

**MATERNAL DEPRESSIVE SYMPTOMS DURING AND AFTER PREGNANCY
AND PSYCHIATRIC PROBLEMS IN CHILDREN**

RUNNING TITLE: PRENATAL DEPRESSION & CHILD DEVELOPMENT

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Acknowledgements

This study was funded by the Academy of Finland, Signe and Ane Gylleberg Foundation, Finnish Graduate School of Psychology, Emil Aaltonen Foundation, EVO (special state

subsidy for health science research), Finnish Medical Foundation, Jane and Aatos Erkkö Foundation, Novo Nordisk Foundation, Päivikki and Sakari Sohlberg Foundation, Sigrid Juselius Foundation, EraNet Neuron, Sir Jules Thorn Charitable Trust and University of Helsinki. The authors thank MA. Jari Lipsanen, University of Helsinki, Finland for his statistical assistance. The authors declare no conflict of interest.

Presentation Information: A preliminary study abstract was presented at the 45th International Society of Psychoneuroendocrinology–Conference in Edinburgh, UK, 2015 and published in [Psychoneuroendocrinology](#). 2015;61:12.

Keywords: antenatal; depression; childhood mental health; psychiatric symptoms; prospective study.

Maternal Depressive Symptoms During and after Pregnancy and Psychiatric Problems in Children

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4 **Objective:** Maternal depressive symptoms during pregnancy are associated with increased risk of
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6 psychiatric problems in children. More precise understanding of the timing of the symptoms during
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8 pregnancy and their independence from other prenatal and postnatal factors in predicting child
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10 psychopathology risk is needed. We examined whether maternal depressive symptoms during pregnancy
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12 predict child psychiatric problems, whether these associations are trimester- or gestational-week-specific
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14 and/or independent of pregnancy disorders, and whether maternal depressive symptoms after pregnancy
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16 mediate or add to the prenatal effects.
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21 **Method:** The study sample comprised 2296 women and their children born in Finland 2006-2010,
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23 participating in the prospective pregnancy cohort study Prediction and Prevention of Preeclampsia and
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25 Intrauterine Growth Restriction (PREDO) and followed up to 1.9-5.9 years of age. The women completed
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27 the Center for Epidemiologic Studies Depression-Scale biweekly between gestational weeks+days
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29 12+0/13+6 and 38+0/39+6 or delivery. In the follow-up, they completed the Beck Depression Inventory-II
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31 and Child Behavior Checklist 1½-5.
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36 **Results:** Maternal depressive symptoms during pregnancy predicted significantly higher internalizing [0.28
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38 standard deviation unit per standard deviation unit increase (95% Confidence Interval=0.24-0.32)],
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40 externalizing [0.26(0.23-0.30)] and total problems [0.31(0.27-0.35)] in children. These associations were
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42 non-specific to gestational week and hence pregnancy trimester, independent of pregnancy disorders, and
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44 independent of, though partially mediated by maternal depressive symptoms after pregnancy. Psychiatric
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46 problems were greatest in children whose mothers reported clinically significant depressive symptoms
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48 across pregnancy trimesters and during and after pregnancy.
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53 **Conclusions:** Maternal depressive symptoms during pregnancy predict increased psychiatric problems in
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55 young children. Preventive interventions from early pregnancy onwards may benefit offspring mental health.
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Maternal depressive symptoms affect a large proportion of pregnancies, with 7.4%-20% of women

1 experiencing clinically significant levels of depressive symptoms at different stages of pregnancy.¹⁻² These
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3 symptoms may alter the intrauterine environment, expose the fetus to unnecessarily high levels of maternal
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5 glucocorticoids³⁻⁵ and pro-inflammatory cytokines,⁶⁻⁷ and “program” an adverse offspring phenotype,
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7 thereby explaining why maternal depressive symptoms during pregnancy predict an increased risk of
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9 psychiatric problems in the offspring.⁸⁻¹⁹
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16 Yet, it still remains unclear whether maternal depressive symptoms during pregnancy are an independent
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18 risk factor for child psychiatric problems.⁸⁻¹⁹ In the Avon Longitudinal Study of Parents and Children
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20 (ALSPAC), which is one of the two largest studies that have examined the consequences of maternal
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22 depressive symptoms during pregnancy on the offspring, maternal depressive symptoms measured at
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24 gestational weeks 18 or 32 predicted higher risks of attention problems in the offspring in early childhood,¹⁷
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26 and emotional and behavioral problems in pre-puberty.¹² In the Generation R-study, the other of the two
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28 largest studies, maternal depressive symptoms at gestational week 20 were associated with higher risks of
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30 offspring attention problems¹⁷ and internalizing and externalizing problems¹⁸ in early childhood. In
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32 ALSPAC, the associations remained significant after adjusting for maternal depressive symptoms at the time
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34 of rating the child’s psychiatric problems.^{12,17} However, in Generation R, the associations were no longer
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36 significant,¹⁷⁻¹⁸ challenging the assumption that the effects of maternal depression would be due to an
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38 adverse intrauterine environment.
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48 While differences in sample characteristics and assessment tools may at least partially explain the
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50 contradictory findings, these and some other smaller-scale previous studies were limited to assessing
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52 maternal depressive symptoms “during the past seven days or last two weeks” only once or twice during
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54 pregnancy.⁸⁻¹⁹ Hence, it remains unknown whether some developmental periods during pregnancy are more
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56 vulnerable than others to the effects of maternal depressive symptoms, and if feeling depressed throughout
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58 pregnancy is more harmful for the offspring than feeling depressed only for a week or two at one or two
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60 arbitrary time-points. However, since depressive symptoms show high stability,^{8,12} disentangling gestation-
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week- or trimester-specific effects of maternal depressive symptoms during pregnancy may prove difficult.

It also remains unclear whether maternal depressive symptoms concurrent to rating the child's problems add to rather than account for, or mediate the effects of prenatal environmental adversities.

Accordingly, we examined whether depressive symptoms measured biweekly from gestational week 12 onwards up to 14 times during pregnancy in a large cohort of pregnant Finnish women predict the levels of psychiatric problems in their 1.9-5.9-year-old children, and whether maternal depressive symptoms at the time of rating the child's problems add to, account for or mediate any effects of maternal depressive symptoms during pregnancy. Another novel contribution of this study was to account for possible confounding by common pregnancy disorders: pre-pregnancy obesity, gestational diabetes and hypertension-spectrum pregnancy disorders. According to previous studies these disorders co-occur with depressive symptoms²⁰⁻²¹ and are associated with offspring psychiatric problems.²²⁻²⁴

METHOD

The Participants

The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) study enrolled 4785 pregnant women, of whom 4777 (8 miscarriages or stillbirths) gave birth to a singleton live-born child between 2006 and 2010.^{4-5,25} The women were recruited to the study when they visited antenatal clinics at one of the ten study hospitals in Southern and Eastern Finland for their first ultrasound screening between 12+0 and 13+6 weeks+days of gestation. Of these women, 3402 (71.2% of those with live-born offspring) filled in the biweekly depressive symptoms questionnaire during pregnancy.

In 2011-2012, 4586 women and their children of the original sample were invited for a follow-up (three children had died after birth and before the follow-up, 33 did not have data in Finnish nation-wide Medical Birth Register, 55 women had declined participation in a follow-up, and for 100 women, addresses were not traceable). Of these, 2667 women and children (58.2% of those invited) participated.

Of the 4586 mothers invited to the follow-up, 3279 had data on depressive symptoms during pregnancy, and 2296 had both pregnancy and follow-up data available. The current study sample comprises these 2296 women and their 1.9- to 5.9-year-old children (1161 boys, 1135 girls; 70.0% of those with data on depressive symptoms during pregnancy and invited to the follow-up).

In comparison to the non-participants in the original sample (n=2489), the current study participants were older at delivery (Mean Difference=0.7 years, $p<.001$), had more often tertiary education (62.8% vs. 54.7%, $p<.001$), were less often obese (body mass index (BMI) ≥ 30 kg/m²) before pregnancy (12.3% vs. 15.9%, $p<.001$) and less often multiparous (58.1% vs. 64.4%, $p<.001$), smoked less often throughout pregnancy (2.8% vs. 7.1%, $p<.001$), and more often had a daughter (49.4% vs. 46.2%, $p=.03$). All participating mothers signed informed consent forms. The PREDO study protocol was approved by ethical committees of the Helsinki and Uusimaa Hospital District.

Maternal Depressive Symptoms

The women completed the Center for Epidemiologic Studies Depression Scale (CES-D)²⁶ biweekly up to 14 times throughout pregnancy starting from 12+0/13+6 gestation weeks+days until 38+0/39+6 gestation weeks+days or delivery. The 20 CES-D questions were rated on a scale from none of the time (0) to all the time (3). Higher scores indicate more depressive symptoms during the past week and a sum-score of ≥ 16 indicates risk for clinical depression.²⁶⁻²⁷

In the follow-up, the women completed the Beck Depression Inventory-II (BDI-II), which comprises 21 items, each containing four statements (scored from 0 to 3) reflecting increasing severity of depressive symptoms during the past two weeks.²⁸ A sum-score of ≥ 14 indicates at least mild depressive symptomatology.²⁸⁻²⁹

Both depression scales have good psychometric properties.²⁶⁻³¹ and the CES-D has been used extensively and validated also in pregnant populations.³⁰⁻³¹ In our sample, the CES-D (Cronbach's α =.88 to .92 in the 14 biweekly measurement points) and the BDI-II (α =.91) showed high internal consistency.

Child Psychiatric Problems

Child Behavior Checklist for ages 1½-5 (CBCL/1½-5), filled in by the child's mother, comprises 99 problem items rated on a scale of not true (0) to very true or often true (2).³² The CBCL/1½-5 yields scores for three main scales (internalizing, externalizing and total problems), seven syndrome scales (emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems, and aggressive behavior) and five Diagnostic and Statistical Manual for Mental Disorders (DSM)-oriented scales (affective, anxiety, pervasive developmental, attention deficit/hyperactivity, and oppositional defiant problems).³⁴ A t-score of ≥ 60 on the main and of ≥ 65 on the syndrome and DSM-oriented scales indicates at least borderline clinically significant problems.³² The CBCL/1½-5 has good test-retest reliability, internal consistency and criterion validity.³²⁻³³

Pregnancy Disorders

Data on maternal pregnancy disorders were extracted from medical reports independently verified by a clinical jury and/or from the Finnish Medical Birth Register.²⁵ These included pre-pregnancy obesity (BMI ≥ 30 kg/m² vs. BMI < 30 kg/m²), hypertension spectrum pregnancy disorders (preeclampsia, gestational hypertension; yes/no), and gestational diabetes (yes/no).^{21,25,34-35}

Covariates

These included maternal age at delivery (years), smoking during pregnancy (did not smoke/quit during first trimester/smoked throughout pregnancy), parity (primiparous/multiparous) chronic hypertension (yes/no), type 1 diabetes (yes/no), child's sex, gestational length (weeks), birth weight (g), and family structure at childbirth (cohabitation/marriage vs. single parent), with data extracted from medical reports and/or Medical Birth Register; maternal history of physician-diagnosed depression before pregnancy (yes/no), psychotropic

medication use during pregnancy [antidepressants, other (barbiturates, sedatives, antipsychotics) vs. no],
1 alcohol use during pregnancy (yes/no) and education level (basic/secondary vs. tertiary), each self-reported
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4 in a questionnaire given to the mothers at 12+0-13+6 weeks+days of gestation; and child's age at follow-up
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6 (years) which was reported in conjunction with filling in the CBCL questionnaire.
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10 **Data Analysis**

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12 We examined the course of depressive symptoms during pregnancy with latent profile analysis and Pearson
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14 Correlation analysis.
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21 Next, we inspected the crude unadjusted mean differences of maternal depressive symptoms across the 14
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23 measurement points during pregnancy according to child internalizing, externalizing and total problems
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25 scores above and below the borderline clinical cutoff, and calculated Cohen's d's for effect sizes.
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30 We then used linear regression analyses to test associations between maternal depressive symptoms during
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32 pregnancy and child internalizing, externalizing, and total problems. We examined gestation-week specific
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34 effects and also calculated a trimester-weighted mean value of depressive symptoms across pregnancy
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36 (mean of the only value from first pregnancy trimester and the mean values of second trimester and third
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38 trimester) and square-root transformed the values to normalize the distributions. Since scores in the
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40 CBCL/1½-5 syndrome and DSM-oriented-scales below 50 were truncated into 50 according to the manual,³²
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42 resulting in strongly skewed distributions and a "floor effect", Tobit regressions were used in the analyses of
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44 these scales. To facilitate interpretation, both the predictor and outcome variables were standardized to the
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46 mean of 0 and SD of 1.
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55 The associations of maternal depressive symptoms during pregnancy with child psychiatric problems were
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57 examined in four different linear or Tobit regression models. Model 1 was adjusted for child's age and sex.
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59 Model 2 was adjusted for the covariates in model 1 and family structure, maternal age at childbirth, parity,
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61 education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy,
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antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy,

1 gestation length and infant's birth weight adjusted for sex and gestation length. Model 3 was adjusted for the
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4 model 2 covariates and pre-pregnancy obesity, gestational diabetes, and hypertension-spectrum pregnancy
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6 disorders. Model 4 was adjusted for the model 3 covariates and maternal depressive symptoms after
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8 pregnancy at the time of rating the child's psychiatric problems.
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13 With linear and/or Tobit regressions, we also tested whether child psychiatric problem scores increased
14 according to the number of pregnancy trimesters (0,1,2,3) during which the mean maternal CES-D score was
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16 above the clinical cut-off of ≥ 16 ; whether child psychiatric problem scores differed between the groups of
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18 mothers identified by a latent profile analysis based on their depressive symptoms scores across pregnancy;
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20 whether maternal pregnancy disorders accounted for the effects of maternal depressive symptoms during
21 pregnancy (analyses were adjusted for the pregnancy disorders and re-run separately in mothers with and
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23 without pregnancy disorders); and whether maternal depressive symptoms after pregnancy accounted for
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25 (postpartum depressive symptoms were added as a covariate into the 4th regression models), mediated
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27 (mediation analyses were performed with the bootstrapping method using 5000 bootstrapping re-samples
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29 with bias-corrected confidence intervals), or added to the effects of maternal depressive symptoms during
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31 pregnancy (interaction term of depressive symptoms during pregnancy x after pregnancy was entered into
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33 the regression equation followed by the main effects).
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45 In additional analyses, we studied age-specific associations by re-running the analyses separately among
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47 children who were 1.9-3.9 years and 4.0-5.9 years at follow-up. We also re-ran the analyses separately
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49 among children born to mothers with and without depression diagnoses before pregnancy. Finally, in a
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51 subsample from whom we had paternal CES-D depressive symptoms data available when the children were
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53 6 months old (n=1237), we examined if paternal depressive symptoms confounded any effects of maternal
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55 depressive symptoms.
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RESULTS

Table 1 shows the characteristics of the study sample. The CES-D scores were highly intercorrelated across pregnancy (Pearson r 's between .44 and .80, p -values<.001). Latent profile analysis identified a solution with three groups as the most optimal (in comparison to solutions with fewer and larger number of groups) to depict depressive symptoms throughout pregnancy (Akaike Information Criterion=184565.50, sample-size-adjusted Bayesian Information Criterion=184714.10, Vuong-Lo-Mendell-Rubin LRT and Lo-Mendell-Rubin Adjusted Likelihood Ratio Test p -values =.02). In all three groups, which differed from each other in their level of depressive symptoms, depressive symptoms showed high stability. One trajectory was described by consistently high, one by consistently moderate and one by consistently low depressive symptom scores (Figure S1, available online). The CES-D mean score during pregnancy also correlated significantly with the BDI-II score in the follow-up (r =.45, p <.001), and child internalizing, externalizing and total problems were highly inter-correlated (r 's from .62 to .90, p -values<.001). Maternal pregnancy disorders were not associated with child psychiatric problems, but maternal history of depression before pregnancy was associated with significantly higher child internalizing, externalizing and total psychiatric problems. Table S1 (Supplement, available online) shows these and the associations of the other covariates with child psychiatric problems.

Maternal depressive symptoms during pregnancy and child psychiatric problems

Figure 1 (Panel A) shows that at each biweekly measurement point during pregnancy, mothers whose children scored above the borderline clinical cutoffs in internalizing, externalizing and total problems, had significantly higher depressive symptoms scores than mothers whose children scored below the cutoffs; these group differences were of medium effect size (Cohen's d 's varying from 0.36 to 0.52).

Figure 1 (Panel B) and Table S2 (Supplement) and Table S3 (Supplement) show that the effects of maternal depressive symptoms across pregnancy and at each biweekly assessment on child internalizing, externalizing and total problems were significant when adjusted for covariates in linear regression models 1-2. Table S2 shows that higher maternal mean depressive symptoms during pregnancy also predicted

significantly higher CBCL syndrome- and DSM-oriented problem scores of the child across Tobit regression models 1-2.

As shown in Figure 2 (Panel A), child internalizing, externalizing and total psychiatric problem scores increased linearly according to the number of pregnancy trimesters during which the mother reported mean depressive symptoms above the clinical cutoff of ≥ 16 . We also compared the psychiatric problems of children of mothers with consistently high, moderate and low depressive symptoms during pregnancy, as identified by the latent profile analysis. Figure 2 (Panel B) shows that child internalizing, externalizing and total psychiatric problem scores were the highest in children born to mothers who had consistently high depressive symptoms during pregnancy. Adjustments for covariates in models 1-4 had no effects on these associations (Figure 2).

Pregnancy disorders, maternal depressive symptoms during pregnancy and child psychiatric problems

When we made further adjustments for maternal pre-pregnancy obesity, hypertension-spectrum pregnancy disorders and gestational diabetes, all the associations between maternal depressive symptoms during pregnancy and child psychiatric problems remained significant (Figures 1 (Panel B, model 3) and 2 and Tables S2-S3, model 3). We re-ran the analyses in groups who were and who were not exposed to maternal pregnancy disorders and in both groups the associations were significant (Figure S2, Supplement).

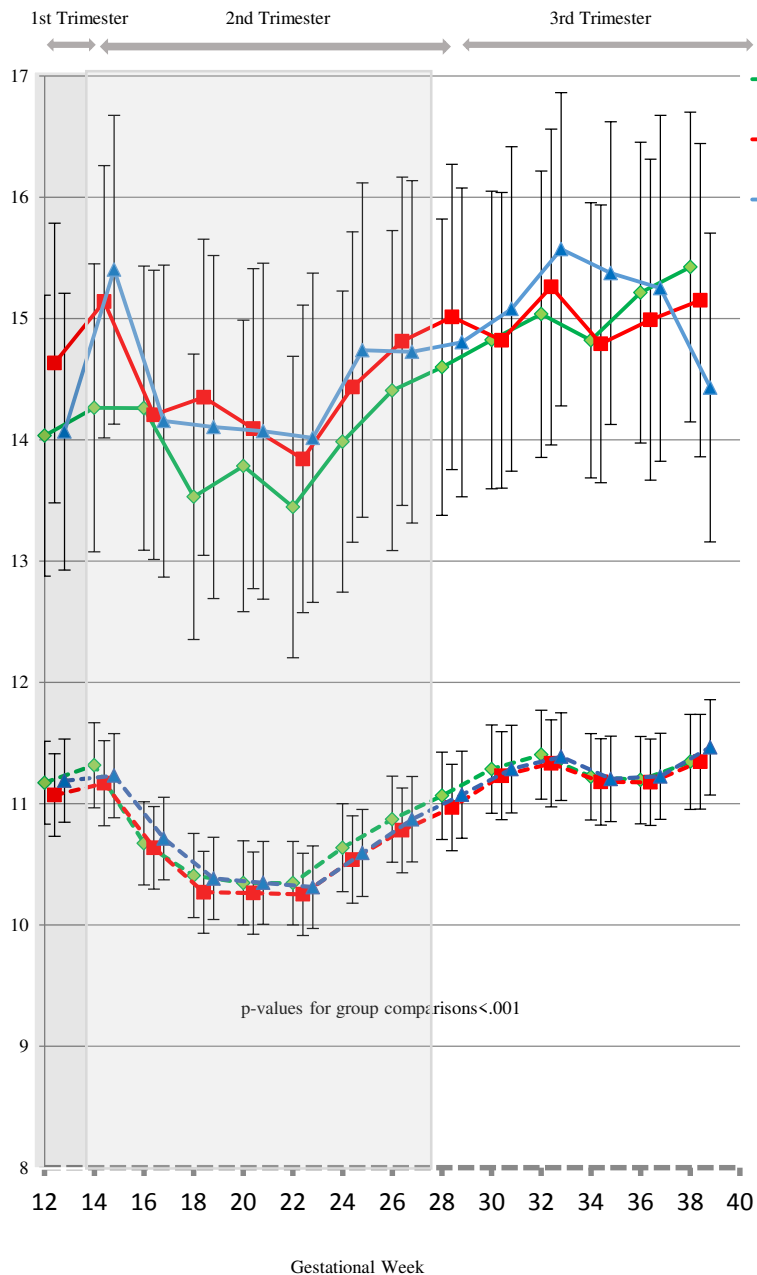
Do maternal depressive symptoms after pregnancy mediate or add to the prenatal effects?

Figures 1 (Panel B, model 4) and 2 and Tables S2-S3 (model 4) show that, although maternal depressive symptoms after pregnancy, concurrently to rating the child psychiatric problems, were significantly associated with higher internalizing, externalizing and total problems as well as syndrome scale- and DSM-oriented problems of the child (unstandardized regression coefficients in 4th regression models =0.22 to 0.47, p-values<.001), maternal depressive symptoms across pregnancy and at each biweekly assessment remained significant predictors of all types of child psychiatric problems after adjustment for maternal depressive

Figure 1

Panel A.

CES-D
sumscore



Panel B.

SD unit increase in child
psychiatric problems per 1 SD
increase in maternal
depressive symptoms during
pregnancy

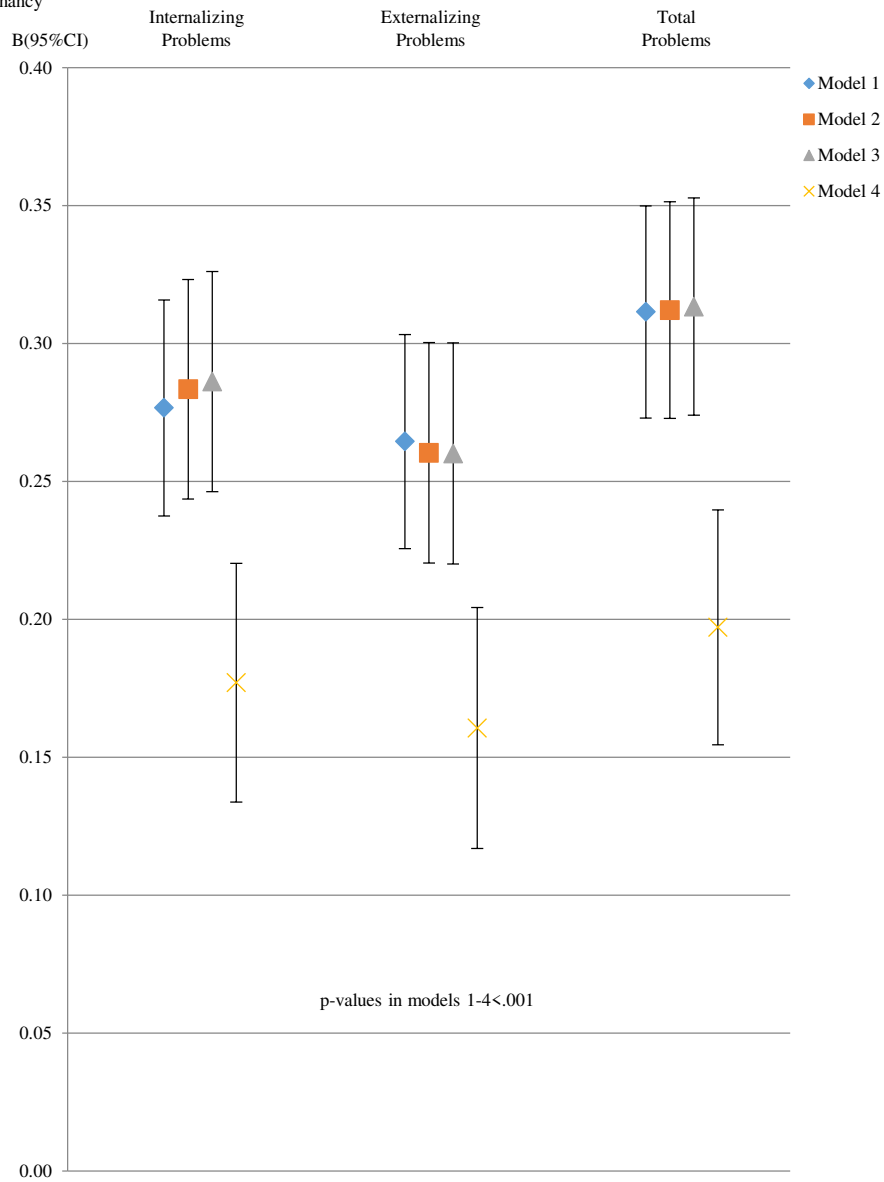
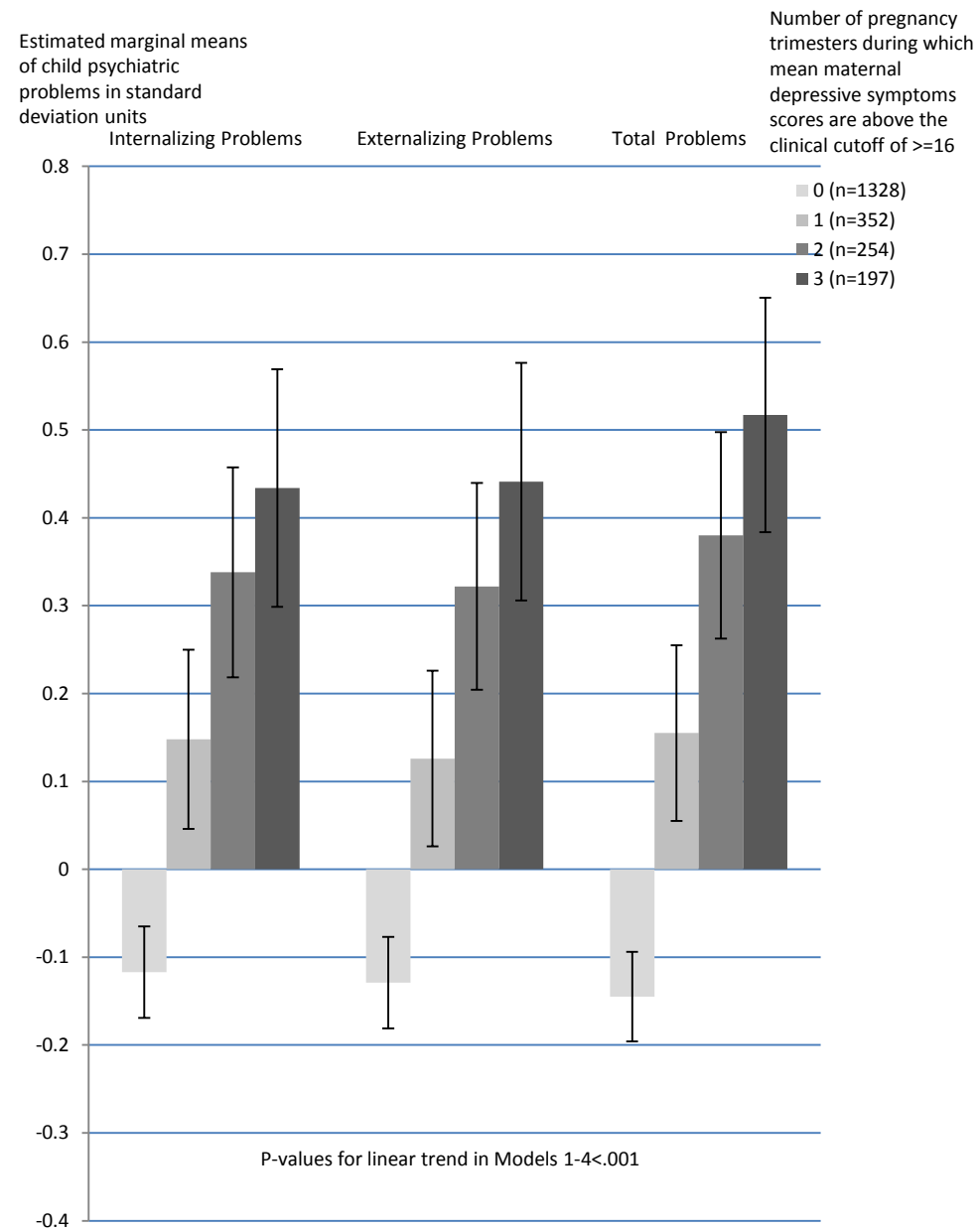


Figure 2



Panel B.

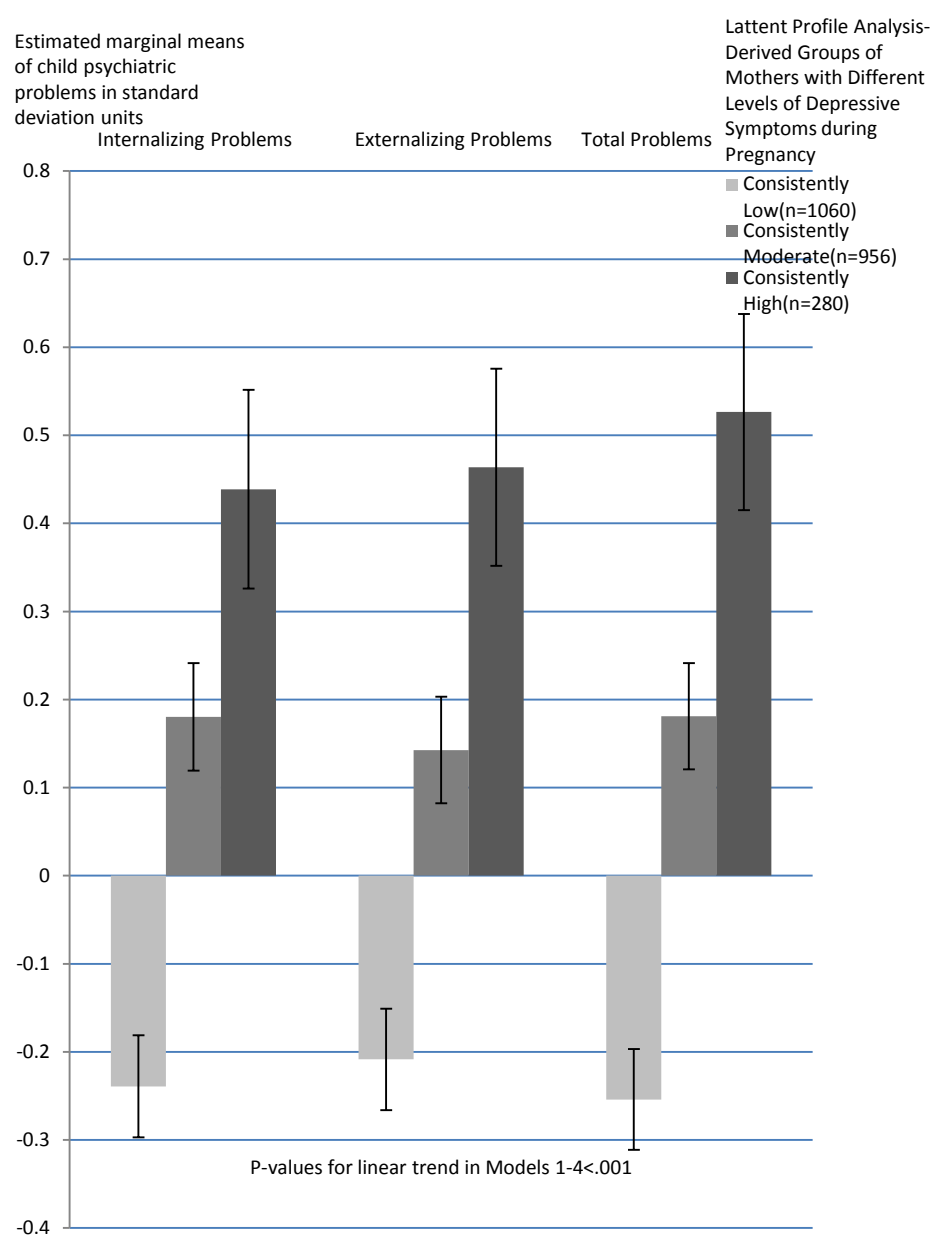
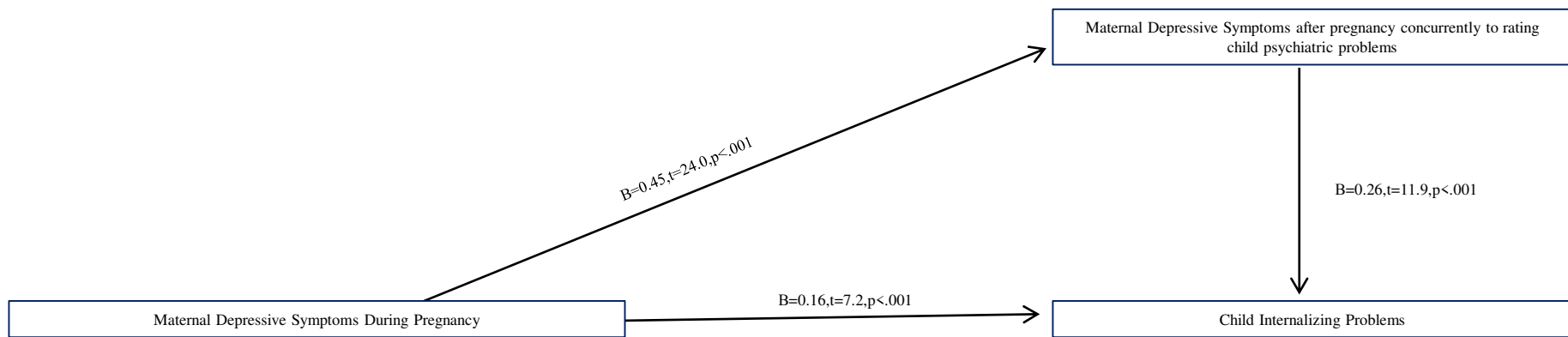


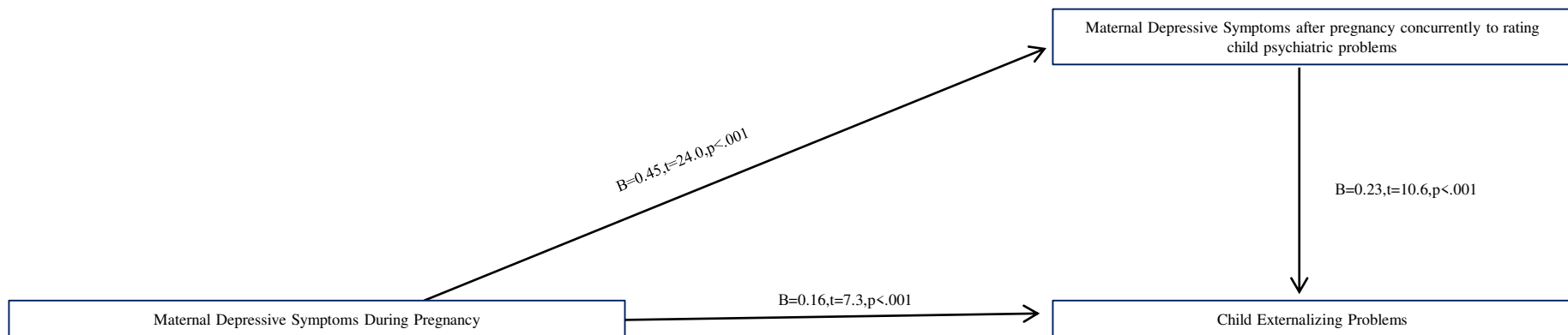
Figure 3

Indirect effect $B=0.12$, 95 % CI= $0.10-0.14$, p-values in models 1-3 $<.001$



Panel B.

Indirect effect $B=0.10$, 95 % CI= $0.08-0.13$, p-values in models 1-3 $<.001$



Panel C.

Indirect effect $B=0.12$, 95 % CI= $0.10-0.15$, p-values in models 1-3 $<.001$

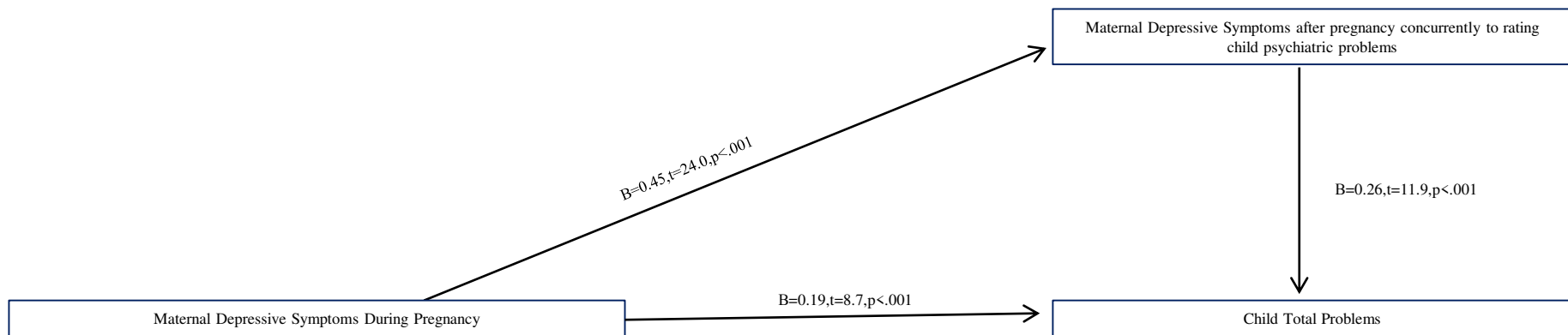
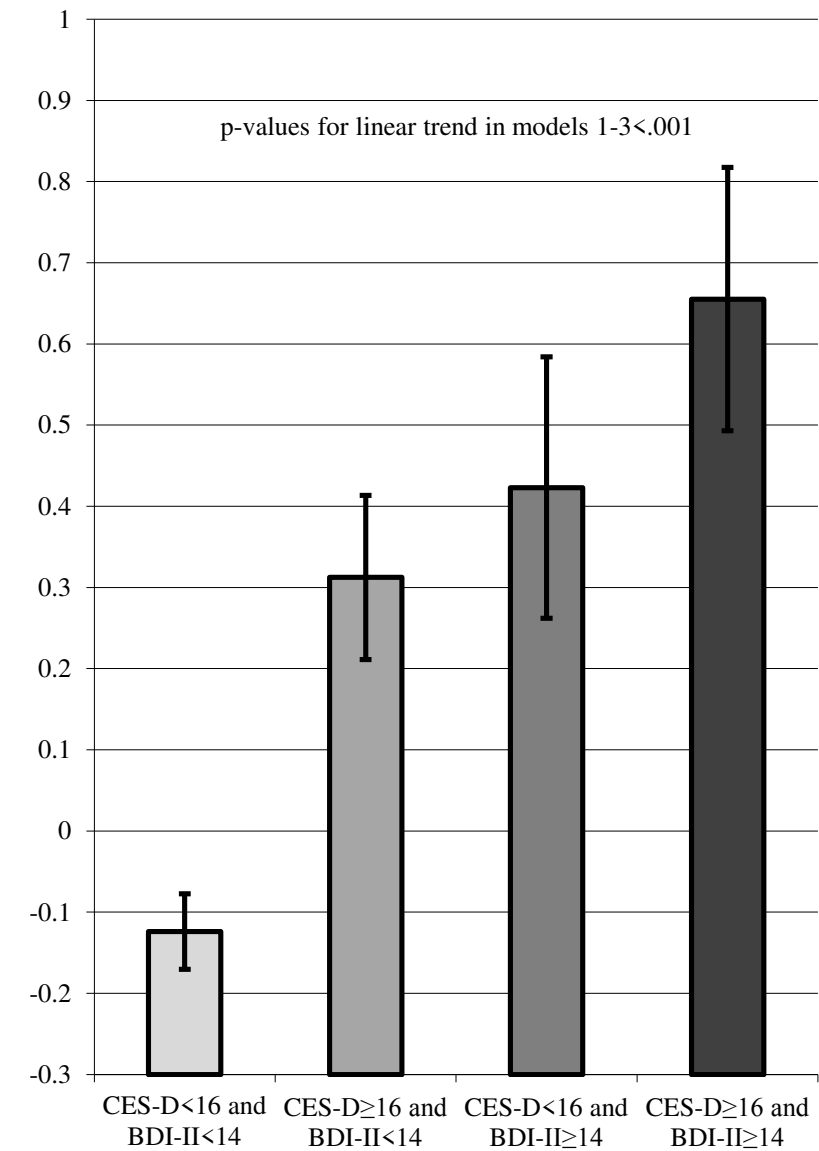


Figure 4

Panel A.

Child internalizing
problems in standard
deviation
units



Panel B.

Child total problems
in standard deviation
units

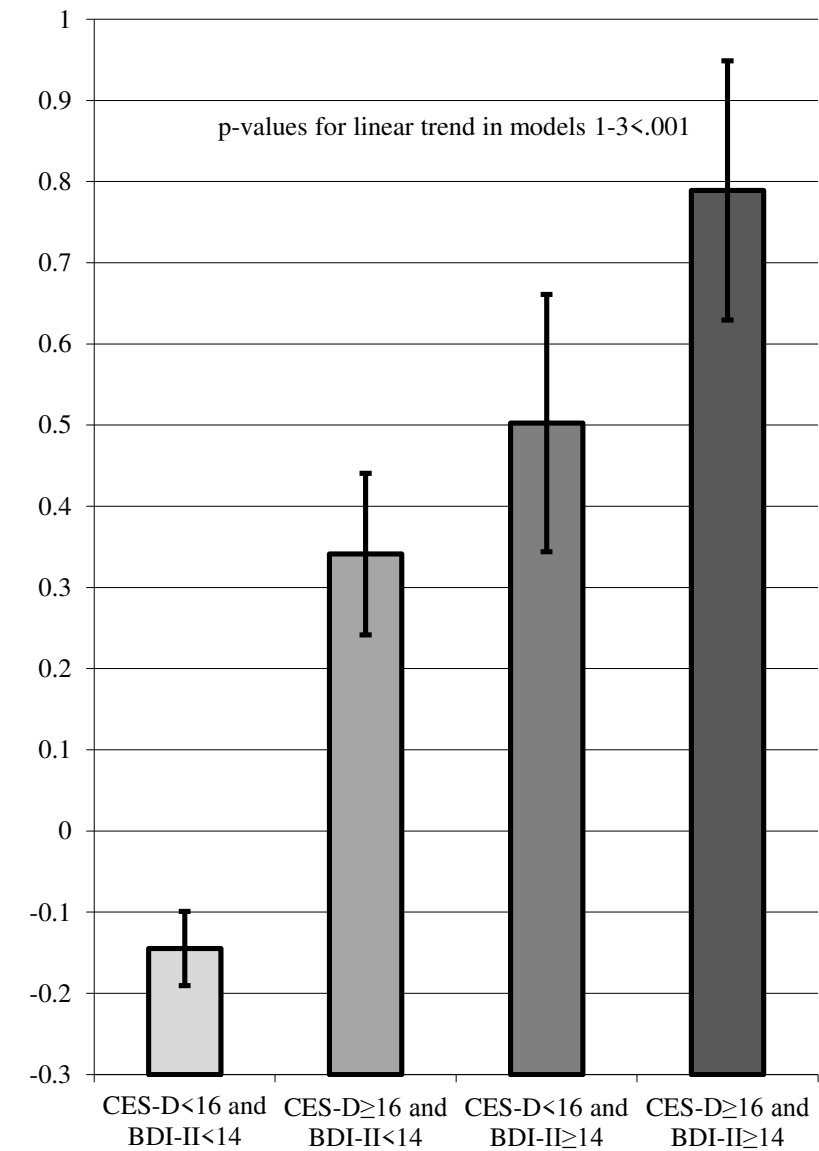


Table S1. The Associations of the Covariates with Child Psychiatric Problems

	CBCL Scale					
	Internalizing Problems^a		Externalizing Problems^a		Total Problems^a	
	r /Mean Difference^b	p	r /Mean Difference^b	p	r /Mean Difference^b	p
Maternal Characteristics						
Age At Delivery	-.09	<.001	-.11	<.001	-.12	<.001
Education: Primary or secondary vs. tertiary	.05	.31	.11	.01	.08	.05
Parity: Primiparous vs. other	.40	<.001	.21	<.001	.34	<.001
Family Structure: Single vs. Cohabiting	.17	.30	.04	.83	.08	.63
History of Depression Before Pregnancy (yes vs. no)	.24	.002	.20	.01	.26	<.001
Antidepressant Use During Pregnancy (yes vs. no)	.02	.88	.26	.07	.21	.14
Other Psychotropic Medication Use During Pregnancy	.37	.17	.43	.11	.44	.10
Alcohol Use During Pregnancy (yes vs. no)	.01	.91	.06	.29	.01	.83
Quit Smoking During First Pregnancy Trimester vs. No Smoking during Pregnancy	.18	.13	.23	.04	.22	.06
Smoked Throughout Pregnancy vs. No Smoking during pregnancy	.31	.01	.49	<.001	.44	.001
Smoked Throughout Pregnancy vs. Quit Smoking during First Pregnancy Trimester	.13	.43	.25	.13	.21	.20
Pre-Pregnancy Obesity (yes/no)	-.03	.63	.09	.18	.04	.56
Gestational Hypertension-Spectrum Disorder (yes/no)	-.00	.95	-.00	.96	-.00	.99
Chronic Hypertension (yes/no)	-.00	>.99	-.08	.50	-.04	.74
Gestational Diabetes (yes/no)	-.02	.80	-.02	.76	-.01	.87
Type 1 Diabetes (yes/no)	.17	.56	.39	.20	.27	.37
Child Characteristics						
Sex (Boy vs. Girl)	-.03	.48	.26	<.001	.15	<.001
Gestational Age	-.03	.13	-.03	.21	-.03	.16
Birth Weight Adjusted for Gestational Age and Sex	-.08	<.001	-.05	.03	-.06	.005
Age at Follow-Up	.07	.002	-.08	<.001	-.04	.03
Paternal Depressive Symptoms in Child's Infancy	.14	<.001	.08	.003	.14	<.001

^a Child Psychiatric Problem Scores are expressed in Standard Deviation Units

^b r refers to Pearson correlation coefficients of continuous covariates with child psychiatric problems; Mean difference refers to mean group differences between the groups of the categorical covariates in child psychiatric problems in independent samples t-test analyses.

Table S2. The Associations Between Trimester-Weighted Mean of Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems

CBCL Scale	Model 1 (N=2296)^a		Model 2 (N=2296)^a		Model 3 (N=2296)^a		Model 4(N=2269)^{a,b}	
Main Scales	B(95 % CI)^c	p	B(95 % CI)^c	p	B(95 % CI)^c	p	B(95 % CI)^c	p
Internalizing Problems	0.28(0.24-0.32)	<.001	0.28(0.24-0.32)	<.001	0.29(0.25-0.33)	<.001	0.18(0.13-0.22)	<.001
Externalizing Problems	0.26(0.23-0.30)	<.001	0.26(0.22-0.30)	<.001	0.26(0.22-0.30)	<.001	0.16(0.12-0.20)	<.001
Total Problems	0.31(0.27-0.35)	<.001	0.31(0.27-0.35)	<.001	0.31(0.27-0.35)	<.001	0.20(0.15-0.24)	<.001
Syndrome Scales								
Emotionally Reactive	0.41(0.33-0.49)	<.001	0.41(0.33-0.48)	<.001	0.42(0.34-0.49)	<.001	0.25(0.17-0.34)	<.001
Anxious/Depressed	0.56(0.44-0.68)	<.001	0.56(0.44-0.68)	<.001	0.56(0.44-0.68)	<.001	0.35(0.23-0.48)	<.001
Somatic Complaints	0.37(0.29-0.45)	<.001	0.38(0.30-0.47)	<.001	0.39(0.30-0.47)	<.001	0.26(0.17-0.35)	<.001
Withdrawn	0.29(0.23-0.36)	<.001	0.33(0.26-0.39)	<.001	0.33(0.26-0.39)	<.001	0.20(0.13-0.27)	<.001
Sleep Problems	0.30(0.24-0.36)	<.001	0.30(0.24-0.36)	<.001	0.30(0.24-0.36)	<.001	0.20(0.13-0.27)	<.001
Attention Problems	0.35(0.28-0.43)	<.001	0.35(0.28-0.43)	<.001	0.35(0.27-0.43)	<.001	0.22(0.13-0.30)	<.001
Aggressive Behaviour	0.46(0.38-0.54)	<.001	0.45(0.37-0.53)	<.001	0.45(0.37-0.53)	<.001	0.28(0.19-0.37)	<.001
DSM^d-Oriented Scales								
Affective Problems	0.30(0.25-0.35)	<.001	0.30(0.25-0.36)	<.001	0.31(0.25-0.36)	<.001	0.20(0.14-0.25)	<.001
Anxiety Problems	0.45(0.36-0.55)	<.001	0.44(0.34-0.54)	<.001	0.44(0.34-0.54)	<.001	0.29(0.19-0.40)	<.001
Pervasive Developmental Problems	0.32(0.26-0.39)	<.001	0.34(0.27-0.41)	<.001	0.34(0.28-0.41)	<.001	0.21(0.14-0.29)	<.001
ADHD ^d Problems	0.39(0.31-0.47)	<.001	0.40(0.32-0.48)	<.001	0.40(0.32-0.48)	<.001	0.25(0.16-0.33)	<.001
Oppositional Defiant Problems	0.31(0.25-0.37)	<.001	0.31(0.24-0.37)	<.001	0.31(0.25-0.37)	<.001	0.18(0.12-0.25)	<.001

^aModel 1 is adjusted for the age and sex of the child; Model 2 further for family structure, maternal age at delivery, parity, education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex; Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders and gestational diabetes; and Model 4 for maternal depressive symptoms after pregnancy at the time of ratings the child's psychiatric problems.

^bThe fourth analytic models include 2269 participants since 27 mothers had missing data on depressive symptoms after pregnancy and were excluded from these analyses. In contrast, participants with missing values on categorical covariates were dummy-coded into separate categories in the regression analysis.

^cB:s and 95% CI:s for main scales are unstandardized regression coefficients and their 95 % confidence intervals from linear regression analyses; B:s and 95% CI:s for syndrome and DSM-Oriented Scales are unstandardized regression coefficients and 95 % confidence intervals from tobit regression analyses. Both the independent and dependent variables are expressed in standard deviation units.

^dDSM=Diagnostic and Statistical Manual for Mental Disorders; ADHD=Attention Deficit Hyperactivity Disorder.

Table S3. Maternal Biweekly Depressive Symptoms during Pregnancy and Child Psychiatric Problems.

Maternal Depressive Symptoms at	Internalizing Problems	Externalizing Problems	Total Problems
	B (95 % CI)	B (95 % CI)	B (95 % CI)
12-13 weeks of gestation (n=2193)			
Model 1	0.22 (0.17-0.26)	0.22 (0.18-0.27)	0.25 (0.21-0.29)
Model 2	0.22 (0.18-0.26)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 3	0.22 (0.18-0.26)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 4	0.12 (0.07-0.16)	0.13 (0.08-0.17)	0.14 (0.10-0.18)
14-15 weeks of gestation (n=2142)			
Model 1	0.22 (0.18-0.26)	0.22 (0.17-0.26)	0.25 (0.21-0.29)
Model 2	0.24 (0.19-0.28)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 3	0.22 (0.18-0.26)	0.20 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.12 (0.08-0.17)	0.12 (0.07-0.16)	0.14 (0.10-0.18)
16-17 weeks of gestation (n=2110)			
Model 1	0.23 (0.19-0.27)	0.21 (0.17-0.25)	0.26 (0.21-0.30)
Model 2	0.23 (0.19-0.28)	0.21 (0.17-0.25)	0.25 (0.21-0.29)
Model 3	0.24 (0.20-0.28)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.14 (0.10-0.18)	0.12 (0.08-0.16)	0.15 (0.11-0.19)
18-19 weeks of gestation (n=2133)			
Model 1	0.21 (0.17-0.25)	0.20 (0.16-0.24)	0.24 (0.20-0.28)
Model 2	0.20 (0.16-0.24)	0.19 (0.15-0.23)	0.23 (0.19-0.27)
Model 3	0.20 (0.16-0.25)	0.19 (0.15-0.23)	0.23 (0.19-0.27)
Model 4	0.12 (0.07-0.16)	0.11 (0.07-0.15)	0.13 (0.09-0.17)
20-21 weeks of gestation (n=2111)			
Model 1	0.23 (0.19-0.27)	0.22 (0.17-0.26)	0.25 (0.21-0.30)
Model 2	0.23 (0.19-0.27)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 3	0.23 (0.19-0.27)	0.20 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.13 (0.09-0.18)	0.12 (0.07-0.16)	0.15 (0.11-0.19)
22-23 weeks of gestation (n=2081)			
Model 1	0.22 (0.17-0.26)	0.22 (0.18-0.26)	0.25 (0.20-0.29)
Model 2	0.21 (0.17-0.25)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 3	0.21 (0.17-0.26)	0.21 (0.16-0.25)	0.24 (0.20-0.28)
Model 4	0.12 (0.07-0.16)	0.12 (0.08-0.16)	0.14 (0.09-0.18)
24-25 weeks of gestation (n=2055)			
Model 1	0.23 (0.19-0.27)	0.21 (0.17-0.25)	0.25 (0.20-0.29)
Model 2	0.22 (0.18-0.26)	0.20 (0.15-0.24)	0.23 (0.19-0.27)
Model 3	0.22 (0.18-0.27)	0.19 (0.15-0.24)	0.23 (0.19-0.28)
Model 4	0.13 (0.09-0.18)	0.11 (0.07-0.16)	0.14 (0.09-0.18)
26-27 weeks of gestation (n=2076)			
Model 1	0.23 (0.18-0.27)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 2	0.22 (0.18-0.26)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 3	0.22 (0.18-0.26)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 4	0.12 (0.08-0.17)	0.12 (0.08-0.17)	0.14 (0.10-0.18)
28-29 weeks of gestation (n=2055)			
Model 1	0.26 (0.22-0.30)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 2	0.26 (0.21-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 3	0.26 (0.22-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 4	0.16 (0.12-0.21)	0.12 (0.08-0.16)	0.16 (0.12-0.20)
30-31 weeks of gestation (n=2056)			
Model 1	0.25 (0.20-0.29)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 2	0.25 (0.21-0.29)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 3	0.25 (0.21-0.30)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 4	0.16 (0.11-0.20)	0.13 (0.08-0.17)	0.16 (0.12-0.21)

Table S3 (cont). Maternal Biweekly Depressive Symptoms during Pregnancy and Child Psychiatric**Problems.**

Maternal Depressive Symptoms at	Internalizing Problems	Externalizing Problems	Total Problems
32-33 weeks of gestation (n=2061)			
Model 1	0.26 (0.22-0.30)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 2	0.27 (0.23-0.31)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 3	0.27 (0.23-0.31)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 4	0.18 (0.13-0.22)	0.14 (0.09-0.18)	0.18 (0.13-0.22)
34-35 weeks of gestation (n=2020)			
Model 1	0.25 (0.20-0.29)	0.22 (0.18-0.26)	0.27 (0.22-0.31)
Model 2	0.25 (0.21-0.29)	0.21 (0.17-0.25)	0.26 (0.22-0.30)
Model 3	0.25 (0.21-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 4	0.16 (0.12-0.21)	0.12 (0.08-0.17)	0.16 (0.12-0.21)
36-37 weeks of gestation (n=1957)			
Model 1	0.23 (0.19-0.27)	0.20 (0.16-0.24)	0.25 (0.21-0.29)
Model 2	0.24 (0.19-0.28)	0.20 (0.16-0.24)	0.25 (0.21-0.30)
Model 3	0.24 (0.20-0.28)	0.20 (0.16-0.24)	0.26 (0.21-0.30)
Model 4	0.16 (0.11-0.20)	0.12 (0.08-0.17)	0.17 (0.12-0.21)
38-39 weeks of gestation (n=1669)			
Model 1	0.22 (0.18-0.27)	0.19 (0.14-0.23)	0.24 (0.19-0.28)
Model 2	0.23 (0.19-0.28)	0.18 (0.14-0.23)	0.24 (0.19-0.28)
Model 3	0.23 (0.19-0.28)	0.19 (0.14-0.23)	0.24 (0.20-0.29)
Model 4	0.15 (0.10-0.20)	0.11 (0.06-0.16)	0.15 (0.10-0.20)

Model 1 is adjusted for child's age and sex; Model 2 further for family structure, maternal age at delivery, parity, education, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex; Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders, and gestational diabetes and Model 4 also for maternal depressive symptoms after pregnancy at the time of rating child's psychiatric problems.

B:s and 95% CI:s are unstandardized regression coefficients and their 95 % confidence intervals from linear regression models. All independent and dependent variables are expressed in standard deviation units.

All the associations are highly statistically significant (p<.001).

Table S4. Age-Specific Associations Between Trimester-Weighted Mean of Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems.								
Age of the child	Model 1		Model 2		Model 3		Model 4	
1.9-3.9 years (n=1564)	B(95 % CI)	p	B(95 % CI)	P	B(95 % CI)	p	B(95 % CI)	p
Internalizing Problems	0.29(0.25-0.34)	<.001	0.30(0.25-0.34)	<.001	0.30(0.25-0.34)	<.001	0.19(0.14-0.24)	<.001
Externalizing Problems	0.27(0.22-0.32)	<.001	0.27(0.22-0.31)	<.001	0.26(0.22-0.31)	<.001	0.17(0.12-0.22)	<.001
Total Problems	0.32(0.28-0.37)	<.001	0.32(0.27-0.37)	<.001	0.32(0.27-0.37)	<.001	0.21(0.16-0.26)	<.001
4-5.9 years (n=732)								
Internalizing Problems	0.25(0.18-0.32)	<.001	0.26(0.18-0.33)	<.001	0.26(0.19-0.34)	<.001	0.15(0.07-0.24)	<.001
Externalizing Problems	0.25(0.18-0.32)	<.001	0.25(0.18-0.32)	<.001	0.25(0.18-0.32)	<.001	0.15(0.06-0.23)	<.001
Total Problems	0.29(0.22-0.36)	<.001	0.29(0.22-0.36)	<.001	0.29(0.22-0.36)	<.001	0.17(0.09-0.25)	<.001
<p>^a Model 1 is adjusted for the age and sex of the child; Model 2 further for family structure, maternal age at delivery, parity, education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex; Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders and gestational diabetes: and Model 4 for maternal depressive symptoms after pregnancy at the time of rating the child's psychiatric problems.</p> <p>^c B:s and 95% CI:s for main scales are unstandardized regression coefficients and their 95 % confidence intervals from linear regression analyses. Both the independent and dependent variables are expressed in standard deviation units.</p>								

Figure S1

Figure S1. Latent profile analysis on the course of maternal depressive symptoms during pregnancy. The figure shows the mean levels of depressive symptoms at different gestational weeks in three latent profile analysis-derived groups of mothers who show consistently low, moderate, and high levels of depressive symptoms throughout pregnancy.

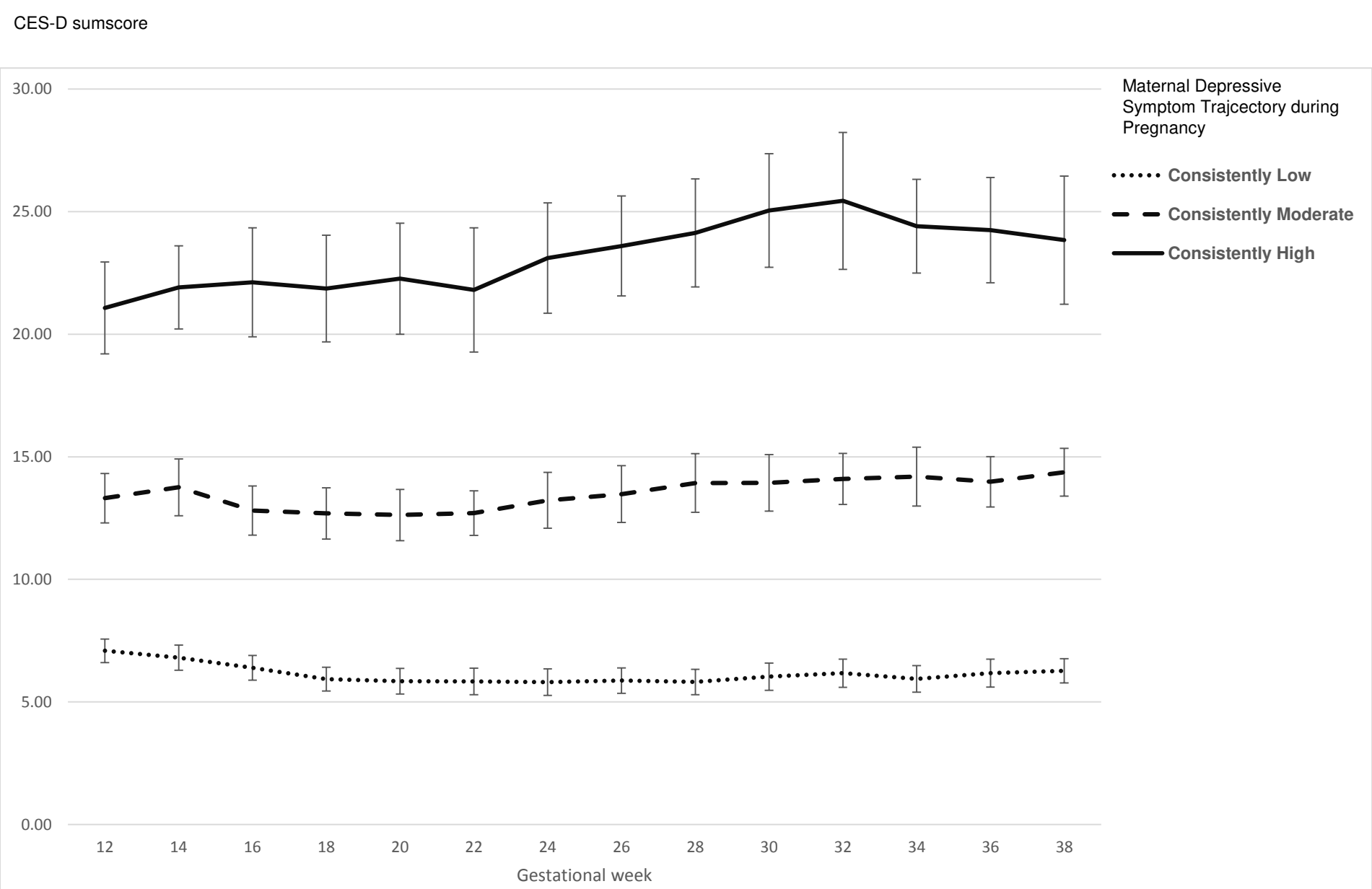


Figure S2

Figure S2. Maternal depressive symptoms during pregnancy and child psychiatric problems in groups with and without pregnancy disorders.

Maternal depressive symptoms during pregnancy and child psychiatric problems among those with maternal pregnancy disorders (pre-pregnancy obesity, gestational hypertensive disorders, and gestational diabetes) (Panel A: n=541) and among those without (Panel B: n=1755). Unstandardized regression coefficients (B) and their 95 % confidence intervals (CI) of linear regression models adjusted for the covariates in models 1-3. The third models refer here to regression models adjusted further for maternal depressive symptoms at the time of rating the child's problems.

Panel A. With pregnancy Disorders

Standard deviation unit increase in child psychiatric problems per 1 standard deviation increase in maternal depressive symptoms during pregnancy

Panel B. Without pregnancy Disorders

Standard deviation unit increase in child psychiatric problems per 1 standard deviation increase in maternal depressive symptoms during pregnancy

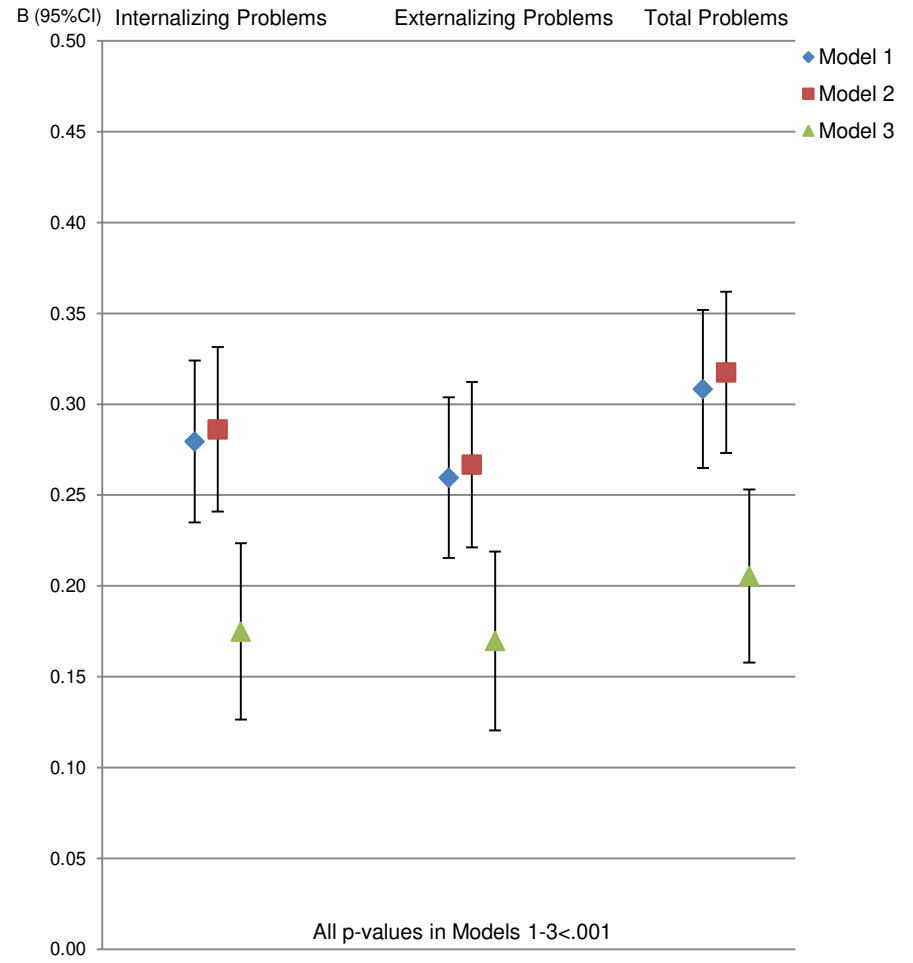
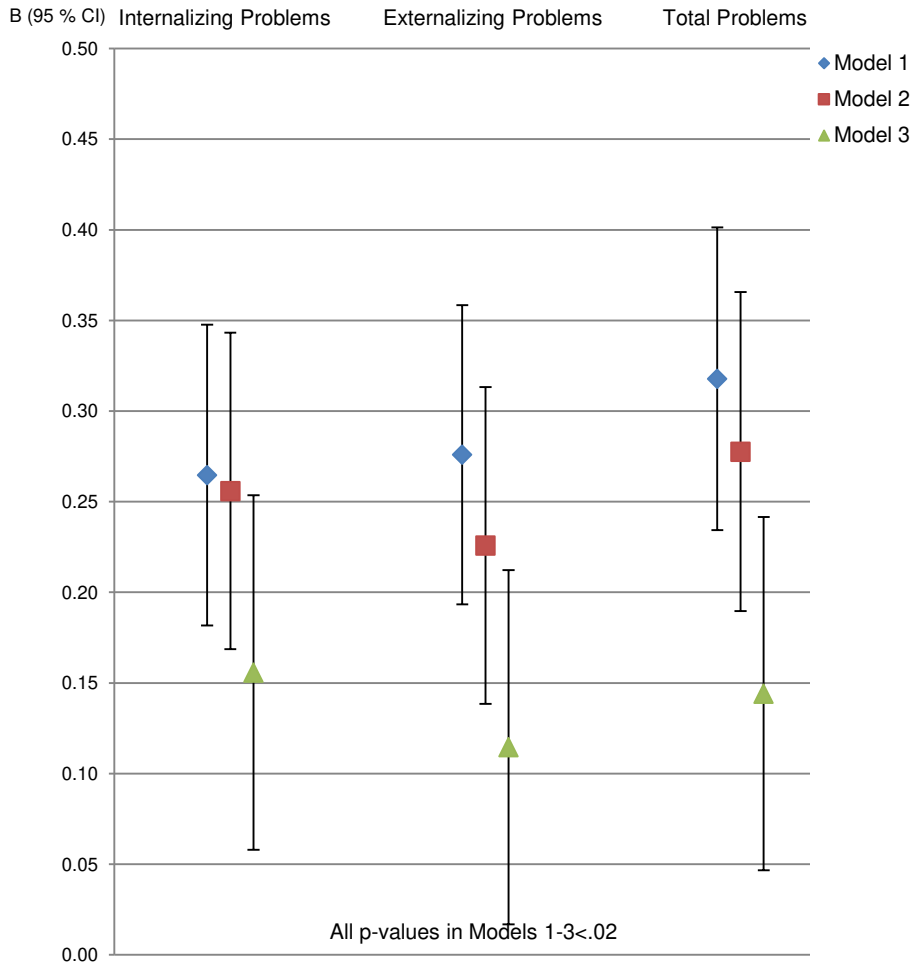


Figure S3

Figure S3. Maternal depressive symptoms during pregnancy and child psychiatric problems in groups with and without maternal diagnosis of depression before pregnancy. Maternal depressive symptoms during pregnancy and child psychiatric problems among those with maternal self-reported history of physician-diagnosed depression before pregnancy (Panel A: n=214) and among those without (Panel B: n=1982). Unstandardized regression coefficients (B) and their 95 % confidence intervals (CI) of linear regression models adjusted for the covariates in models 1-4.

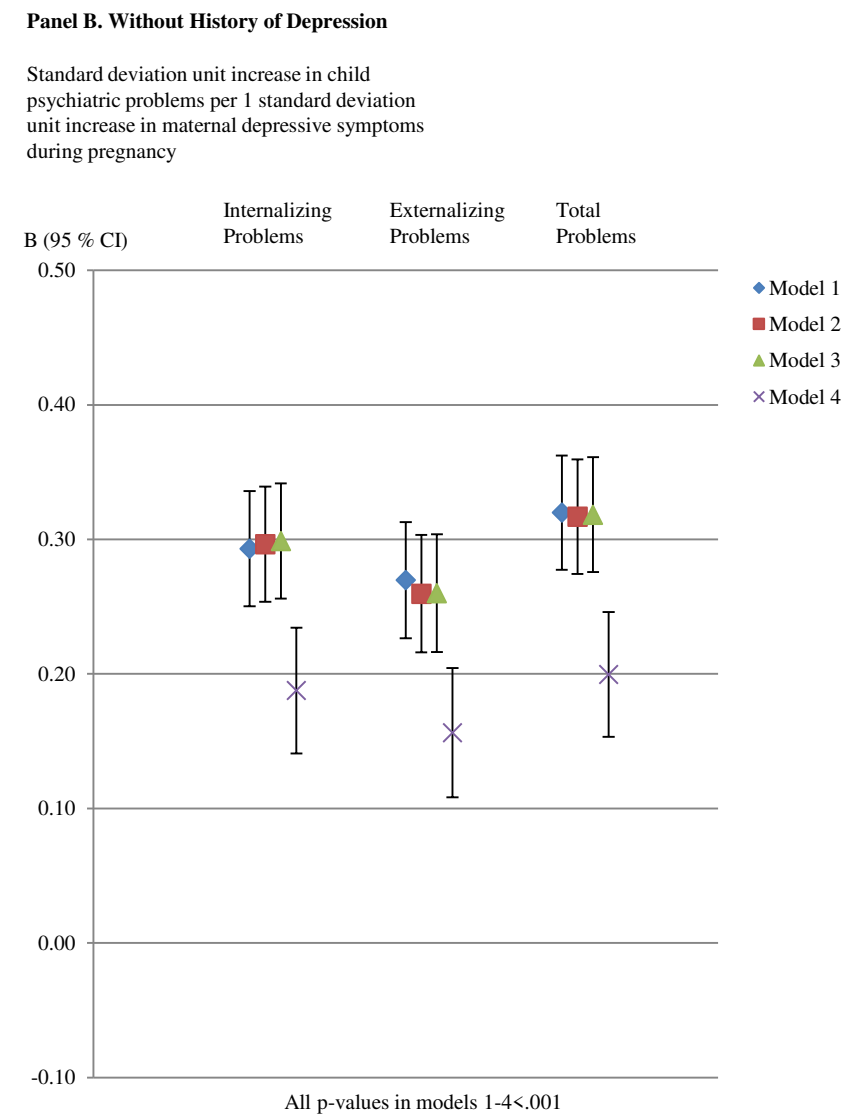
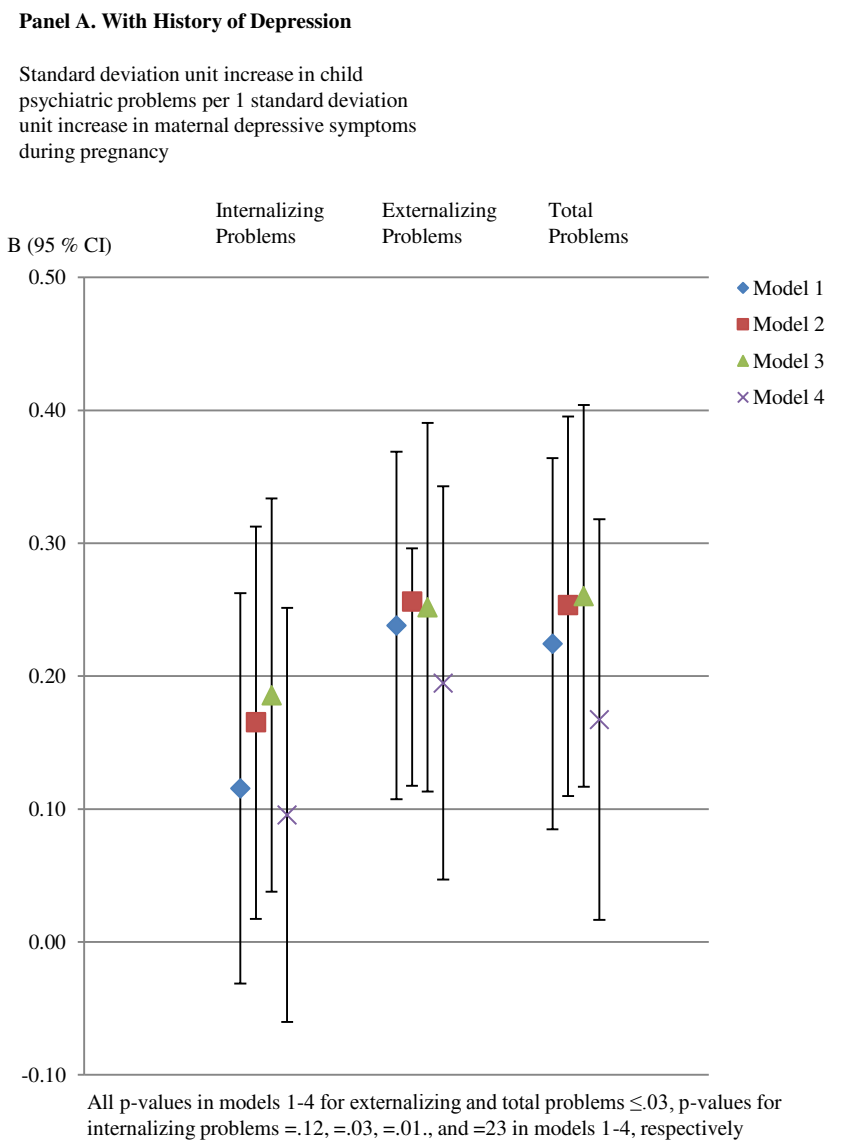


Figure 1 black and white for print version

