and anxiety disorders. *Acta Psychiatr Scand* 2012 126, 198-207.
13. Kinsley CH, Amory-Meyer E. Why the maternal brain? *J Neuroendocrinol* 2011 23, 974-983.
14. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Statistics in Medicine* 2010 30, 377-399.
15. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. John Wiley and Sons, 1987 New York
16. Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* 1992 31, 301-306.
17. Bowen A, Muhajarine N. Prevalence of antenatal depression in women enrolled in an outreach program in Canada. *J Obstet Gynecol Neonatal Nurs* 2006 35, 491-498.
18. Golding J, Pembrey M, Jones R; ALSPAC Study Team. ALSPAC--the Avon Longitudinal Study of Parents and Children. I. Study methodology. *Paediatr Perinat Epidemiol* 2010 15, 74-87. ALSPAC questionnaires; <http://www.bristol.ac.uk/alspac>.
19. Garnefski N, Kraaij V. Negative Life Events Scale 2001 (<http://www.socialsciences.leiden.edu/psychology/organisation/chn/health/research/instruments/life-events-scale.html>).
20. Hoekstra HA, Ormel J, De Fruyt F. NEO persoonlijkheidsvragenlijsten NEOPI-R en NEO-FFI. Handleiding. 1996 Lisse: Swets & Zeitlinger.
21. Costa PT Jr., McCrae RR. Revised NEO Personality Inventory (NEO-PI-R) and NEO Five-Factor Inventory (NEO-FFI) professional manual. 1992 FL: Psychological Assessment Resources.
22. Van Batenburg-Eddes T, De Groot L, Huizink AC, Steegers EA, Hofman A, Jaddoe VW, Verhulst FC, Tiemeier H. Maternal symptoms of anxiety during pregnancy affect infant neuromotor development: the generation R study. *Dev Neuropsychol* 2009 34, 476-493.
23. Kowalcek I, Huber G, Lammers C, Brunk J, Bieniakiewicz I, Gembruch U. Anxiety scores before and after prenatal testing for congenital anomalies. *Arch Gynecol Obstet* 2003 267, 126-129.
24. Leithner K, Maar A, Fischer-Kern M, Hilger E, Löffler-Stastka H, Ponocny-Seliger E. Affective state of women following a prenatal diagnosis: predictors of a negative psychological outcome. *Ultrasound Obstet Gynecol* 2004 23, 240-246.
25. Kaasen A, Helbig A, Malt UF, et al. The relation of psychological distress to salivary and serum cortisol levels in pregnant women shortly after the diagnosis

- of a structural fetal anomaly. *Acta Obstet Gynecol Scand* 2011 91, 68-78.
26. Rychik J, Donaghue DD, Levy S, Fajardo C, Combs J, Zhang X, Szwasz A, Diamond GS. Maternal Psychological Stress after Prenatal Diagnosis of Congenital Heart Disease. *J Pediatr* 2012 doi: 10.1016/j.jpeds.2012.07.023.
 27. Kleinveld JH, Timmermans DR, De Smit DJ, Adér HJ, Van der Wal G, Ten Kate LP. Does prenatal screening influence anxiety levels of pregnant women? A longitudinal randomised controlled trial. *Prenat Diagn* 2006 26, 354-361.
 28. Karaçam Z, Ançel G. Depression, anxiety and influencing factors in pregnancy: a study in a Turkish population. *Midwifery* 2009 25, 344-56.
 29. Traviss GD, Meer S, West RM, House AO. Life events and difficulties and their association with antenatal distress in White and South Asian women in the UK. *Soc Psychiatry Psychiatr Epidemiol* 2012 Sep 18.
 30. Spinhoven P, Elzinga BM, Hovens JG, Roelofs K, Zitman FG, Van Oppen P, Penninx BW. The specificity of childhood adversities and negative life events across the life span to anxiety and depressive disorders. *J Affect Disord* 2010 126, 103-112.
 31. Comijs HC, Beekman AT, Smit F, Bremmer M, Van Tilburg T, Deeg DJ. Childhood adversity, recent life events and depression in late life. *J Affect Disord* 2007 103, 243-246.
 32. Bifulco A, Bernazzani O, Moran PM, Ball C. Lifetime stressors and recurrent depression: preliminary findings of the Adult Life Phase Interview (ALPHI). *Soc Psychiatry Psychiatr Epidemiol* 2000 35, 264-275.
 33. Grant KE, Compas BE, Thurm AE, et al. Stressors and child and adolescent psychopathology: Evidence of moderating and mediating effects. *Clin Psychol Rev* 2006 26, 257-283.
 34. Cuijpers P, Smit F. Subthreshold depression as a risk indicator for major depressive disorder: a systematic review of prospective studies. *Acta Psychiatr Scand* 2004 109, 325-31.

