




Positive maternal mental health during pregnancy and mental and behavioral disorders in children: A prospective pregnancy cohort study

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Background: The role of positive maternal mental health during pregnancy in child mental health remains largely unknown. We investigated whether positive maternal mental health during pregnancy is associated with lower hazards of mental and behavioral disorders in children and mitigates the adverse effects of negative maternal mental health. **Methods:** Among 3,378 mother-child dyads of the Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction study, mothers reported their positive mental health biweekly throughout pregnancy with the Positive and Negative Affect Schedule, the Spielberger State Anxiety Inventory Curiosity scale, and a visual analogue scale for social support, and negative mental health with the Center for Epidemiologic Studies Depression Scale. We extracted data on their mental and behavioral disorder diagnoses from a nationwide medical register. This register provided data on their children's mental and behavioral disorder diagnoses as well, from birth until 8.4–12.8 (Median = 10.2, Interquartile Range 9.7–10.8) years of age. **Results:** A positive maternal mental health composite score during pregnancy was associated with a lower hazard of any mental and behavioral disorder among all children [Hazard Ratio (HR) = 0.79, 95% Confidence Interval (CI) 0.71 – 0.87] and among children of mothers experiencing clinically relevant depressive symptoms during pregnancy [HR = 0.80, 95%CI 0.64 – 1.00] and/or mental and behavioral disorders before or during pregnancy [HR = 0.69, 95%CI 0.55–0.86]. These associations were independent of covariates. **Conclusions:** Children whose mothers had more positive mental health during pregnancy were less likely to develop mental and behavioral disorders. Protective effects were seen also among children of mothers facing mental health adversities before or during pregnancy. **Keywords:** Positive mental health; prenatal well-being; child psychiatry.

Introduction

Ample empirical evidence suggests that negative maternal mental health during pregnancy, including mental and behavioral disorders and their symptoms, predicts an increased risk of mental and behavioral disorders in children (Madigan et al., 2018; Robinson, Lahti-Pulkkinen, Heinonen, Reynolds, & Räikkönen, 2019; Van den Bergh et al., 2020). These findings support the Developmental Origins of Health and Disease (DOHaD) -framework (O'Donnell & Meaney, 2017; Van den Bergh et al., 2020), which suggests that exposure to environmental adversities in prenatal life may program brain development in ways that increase mental and behavioral disorder risk in subsequent life.

However, not all children suffer from the adverse effects of negative maternal mental health during pregnancy. While there may be several contributors to this, it has been hypothesized that the prenatal environment may also convey protective characteristics, such as positive maternal mental health, including positive emotions and perceived social support (Phua, Kee, & Meaney, 2020). Although negative and positive mental health are inversely correlated, they are independent constructs (Phua et al., 2017) which only partially share developmental origins, biological correlates, and health consequences (Kendler, Myers, Maes, & Keyes, 2011; Ryff et al., 2006). Co-occurring positive maternal mental health may thus carry protection from the adverse effects of negative maternal mental health.

Whether positive maternal mental health during pregnancy mitigates the mental and behavioral

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disorder risk in children remains unknown. Some preliminary evidence exists, but it is limited by relatively small sample sizes, and to adaptive development (Braeken, Jones, Otte, Nyklíček, & Van den Bergh, 2017; DiPietro, Novak, Costigan, Atella, & Reusing, 2006; van den Heuvel, Johannes, Henrichs, & Van den Bergh, 2015; Phua et al., 2017) and psychiatric symptoms (Phua et al., 2017) in children, rather than diagnosed mental and behavioral disorders, which represent the more severe end on the continuum of psychiatric symptoms. Moreover, the one study on psychiatric symptoms in children reported inconsistent findings: higher positive maternal mood latent factor score at 26 gestational weeks was associated with higher peer aggression, but not with other externalizing or internalizing problems in their 12-month-old-children. However, this positive maternal mood score was associated with lower autism-related symptoms score when the children were 18 months old. Furthermore, none of the existing studies have extended follow-up of the children beyond toddlerhood or examined if indices of positive maternal mental health were independent of, or protected the children from, the adverse effects of negative maternal mental health during pregnancy.

In a large sample of pregnant women and their children, we investigated whether positive maternal mental health, assessed biweekly throughout pregnancy, was associated with lower hazards of mental and behavioral disorders in children followed from birth until age 8.4–12.8 years, and whether the associations were specific to gestation stage. We also investigated whether these associations were independent of maternal depressive symptoms during pregnancy or mental and behavioral disorder diagnoses before or during pregnancy. Further, we studied whether positive maternal mental health during pregnancy protected the children whose mothers experienced these mental health adversities from developing mental and behavioral disorders.

Methods

Participants

The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) study (Girchenko et al., 2017) comprises 4,777 pregnant women who gave birth to a singleton live child between 2006 and 2010. The women were recruited during their first ultrasound screening visit between 12 + 0 and 13 + 6 gestational weeks+days at one of the ten study hospitals in Finland. Three women subsequently withdrew from the study. Of the participating 4,774 women, 3,403 (71.3%) completed questionnaires addressing positive and negative mental health during pregnancy. Data on mental and behavioral disorder diagnoses were available for 3,378 of their children (99.3%) in a follow-up from birth until 8.4–12.8 (median = 10.2, interquartile range 9.7–10.8) years-of-age.

Compared to non-responders of the initial sample, the women in our analytic subsample were older, more often with higher education, married or cohabiting, and primiparous, and

less often used substances (tobacco/alcohol) during early pregnancy or had cardio-metabolic pregnancy conditions (overweight/obesity, diabetes, or hypertensive disorders) or mental and behavioral disorder diagnoses, and their children were less often diagnosed with any mental and behavioral disorder (Table S1).

Ethical considerations

The PREDO study protocol was approved by the Ethics committee of the Helsinki and Uusimaa Hospital District. Written informed consent was obtained from all participants, also enabling linkage of nationwide health register data for the women, their spouses, and children with the permission of relevant register authorities.

Measures

Positive maternal mental health. The mothers completed questionnaires addressing positive emotions and social support biweekly up to 14 times throughout pregnancy from 12–13 to 38–39 gestational weeks/delivery. Positive emotions were assessed with the Positive affect scale of the Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988) and the Curiosity scale of the Spielberger State-Trait Anxiety Inventory (STAI), state version (Spielberger, 1983). The PANAS comprises 10 positive affect items (e.g. 'excited', 'interested') rated on a 5-point scale ranging from 'not at all' (1) to 'very much' (5), according to how strongly the affect is currently experienced. The STAI Curiosity scale comprises 10 positively worded items (e.g., 'I feel pleasant', 'I feel secure') rated on a 4-point scale ranging from 'not at all' (1) to 'very much' (4) (Spielberger & Reheiser, 2009).

Perceived social support was assessed using a visual analogue scale (VAS). The mothers marked on a 65-mm long line how much support they felt they had received during the past two weeks ranging from 'not at all' (0) to 'very much' (65 mm).

Psychometric properties are good for PANAS (Crawford & Henry, 2004; Watson et al., 1988) and STAI Curiosity scales (Spielberger, 1983). In our sample, the scales showed good internal consistencies, $\alpha = .91-.94$ for PANAS and $\alpha = .94-.95$ for STAI Curiosity. Since positive affect, curiosity, and social support showed high stability throughout the biweekly assessment points during pregnancy ($r = .47-.76$ for PANAS, $r = .45-.69$ for STAI Curiosity, and $r = .41-.75$ for VAS), we calculated mean scores across all available observations.

Further, because the scales were interrelated ($r = .68$ between PANAS and STAI Curiosity, $r = .40$ between PANAS and VAS, and 0.41 between STAI Curiosity and VAS; $p < .001$ for all of the correlations), we conducted a principal component analysis (PCA) that yielded one principal component (eigenvalue = 2.00; loadings 0.87, 0.87 and 0.70 for PANAS, STAI Curiosity and VAS, respectively), explaining 66.6% of the total variance. In the analyses, we used this PCA-based composite score as the primary index of positive maternal mental health during pregnancy. However, we also show associations from analyses using the individual scales, which we additionally used when investigating whether their associations with mental and behavioral disorders in children varied by gestational stage, that is, whether associations were different across the biweekly assessment points.

Negative maternal mental health. The mothers completed the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977) at the same biweekly time points as the questionnaires addressing positive mental health. The 20 CES-D items on depressive symptoms during the past week are rated from none (0) to all (3) of the time. The CES-D has excellent psychometric properties (Radloff, 1977). A cut-off

score of 16 was used to identify women with clinically relevant depressive symptoms (Radloff, 1977).

We identified maternal mental and behavioral disorder diagnoses before or during pregnancy from the Finnish nationwide Care Register for Health Care (HILMO). This register carries diagnoses classified using the International Classification of Diseases 8th (ICD-8; codes 290–315) and 9th (ICD-9; codes 290–319) Revisions and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10; codes F00–F99). By using the ICD-8, ICD-9, and ICD-10 codes, we identified all primary and subsidiary diagnoses of all maternal hospital treatments since 1969 and of all outpatient treatments in public specialized medical care since 1998 until the birth of the child. The HILMO has been validated for mental and behavioral disorder diagnoses (Sund, 2012).

Mental and behavioral disorders in children. We identified mental and behavioral disorder diagnoses in children from the HILMO from birth until 31/12/2018. As an outcome, we used any mental and behavioral disorder (ICD-10 codes: F00–F99) in children. Apart from being a validated research tool (Sund, 2012), the HILMO has also been validated for certain childhood mental and behavioral disorders (Joelson et al., 2016; Lampi et al., 2010).

Covariates. Covariates derived from the nationwide Medical Birth Register (MBR; Gissler, Louhiala, & Hemminki, 1997), HILMO, and/or the Population Information System included maternal age at delivery (years), parity (primiparous/multiparous), marital status (cohabiting or married/single), cardio-metabolic pregnancy conditions (no pregnancy condition/hypertension or gestational diabetes only before current pregnancy/early pregnancy body mass index [BMI] ≥ 25 kg/m², chronic hypertension, preeclampsia, gestational hypertension or unspecified hypertension in current pregnancy [ICD-10: I10, O10–O11, O13–O16], and/or type 1 or type 2 diabetes or gestational diabetes in current pregnancy [ICD-10: E08–E14, O24]), and child's sex, birth year, gestational age (weeks), and birth weight (grams). Maternal education level (basic/secondary/tertiary) was self-reported in early pregnancy. Maternal substance use during pregnancy comprised MBR data on smoking (no smoking/quit during 1st trimester or smoked throughout pregnancy) and self-reported data on alcohol consumption (no/yes) during early pregnancy. Additionally, we included HILMO data on maternal and paternal mental and behavioral disorders (identified with ICD-8: codes 290–315; ICD-9: codes 290–319; ICD-10: codes F00–F99) diagnosed by the child's first mental and behavioral disorder or by the end of the follow-up (31/12/2018) as covariates.

Statistical analyses

Positive maternal mental health and mental and behavioral disorders in children. To investigate whether the PCA-based positive maternal mental health composite score during pregnancy (independent variable) was associated with our outcome, namely any mental and behavioral disorder in children, we used Cox proportional hazards models. The children were followed from birth until the first mental and behavioral disorder diagnosis, and were censored from the analyses at death, moving abroad, or at the end of the follow-up in 31/12/2018. The Cox models are well-suited for analyses where the length of the follow-up varies by individual, and yield hazard ratios (HR) and 95% Confidence Intervals (CI). We also show the associations of maternal positive affect, curiosity, and social support during pregnancy as separate

independent predictors of any mental and behavioral disorder in children as the outcome.

Before applying the Cox models, we tested whether the HRs changed across time by applying time-dependent Cox regression. We found only one time-dependent effect: the HR of maternal substance use on any mental and behavioral disorder in children varied across time ($p = .007$). Cox models were thus stratified for substance use.

For each analysis, we made adjustments for child's sex and birth year (Model 1) and additionally for birth weight, gestational age, maternal parity, marital status, age, education, and cardio-metabolic pregnancy conditions (Model 2).

Gestation stage-specificity of the associations. To study if the associations between positive maternal mental health and mental and behavioral disorders in children were gestation stage-specific, we used reverse temporal mixed effects models. In these models, maternal biweekly reports of positive affect/curiosity/social support were defined as outcomes, each tested in a separate model. Between-person predictor was any mental and behavioral disorder in children, within-person predictor was gestational week at the time of assessment of positive maternal mental health, and their interaction tested if the associations varied by gestational week. In these models, child's sex was included as a fixed effect and length of diagnostic follow-up for the child as both a fixed and random effect covariate.

Negative maternal mental health: independent and protective effects of positive maternal mental health on any mental and behavioral disorder in children. To investigate if the associations between maternal PCA-based positive mental health score and any mental and behavioral disorder in children were independent of maternal clinically relevant depressive symptoms during pregnancy and mental and behavioral disorders diagnosed before or during pregnancy, we ran Cox models adjusting for these negative maternal mental health variables and the covariates in model 2 (see above). We also present these associations from analyses in which we included both maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder or by 31/12/2018 as covariates.

Cox proportional hazards models were also used to investigate whether positive maternal mental health during pregnancy protected the children whose mothers experienced negative mental health before or during pregnancy from developing any mental and behavioral disorder. As independent variables in these models, we included interaction terms of 'PCA-based positive maternal mental health composite score \times maternal clinically relevant depressive symptoms' and 'PCA-based positive maternal mental health composite score \times maternal mental and behavioral disorder diagnosis before or during pregnancy', following the main effects of these variables. We then ran separate Cox models studying the association of the PCA-based positive maternal mental health composite score with any mental and behavioral disorder in children as an outcome variable in groups with and without maternal clinically relevant depressive symptoms and in groups with and without maternal mental and behavioral disorders before or during pregnancy.

All continuous measures were standardized to facilitate effect size interpretation. Because missingness on covariates was minimal ($\leq 0.3\%$ of observations; Table 1), we used complete case analyses. For paternal mental and behavioral disorders, for which missingness was substantial (46.5%; Table 1) and not-at-random, missing data was coded as a separate analytic category. We also present the complete case associations by excluding participants with missing paternal

data. Statistical analyses were conducted using IBM SPSS Statistics 26 and R4.0.3.

Results

Table 1 shows characteristics of the participants. Of the children, 10.6% were diagnosed with any mental and behavioral disorder during the follow-up. The incidence of specific mental and behavioral disorder categories are shown in Table S2 for the children and in Table S3 for the mothers. Table S4 shows that of the covariates, child's male sex and maternal lower education, single parenthood, substance use during early pregnancy, cardio-metabolic pregnancy conditions, and mental and behavioral disorders were all associated with higher hazards of mental and behavioral disorders in children.

Importantly, mothers with clinically relevant depressive symptoms and mental and behavioral disorders diagnosed before or during pregnancy scored lower across all positive mental health scales than mothers without these conditions (e.g., the standardized mean (SD) for positive mental health composite score was -1.04 (0.80) vs. 0.29 (0.85) for mothers with vs. without clinically relevant depressive symptoms during pregnancy ($t = 39.21$, $p < .001$), and -0.46 (1.07) vs. 0.04 (0.98) for mothers with and without any mental and behavioral disorder before or during pregnancy ($t = 7.79$, $p < .001$), respectively; Table S5).

Positive maternal mental health and mental and behavioral disorders in children

Higher maternal PCA-based positive mental health composite score during pregnancy was associated with a lower hazard of any mental and behavioral disorder in children (Table 2). This association was significant across the adjustment models. The associations were similar when we used positive affect (PANAS), curiosity (STAI), and social support (VAS) scores during pregnancy as independent variables (Table 2).

Gestation stage-specificity of the associations

Associations of positive affect (PANAS), curiosity (STAI), and social support (VAS) with any mental and behavioral disorder in children were not specific to gestational week (estimates < 0.01 , 95% CIs $-0.04 - 0.05$, p -values $\geq .24$ for interactions between gestational week \times any mental and behavioral disorder in children; Figure S1). Figure S1 shows the trajectories of positive affect (PANAS, Panel A), curiosity (STAI, Panel B), and social support (VAS, Panel C) across pregnancy for mothers whose children did or did not have any mental and behavioral disorder.

Negative maternal mental health: independent and protective effects of positive maternal mental health on any mental and behavioral disorder in children

The PCA-based positive maternal mental health composite score was associated with a lower hazard of any mental and behavioral disorder in children independently of negative maternal mental health, as indicated by maternal depressive symptoms during pregnancy and maternal mental and behavioral disorders before or during pregnancy (HR = 0.86, 95% CI = 0.76–0.98, $p = .02$). This association was also independent of maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder diagnosis or by 31/12/2018 (HR = 0.87, 95% CI = 0.77–0.99, $p = .03$).

When we restricted the analyses to those for whom paternal data were available ($n = 1,806$; the 1,572 participants with missing paternal data were excluded), first without adjusting for paternal mental and behavioral disorders, the direction of the association between positive maternal mental health and mental and behavioral disorders in children remained the same but the association was not significant (HR = 0.91, 95% CI = 0.75–1.11, $p = .35$). This association within this subsample was identical when further adjusted for paternal mental and behavioral disorders (HR = 0.91, 95% CI = 0.75–1.11, $p = .35$). Of note, the incidence of mental and behavioral disorders in children was significantly lower among the subsample with available paternal data (8.5% vs. 10.6% in the full analytic sample).

Figure 1 shows that the higher PCA-based positive maternal mental health composite score during pregnancy was associated with a lower hazard of any mental and behavioral disorder among children of mothers with (Panel A) but not among children of mothers without (Panel B) clinically relevant depressive symptoms during pregnancy, and both among children of mothers with (Panel C) and without (Panel D) any mental and behavioral disorder before or during pregnancy. However, the interaction effects of 'PCA-based positive maternal mental health composite score \times maternal depressive symptoms during pregnancy' (HR = 0.89, 95% CI 0.68–1.16; $p = .37$) and 'PCA-based positive maternal mental health composite score \times maternal mental and behavioral disorders before or during pregnancy' (HR = 0.80, 95% CI 0.62–1.02; $p = .07$) on any mental and behavioral disorder in children were not significant.

Discussion

In this prospective cohort study of 3,378 mother-child dyads, a PCA-based composite score of positive maternal mental health during pregnancy, comprising positive affect, curiosity, and social support, was

Table 1 Characteristics of the study participants (*n* = 3378)

	Mean (SD)/ <i>n</i> (%)
<i>Maternal characteristics</i>	
Age at childbirth, mean (SD), years	31.8 (4.7)
Education level, <i>n</i> (%)	
Primary or secondary	1348 (39.9)
Lower tertiary	872 (25.8)
Upper tertiary	1153 (34.1)
Unknown	5 (0.1)
Marital status, <i>n</i> (%)	
Single	76 (2.2)
Married or cohabiting	3293 (97.5)
Unknown	9 (0.3)
Parity, <i>n</i> (%)	
Primiparous	1379 (40.8)
Multiparous	1999 (59.2)
Substance use during pregnancy, <i>n</i> (%)	
Yes	687 (20.3)
No	2690 (79.7)
Unknown	1 (0.03)
Cardio-metabolic pregnancy conditions ^a , <i>n</i> (%)	
Yes	1432 (42.4)
No	1706 (50.5)
Only before current pregnancy	234 (6.9)
Unknown	6 (0.2)
Any mental and behavioral disorder diagnosed before or during pregnancy ^b , <i>n</i> (%)	
Yes	294 (8.7)
No	3084 (91.3)
Any mental and behavioral disorder diagnosed by the child's first mental and behavioral disorder or by 31/12/2018 ^b , <i>n</i> (%)	
Yes	529 (15.7)
No	2849 (84.3)
Depressive symptoms (CES-D) during pregnancy, mean (SD)	11.47 (6.39)
Below clinically relevant threshold (<16), <i>n</i> (%)	2649 (78.4)
Above clinically relevant threshold (≥16), <i>n</i> (%)	728 (21.6)
Unknown, <i>n</i> (%)	1 (0.03)
Positive mental health during pregnancy, mean (SD)	
Positive affect (PANAS)	30.28 (6.76)
Curiosity (STAI)	31.40 (4.87)
Social support (VAS)	44.22 (11.19)
<i>Paternal Characteristics</i>	
Any mental and behavioral disorder diagnosed by the child's first mental and behavioral disorder or by 31/12/2018 ^b , <i>n</i> (%)	
Yes	126 (3.7)
No	1680 (49.7)
Unknown	1572 (46.5)
<i>Child Characteristics</i>	
Sex, <i>n</i> (%)	
Girl	1635 (48.4)
Boy	1743 (51.6)
Birth weight, mean (SD), grams	3526.5 (517.2)
Unknown, <i>n</i> (%)	11 (0.3)
Gestational age at birth, mean (SD), weeks	39.9 (1.6)
Any mental and behavioral disorder ^c , <i>n</i> (%)	
Yes	359 (10.6)
No	3019 (89.4)

CES-D, Center for Epidemiologic Studies Depression Scale; PANAS, Positive and Negative Affect Schedule; SD, Standard deviation; STAI, Spielberger State Anxiety Inventory; VAS, Visual Analogue Scale.

^aCardio-metabolic pregnancy conditions included early pregnancy body mass index [BMI] ≥ 25 kg/m², chronic hypertension, preeclampsia, gestational hypertension or unspecified hypertension in current pregnancy [ICD-10: I1, O10–O11, O13–O16], and/or type 1, type 2, or gestational diabetes [ICD-10: E08–E14, O24].

^bAll mental and behavioral disorder diagnoses classified using the International Classification of Diseases, 8th (ICD-8; codes 290–315) and 9th (ICD-9; codes 290–319) Revisions and the International Statistical Classification of Diseases and Related Health Problems, 10th (ICD-10) Revision (codes F00–F99).

^cAll mental and behavioral disorder diagnoses classified using the International Statistical Classification of Diseases and Related Health Problems, 10th (ICD-10) Revision (codes F00–F99).

associated with a lower hazard of any mental and behavioral disorder in children followed up from birth until 8.4–12.8 years-of-age. This association was independent of negative maternal mental health before or during pregnancy. Moreover, the associations of positive affect, curiosity, and social support with any mental and behavioral disorder in children were not specific to gestational stage, presumably reflecting the high stability of these positive maternal experiences throughout pregnancy. This association was also independent of important covariates, including maternal and paternal mental and behavioral disorders diagnosed by the child's first mental and behavioral disorder diagnosis or by the end of the follow-up (31/12/2018).

To our knowledge, this study is the first to investigate associations between positive maternal mental health during pregnancy and mental and behavioral disorders in children. Hence, it adds novel information to the preliminary evidence suggesting that positive maternal mental health during pregnancy carries beneficial effects on child psychological development and on the risk of psychiatric symptoms (Braeken et al., 2017; DiPietro et al., 2006; van den Heuvel et al., 2015; Phua et al., 2017). Our study broadens this perspective to the more severe end on the continuum of psychiatric symptoms, namely, to diagnosed mental and behavioral disorders, and extends the follow-up beyond toddlerhood into childhood and early adolescence.

Table 2 Associations between positive maternal mental health during pregnancy and any mental and behavioral disorder in children

	Any mental and behavioral disorder in children (F00-F99)		
	HR	95%CI	<i>p</i> -Value
Principal component analysis-based positive mental health composite score, SD units			
Model 1	0.79	0.71, 0.87	<.001
Model 2	0.79	0.71, 0.88	<.001
Positive affect (PANAS), SD units			
Model 1	0.86	0.78, 0.96	.005
Model 2	0.85	0.77, 0.95	.003
Curiosity (STAI), SD units			
Model 1	0.77	0.70, 0.85	<.001
Model 2	0.79	0.72, 0.88	<.001
Social support (VAS), SD units			
Model 1	0.86	0.78, 0.95	.004
Model 2	0.84	0.76, 0.93	.001

CI, Confidence interval; F, International Statistical Classification of Diseases and Related Health Problems 10th (ICD-10) Revision diagnostic codes; HR, Hazard ratio; PANAS, Positive and Negative Affect Schedule; SD, Standard deviation; STAI, Spielberger State Anxiety Inventory; VAS, Visual Analogue Scale.

Model 1 is adjusted for child's sex and birth year.

Model 2 is stratified for maternal substance use and adjusted for Model 1 covariates and maternal age, marital status, education level, parity, cardio-metabolic pregnancy conditions, and child's birth weight and gestational age.

Our findings also demonstrated that the association of PCA-based positive maternal mental health composite score during pregnancy with lower hazard of any mental and behavioral disorder in children was evident among mothers who reported clinically relevant depressive symptoms during pregnancy and among mothers who had been diagnosed with a mental and behavioral disorder before or during pregnancy. Our findings thus suggest that positive maternal mental health during pregnancy may provide mental health benefits for all children, including children whose mothers experienced mental health adversities.

Extensive research has identified potential mechanisms underlying the association between prenatal maternal stress and mental and behavioral disorders in children, including, for example, epigenetic modifications and genetic variation in the regulation of hypothalamic-pituitary-adrenal axis and inflammatory system functioning (Girchenko et al., 2020; O'Donnell & Meaney, 2017; Van den Bergh et al., 2020). Whether the same mechanisms mediate the associations of positive maternal mental health during pregnancy with lower hazards of mental and behavioral disorders in children remains uninvestigated. However, since positive mental health is associated with lower physiological stress responses among pregnant women (Nierop, Wirtz, Bratsikas, Zimmermann, & Ehlert, 2008), positive maternal mental health during pregnancy may alleviate the biological effects of prenatal stress on the fetus.

Other potential mechanisms also exist. A previous study in the PREDO cohort showed that positive maternal mental health during pregnancy was associated with longer cord blood leukocyte telomere length in the newborn particularly when the mother had faced higher prenatal stress (Verner et al., 2021). As shorter telomere length has been associated with stress biology and mental and behavioral disorders (Van den Bergh et al., 2020), longer telomeres may underlie the protective effects of positive maternal mental health on child mental and behavioral disorders. Furthermore, shared genetic variation of the mother-child-dyad may partly underlie the association between positive maternal mental health and child mental health (Okbay et al., 2016). However, we partly addressed familial confounding by controlling for maternal and paternal mental and behavioral disorders, which are key risk factors for child mental and behavioral disorders (Rasic, Hajek, Alda, & Uher, 2014). Our results thus suggest that inherited confounding may not at least fully account for the associations found. However, future studies addressing these study questions would benefit from a genetically informative design (Jami, Hammerschlag, Bartels, & Middeldorp, 2021).

The association may also be mediated by behavioral factors. For example, experiencing positive emotions during pregnancy has been associated

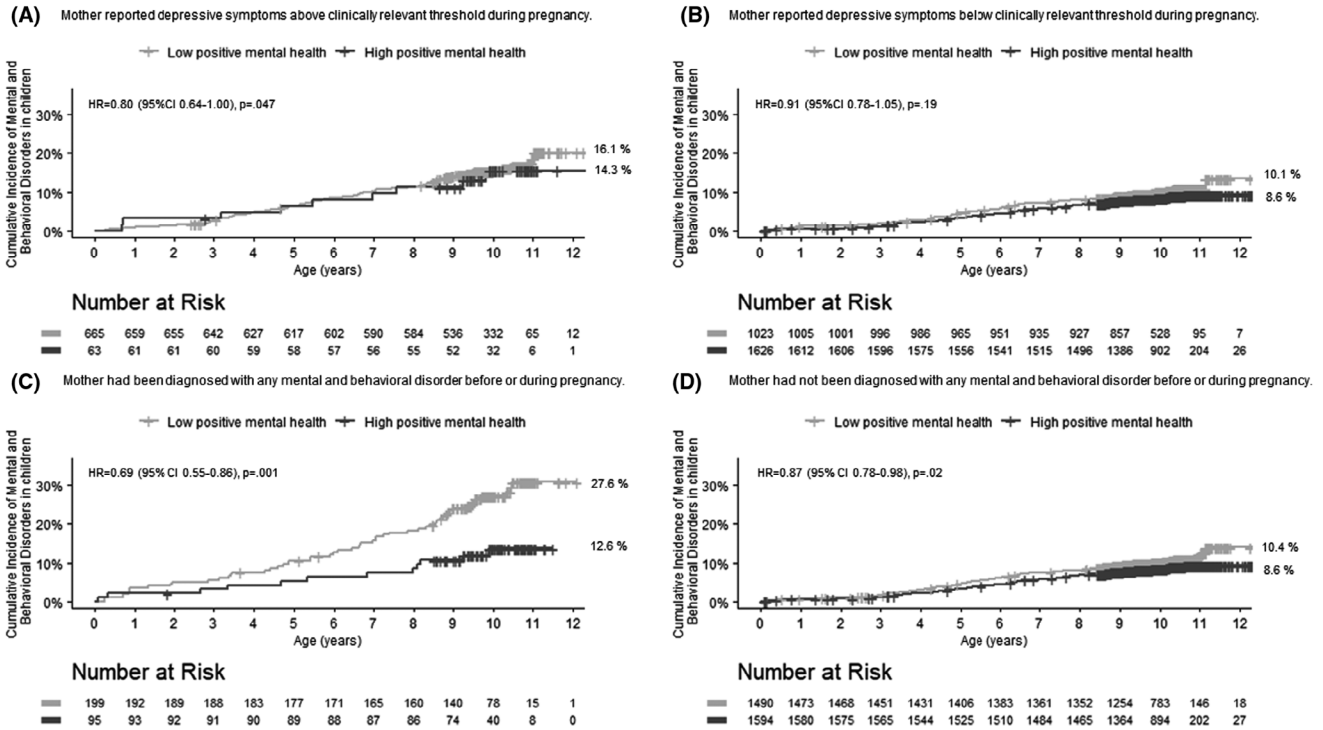


Figure 1 Cumulative incidence of mental and behavioral disorders in children whose mothers reported low (below median) and high (at or above median) levels of positive mental health in the principal component analysis-based positive mental health composite score, and depressive symptoms during pregnancy that were above (Panel A; Center for Epidemiologic Studies Depression Scale score ≥ 16) and below (Panel B; Center for Epidemiologic Studies Depression Scale score < 16) the clinically relevant threshold, and who had (Panel C) and had not been (Panel D) diagnosed with mental and behavioral disorders before or during pregnancy (the International Classification of Diseases 8th Revision codes 290–315; 9th Revision codes 290–319; and the International Statistical Classification of Diseases and Related Health Problems, 10th Revision codes F00–F99). Hazard ratios (HRs), 95% CIs, and p values present Cox proportional hazard models adjusting for child sex and birth year

with engaging in positive feeding practices postpartum (McManus, Khalessi, Lin, Ashraf, & Reich, 2017). Also, positive emotions, which show continuity across pregnancy and postpartum, and related biological oxytocin-dopamine correlates have been associated with positive parenting (Phua et al., 2020). Subsequent positive parenting may thus mediate the association between positive maternal mental health during pregnancy and positive child outcomes. In addition, positive maternal mental health during pregnancy may enhance maternal pre- and postnatal bonding to the child: while we are not aware of previous studies investigating this, one study has found that negative maternal mental health during pregnancy predicted poorer maternal bonding postpartum (Le Bas, Youssef, Macdonald, Mattick, et al., 2021). Higher maternal bonding both pre- and postnatally, in turn, predicts positive developmental outcomes in children (Le Bas et al., 2020; Le Bas, Youssef, Macdonald, Teague, et al., 2021).

Timely interventions and prevention for childhood-onset mental and behavioral disorders are urgently needed. Identification of protective factors may help in risk stratification and in developing more effective and personalized interventions targeted not merely on decreasing prenatal maternal stress, but also on increasing positive

maternal mental health. This may be particularly beneficial among mothers with prenatal stress or a history of mental and behavioral disorders. Combining current treatments with interventions targeting positive maternal mental health, such as mindfulness interventions, may prove beneficial, although evidence on their benefits among pregnant women is still mixed (Phua et al., 2020).

Strengths and limitations

Our study has several strengths, including a prospective design and a large study sample. Furthermore, we measured positive maternal mental health biweekly throughout pregnancy, using validated questionnaires, and identified physician-diagnosed mental and behavioral disorders in parents and children from a nationwide health register that has been validated for mental and behavioral disorder diagnoses (Joelsson et al., 2016; Lampi et al., 2010; Sund, 2012). Our methodology thus precludes the bias related to shared method variance inherent in many studies that use mother-reports of both her own and her child’s mental health. We also took into account maternal depressive symptoms during pregnancy and mental and behavioral disorders of both parents, thus forming a comprehensive picture of mental health of the parents.

Our study also has its limitations. First, women of the PREDO cohort who provided data on mental health during pregnancy had fewer sociodemographic and health-related risk factors for child psychiatric outcomes, and their children had a lower incidence of mental and behavioral disorders compared to non-responders. Furthermore, the cohort comprised mostly people of Northern European ancestry in a high-resource setting. These aspects may limit the generalizability of our findings to populations that differ in these characteristics. Also, since we focused on diagnosed mental and behavioral disorders, our findings do not capture subclinical psychiatric symptoms in children. Finally, missingness of data on paternal mental and behavioral disorders was nearly 50%, resulting in decreased statistical power in the complete case subsample analyses providing paternal data. An earlier study has shown that when the amount of missing data is substantial, complete case analyses may result in wider confidence intervals and biased estimates when compared with other imputation methods (Ayilara et al., 2019). Hence, while our findings are suggestive that the associations were not explained by paternal mental and behavioral disorders, further studies with larger samples of mothers, fathers and their children are warranted.

Conclusions

In our large, longitudinal study, positive maternal mental health during pregnancy was associated with lower hazards of mental and behavioral disorders in all children and in children whose mothers experienced negative mental health before or during pregnancy. Our findings suggest that positive maternal mental health during pregnancy may carry mental health benefits in children regardless of maternal mental health adversities. This highlights the need to support positive maternal mental health in prenatal intervention and prevention programs.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Differences between the participants of the analytic subsample and the non-responders of the initial cohort that were not included in the analyses.

Table S2. Number of children with mental and behavioral disorders and median age (interquartile range) at first diagnosis in the initial PREDO cohort and in the analytic sample of the current study.

Table S3. Number of mothers with mental and behavioral disorders diagnosed before or during pregnancy in the initial PREDO cohort and in the analytic sample of the current study.

Table S4. Associations between covariates and mental and behavioral disorders in children.

Table S5. Mean scores, standard deviations and group differences of PCA-based positive maternal mental health composite score and the positive affect (PANAS), curiosity (STAI) and social support (VAS) scores among the subgroups of women with depressive symptoms during pregnancy that were above or below the clinically relevant threshold, and among the subgroups of women who had and had not been diagnosed with mental and behavioral disorders before or during pregnancy.

Figure S1. Trajectories of PANAS (Panel A), STAI Curiosity (Panel B) and VAS (Panel C) across the biweekly assessment points for mothers whose children did or did not have any mental and behavioral disorder at follow-up.

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Key points

- Maternal prenatal stress increases the risk of mental and behavioral disorders in children. Whether positive maternal mental health during pregnancy protects child mental health remains unknown.
- In our prospective study, children whose mothers experienced more positive mental health during pregnancy were less likely to develop mental and behavioral disorders. This included children whose mothers experienced negative mental health before or during pregnancy.

- Our results suggest that positive maternal mental health during pregnancy is associated with mental health benefits in children and may mitigate the negative effects of maternal mental health adversities.
- Prenatal intervention programs may benefit from supporting positive maternal mental health, particularly among mothers facing mental health adversities.

References

- Ayilara, O.G., Zhang, L., Sajobi, T.T., Sawatzky, R., Bohm, E., & Lix, L.M. (2019). Impact of missing data on bias and precision when estimating change in patient-reported outcomes from a clinical registry. *Health and Quality of Life Outcomes, 17*, 106.
- Braeken, M.A.K.A., Jones, A., Otte, R.A., Nyklíček, I., & Van den Bergh, B.R.H. (2017). Potential benefits of mindfulness during pregnancy on maternal autonomic nervous system function and infant development. *Psychophysiology, 54*, 279–288.
- Crawford, J.R., & Henry, J.D. (2004). The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *British Journal of Clinical Psychology, 43*, 245–265.
- DiPietro, J.A., Novak, M.F.S.X., Costigan, K.A., Atella, L.D., & Reusing, S.P. (2006). Maternal psychological distress during pregnancy in relation to child development at age two. *Child Development, 77*, 573–587.
- Girchenko, P., Lahti, M., Tuovinen, S., Savolainen, K., Lahti, J., Binder, E.B., ... & Räikkönen, K. (2017). Cohort Profile: Prediction and prevention of preeclampsia and intrauterine growth restriction (PREDO) study. *International Journal of Epidemiology, 46*, 1380–1381.
- Girchenko, P., Lahti-Pulkkinen, M., Heinonen, K., Reynolds, R.M., Laivuori, H., Lipsanen, J., ... & Räikkönen, K. (2020). Persistently high levels of maternal antenatal inflammation are associated with and mediate the effect of prenatal environmental adversities on neurodevelopmental delay in the offspring. *Biological Psychiatry, 87*, 898–907.
- Gissler, M., Louhiala, P., & Hemminki, E. (1997). Nordic Medical Birth Registers in epidemiological research. *European Journal of Epidemiology, 13*, 169–175.
- Jami, E.S., Hammerschlag, A.R., Bartels, M., & Middeldorp, C.M. (2021). Parental characteristics and offspring mental health and related outcomes: A systematic review of genetically informative literature. *Translational Psychiatry, 11*, 197.
- Joelsson, P., Chudal, R., Gyllenberg, D., Kesti, A.K., Hinkka-Yli-Salomäki, S., Virtanen, J.P., ... & Sourander, A. (2016). Demographic characteristics and psychiatric comorbidity of children and adolescents diagnosed with ADHD in specialized healthcare. *Child Psychiatry and Human Development, 47*, 574–582.
- Kendler, K.S., Myers, J.M., Maes, H.H., & Keyes, C.L.M. (2011). The relationship between the genetic and environmental influences on common internalizing psychiatric disorders and mental Well-being. *Behavior Genetics, 41*, 641–650.
- Lampi, K., Sourander, A., Gissler, M., Niemelä, S., Rehnström, K., Pulkkinen, E., ... & Von Wendt, L. (2010). Brief report: validity of Finnish registry-based diagnoses of autism with the ADI-R. *Acta Paediatrica, 99*, 1425–1428.
- Le Bas, G.A., Youssef, G.J., Macdonald, J.A., Mattick, R., Teague, S.J., Honan, I., ... & Hutchinson, D.M. (2021). Maternal bonding, negative affect, and infant social-emotional development: A prospective cohort study. *Journal of Affective Disorders, 281*, 926–934.
- Le Bas, G.A., Youssef, G.J., Macdonald, J.A., Rossen, L., Teague, S.J., Kothe, E.J., ... & Hutchinson, D.M. (2020). The role of antenatal and postnatal maternal bonding in infant development: A systematic review and meta-analysis. *Social Development, 29*, 3–20.
- Le Bas, G., Youssef, G., Macdonald, J.A., Teague, S., Mattick, R., Honan, I., ... & Hutchinson, D. (2021). The role of antenatal and postnatal maternal bonding in infant development. *Journal of the American Academy of Child & Adolescent Psychiatry*, published online. <https://doi.org/10.1016/j.jaac.2021.08.024> Online ahead of print.
- Madigan, S., Oatley, H., Racine, N., Fearon, R.M.P., Schumacher, L., Akbari, E., ... & Tarabulsy, G.M. (2018). A meta-analysis of maternal prenatal depression and anxiety on child socioemotional development. *Journal of the American Academy of Child and Adolescent Psychiatry, 57*, 645–657.e8.
- McManus, M.A., Khalessi, A.A., Lin, J., Ashraf, J., & Reich, S.M. (2017). Positive feelings during pregnancy, early feeding practices, and infant health. *Pediatrics International, 59*, 593–599.
- Nierop, A., Wirtz, P.H., Bratsikas, A., Zimmermann, R., & Ehlert, U. (2008). Stress-buffering effects of psychosocial resources on physiological and psychological stress response in pregnant women. *Biological Psychology, 78*, 261–268.
- O'Donnell, K.J., & Meaney, M.J. (2017). Fetal origins of mental health: The developmental origins of health and disease hypothesis. *American Journal of Psychiatry, 174*, 319–328.
- Okbay, A., Baselmans, B.M.L., De Neve, J.-E., Turley, P., Nivard, M.G., Fontana, M.A., ... & Cesarini, D. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics, 48*, 624–633.
- Phua, D.Y., Kee, M.K.Z.L., Koh, D.X.P., Rifkin-Graboi, A., Daniels, M., Chen, H., ... & Meaney, M.J. (2017). Positive maternal mental health during pregnancy associated with specific forms of adaptive development in early childhood: Evidence from a longitudinal study. *Development and Psychopathology, 29*, 1573–1587.
- Phua, D.Y., Kee, M.Z.L., & Meaney, M.J. (2020). Positive maternal mental health, parenting, and child development. *Biological Psychiatry, 87*, 328–337.
- Radloff, L.S. (1977). The CES-D Scale. *Applied Psychological Measurement, 1*, 385–401.
- Rasic, D., Hajek, T., Alda, M., & Uher, R. (2014). Risk of mental illness in offspring of parents with schizophrenia, bipolar disorder, and major depressive disorder: A meta-analysis of family high-risk studies. *Schizophrenia Bulletin, 40*, 28–38.
- Robinson, R., Lahti-Pulkkinen, M., Heinonen, K., Reynolds, R.M., & Räikkönen, K. (2019). Fetal programming of neuropsychiatric disorders by maternal pregnancy depression: A systematic mini review. *Pediatric Research, 85*, 134–145.
- Ryff, C.D., Dienberg Love, G., Urry, H.L., Muller, D., Rosenkranz, M.A., Friedman, E.M., ... & Singer, B. (2006). Psychological well-being and ill-being: Do they have distinct or mirrored biological correlates? *Psychotherapy and Psychosomatics, 75*, 85–95.
- Spielberger, C.D., & Reheiser, E.C. (2009). Assessment of emotions: Anxiety, anger, depression, and curiosity. *Applied Psychology: Health and Well-Being, 1*, 271–302.
- Spielberger, C.D. (1983). *Manual for the state-trait anxiety inventory*. Palo Alto, CA: Consulting Psychological Press.
- Sund, R. (2012). Quality of the Finnish Hospital Discharge Register: A systematic review. *Scandinavian Journal of Public Health, 40*, 505–515.

- Van den Bergh, B.R.H., van den Heuvel, M.I., Lahti, M., Braeken, M., de Rooij, S.R., Entringer, S., ... & Schwab, M. (2020). Prenatal developmental origins of behavior and mental health: The influence of maternal stress in pregnancy. *Neuroscience and Biobehavioral Reviews*, *117*, 26–64.
- van den Heuvel, M.I., Johannes, M.A., Henrichs, J., & Van den Bergh, B.R.H. (2015). Maternal mindfulness during pregnancy and infant socio-emotional development and temperament: The mediating role of maternal anxiety. *Early Human Development*, *91*, 103–108.
- Verner, G., Epel, E., Lahti-Pulkkinen, M., Kajantie, E., Buss, C., Lin, J., ... & Entringer, S. (2021). Maternal psychological resilience during pregnancy and newborn telomere length: A prospective study. *American Journal of Psychiatry*, *178*, 183–192.
- Watson, D., Clark, L.A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063–1070.

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