

Maternal Psychosocial Stress Associates With Increased Risk of Asthma Development in Offspring

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ABSTRACT

Prenatal maternal psychosocial stress might influence childhood asthma development.

Evaluating paternal psychosocial stress and conducting a sibling comparison could provide further insight into the role of unmeasured confounding. We examined the associations of parental psychosocial stress during and after pregnancy with asthma at 7 years in the Norwegian Mother and Child Cohort Study (n=63,626). Measures of psychosocial stress included lifetime major depressive symptoms, current anxiety/depression symptoms, use of antidepressants, anxiolytics and/or hypnotics, life satisfaction, relationship satisfaction, work stress and social support. Childhood asthma was associated with maternal lifetime major depressive symptoms, adjusted relative risk (aRR) 1.19 (95% CI: 1.09, 1.30), in addition to symptoms of anxiety/depression during pregnancy, aRR 1.17 (95% CI: 1.06, 1.29), and 6 months after delivery, aRR 1.17 (95% CI: 1.07, 1.28). Maternal negative life events during pregnancy, aRR 1.10 (95% CI: 1.06, 1.13), and 6 months after delivery, aRR 1.14 (95% CI: 1.11, 1.18), were also associated with asthma. These associations were not replicated when evaluated within sibling groups. There were no associations with paternal psychosocial stress. In conclusion, maternal anxiety/depression and negative life events was associated with offspring asthma, but this might be explained by unmeasured maternal background characteristics that remain stable across deliveries.

Key words: asthma; maternal; paternal; pregnancy; psychosocial stress.

Abbreviations: ATC, Anatomical Therapeutic Chemical classification system; CI, confidence interval; MBRN, the Medical Birth Registry of Norway; MoBa, the Norwegian Mother and Child Cohort Study; NorPD, the Norwegian Prescription Database, OR, odds ratio; RR, Relative Risk.

Prenatal exposure to maternal psychosocial stress is associated with increased risk of childhood asthma (1-16). Previous studies mostly evaluated single or a limited number of measures of psychosocial stress or stress correlates (e.g. psychological functioning), hereafter denoted as psychosocial stress, including maternal negative life events (1, 4, 7, 11, 15), depression/anxiety (3, 6, 12, 14, 16), community violence (2), bereavement (5, 8, 13), job strain (9) and demoralization (10). These studies also varied in the outcome definition, where some evaluated wheezing symptoms (2, 10-12, 15) while others evaluated asthma (1, 3-9, 13, 14). Furthermore, most of these studies relied on maternal report of childhood asthma, while only a few used information from national registries/administrative databases (5, 8, 13, 14).

We wanted to further examine whether the previously reported associations of maternal psychosocial stress and risk of childhood asthma might be explained by unmeasured confounding, by using paternal psychosocial stress as a negative control and by conducting a sibling analysis (17, 18). If similar associations of maternal and paternal psychosocial stress is observed with childhood asthma, this could indicate that the reported association between maternal psychosocial stress and childhood asthma is explained by unmeasured background characteristics linked to psychosocial stress in both parents. A few previous studies examined paternal anxiety/depression while the mother was pregnant in relation to childhood asthma, reporting contradictory findings (6, 14). To the best of our knowledge, no previous study of parental psychosocial stress and childhood asthma explored a sibling comparison, in order to evaluate the potential role of unmeasured confounding by maternal background characteristics that remain stable between deliveries.

Our aim was therefore to estimate the associations of maternal psychosocial stress during and after pregnancy with childhood asthma. We also evaluated associations with paternal psychosocial stress and explored a sibling analysis to evaluate the role of unmeasured confounding. By performing this study in Norway, a country with universal access to health

care services and relatively low levels of social inequality, potential confounding by socio-economic factors is less likely compared to many other locations.

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METHODS

Study population

We used data from the Norwegian Mother and Child Cohort Study (MoBa) (19, 20), which recruited pregnant women from all over Norway between 1999 and 2008, at approximately 18 weeks gestation. All participants gave a written informed consent, and the participation rate was 41%. Mothers could participate with more than one pregnancy, resulting in approximately 95,200 mothers and 114,500 children. Information collected through MoBa questionnaires was subsequently linked to the Medical Birth Registry of Norway (MBRN), and the Norwegian Prescription Database (NorPD), using national identification numbers. Dispensed prescriptions in the NorPD are coded according to the Anatomical Therapeutic Chemical (ATC) classification system. A total of 83,767 live-born singletons born before July 1st 2007, who had reached age 7 by July 1st 2014, were eligible for the current study. Among these children, 63,626 had information on maternal psychosocial stress gathered at 18 gestational weeks, 30 gestational weeks and 6 months after delivery (Figure 1), and were included in the analysis of maternal psychosocial stress. In comparison, 47,619 children were available for the analysis of paternal psychosocial stress (Figure 1). This study was approved by the Norwegian Data Inspectorate and the Regional Committee for Medical and Health Research Ethics of South/East Norway.

Maternal psychosocial stress during pregnancy

The specific questions asked to capture psychosocial stress are displayed in Web Table 1. We defined maternal lifetime history of major depressive symptoms based on at least three affirmative answers to a previously validated five-item scale (21). Current self-reported symptoms of anxiety/depression was measured by a five-item symptom checklist

(SCL-5) at both 18 and 30 gestational weeks (22). The answers were obtained on a 4 point Likert scale (Cronbach's $\alpha=0.80/0.81$, at weeks 18 and 30, respectively), and we used the mean to indicate the overall burden of symptoms. Mothers also self-reported their use of antidepressants, anxiolytics and hypnotics during pregnancy at 18 and 30 gestational weeks, and retrospectively when the child was 6 months. Specific medications included *antidepressants* (N06AB, N06AF, N06AG and N06AX), *benzodiazepines and benzodiazepine-related drugs* (N05BA, N05CD, N03AE01 and N05CF), *buspiron* (N05BE01), *pregabalin* (N03AX16), and the hypnotic drug *melatonin* (N05CH01).

We also measured maternal self-reported life satisfaction with a five-item scale at both 18 and 30 gestational weeks (23-25), where overall life satisfaction was defined as the mean of the responses gathered on a 7 point Likert scale, and low scores represents dissatisfaction (Cronbach's $\alpha=0.89$, at both 18 and 30 weeks). Mothers also responded to 10 questions related to relationship satisfaction at both 18 and 30 gestational weeks (26). The answers were gathered on a 6 point Likert scale, where the scale was reversed for negatively phrased questions, and the mean across the ten items was used as a measure of overall relationship satisfaction (Cronbach's $\alpha=0.91$, at both weeks 18 and 30). Participants also reported whether they had experienced eight different negative life-events during the past year at 30 gestational weeks (27, 28), and the answers were added to indicate the total burden of negative life-events. Work stress was reported at 18 gestational weeks using eight questions with answers on a 4 point Likert scale. After reversing the answers to positively phrased questions, the mean was used as an overall measure of work stress, with higher values indicating higher levels of work stress. Finally, we defined social support as the mean of the answers to three questions at 18 gestational weeks.

Paternal psychosocial stress during pregnancy and maternal psychosocial stress after pregnancy

We also obtained information on paternal self-reported lifetime history of major depressive symptoms, current symptoms of anxiety/depression (SCL-5), use of antidepressants, anxiolytics and/or hypnotics, self-reported satisfaction with life, and relationship satisfaction at the time of recruitment. Mothers further reported current symptoms of anxiety/depression (SCL-5), use of antidepressants, anxiolytics and/or hypnotics, satisfaction with life, relationship satisfaction, in addition to negative life events occurring after 30 gestational weeks, when the child was 6 months.

Childhood asthma

We defined asthma at age 7 based on a dispensed asthma medication during the past year, in addition to a second dispensed prescription within one year after the first, as registered in the NorPD. Asthma medications included long-acting beta(2)-agonists (R03AC), inhaled corticosteroids (R03BA), fixed-dose combinations of inhaled beta(2)-agonists and corticosteroids (R03AK), and/or leukotriene antagonists (R03DC). We also assessed maternal report of current asthma in the 7 year questionnaire as a secondary outcome, defined as maternal report of doctor diagnosed asthma, in combination with either current symptoms or use of asthma medications in the past year.

Covariates

We obtained additional information on characteristics that could plausibly be associated with psychosocial stress and childhood asthma. Maternal characteristics included age at delivery, parity (0, 1, 2, 3 or more), education (less than high school, high school, up to four

years of college, more than four years of college), pre-pregnancy body-mass index (<18.5, 18.5-24.9, 25-29.9, 30 or higher), smoking during pregnancy (no, quit by 18 weeks, smoked after 18 weeks), smoking the first 6 months of the child's life (no, occasionally, daily) and history of asthma. Paternal characteristics included age at delivery (<25, 25-29, 30-34, 35 and higher), education (less than high school, high school, up to four years of college, more than four years of college), body-mass index (<18.5, 18.5-24.9, 25-29.9, 30 or higher), smoking (yes versus no) and history of asthma. Finally, child characteristics included gender, birth weight in grams, gestational age in weeks and whether the child was still breastfed at 6 months (yes versus no).

Statistical analysis

We evaluated parental psychosocial stress in relation to childhood asthma using log-binomial regression, reporting relative risks (RR) and 95% confidence intervals (CI). In order to account for the presence of siblings, we used robust cluster variance estimation. We adjusted the analysis of maternal psychosocial stress during pregnancy in relation to childhood asthma for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma. We did not adjust the association between maternal psychosocial stress during pregnancy and childhood asthma for pregnancy complications, since they could be on the causal pathway, and we were interested in examining the total association. However, maternal psychosocial stress 6 months after delivery was further adjusted for smoking 6 months after delivery, child gender, birth weight, gestational age, and whether the child was still breastfed at 6 months. The associations with paternal psychosocial stress were adjusted for paternal age, education, smoking, body-mass index and history of asthma.

We conducted a number of sensitivity analyses. First, we adjusted maternal symptoms of anxiety/depression for the use of antidepressants, anxiolytics and/or hypnotics during pregnancy. Second, we adjusted the associations with maternal psychosocial stress 6 months after delivery for the same measures of psychosocial stress during pregnancy. Third, we evaluated the associations with maternal prenatal psychosocial stress in the subsample with information on paternal psychosocial stress. Fourth, we explored mutual adjustment of the same measures of maternal and paternal psychosocial stress. To examine a selection bias due to the restriction of the main analysis to those with information from the questionnaires administered at 18 gestational weeks, 30 gestational weeks and 6 months after delivery, these analyses were re-evaluated without restricting to those with information from the questionnaire administered 6 months after delivery. We also conducted a secondary analysis of maternal report of asthma at age 7 in the subgroup with information from the 7-year follow-up questionnaire (n= 37,694). Finally, we also conducted a sibling analysis using fixed effects logistic regression, reporting odds ratios (OR) and 95% CI. The fixed-effects logistic regression compares the distribution of the exposure among sibling pairs discordant for the outcome of interest. The analysis is therefore restricted to discordant sibling pairs, and is equivalent to a conditional logistic regression used for matched case-control studies, where the discordant sibling pairs are the matched pairs of interest.

Less than 5% of observations were excluded from any of the multivariable analyses because of missing information on one or more covariates. The results presented are therefore from a complete case analysis. We conducted the analyses using Stata version 14 (Statacorp LLC, Texas).

RESULTS

The distribution of background characteristics among children included in the analyses of maternal and paternal psychosocial stress is given in Table 1. When we compared included and excluded children based on necessary follow-up information, the children included had parents who were older, more educated, less likely to be smokers and more mothers who were nulliparous (Web Table 2). There was no appreciable difference in the proportion of children with asthma among those with (4.2%) and without (4.5%) information on measures of maternal psychosocial stress (Web Table 2). Likewise, the proportion of children with asthma among children with (4.1%) and without (4.5%) information on measures of paternal psychosocial stress was very similar (Web Table 2).

There was a modest correlation between the different measures of maternal psychosocial stress during pregnancy, ranging from 0.11 to 0.78 (Web Table 3). Maternal lifetime history of major depressive symptoms, adjusted RR 1.19 (95% CI: 1.09, 1.30), in addition to symptoms of anxiety/depression during pregnancy (SCL5), adjusted RR 1.19 (95% CI: 1.09, 1.30) per unit increase in the symptom score, was positively associated with asthma at age 7 (Table 2). There was no strong evidence for an association with maternal use of antidepressants, anxiolytics and/or hypnotics during pregnancy (Table 2). Additional adjustment of the association between maternal symptoms of anxiety/depression during pregnancy and childhood asthma for the use of antidepressants, anxiolytics and/or hypnotics did not change the associations (Web Table 4). When we evaluated maternal use of antidepressants, anxiolytics and hypnotics during pregnancy separately, we found no strong evidence for an association between any of these medication groups and childhood asthma (Web Table 5). Maternal negative life-events during pregnancy was also positively associated with asthma at 7 years, adjusted RR 1.10 (95% CI: 1.06, 1.13) per additional negative life-event (Table 2). There was no strong evidence of associations with maternal satisfaction with

life, relationship satisfaction or work stress (Table 2). The sensitivity analysis re-examining the associations with maternal psychosocial stress at 18 and 30 gestational weeks without restricting to those with information from the questionnaire administered 6 months after delivery yielded similar findings (Web Table 6).

We also evaluated associations of paternal psychosocial stress at the time of recruitment (during pregnancy) with asthma at 7 years, and the correlation between the different measures of paternal psychosocial stress is portrayed in Web Table 7. The correlations between the same measures of parental psychosocial stress at the time of recruitment ranged from 0.18 to 0.55, with the strongest correlation seen for relationship satisfaction (Web Table 8). We observed no strong evidence for associations of paternal psychosocial stress with asthma at 7 years (Table 3). For example, the association between paternal symptoms of anxiety/depression and asthma yielded an adjusted RR of 1.05 (95% CI: 0.90, 1.23) per unit increase in the symptom score (Table 3). Examining the associations with maternal psychosocial stress during pregnancy in the subsample in the analysis of paternal psychosocial stress yielded similar associations with maternal psychosocial stress (Web Table 9). Mutual adjustment of the same measures of parental psychosocial stress during pregnancy also did not change the associations observed with maternal psychosocial stress during pregnancy (Web Table 10).

The correlation between the same measures of maternal psychosocial stress during pregnancy and 6 months after delivery ranged from 0.56 to 0.78. Maternal symptoms of anxiety/depression reported 6 months after delivery, adjusted RR 1.17 (95% CI: 1.07, 1.28) per unit increase in the symptoms score, in addition to negative life events, adjusted RR 1.12 (95% CI: 1.09, 1.16) per additional negative life event, was positively associated with asthma at age 7 (Table 4). The association between maternal symptoms of anxiety/depression reported 6 months after delivery and asthma at 7 years was attenuated after adjustment for

symptoms during pregnancy (Table 4). In contrast, the association between negative life-events reported 6 months after delivery and asthma at 7 years remained largely unchanged after adjusting for negative life-events reported during pregnancy (Table 4).

The secondary analyses of parental psychosocial stress with asthma at age 7 defined based on maternal report through questionnaires yielded similar results as the main analysis (Web Tables 11-13). When we evaluated the associations within sibling groups, maternal symptoms of anxiety/depression before, during or after pregnancy showed no evidence of an association with offspring asthma at 7 years (Tables 5 and 6). However, the sibling analyses indicated a positive association between maternal relationship satisfaction and offspring asthma at 7 years not observed in the primary/population overall analysis (Tables 5 and 6). The sibling analyses yielded similar associations with paternal psychosocial stress (Web Table 14).

DISCUSSION

In this large-scale pregnancy cohort, maternal symptoms of anxiety/depression and negative life-events both during pregnancy and the first 6 months after delivery was positively associated with asthma at 7 years. Our findings were not explained by unmeasured confounding by background characteristics linked to these measures of psychosocial stress in both parents, since we observed no associations with paternal anxiety/depression. However, we cannot exclude unmeasured confounding by maternal background characteristics that remain stable between deliveries based on our sibling analysis. Other measures of maternal psychosocial stress, such as satisfaction with life, relationship satisfaction or work stress, showed no strong evidence of associations with the risk of childhood asthma.

Strengths of this study include the range of measures of psychosocial stress, the inclusion of paternal psychosocial stress as a negative control, the inclusion of a sibling comparison, and the modest likelihood of confounding due to social inequality. Selection bias could arise if either participation in MoBa or loss-to-follow-up are jointly associated with parental psychosocial stress and the child's risk of asthma. Very reassuringly, the prevalence of asthma medication use in the past year at age 7 among MoBa participants is very similar to the national estimated prevalence (29), and the proportion of children with asthma was similar among those with and without information on parental psychosocial stress. This indicates that neither participation in the cohort nor loss-to-follow-up was associated with our outcome of interest. Relying on self-report of parental psychosocial stress could have resulted in misclassification. Assuming that any misclassification of parental psychosocial stress is not differential by offspring asthma, this would have attenuated the observed associations. In contrast, if mothers with higher levels of psychosocial stress are more likely to obtain health care services for respiratory symptoms in the child, which could result in a higher proportion of their offspring being diagnosed with asthma, there is a chance of an ascertainment bias that

could have led us to overestimate the true association. We relied on dispensed asthma medications as registered in the prescription registry to define asthma. However, there is a high concordance between maternal report that the child use asthma medications when the child was 7 years and dispensed asthma medications (30). We also did not adjust for multiple testing due to the correlation between the measures of parental psychosocial stress, indicating that the tests are not strictly independent, and we can therefore not fully exclude the possibility of chance findings. We also can't exclude the possibility of unobserved confounding of the observed associations by factors that we could not adjust for, such as for example whether participants lived in an urban versus a rural environment. Finally, due to the modest number of discordant sibling groups, our sibling analysis is less well powered than the much larger primary analysis, which is reflected in the wider confidence intervals for the estimates obtained from this analysis. The sibling analysis is also more prone to bias by unmeasured parental background characteristics that change between deliveries in addition to misclassification (31). For example, if siblings differ to a greater extent with regard to distributions of potential confounders than with regard to the exposure of interest, the sibling analysis may be more biased than a standard analysis (31, 32).

Our main findings supports previously reported positive associations between maternal depression/anxiety and offspring asthma (3, 6, 14). The Generation R cohort reported an association between maternal symptoms of depression/anxiety during pregnancy with maternal report of wheezing symptoms the first 6 years of life (6). This association was seemingly independent of paternal anxiety/depression and maternal anxiety/depression after delivery (6). Results from the ALSPAC cohort further showed that maternal symptoms of anxiety during pregnancy was positively associated with maternal report of asthma at 7 years (3). Finally, a large Danish registry-based study showed a positive association between maternal depression both before and during pregnancy with childhood asthma defined by

hospital discharge codes and dispensed prescriptions, while there was no association with maternal use of medications for anxiety/depression, very similar to our findings (14). Our findings also supports previous studies indicating a positive association between maternal negative life events and childhood asthma (1, 4, 7, 11, 15), although the measures of negative life events varied greatly across studies. In contrast, our findings are not in line with the previous report that maternal work stress during pregnancy is positively associated with asthma (9).

Since we did not observe an association with paternal anxiety/depression, the association between maternal anxiety/depression and childhood asthma might not be explained by unmeasured characteristic linked to this measure of psychosocial stress in both parents (17). These results correspond to what was reported for paternal anxiety/depression from the Generation R cohort (6), but are in contrast to the findings from the Danish registry study (14). Seemingly negating the findings from the negative control analysis, the findings from our sibling analyses indicate that the associations of maternal symptoms of anxiety/depression and negative life events with offspring asthma could be explained by unmeasured maternal background characteristics that remain stable between deliveries. However, due to the modest number of discordant sibling groups available for the sibling analyses, and the fact that sibling analyses can actually be more biased under certain scenarios (31), we remain cautious in the interpretation of these findings.

Potential biological mechanisms exist for an influence of maternal psychosocial stress during pregnancy on offspring asthma development. In humans, exposure to prenatal psychosocial stress is also associated with altered cord blood cytokine responses (33) and elevated IgE levels (34-36), which might predispose the child to allergic airway disease. One might also speculate that maternal psychosocial stress during pregnancy could influence epigenetic changes in the developing offspring (37, 38) and/or result in shortening of telomere

length (39, 40), with potential consequences for asthma in the offspring. Additional research is necessary to further explore these potential mechanisms. The fact that we only observed associations with maternal symptoms of anxiety/depression and negative life events, but not other measures of psychosocial stress (satisfaction with life, relationship satisfaction and work stress), could indicate that these two measures were capturing something more severe.

In conclusion, maternal anxiety/depression and negative life events both during pregnancy and the first 6 months after delivery was associated with increased risk of asthma in the offspring, but this might be explained by unmeasured maternal background characteristics that remain stable across deliveries. The relatively modest levels of other measures of parental psychosocial stress (satisfaction with life, relationship satisfaction and work stress) were not associated with childhood asthma in this cohort from a country with universal access to health care and relatively modest social inequality.

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References

1. Lee A, Mathilda Chiu YH, Rosa MJ, et al. Prenatal and postnatal stress and asthma in children: Temporal- and sex-specific associations. *J Allergy Clin Immunol* 2016;138(3):740-747.
2. Chiu YH, Coull BA, Sternthal MJ, et al. Effects of prenatal community violence and ambient air pollution on childhood wheeze in an urban population. *J Allergy Clin Immunol* 2014;133(3):713-722.
3. Cookson H, Granell R, Joinson C, et al. Mothers' anxiety during pregnancy is associated with asthma in their children. *J Allergy Clin Immunol* 2009;123(4):847-853.
4. de Marco R, Pesce G, Girardi P, et al. Foetal exposure to maternal stressful events increases the risk of having asthma and atopic diseases in childhood. *Pediatr Allergy Immunol* 2012;23(8):724-729.
5. Fang F, Hoglund CO, Arck P, et al. Maternal bereavement and childhood asthma-analyses in two large samples of Swedish children. *PLoS One* 2011;6(11):e27202.
6. Guxens M, Sonnenschein-van der Voort AM, Tiemeier H, et al. Parental psychological distress during pregnancy and wheezing in preschool children: the Generation R Study. *J Allergy Clin Immunol* 2014;133(1):59-67.
7. Hartwig IR, Sly PD, Schmidt LA, et al. Prenatal adverse life events increase the risk for atopic diseases in children, which is enhanced in the absence of a maternal atopic predisposition. *J Allergy Clin Immunol* 2014;134(1):160-169.
8. Khashan AS, Wicks S, Dalman C, et al. Prenatal stress and risk of asthma hospitalization in the offspring: a Swedish population-based study. *Psychosom Med* 2012;74(6):635-641.
9. Larsen AD, Schlunssen V, Christensen BH, et al. Exposure to psychosocial job strain during pregnancy and odds of asthma and atopic dermatitis among 7-year old children - a prospective cohort study. *Scand J Work Environ Health* 2014;40(6):639-648.
10. Reyes M, Perzanowski MS, Whyatt RM, et al. Relationship between maternal demoralization, wheeze, and immunoglobulin E among inner-city children. *Ann Allergy Asthma Immunol* 2011;107(1):42-49.
11. Mathilda Chiu YH, Coull BA, Cohen S, et al. Prenatal and postnatal maternal stress and wheeze in urban children: effect of maternal sensitization. *Am J Respir Crit Care Med* 2012;186(2):147-154.
12. Ramratnam SK, Visness CM, Jaffee KFM, et al. Relationships Among Maternal Stress and Depression, Type 2 Responses, and Recurrent Wheezing at Age 3 Years in Low Income Urban Families. *Am J Respir Crit Care Med* 2017;195(5):674-681.
13. Liu X, Olsen J, Agerbo E, et al. Prenatal stress and childhood asthma in the offspring: role of age at onset. *Eur J Public Health* 2015;25(6):1042-1046.
14. Liu X, Olsen J, Pedersen LH, et al. Antidepressant use during pregnancy and asthma in the offspring. *Pediatrics* 2015;135(4):e911-917.
15. Rosa MJ, Just AC, Tamayo YOM, et al. Prenatal and postnatal stress and wheeze in Mexican children: Sex-specific differences. *Ann Allergy Asthma Immunol* 2016;116(4):306-312.
16. Lefevre F, Moreau D, Semon E, et al. Maternal depression related to infant's wheezing. *Pediatr Allergy Immunol* 2011;22(6):608-613.
17. Richmond RC, Al-Amin A, Smith GD, et al. Approaches for drawing causal inferences from epidemiological birth cohorts: a review. *Early Hum Dev* 2014;90(11):769-780.
18. Lawlor DA, Tilling K, Davey Smith G. Triangulation in aetiological epidemiology. *Int J Epidemiol* 2016;45(6):1866-1886.
19. Nilsen RM, Vollset SE, Gjessing HK, et al. Self-selection and bias in a large prospective pregnancy cohort in Norway. *Paediatr Perinat Epidemiol* 2009;23(6):597-608.
20. Magnus P, Birke C, Vejrup K, et al. Cohort Profile Update: The Norwegian Mother and Child Cohort Study (MoBa). *Int J Epidemiol* 2016;45(2):382-388.
21. Kendler KS, Neale MC, Kessler RC, et al. The lifetime history of major depression in women. Reliability of diagnosis and heritability. *Arch Gen Psychiatry* 1993;50(11):863-870.
22. Tambs K, Moum T. How well can a few questionnaire items indicate anxiety and depression? *Acta Psychiatr Scand* 1993;87(5):364-367.

23. Clench-Aas J, Nes RB, Dalgard OS, et al. Dimensionality and measurement invariance in the Satisfaction with Life Scale in Norway. *Qual Life Res* 2011;20(8):1307-1317.
24. Diener E, Emmons RA, Larsen RJ, et al. The Satisfaction With Life Scale. *J Pers Assess* 1985;49(1):71-75.
25. Lucas RE, Diener E, Suh E. Discriminant validity of well-being measures. *J Pers Soc Psychol* 1996;71(3):616-628.
26. Mellingen S, Torsheim T, Thuen F. Changes in alcohol use and relationship satisfaction in Norwegian couples during pregnancy. *Subst Abuse Treat Prev Policy* 2013;8:5.
27. Coddington RD. The significance of life events as etiologic factors in the diseases of children. II. A study of a normal population. *J Psychosom Res* 1972;16(3):205-213.
28. Rosand GM, Slinning K, Roysamb E, et al. Relationship dissatisfaction and other risk factors for future relationship dissolution: a population-based study of 18,523 couples. *Soc Psychiatry Psychiatr Epidemiol* 2014;49(1):109-119.
29. Karlstad O, Nafstad P, Tverdal A, et al. Prevalence, incidence and persistence of anti-asthma medication use in 2- to 29-year-olds: a nationwide prescription study. *Eur J Clin Pharmacol* 2010;66(4):399-406.
30. Furu K, Karlstad O, Skurtveit S, et al. High validity of mother-reported use of antiasthmatics among children: a comparison with a population-based prescription database. *J Clin Epidemiol* 2011;64(8):878-884.
31. Frisell T, Oberg S, Kuja-Halkola R, et al. Sibling comparison designs: bias from non-shared confounders and measurement error. *Epidemiology* 2012;23(5):713-720.
32. Keyes KM, Smith GD, Susser E. On sibling designs. *Epidemiology* 2013;24(3):473-474.
33. Wright RJ, Visness CM, Calatroni A, et al. Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner-city cohort. *Am J Respir Crit Care Med* 2010;182(1):25-33.
34. Peters JL, Cohen S, Staudenmayer J, et al. Prenatal negative life events increases cord blood IgE: interactions with dust mite allergen and maternal atopy. *Allergy* 2012;67(4):545-551.
35. Lin YC, Wen HJ, Lee YL, et al. Are maternal psychosocial factors associated with cord immunoglobulin E in addition to family atopic history and mother immunoglobulin E? *Clin Exp Allergy* 2004;34(4):548-554.
36. Wen HJ, Wang YJ, Lin YC, et al. Prediction of atopic dermatitis in 2-yr-old children by cord blood IgE, genetic polymorphisms in cytokine genes, and maternal mentality during pregnancy. *Pediatr Allergy Immunol* 2011;22(7):695-703.
37. Trump S, Bieg M, Gu Z, et al. Prenatal maternal stress and wheeze in children: novel insights into epigenetic regulation. *Sci Rep* 2016;6:28616.
38. Palma-Gudiel H, Cordova-Palomera A, Eixarch E, et al. Maternal psychosocial stress during pregnancy alters the epigenetic signature of the glucocorticoid receptor gene promoter in their offspring: a meta-analysis. *Epigenetics* 2015;10(10):893-902.
39. Entringer S, Epel ES, Lin J, et al. Maternal psychosocial stress during pregnancy is associated with newborn leukocyte telomere length. *Am J Obstet Gynecol* 2013;208(2):e131-137.
40. Marchetto NM, Glynn RA, Ferry ML, et al. Prenatal stress and newborn telomere length. *Am J Obstet Gynecol* 2016;215(1):e91-98.

Figure legends:

Figure 1 Illustration of study sample

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Table 1. Distribution of background characteristics among children included in the analysis of maternal and paternal stress, the Norwegian Mother and Child Cohort Study, 2000-2007

Background characteristic	Maternal psychosocial stress (N=63,626)		Paternal psychosocial stress (N=47,619)	
	N	%	N	%
Maternal age at delivery ^a	30.1 (4.5)		30.1 (4.4)	
Maternal parity				
0	28,413	44.7	22,374	47.0
1	22,650	35.6	16,617	34.9
2	9,849	15.5	6,860	14.4
3+	2,714	4.3	1,768	3.7
Maternal education				
Less than high school	4,795	7.5	3,274	6.9
High school	19,318	30.4	13,851	29.1
Up to four years of college	26,261	41.3	20,021	42.0
More than four years of college	12,996	20.4	10,267	21.6
Missing	256	0.4	206	0.4
Maternal pre-pregnancy body-mass index ^b				
<18.5	1,817	2.9	1,340	2.8
18.5–24.9	40,453	63.6	30,259	63.5
25–29.9	13,854	21.8	10,397	21.8
≥30	5,858	9.2	4,435	9.3
Missing	1,644	2.6	1,188	2.5
Maternal smoking during pregnancy				
No	48,184	75.7	36,654	77.0
Quit by 18 weeks	8,991	14.1	6,661	14.0
Smoked after 18 weeks	6,182	9.7	4,112	8.6
Missing	269	0.4	192	0.4
Maternal smoking during the first 6 months of the child's life				
No	52,124	81.9	39,517	83.0
Yes	8,879	14.0	6,174	13.0
Missing	2,623	4.1	1,928	4.1
Maternal history of asthma				
No	58,924	92.6	44,027	92.5
Yes	4,702	7.4	3,592	7.5
Paternal age				
<25	2,851	4.5	2,083	4.4
25–29	14,592	22.9	11,040	23.2
30–34	25,101	39.5	19,235	40.4
≥35	20,955	32.9	15,259	32.0
Missing	127	0.2	2	0
Paternal education				
Less than high school	6,772	10.6	4,441	9.3
High school	25,631	40.3	18,691	39.3
Up to four years of college	16,679	26.2	13,082	27.5
More than four years of college	12,638	19.9	10,089	21.2
Missing	1,906	3.0	1,316	2.8

Paternal body-mass index				
<18.5	128	0.2	99	0.2
18.5–24.9	27,149	42.7	20,122	42.3
25–29.9	27,565	43.3	20,846	43.8
≥30	5,829	9.2	4,560	9.6
Missing	2,955	4.6	1,992	4.2
Paternal smoking				
No	45,830	72.0	35,388	74.3
Yes	17,490	27.5	12,050	25.3
Missing	306	0.5	181	0.4
Paternal history of asthma				
No	43,462	68.3	43,462	91.3
Yes	4,157	6.5	4,157	8.7
Missing	16,007	25.2	0	0
Child gender				
Male	32,562	51.2	24,329	51.1
Female	31,064	48.8	23,290	48.9
Child birth weight (grams)	3,621	545	3,613	543
Missing	31	0.1	22	0.1
Child gestational age (weeks)	39.5	1.7	39.5	1.7
Missing	244	0.4	188	0.4
Child still breastfeeding at 6 months				
No	11,554	18.2	8,574	18.0
Yes	52,072	81.8	39,045	82.9

^a Values are expressed as mean (standard deviation)

^b Weight (kg)/height (m)²

Table 2. Association between maternal psychosocial stress during pregnancy and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) at 18 gestational weeks ^b	1-4	62,438	2,610	1.0 (1.0, 1.4)	1.31	1.20, 1.42	1.19	1.09, 1.30
Satisfaction With Life Scale at 18 gestational weeks ^c	1-7	62,877	2,629	5.8 (5.2, 6.4)	0.94	0.91, 0.98	0.99	0.95, 1.03
Relationship satisfaction at 18 gestational weeks ^c	1-6	61,039	2,534	5.5 (5.0, 5.8)	0.97	0.92, 1.03	1.01	0.96, 1.08
Work stress at 18 gestational weeks ^b	1-4	58,547	2,374	2.0 (1.8, 2.3)	1.21	1.10, 1.33	1.08	0.97, 1.20
Social support at 18 gestational weeks ^c	1-3	61,742	2,575	3.3 (3.0, 3.7)	0.86	0.79, 0.94	0.94	0.86, 1.03
Lifetime symptoms of depression at 18 gestational weeks ^b	0-5	62,922	2,630	2.0 (0.0, 3.0)	1.08	1.06, 1.10	1.05	1.02, 1.07
Lifetime history of major depressive symptoms at 18 gestational weeks	No	49,056	1,920	NA	Referent		Referent	
	Yes	13,866	710	NA	1.31	1.20, 1.42	1.19	1.09, 1.30
Symptom Check List 5 (SCL-5) at 30 gestational weeks ^b	1-4	63,112	2,631	1.1 (1.0, 1.4)	1.30	1.18, 1.43	1.17	1.06, 1.29
Satisfaction With Life Scale at 30 gestational weeks ^c	1-7	63,158	2,636	6.0 (5.4, 6.2)	0.98	0.94, 1.02	1.02	0.98, 1.07
Relationship satisfaction at 30 gestational weeks ^c	1-6	62,487	2,602	5.5 (5.1, 5.8)	1.02	0.96, 1.09	1.06	0.99, 1.13
Negative life events during the past year at 30 gestational weeks ^b	0-8	63,626	2,659	1.0 (0.0, 1.0)	1.15	1.11, 1.19	1.10	1.06, 1.13
Use of antidepressants, anxiolytics and/or hypnotics during pregnancy	No	62,560	2,602	NA	Referent		Referent	
	Yes	1,066	57	NA	1.29	1.00, 1.66	1.16	0.90, 1.50

CI=confidence interval; IQR=inter quartile range; NA=not applicable; RR=relative risk.

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Table 3. Association between paternal psychosocial stress and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of paternal psychosocial stress	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^b	1-4	47,133	1,925	1.0 (1.0, 1.2)	1.10	0.95, 1.27	1.05	0.90, 1.23
Satisfaction With Life Scale ^c	1-7	47,191	1,924	5.8 (5.2, 6.2)	0.96	0.92, 1.01	0.97	0.93, 1.02
Relationship Satisfaction ^c	1-6	47,033	1,917	5.4 (5.0, 5.8)	1.03	0.95, 1.11	1.03	0.95, 1.12
Lifetime symptoms of depression ^b	0-5	47,088	1,925	0.0 (0.0, 2.0)	1.05	1.02, 1.09	1.03	1.00, 1.07
Lifetime history of major depressive symptoms	No	42,568	1,746	NA	Referent		Referent	
	Yes	4,520	179	NA	0.97	0.83, 1.12	0.95	0.81, 1.11
Use of antidepressants, anxiolytics and/or hypnotics	No	46,894	1,911	NA	Referent		Referent	
	Yes	725	28	NA	0.95	0.66, 1.37	0.81	0.55, 1.20

CI=confidence interval; IQR=inter quartile range; NA=not applicable; RR=relative risk.

^a Adjusted for paternal age, education, body-mass index, smoking and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Table 4. Association between maternal psychosocial stress 6 months after delivery and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress 6 months after delivery	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted Model 1 ^a		Adjusted Model 2 ^b	
					RR	95% CI	RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^c	1-4	63,332	2,649	1.0 (1.0, 1.4)	1.30	1.19, 1.41	1.17	1.07, 1.28	1.09	0.98, 1.21
Satisfaction With Life Scale ^d	1-7	62,844	2,626	6.0 (5.4, 6.4)	0.92	0.89, 0.95	0.96	0.93, 1.00	0.96	0.91, 1.00
Relationship Satisfaction ^d	1-6	61,679	2,553	5.4 (5.0, 5.8)	0.96	0.91, 1.01	1.00	0.95, 1.06	1.00	0.93, 1.08
Negative life events after 30 gestational weeks ^c	0-10	63,626	2,659	0.0 (0.0, 1.0)	1.20	1.17, 1.24	1.14	1.11, 1.18	1.12	1.09, 1.16
Use of antidepressants, anxiolytics and/or hypnotics (yes/no)	No	62,860	2,621	NA	Referent		Referent		Referent	
	Yes	766	38	NA	1.19	0.87, 1.63	1.01	0.73, 1.41	0.95	0.67, 1.34

CI=confidence interval; NA=not applicable; IQR=inter quartile range; RR=relative risk.

^a Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy body-mass index, smoking the first 6 months of the child's life and history of asthma, in addition to child gender, birth weight, gestational age and breastfeeding the first 6 months

^b Adjusted for the same characteristics as described in model 1 and the same measure of psychosocial stress during pregnancy

^c Higher scores indicates more stress

^d Higher scores indicates less stress

Table 5. A sibling analysis of maternal psychosocial stress during pregnancy and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress	Range of scale	N	n cases	Unadjusted		Adjusted ^a	
				OR	95% CI	OR	95% CI
Symptom Check List 5 (SCL-5) at 18 gestational weeks ^b	1-4	848	416	0.97	0.58, 1.61	1.00	0.56, 1.77
Satisfaction With Life Scale at 18 gestational weeks ^c	1-7	857	437	0.98	0.83, 1.17	1.00	0.84, 1.20
Relationship satisfaction at 18 gestational weeks ^c	1-6	781	381	1.19	0.82, 1.75	1.37	0.88, 2.14
Work stress ^b	1-4	725	354	0.72	0.42, 1.26	0.69	0.37, 1.29
Social support at 18 gestational weeks ^c	1-3	795	388	1.04	0.62, 1.74	0.88	0.50, 1.56
Lifetime symptoms of depression at 18 gestational weeks ^b	0-5	860	421	0.89	0.76, 1.03	0.89	0.75, 1.04
Lifetime history of major depressive symptoms at 18 gestational weeks	No	656	323	Referent		Referent	
	Yes	204	98	0.88	0.56, 1.39	0.90	0.55, 1.50
Symptom Check List 5 (SCL-5) at 30 gestational weeks ^b	1-4	865	423	0.74	0.43, 1.27	0.74	0.42, 1.33
Satisfaction With Life Scale at 30 gestational weeks ^c	1-7	861	421	1.05	0.86, 1.27	1.03	0.83, 1.27
Relationship satisfaction at 30 gestational weeks ^c	1-6	853	417	1.74	1.23, 2.48	2.06	1.33, 3.19
Negative life events during the past year at 30 gestational weeks ^b	0-8	867	424	1.07	0.92, 1.25	1.05	0.89, 1.24
Use of antidepressants, anxiolytics and/or hypnotics during pregnancy	No	855	418	Referent		Referent	
	Yes	12	6	1.00	0.29, 3.45	1.02	0.26, 3.96

CI=confidence interval; OR=odds ratio.

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Table 6. A sibling analysis of maternal psychosocial stress 6 months after delivery and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress 6 months after delivery	Range of scale	N	n cases	Unadjusted		Adjusted Model 1 ^a		Adjusted Model 2 ^b	
				OR	95% CI	OR	95% CI	OR	95% CI
Symptom Check List 5 (SCL-5) ^c	1-4	865	423	1.37	0.80, 2.34	1.52	0.79, 2.91	1.46	0.75, 2.84
Satisfaction With Life Scale ^d	1-7	846	414	1.15	0.89, 1.48	1.28	0.94, 1.74	1.32	0.96, 1.80
Relationship Satisfaction ^d	1-6	840	411	1.39	1.01, 1.90	1.35	0.91, 2.00	1.30	0.86, 1.96
Negative life events after 30 gestational weeks ^c	0-10	867	424	1.07	0.91, 1.26	1.10	0.91, 1.32	1.09	0.91, 1.32
Use of antidepressants, anxiolytics and/or hypnotics	No	857	420	Referent		Referent		Referent	
	Yes	10	4	0.60	0.14, 2.51	0.82	0.15, 4.42	0.82	0.15, 4.50

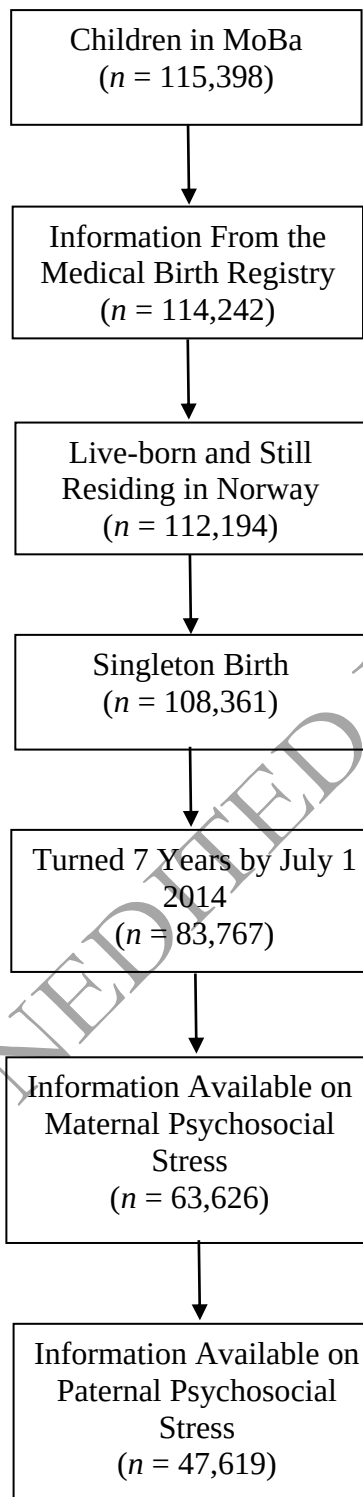
CI=confidence interval; OR=odds ratio.

^a Model 1 Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy body-mass index, smoking the first 6 months of the child's life and history of asthma, in addition to child gender, birth weight, gestational age and breastfeeding the first 6 months

^b Model 2 Adjusted for the same characteristics as described in model 1 and the same measure of psychosocial stress during pregnancy

^c Higher scores indicates more stress

^d Higher scores indicates less stress



Web Table 1. Questions used to obtain information of psychosocial stress, the Norwegian Mother and Child Cohort Study, 2000-2007

Scale capturing psychosocial stress	Questions	Answer options
Life-time history of major depressive symptoms	Felt depressed, sad?	Yes versus no
	Had problems with appetite or eaten too much?	
	Been bothered by feeling weak or a lack of energy?	
	Really blamed yourself and felt worthless?	
	Had problems with concentration or had problems making decisions?	
Five item symptom checklist (SCL-5) for anxiety/depression	Constantly frightened or anxious?	A four point Likert scale ranging from 1 (not at all bothered) to 4 (very much bothered)
	Nervous, inner turmoil?	
	Feeling of hopelessness with regard to the future?	
	Depressed, sad?	
	Frequently worried or uneasy?	
Satisfaction With Life Scale (SWLS)	My life is largely what I wanted it to be	A seven point Likert scale ranging from disagree completely (1) to agree completely (7)
	My life is very good	
	I am satisfied with my life	
	To date, I have achieved what is important for me in my life	
	If I could start all over, there is very little I would do differently	
Social support	Do you have anyone other than your husband/partner you can ask for advice in a difficult situation? (Answer options	1-No, 2-Yes, 1 or 2 people, and 3-Yes, more than 2 people
	How often do you meet or talk on the telephone with your family (other than your husband/partner and children) or close friends?	1-Once a month or less, 2-2-8 times a month, and 3-More than twice a week
	Do you feel lonely?	1-Almost never, 2-Infrequently, 3-Sometimes, 4-Usually, and 5-Almost always
10-item Relationship Satisfaction (RS) scale	My husband/partner and I have a close relationship	A six point Likert scale ranging from (1) strongly disagree to (6) strongly agree
	My partner and I have problems in our relationship	
	I am very happy in my relationship	
	My partner is usually understanding	
	I often think about ending our relationship	
	I am satisfied with my relationship with my partner	
	We often disagree about important decisions	
	I have been lucky in my choice of a partner	
	We agree about how children should be raised	
	I think my partner is satisfied with our relationship	
Negative life events	Have you had problems at work or where you study?	Yes versus no
	Have you had financial problems?	
	Have you been divorced, separated or ended your relationship with your partner?	
	Have you had problems or conflicts with your family, friends or neighbors?	
	Have you been seriously ill or injured?	
	Has anyone close to you been seriously ill or injured?	
	Have you been involved in a serious accident, fire or robbery?	
	Have you lost someone close to you?	
Work stress	I have physically heavy work	A four point Likert scale ranging from (1) agree to (4) disagree
	My work is very stressful	
	I learn a lot at work	
	My work is very monotonous	
	My work demands a lot of me	
	I am able to decide how my work is to be carried out	
	There is a good team spirit at my place of work	
	I enjoy my work	

Web Table 2. Distribution of background characteristics among included and excluded individuals, the Norwegian Mother and Child Cohort Study, 2000-2007

Background characteristic	Maternal psychosocial stress		Paternal psychosocial stress	
	Included (N=63,626)	Excluded (N= 20,141)	Included (N=47,619)	Excluded (N=16,007)
	N (%)	N (%)	N (%)	N (%)
Child asthma use of asthma medications at 7 years in the NorPD				
No	60,967 (95.8)	19,230 (95.5)	45,680 (95.9)	15,287 (95.5)
Yes	2,659 (4.2)	911 (4.5)	1,939 (4.1)	720 (4.5)
Maternal age at delivery ^a	30.1 (4.5)	29.5 (5.1)	30.1 (4.4)	30.2 (4.7)
Maternal parity				
0	28,413 (44.7)	7,382 (36.7)	22,374 (47.0)	6,039 (37.7)
1	22,650 (35.6)	7,776 (38.6)	16,617 (34.9)	6,033 (37.7)
2	9,849 (15.5)	3,693 (18.3)	6,860 (14.4)	2,989 (18.7)
3+	2,714 (4.3)	1,290 (6.4)	1,768 (3.7)	946 (5.9)
Maternal education				
Less than high school	4,795 (7.6)	1,903 (15.8)	3,274 (6.9)	1,521 (9.5)
High school	19,318 (30.5)	4,167 (34.6)	13,851 (29.2)	5,467 (34.3)
Up to four years of college	26,261 (41.4)	3,962 (32.9)	20,021 (42.2)	6,240 (39.1)
More than four years of college	12,996 (20.5)	2,022 (16.8)	10,267 (21.7)	2,729 (17.1)
Missing	256	8,087	206	50
Maternal pre-pregnancy body-mass index ^b				
<18.5	1,817 (2.9)	496 (4.3)	1,340 (2.9)	477 (3.1)
18.5-24.9	40,453 (65.3)	7,315 (63.0)	30,259 (65.2)	10,194 (65.6)
25-29.9	13,854 (22.4)	2,537 (21.9)	10,397 (22.4)	3,457 (22.2)
30 or higher	5,858 (9.5)	1,264 (10.9)	4,435 (9.6)	1,423 (9.2)
Missing	1,644	8,529	1,188	456
Maternal smoking during pregnancy				
No	48,184 (76.2)	8,380 (67.7)	36,654 (77.3)	11,530 (72.4)
Quit by 18 weeks	8,991 (14.2)	1,941 (15.7)	6,661 (14.0)	2,330 (14.6)
Smoked after 18 weeks	6,182 (9.8)	2,058 (16.6)	4,112 (8.7)	2,070 (13.0)
Missing	269	7,762	192	77
Maternal history of asthma				
No	58,924 (92.6)	11,159 (92.6)	44,027 (92.5)	14,897 (93.1)
Yes	4,702 (7.4)	1,012 (7.4)	3,592 (7.5)	1,110 (6.9)
Missing	0	7,970	0	0
Paternal age				
<25	2,851 (4.5)	1,623 (8.1)	2,083 (4.4)	768 (4.8)
25-29	14,592 (22.9)	4,657 (23.2)	11,040 (23.2)	3,552 (22.4)
30-34	25,101 (39.5)	7,161 (35.7)	19,235 (40.4)	5,866 (36.9)
35 and higher	20,955 (33.0)	6,609 (33.0)	15,259 (32.1)	5,696 (35.9)
Missing	127	91	2	125

Paternal education				
Less than high school	6,772 (11.0)	1,749 (15.2)	4,441 (9.6)	2,331 (15.1)
High school	25,631 (41.5)	5,003 (43.5)	18,691 (40.4)	6,940 (45.0)
Up to four years of college	16,679 (27.0)	2,593 (22.6)	13,082 (28.3)	3,597 (23.3)
More than four years of college	12,638 (20.5)	2,146 (18.7)	10,089 (21.8)	2,549 (16.5)
Missing	1,906	8,650	1,316	590
Paternal body-mass index				
<18.5	128 (0.2)	34 (0.3)	99 (0.2)	29 (0.2)
18.5-24.9	27,149 (44.8)	5,059 (44.8)	20,122 (44.1)	7,027 (46.7)
25-29.9	27,565 (45.4)	5,005 (44.4)	20,846 (45.7)	6,719 (44.7)
30 or higher	5,829 (9.6)	1,186 (10.5)	4,560 (10.0)	1,269 (8.4)
Missing	2,955	8,857	1,992	963
Paternal smoking				
No	45,830 (72.4)	8,363 (67.5)	35,388 (74.6)	10,442 (65.8)
Yes	17,490 (27.6)	4,033 (32.5)	12,050 (25.4)	5,440 (34.3)
Missing	306	7,745	181	125
Paternal history of asthma				
No	43,462 (91.3)	7,510 (90.9)	43,462 (91.3)	NA
Yes	4,157 (8.7)	751 (9.1)	4,157 (8.7)	NA
Missing	16,007	11,880	0	NA

^a Values are expressed as mean (standard deviation)

^b Weight (kg)/height (m)²

Web Table 3. The pairwise correlation coefficients between the different measures of maternal psychosocial stress during pregnancy, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress	Symptom Check List 5 (SCL-5) at 18 gw ^a	Satisfaction With Life Scale at 18 gw ^b	Relationship satisfaction at 18 gw ^b	Work stress at 18 gw ^a	Social support at 18 gw ^b	Lifetime symptoms of depression ^a	Symptom Check List 5 (SCL-5) at 30 gw ^a	Satisfaction With Life Scale at 30 gw ^b	Relationship satisfaction at 30 gw ^b	Negative life events the past 12 months at 30 gw ^a
Symptom Check List 5 (SCL-5) at 18 gw ^a	1									
Satisfaction With Life Scale at 18 gw ^b	-0.39	1								
Relationship satisfaction at 18 gw ^b	-0.31	0.44	1							
Work stress at 18 gw ^a	0.19	-0.23	-0.11	1						
Social support at 18 gw ^b	-0.32	0.33	0.30	-0.18	1					
Lifetime symptoms of depression ^a	0.38	-0.27	-0.19	0.13	-0.24	1				
Symptom Check List 5 (SCL-5) at 30 gw ^a	0.58	-0.30	-0.24	0.16	-0.28	0.37	1			
Satisfaction With Life Scale at 30 gw ^b	-0.35	0.56	0.43	-0.20	0.32	-0.25	-0.37	1		
Relationship satisfaction at 30 gw ^b	-0.26	0.38	0.78	-0.11	0.29	-0.17	-0.31	0.49	1	
Negative life events the past 12 months at 30 gw ^a	0.28	-0.20	-0.15	0.16	-0.16	0.27	0.28	-0.21	-0.16	1

Web Table 4. Association between maternal symptoms of anxiety/depression during pregnancy and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Symptom Check List 5 (SCL-5) ^a	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^b	
					RR	95% CI	RR	95% CI
18 gestational weeks	1-4	62,438	2,610	1.0 (1.0, 1.4)	1.31	1.20, 1.42	1.19	1.09, 1.30
30 gestational weeks	1-4	63,112	2,631	1.1 (1.0, 1.4)	1.30	1.18, 1.43	1.16	1.05, 1.28

CI=confidence interval; IQR=inter quartile range; RR=relative risk.

^a Higher scores indicate more stress

^b Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy, history of asthma and use of medications for anxiety/depression during pregnancy.

Web Table 5. Associations of maternal use of anxiolytics, antidepressants and hypnotics during pregnancy with offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Medication group	Range of scale	N	n cases	Unadjusted		Adjusted ^a	
				RR	95% CI	RR	95% CI
Anxiolytics	No	63,273	2,642	Referent		Referent	
	Yes	353	17	1.15	0.72, 1.84	1.04	0.65, 1.64
Antidepressants	No	63,009	2,621	Referent		Referent	
	Yes	617	38	1.48	1.09, 2.02	1.27	0.92, 1.74
Hypnotics	No	63,381	2,650	Referent		Referent	
	Yes	245	9	0.88	0.46, 1.67	0.85	0.45, 1.62

CI=confidence interval; RR=relative risk

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy, and history of asthma.

Web Table 6. Association of maternal psychosocial stress during pregnancy with offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007: sensitivity analysis without restricting to individuals with information from the questionnaire administered 6 months after delivery

Measures of maternal psychosocial stress during pregnancy	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) at 18 gestational weeks ^b	1-4	74,071	3,147	1.0 (1.0, 1.4)	1.26	1.17, 1.36	1.17	1.08, 1.26
Satisfaction With Life Scale at 18 gestational weeks ^c	1-7	74,703	3,180	5.8 (5.2, 6.4)	0.96	0.93, 0.99	1.00	0.97, 1.03
Relationship satisfaction at 18 gestational weeks ^c	1-6	71,833	3,026	5.4 (5.0, 5.8)	0.97	0.92, 1.02	1.00	0.95, 1.06
Work stress at 18 gestational weeks ^b	1-4	68,830	2,855	3.0 (2.8, 3.3)	0.84	0.77, 0.92	0.94	0.85, 1.03
Social support at 18 gestational weeks ^c	1-3	72,857	3,086	3.3 (3.0, 3.7)	0.89	0.83, 0.96	0.96	0.88, 1.04
Lifetime symptoms of depression at 18 gestational weeks ^b	0-5	74,762	3,182	2.0 (0.0, 3.0)	1.08	1.06, 1.11	1.06	1.03, 1.08
Lifetime history of major depressive symptoms at 18 gestational weeks	No	57,692	2,298	NA	Referent		Referent	
	Yes	17,070	884	NA	1.30	1.20, 1.40	1.20	1.11, 1.30
Symptom Check List 5 (SCL-5) at 30 gestational weeks ^b	1-4	69,296	2,910	1.1 (1.0, 1.4)	1.27	1.16, 1.38	1.15	1.04, 1.26
Satisfaction With Life Scale at 30 gestational weeks ^c	1-7	69,341	2,911	6.0 (5.4, 6.2)	0.97	0.94, 1.01	1.02	0.98, 1.05
Relationship satisfaction at 30 gestational weeks ^c	1-6	68,552	2,866	5.5 (5.0, 5.8)	1.01	0.95, 1.07	1.04	0.98, 1.10
Negative life events the past 12 months at 30 gestational weeks ^b	0-8	69,934	2,939	1.0 (0.0, 2.0)	1.14	1.11, 1.18	1.10	1.06, 1.13

CI=confidence interval; IQR=inter quartile range; RR=relative risk.

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Web Table 7 The pairwise correlation coefficients between the different measures of paternal psychosocial stress ascertained at recruitment, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of paternal psychosocial stress	Symptom Check List 5 (SCL-5)	Satisfaction With Life Scale at 18 gw	Relationship satisfaction at 18 gw	Lifetime symptoms of depression
Symptom Check List 5 (SCL-5)	1			
Satisfaction With Life Scale	-0.36	1		
Relationship satisfaction	-0.26	0.41	1	
Lifetime symptoms of depression	0.41	-0.29	-0.18	1

Web Table 8. The pairwise correlation coefficients of maternal and paternal psychosocial stress at recruitment around 18 gestational weeks, the Norwegian Mother and Child Cohort Study, 2000-2007

Measure of parental psychosocial stress	Correlation coefficient
Symptom Check List 5 (SCL-5)	0.19
Satisfaction With Life Scale	0.25
Relationship satisfaction	0.55
Lifetime symptoms of depression	0.18

Web Table 9. Association between maternal psychosocial stress during pregnancy and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007: sensitivity analysis among study sample used to evaluate paternal psychosocial stress

Measures of maternal psychosocial stress during pregnancy	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) at 18 gestational weeks ^b	1-4	46,813	1,907	1.0 (1.0, 1.4)	1.29	1.17, 1.43	1.18	1.06, 1.31
Satisfaction With Life Scale at 18 gestational weeks ^c	1-7	47,108	1,915	6.0 (5.4, 6.4)	0.96	0.92, 1.00	1.01	0.96, 1.05
Relationship Satisfaction at 18 gestational weeks ^c	1-6	47,173	1,914	5.5 (5.1, 5.8)	0.99	0.92, 1.07	1.03	0.95, 1.12
Work stress at 18 gestational weeks ^b	1-4	43,980	1,736	3.0 (2.8, 3.3)	1.17	1.05, 1.31	1.02	0.90, 1.15
Social support at 18 gestational weeks ^c	1-3	47,378	1,926	3.3 (3.0, 3.7)	0.87	0.79, 0.96	0.95	0.85, 1.05
Lifetime symptoms of depression at 18 gestational weeks ^b	0-5	47,113	1,917	2.0 (0.0, 3.0)	1.07	1.05, 1.10	1.05	1.02, 1.07
Lifetime history of major depressive symptoms at 18 gestational weeks	No	36,816	1,419	NA	Referent		Referent	
	Yes	10,297	498	NA	1.25	1.14, 1.39	1.14	1.03, 1.27
Symptom Check List 5 (SCL-5) at 30 gestational weeks ^b	1-4	47,273	1,921	1.1 (1.0, 1.4)	1.24	1.10, 1.39	1.10	0.97, 1.24
Satisfaction With Life Scale at 30 gestational weeks ^c	1-7	47,296	1,922	6.0 (5.4, 6.4)	1.00	0.95, 1.05	1.05	1.00, 1.10
Relationship Satisfaction at 30 gestational weeks ^c	1-6	47,161	1,922	5.5 (5.1, 5.8)	1.05	0.97, 1.14	1.09	1.01, 1.19
Negative Life Events at 30 gestational weeks ^b	0-8	47,619	1,939	1.0 (0.0, 1.0)	1.15	1.11, 1.12	1.10	1.06, 1.15
Use of antidepressants, anxiolytics and/or hypnotics during pregnancy	No	46,836	1,895	NA	Referent		Referent	
	Yes	783	44	NA	1.39	1.04, 1.86	1.23	0.91, 1.65

CI= confidence interval; IQR=inter quartile range; RR=relative risk.

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Web Table 10. Associations of maternal and paternal psychosocial stress with offspring asthma at 7 years defined by the Norwegian Prescription Database after mutual adjustment, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress during pregnancy at 18 gestational weeks	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^b	1-4	46,813	1,907	1.0 (1.0, 1.4)	1.29	1.17, 1.43	1.18	1.06, 1.32
Satisfaction With Life Scale ^c	1-7	47,108	1,915	6.0 (5.4, 6.4)	0.96	0.92, 1.00	1.01	0.94, 1.03
Relationship satisfaction ^c	1-6	47,173	47,173	5.5 (5.1, 5.8)	0.99	0.92, 1.07	1.00	0.91, 1.09
Lifetime symptoms of depression ^b	0-5	47,113	1,917	2.0 (0.0, 3.0)	1.07	1.05, 1.10	1.04	1.01, 1.07
Lifetime history of major depressive symptoms	No	36,816	1,419	NA	Referent		Referent	
	Yes	10,297	498	NA	1.25	1.14, 1.39	1.14	1.03, 1.27
Measures of maternal psychosocial stress during pregnancy at 30 gestational weeks	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL5) ^b	1-4	47,273	1,921	1.1 (1.0, 1.4)	1.24	1.10, 1.39	1.10	0.97, 1.24
Satisfaction With Life Scale ^c	1-7	47,296	1,922	6.0 (5.4, 6.4)	1.00	0.95, 1.05	1.06	1.00, 1.11
Relationship satisfaction ^c	1-6	47,161	1,922	5.5 (5.1, 5.8)	1.05	0.97, 1.14	1.08	0.99, 1.18
Use of antidepressants, anxiolytics and/or hypnotics	No	46,836	1,895	NA	Referent		Referent	
	Yes	783	44	NA	1.39	1.04, 1.86	1.24	0.92, 1.67
Measures of paternal psychosocial stress	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^b	1-4	47,133	1,925	1.0 (1.0, 1.2)	1.10	0.95, 1.27	0.99	0.84, 1.17
Satisfaction With Life Scale ^c	1-7	47,191	1,924	5.8 (5.2, 6.2)	0.96	0.92, 1.01	0.98	0.93, 1.03
Relationship Satisfaction ^c	1-6	47,033	1,917	5.4 (5.0, 5.8)	1.03	0.95, 1.11	1.02	0.93, 1.12
Lifetime symptoms of depression ^b	0-5	47,088	1,925	0.0 (0.0, 2.0)	1.05	1.02, 1.09	1.02	0.98, 1.05
Lifetime history of major depressive symptoms	No	42,568	1,746	NA	Referent		Referent	
	Yes	4,520	179	NA	0.97	0.83, 1.12	0.92	0.79, 1.08
Use of antidepressants, anxiolytics and/or hypnotics	No	46,894	1,911	NA	Referent		Referent	
	Yes	725	28	NA	0.95	0.66, 1.37	0.79	0.53, 1.18

CI=confidence interval; NA=not applicable; IQR=inter quartile range; RR=relative risk.

^a Maternal psychosocial stress adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy, history of asthma, in addition to the same measure of paternal psychosocial stress. Paternal psychosocial stress adjusted for paternal age, education, body-mass index, smoking, history of asthma, in addition to the same measure of maternal psychosocial stress.

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Web Table 11. Association between maternal psychosocial stress during pregnancy and offspring asthma at 7 years defined by maternal report through questionnaire, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress during pregnancy	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) at 18 gestational weeks ^b	1-4	36,350	2,004	1.0 (1.0, 1.4)	1.30	1.18, 1.43	1.21	1.09, 1.34
Satisfaction With Life Scale at 18 gestational weeks ^c	1-7	36,586	2,016	6.0 (5.4, 6.4)	0.96	0.92, 0.99	0.99	0.95, 1.03
Relationship Satisfaction at 18 gestational weeks ^c	1-6	35,381	1,940	5.5 (5.0, 5.8)	0.94	0.88, 1.01	0.96	0.90, 1.03
Work stress at 18 gestational weeks ^b	1-4	34,478	1,855	2.0 (1.8, 2.3)	1.24	1.11, 1.38	1.10	0.97, 1.23
Social support at 18 gestational weeks ^c	1-3	35,700	1,960	3.3 (3.0, 3.7)	0.94	0.85, 1.04	1.00	0.90, 1.11
Lifetime symptoms of depression at 18 gestational weeks ^b	0-5	36,584	2,010	1.0 (0.0, 3.0)	1.09	1.06, 1.12	1.07	1.04, 1.10
Lifetime history of major depressive symptoms at 18 gestational weeks	No	28,916	1,495	NA	Referent		Referent	
	Yes	7,668	515	NA	1.30	1.18, 1.43	1.22	1.11, 1.35
Symptom Check List 5 (SCL-5) at 30 gestational weeks ^b	1-4	36,688	2,017	1.1 (1.0, 1.4)	1.44	1.29, 1.60	1.32	1.18, 1.47
Satisfaction With Life Scale at 30 gestational weeks ^c	1-7	36,743	2,019	6.0 (5.4, 6.4)	0.96	0.92, 1.00	0.99	0.94, 1.03
Relationship satisfaction at 30 gestational weeks ^c	1-6	36,407	2,003	5.5 (5.1, 5.8)	0.96	0.90, 1.03	0.98	0.92, 1.05
Negative life events at 30 gestational weeks ^b	0-8	36,925	2,029	1.0 (0.0, 1.0)	1.18	1.13, 1.22	1.12	1.08, 1.17
Use of antidepressants, anxiolytics and/or hypnotics	No	36,355	1,996	NA	Referent		Referent	
	Yes	570	33	NA	1.05	0.75, 1.47	1.02	0.73, 1.42

CI=confidence interval; IQR=inter quartile range; NA=not applicable; RR= relative risk.

^a Adjusted for maternal age, parity, education, pre-pregnancy body-mass index, smoking during pregnancy and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Web Table 12. Association between paternal psychosocial stress and offspring asthma at 7 years defined by maternal report through questionnaire, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of paternal psychosocial stress	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted ^a	
					RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^b	1-4	28,384	1,552	1.0 (1.0, 1.2)	1.12	0.94, 1.33	1.11	0.94, 1.32
Satisfaction With Life Scale ^c	1-7	28,387	1,552	5.8 (5.2, 6.2)	0.98	0.93, 1.03	0.98	0.93, 1.03
Relationship satisfaction ^c	1-6	28,298	1,552	5.4 (5.0, 5.8)	0.97	0.89, 1.06	0.96	0.88, 1.05
Lifetime symptoms of depression ^b	0-5	28,358	1,553	0.0 (0.0, 2.0)	1.07	1.04, 1.11	1.06	1.03, 1.10
Lifetime history of major depressive symptoms	No	25,755	1,393	NA	Referent		Referent	
	Yes	2,603	160	NA	1.14	0.97, 1.33	1.16	0.98, 1.37
Use of antidepressants, anxiolytics and/or hypnotics	No	28,189	1,536	NA	Referent		Referent	
	Yes	429	429	NA	1.28	0.91, 1.82	1.13	0.77, 1.65

CI=confidence interval; NA=not applicable; IQR=inter quartile range; RR=relative risk.

^a Adjusted for paternal age, education, body-mass index, smoking and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress

Web Table 13. Association between maternal psychosocial stress 6 months after delivery and offspring asthma at 7 years defined by maternal report through questionnaire, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of maternal psychosocial stress 6 months after delivery	Range of scale	N	n cases	Median (IQR)	Unadjusted		Adjusted Model 1 ^a		Adjusted Model 2 ^b	
					RR	95% CI	RR	95% CI	RR	95% CI
Symptom Check List 5 (SCL-5) ^c	1-4	36,824	2,022	1.0 (1.0, 1.4)	1.37	1.24, 1.51	1.29	1.15, 1.44	1.22	1.07, 1.39
Satisfaction With Life Scale ^d	1-7	36,562	2,004	6.0 (5.4, 6.4)	0.92	0.88, 0.96	0.95	0.91, 1.00	0.94	0.89, 1.00
Relationship satisfaction ^d	1-6	36,012	1,966	5.4 (5.0, 5.8)	0.92	0.87, 0.98	0.94	0.88, 1.01	0.95	0.87, 1.04
Negative life events ^c	0-10	36,925	2,029	0.0 (0.0, 1.0)	1.23	1.19, 1.28	1.19	1.14, 1.24	1.16	1.11, 1.21
Use of antidepressants, anxiolytics and/or hypnotics	No	36,516	2,007	NA	Referent		Referent		Referent	
	Yes	409	22	NA	0.98	0.65, 1.47	0.84	0.53, 1.33	0.81	0.50, 1.33

CI=confidence interval; NA=not applicable; IQR=inter quartile range; RR=relative risk.

^a Model 1 Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy body-mass index, smoking the first 6 months of the child's life and history of asthma, in addition to child gender, birth weight, gestational age and breastfeeding the first 6 months

^b Model 2 Adjusted the same covariates described in model 1 and the same measure of psychosocial stress during pregnancy

^c Higher scores indicates more stress

^d Higher scores indicates less stress

Web Table 14. A sibling analysis of paternal psychosocial stress and offspring asthma at 7 years defined by the Norwegian Prescription Database, the Norwegian Mother and Child Cohort Study, 2000-2007

Measures of paternal psychosocial stress	Range of scale	N	n cases	Unadjusted		Adjusted ^a	
				OR	95% CI	OR	95% CI
Symptom Check List 5 (SCL-5) ^b	1-4	481	237	0.60	0.24, 1.51	0.46	0.16, 1.31
Satisfaction With Life Scale ^c	1-7	483	238	1.22	0.95, 1.57	1.24	0.95, 1.62
Relationship Satisfaction ^c	1-6	479	236	1.33	0.81, 2.20	1.50	0.82, 2.73
Lifetime symptoms of depression ^b	0-5	481	237	1.12	0.90, 1.40	1.16	0.90, 1.49
Lifetime history of major depressive symptoms	No	449	226	Referent		Referent	
	Yes	32	11	0.40	0.15, 1.01	0.46	0.15, 1.36

CI=confidence interval; OR=odds ratio.

^a Adjusted for paternal age, education, body-mass index, smoking and history of asthma

^b Higher scores indicate more stress

^c Higher scores indicate less stress