



HHS Public Access

Author manuscript

Obesity (Silver Spring). Author manuscript; available in PMC 2018 May 01.

Published in final edited form as:

Obesity (Silver Spring). 2018 January ; 26(1): 160–166. doi:10.1002/oby.22039.

Timing of Maternal Depression and Sex-specific Child Growth, the Upstate KIDS Study

Hyojun Park, PhD,

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Rajeshwari Sundaram, PhD,

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Stephen E. Gilman, ScD,

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Department of Social and Behavioral Sciences and Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA, USA

Griffith Bell, PhD,

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Germaine M. Buck Louis, Ph.D., M.S., and

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Edwina H. Yeung, PhD

Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

Abstract

Objective—Equivocal findings have been reported between maternal depression and children’s growth possibly given limited attention to its disproportionate impact by child sex. We assessed

Users may view, print, copy, and download text and data-mine the content in such documents, for the purposes of academic research, subject always to the full Conditions of use:http://www.nature.com/authors/editorial_policies/license.html#terms

Corresponding author: Edwina H. Yeung, PhD; Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA (veungedw@mail.nih.gov; 301-435-6921; 6710B Rockledge drive, Rm 3122, MSC 7004, Rockville, MD 20817.

Disclosure: The authors declared no conflict of interest.

Author contributions: H.P. wrote the first draft of the manuscript. All authors contributed to this manuscript: conception and design (H.P., R.S., S.G., G.B., G.L., and E.Y.), acquisition of the data and analysis (H.P., R.S., G.B., and E.Y.), and interpretation of data (H.P., R.S., S.G., G.B., G.L., and E.Y.). All authors reviewed the manuscript and revised it critically and have approved the final version of the manuscript.

the relationship between the timing of maternal depression and children's growth in a population-based prospective birth cohort with particular attention to sex differences.

Methods—The Upstate KIDS Study comprised 4,394 children followed through 3 years of age from 2008 to 2010. Maternal depression was measured antenatally by linkage with hospital discharge records before delivery, and postnatally, by depressive symptoms reported from questionnaires. Child's growth was measured by sex-and-age-specific weight, height, weight-for-height, and body mass index. Adjusted linear mixed effects models were used to estimate growth outcomes for the full sample and separately by plurality and sex.

Results—Antenatal depression was associated with lower weight-for-age (−0.24 z-score units; 95% CI: −0.43, −0.05) and height-for-age (−0.26; −0.51, −0.02) among singleton boys. Postnatal depressive symptoms were associated with higher weight-for-height (0.21; 0.01, 0.42) among singleton girls.

Conclusions—Our findings suggest that antenatal depression was associated with lower weight and smaller height only for boys, while postnatal depressive symptom was associated with higher weight-for-height only for girls. Timing of depression and the mechanisms of sex-specific responses require further examination.

Keywords

Depression; Childhood Obesity; Body-Mass Index; Population Studies; Longitudinal

Introduction

Depression is common among reproductive-aged women. In the U.S., 14% – 23% of women may experience antenatal (during pregnancy) depression(1), and 12% of women experience postnatal (within a year after delivery) depression(2). In addition to the considerable impact of depression to the mother's health and social functioning(3), there is also concern that maternal depression impacts offspring development.

Antenatal depression may have adverse effects on the developing fetus through intrauterine pathways.(4) For example, antenatal depression may cause a dysregulation of the maternal hypothalamic- pituitary-adrenal (HPA) axis with corresponding elevated maternal cortisol levels, potentially affecting fetal HPA regulation and infant adiposity(5). Also antenatal depression may increase proinflammatory cytokines during pregnancy(6) which is associated with higher childhood adiposity(7). Postnatal depression has been associated with delays in children's cognitive, mental, and physical development through several mechanisms.(8) Mothers with postnatal depression are less likely to engage in earlier initiation or longer duration of breastfeeding(9) which are protective against childhood obesity(10). They are also more likely to have impaired mother-infant interactions, such as lower responsiveness to infants in needs and difficulties in providing appropriate child care. (11, 12) Parenting practices related to other child behavioral factors, such as unhealthy diet, food fussiness, low physical activity, and sedentary behaviors have been also suggested as potential pathways for the impact of postnatal depression.(13, 14)

Empirical evidence is inconclusive regarding the association between maternal depression and child growth.(8, 15) Some studies found that antenatal depression was associated with smaller child size and greater central adiposity(5), and postnatal depression was associated with higher overall adiposity(5) and increased risk of being overweight or obese at 3 years of age(16). However, other studies found no association between antenatal depression and preschooler's growth(4) or postnatal depression and child body index (BMI) z-score at the age of 3 years(17). One study documented that postnatal depression was associated with sex and age-specific child growth by which the earlier onset of BMI increases in girls exposed to postnatal maternal depressive symptoms as compared to boys.(18)

The inconsistency in evidence may be partly due to differences associated with the timing of maternal depression relative to pregnancy and possible sex-specific growth patterns in offspring of mothers with depression.(5, 16, 18) It has been proposed that fetal sex-specific placental responsiveness to maternal stress and sex hormones may result in sexually dimorphic growth responses *in utero* and *ex utero*. Male fetuses need to maintain an accelerated growth pattern, thus they are more vulnerable to adverse conditions *in utero*.(19) Female fetuses, however, maintain flexible and adaptable growth patterns in response to adverse conditions *in utero*, but may be more vulnerable to adverse conditions *ex utero*.(19) Therefore, this study investigated the relationship between the timing of maternal depression and children's growth through 3 years of age in a population-based prospective birth cohort with particular attention to sex-specific differences.

Methods

The Upstate KIDS Study is a population-based birth cohort originally designed to evaluate the impact of infertility treatment on child growth and development through age 3 years from 2008 to 2010.(20) Using birth certificates from the 57 counties in New York State (NYS) except for the 5 New York City boroughs, infants were oversampled on recorded infertility treatment and all twins and higher order infants were eligible to participate regardless of conception mode, such as spontaneous or medically assisted conception. The study cohort comprised 4,394 children including 3,440 singletons and 954 randomly selected siblings from twin pairs for whom growth was measured at least once during follow-up.

Antenatal depression was derived from the Statewide Planning and Research Cooperative System (SPARCS)(21), a statewide reporting system for discharge data to which the Upstate KIDS Study Cohort was linked to ascertain maternal depression. Maternal records were linked capturing in- or out-patient hospital care 1–3 years prior to or after delivery (i.e., 2007 – 2011).(21) Specifically, mothers were categorized as having antenatal depression if they had any linkable in- or out-patient discharge records with relevant International Code for Diseases (ICD-9-CM 296.X; 311; 300.4; 648.4X)(22) in the 3 years preceding delivery of the index birth (i.e. 'Antenatal depression : SPARCS'). Any in- or out-patient discharge records up to 3 years after delivery from SPARCS was used to define postnatal depression (i.e., 'Postnatal depression requiring hospital care: SPARCS'). The hospital records from SPARCS data include mothers with depression requiring hospital care as well as depression affecting treatment or length of stay but may not be the primary reasons for hospital care.

We additionally examined maternal depression using 2 other sources of data. Postnatal depressive symptoms were measured by the abridged Edinburgh postnatal depression scale (EPDS) administered to mothers when the infants were 4, 12, 24, and 36 months of age. The EPDS encompasses 5 items assessing emotional experiences over the past seven days.(23) Each item ranges from 0 (i.e., absence of symptoms) to 3 (i.e., maximum severity), thus total scores range from 0 to 15.(23) A longitudinal measure for severe postnatal depressive symptoms were defined as a score > 8(23) and scored at 4, 12, 24, and 36 months after delivery (i.e. ‘Severe postnatal depressive symptoms: EPDS’). Lastly, mothers reported depression during pregnancy on the NYS birth certificate, ranging from not depressed to depression requiring help. We categorized mothers with antenatal depressive symptoms as whose answer includes ‘moderately depressed’, ‘very depressed’, and ‘very depressed and had to get help’ (i.e. ‘Self-reported antenatal depressive symptoms: Birth certificate’).

Combining clinical and self-reported depression measures would be useful to address comprehensive assessment of depression status as each depression measure may capture a unique aspect that may not captured by other measures.(24) Thus we constructed a combined antenatal depression or depressive measure from self-reported depressive symptoms on birth certificates and depression records in SPARCS. Similarly, a combined postnatal depression or depressive symptoms was constructed by aggregating EPDS and SPARCS data. We additionally evaluated the combined effects of both antenatal and postnatal depression on child growth in any four measures. We reported combined depression measures, defining depression as present if either a diagnosis was present or the participant reported a high level of symptoms. In subsequent analyses, we investigated their independent associations as different methods also correspond to different time points of exposure.

Children’s growth was assessed longitudinally from mothers. Mothers completed health journals designed to capture children’s height, weight, and head circumference that were measured by health care personnel during well baby and child visits at 4, 8, 12, 18, 24, 30, and 36 months. These data were then used to calculate sex and age specific standardized weight, height, BMI and weight-for-height z-scores using the World Health Organization child growth standards.(25)

Statistical analyses

Descriptive statistics for the study population were summarized and compared by the timing of maternal depression, with significance ($p < 0.05$) formally tested using either the chi-square and Student t- tests for categorical and continuous variables, respectively. Linear mixed effects models with random intercepts for age and robust standard errors(25) were used to estimate mean differences of four growth outcomes from birth through 3 years of age between children of mothers with depression and those without. Nested infant-level random effects accounted for correlations between repeated growth measures. Models were analyzed for all study participants, and then estimated separately for singletons, singleton boys and girls, and twins. Unadjusted models assessed the relations between antenatal depression and child growth (results were not shown), and were then adjusted for *a priori* selected potential confounders from previous research(26) informed by the study’s directed acyclic graph.

These include maternal age at delivery (years, continuous), race (white, non-white), education (high school or less, some college or associate degree, bachelor's degree or higher), marital status (married or living with partner, single), infertility treatment for index birth (yes, no), health insurance (yes, no), and prepregnancy BMI (underweight/normal, overweight, or obese). Similarly, unadjusted models for the associations between longitudinal postnatal depressive symptoms and child growth (results were not shown) were followed by adjusted models of postnatal depressive symptoms on child growth. We additionally adjusted for antenatal depression(27) (yes, no), cigarette smoking during pregnancy (yes, no), alcohol usage during pregnancy (yes, no), gestational diabetes(28) (yes, no), gestational hypertension (yes, no), and breastfeeding at hospital discharge(29) (yes, no) as well as confounders listed above. All models were adjusted for the children's age at last assessment of growth. Given the Upstate KIDS Study oversampling of births conceived with infertility treatment, we applied sampling weights in all analyses.(25) Missing values for maternal depressive symptoms and covariates were imputed by generating 25 imputed datasets using the MICE algorithm and statistics were aggregated by using the standard combination rules for multiple imputation. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Sociodemographic characteristics and behavioral factors were associated with maternal depression (Table 1). As compared to mothers without any depression, those with either antenatal depression or postnatal depressive symptoms were younger, had lower educational attainment, and more likely to be unmarried, obese before pregnancy, to have smoked during pregnancy, and to lack private health insurance; they were less likely to be breastfeeding at hospital discharge or to have received infertility treatment. In addition, mothers with postnatal depressive symptoms were more likely to be non-white as compared to mothers without postnatal depressive symptoms. Children of mothers with antenatal depression were shorter than their counterparts, but similar on all other growth measures. Children of mothers reporting postnatal depressive symptoms were born earlier and weighed less than children whose mothers did not report such symptoms.

Table 2 summarizes the associations of antenatal and postnatal depression with early child growth. Regression coefficients indicate the differences of z-scores for children's growth between children whose mother had antenatal depression and those without. Antenatal depression was associated with lower weight-for-age (-0.24; -0.43, -0.05) and height-for-age (-0.26; -0.51, -0.02) among singleton boys. Postnatal depression or depressive symptoms was associated with higher weight-for-height ratios (0.21; 0.01, 0.42), but only for singleton girls. As compared to male offspring of mothers without any depression, children whose mothers had both antenatal and postnatal depression weighed less (-0.26; -0.47, -0.05) and were shorter (-0.43; -0.70, -0.16) for singleton boys and twins (-0.33; -0.65, -0.02). No association was observed for singleton girls.

Table 3 summarizes the associations between antenatal depression and children's growth through 3 years, evaluated by two severity levels, one is self-reported depressive symptoms on birth certificates and the other is depression requiring hospital care in SPARCS. Singleton

boys whose mothers had antenatal depression requiring hospital care weighed less ($b=-0.27$, 95% CI= $-0.48, -0.06$) and were shorter ($b=-0.42$, 95% CI= $-0.69, -0.14$) as compared to boys whose mothers did not have antenatal depression after adjusting for covariates. Self-reported antenatal depressive symptoms from birth certificate data were not associated with growth measures.

Table 4 captures postnatal associations. Again, associations were made stratified by source of data to provide indications of severity. In general, we found some indications that postnatal depressive symptoms were associated with increased growth among singletons but differed by severity and infant sex. For girls, depressive symptoms were associated with increased weight for height ($b=0.27$; 0.1, 0.54) and BMI (0.21; $-0.07, 0.49$; not significant). For boys, depression requiring hospitalization rather than depressive symptoms alone tended to be associated with increased weight-for-height (0.24; $-0.01, 0.49$) and BMI (0.26; $-0.03, 0.55$; not significant). Again, these associations may be driven by the persisting depressive episodes and findings were only marginally significant.

We conducted sensitivity analyses to assess missingness, including the complete case analyses for exposures and outcomes and multiple imputation, and our findings remained robust (data not shown).

Discussion

We observed no consistent associations between various maternal depression measures and children's growth through 3 years of age. Overall, maternal depression or depressive symptoms during both antenatal and postnatal was associated with decreased weight and height only for singleton boys. We also found sex-specific associations between the timing of maternal depression and children's growth among singletons. Antenatal depression or depressive symptoms was associated with decreased weight- and height-for-age among singleton boys, while postnatal depression or depressive symptoms was associated with decreased height-for-age. When examining individual measures, antenatal depression from SPARCS records was associated with decreased height for age only for singleton boys, while severe postnatal depressive symptoms from EPDS was associated with increased weight for height only for singleton girls. Exact mechanisms remain unknown, but several explanations can be suggested to better understand our findings on how depression would be associated with child growth. Antenatal depression may increase cortisol and ovarian hormone levels which are associated with a dysregulation of the maternal HPA axis.(12) These changes may reprogram fetal HPA regulation and increased infant's cortisol stress responses, and potentially resulting in infant adiposity or impaired mother-child interaction or attachment(12). As compared to mothers without depression, mothers with depression were less sensitive to children's signs of interest(32), less likely to support or be attached towards their children(33), and less likely to complete well-child visits(34).

Different responsiveness and vulnerability to maternal depression by infant sex may determine sexually dimorphic growth patterns *in utero* and *ex utero*.(19, 35) Previous studies have suggested that males may be more vulnerable to adverse conditions *in utero*, while females may be more vulnerable *ex utero*.(19, 35, 36) Relatively higher fetal and neonatal

mortality and morbidity among males than females despite their larger size could be due to different survival strategies between male and female fetuses.(35) Meanwhile, relatively higher adaptability *in utero* among female fetuses may be related to higher variabilities in growth *ex utero*, resulting in higher susceptibility and vulnerability to behavioral or environmental conditions.(36) Although mechanisms are not fully understood yet, sex-specific growth patterns *in utero* and *ex utero* may be due to the differential responses in the placenta by sex. Female placenta is known to be more responsive to maternal glucocorticoid concentration.(36) Studies also documented sex-specific differences in placental cytokine expression or insulin-like growth factor pathways, as well as fetal growth, survival, and obstetric outcomes.(35) For example, different caloric density in breast milk by infant sex demonstrates potential sexually dimorphic programming *in utero* that subsequently affect child growth *ex utero*.(37) Cheng and colleagues documented that caloric density in breast milk differ by infant sex - on average, 63–64 kcal/100mL for girls and 68–78 kcal/100ml for boys. Formula-fed girls grew faster than formula-fed boys since caloric density in formula milk (67 kcal/100ml) is greater than in breast milk for girls but similar to breast milk for boys.(37) It is also possible sex- specific growth is the result of differential child care practices varying by infant sex. Differential child care practices by infant sex among humans have not been investigated yet, but animal studies have documented that maternal child care practices may vary by infant sex.(38) However, it is unclear if the observed sex-specific maternal child care practices are embedded behaviors of mothers or a reflection of sex differences of newborns.(38)

Our study is one of few studies indicating potential sex-specific associations between the timing of maternal depression and child growth.(5, 16, 18) This study advanced the area by examining both antenatal and postnatal depression using medical records, self-reported antenatal depression status, and longitudinal assessment of postnatal depressive symptoms. Therefore, given the number of sources of data used along with the timing of depression, this remains one of the most comprehensive studies on the topic of maternal depression on growth using a population-based cohort study.

Despite notable strengths including our population-based cohort with longitudinal measurement of children's growth in relation to a set of maternal depression measures at various critical windows, our findings need to be cautiously interpreted in the context of important limitations. Our self-reported measure for antenatal depression or depressive symptoms is likely to be subject to under-reporting.(39) Hospital discharge data from SPARCS may have high specificity but low sensitivity for depression, as SPARCS data do not include subclinical depression or claims from state psychiatric centers or private psychiatric hospitals and only covered 61% of inpatient bed capacity in the NYS as of 2016. (40)

Although our measure for postnatal depressive symptoms, the abridged EPDS, was found to have good psychometric properties for research purposes in postnatal women(23) as the full EPDS, it may not be directly comparable to clinically diagnosed depression measure. Given the number of comparisons using different definitions and measures of maternal depression, we cannot rule out chance findings that resulted in only a couple of associations attaining conventional 5% levels of significance.

In conclusion, we found some evidence that maternal depression is differentially associated with children's growth depending upon its timing. Specifically, antenatal depression was associated with lower weight and smaller height among boys but not girls', while postnatal depression was associated with higher weight-for-height among girls. These findings underscore the importance of the timing of depression and children's sex for growth, although underlying mechanisms remain unknown.

Acknowledgments

All individuals listed as authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding: This study was supported by the Intramural Research Program of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD contracts #HHSN275201200005C, #HHSN267200700019C). The sponsor played no role in the study design, data collection, data analysis or interpretation, writing of the manuscript, or the decision to submit the article for publication.

References

1. Yonkers KA, Wisner KL, Stewart DE, Oberlander TF, Dell DL, Stotland N, et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. *Gen Hosp Psychiatry*. 2009; 31(5):403–13. DOI: 10.1016/j.genhosppsy.2009.04.003 [PubMed: 19703633]
2. Ko KMR, Jean Y., Tong, Van T., Morrow, Brian, Farr, Sherry L. Trends in Postpartum Depressive Symptoms - 27 States, 2004, 2008 and 2012. *Morbidity and Mortality Weekly Report*. 2017; 66(6)
3. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJ, et al. Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. *PLoS Med*. 2013; 10(11):e1001547.doi: 10.1371/journal.pmed.1001547 [PubMed: 24223526]
4. Guxens M, Tiemeier H, Jansen PW, Raat H, Hofman A, Sunyer J, et al. Parental psychological distress during pregnancy and early growth in preschool children: the generation R study. *Am J Epidemiol*. 2013; 177(6):538–47. DOI: 10.1093/aje/kws275 [PubMed: 23436897]
5. Ertel KA, Koenen KC, Rich-Edwards JW, Gillman MW. Antenatal and postpartum depressive symptoms are differentially associated with early childhood weight and adiposity. *Paediatr Perinat Epidemiol*. 2010; 24(2):179–89. DOI: 10.1111/j.1365-3016.2010.01098.x [PubMed: 20415775]
6. Christian LM, Franco A, Glaser R, Iams JD. Depressive symptoms are associated with elevated serum proinflammatory cytokines among pregnant women. *Brain Behav Immun*. 2009; 23(6):750–4. DOI: 10.1016/j.bbi.2009.02.012 [PubMed: 19258033]
7. Gaillard R, Rifas-Shiman SL, Perng W, Oken E, Gillman MW. Maternal inflammation during pregnancy and childhood adiposity. *Obesity (Silver Spring)*. 2016; 24(6):1320–7. DOI: 10.1002/oby.21484 [PubMed: 27094573]
8. Lampard AM, Franckle RL, Davison KK. Maternal depression and childhood obesity: a systematic review. *Prev Med*. 2014; 59:60–7. DOI: 10.1016/j.ypmed.2013.11.020 [PubMed: 24291685]
9. Dennis CL, McQueen K. The relationship between infant-feeding outcomes and postpartum depression: a qualitative systematic review. *Pediatrics*. 2009; 123(4):e736–51. DOI: 10.1542/peds.2008-1629 [PubMed: 19336362]
10. Yan J, Liu L, Zhu Y, Huang GW, Wang PP. The association between breastfeeding and childhood obesity: a meta-analysis. *Bmc Public Health*. 2014; 14 Artn 1267. doi: 10.1186/1471-2458-14-1267
11. Ertel KA, Rich-Edwards JW, Koenen KC. Maternal depression in the United States: nationally representative rates and risks. *J Womens Health (Larchmt)*. 2011; 20(11):1609–17. DOI: 10.1089/jwh.2010.2657 [PubMed: 21877915]
12. Brummelte S, Galea LA. Postpartum depression: Etiology, treatment and consequences for maternal care. *Horm Behav*. 2016; 77:153–66. DOI: 10.1016/j.yhbeh.2015.08.008 [PubMed: 26319224]

13. de Barse LM, Cardona Cano S, Jansen PW, Jaddoe VV, Verhulst FC, Franco OH, et al. Are parents' anxiety and depression related to child fussy eating? *Arch Dis Child*. 2016; 101(6):533–8. DOI: 10.1136/archdischild-2015-309101 [PubMed: 26916538]
14. McConley RL, Mrug S, Gilliland MJ, Lowry R, Elliott MN, Schuster MA, et al. Mediators of maternal depression and family structure on child BMI: parenting quality and risk factors for child overweight. *Obesity (Silver Spring)*. 2011; 19(2):345–52. DOI: 10.1038/oby.2010.177 [PubMed: 20798670]
15. Milgrom J, Skouteris H, Worotniuk T, Henwood A, Bruce L. The association between ante- and postnatal depressive symptoms and obesity in both mother and child: a systematic review of the literature. *Womens Health Issues*. 2012; 22(3):e319–28. DOI: 10.1016/j.whi.2011.12.001 [PubMed: 22341777]
16. Wang L, Anderson JL, Dalton WT III, Wu T, Liu X, Zheng S, et al. Maternal depressive symptoms and the risk of overweight in their children. *Matern Child Health J*. 2013; 17(5):940–8. DOI: 10.1007/s10995-012-1080-1 [PubMed: 22833333]
17. Ertel KA, Kleinman K, van Rossem L, Sagiv S, Tiemeier H, Hofman A, et al. Maternal perinatal depression is not independently associated with child body mass index in the Generation R Study: methods and missing data matter. *J Clin Epidemiol*. 2012; 65(12):1300–9. DOI: 10.1016/j.jclinepi.2012.05.013 [PubMed: 22974499]
18. Duarte CS, Shen S, Wu P, Must A. Maternal depression and child BMI: longitudinal findings from a US sample. *Pediatr Obes*. 2012; 7(2):124–33. DOI: 10.1111/i.2047-6310.2011.00012.x [PubMed: 22434752]
19. Cheong JN, Wlodek ME, Moritz KM, Cuffe JS. Programming of maternal and offspring disease: impact of growth restriction, fetal sex and transmission across generations. *J Physiol*. 2016; 594(17):4727–40. DOI: 10.1113/JP271745 [PubMed: 26970222]
20. Buck Louis GM, Hediger ML, Bell EM, Kus CA, Sundaram R, McLain AC, et al. Methodology for establishing a population-based birth cohort focusing on couple fertility and children's development, the Upstate KIDS Study. *Paediatr Perinat Epidemiol*. 2014; 28(3):191–202. DOI: 10.1111/ppe.12121 [PubMed: 24665916]
21. NYSDOH. Statewide Planning and Research Cooperative System (SPARCS): New York State Department of Health. 2016. [updated Jun 2016; cited 2016 Sept 20]. Available from: <http://www.health.ny.gov/statistics/sparcs/>
22. Laurence B, Mould-Millman NK, Nero KE Jr, Salter RO, Sagoo PK. Depression and hospital admission in older patients with head and neck cancer: analysis of a national healthcare database. *Gerodontology*. 2016; doi: 10.1111/ger.12247
23. Eberhard-Gran M, Eskild A, Samuelsen SO, Tambs K. A short matrix-version of the Edinburgh Depression Scale. *Acta Psychiatr Scand*. 2007; 116(3):195–200. DOI: 10.1111/j.1600-0447.2006.00934.x [PubMed: 17655561]
24. Uher R, Perlis RH, Placentino A, Dernovsek MZ, Henigsberg N, Mors O, et al. Self-report and clinician-rated measures of depression severity: can one replace the other? *Depress Anxiety*. 2012; 29(12):1043–9. DOI: 10.1002/da.21993 [PubMed: 22933451]
25. Yeung EH, Sundaram R, Bell EM, Druschel C, Kus C, Xie Y, et al. Infertility treatment and children's longitudinal growth between birth and 3 years of age. *Hum Reprod*. 2016; 31(7):1621–8. DOI: 10.1093/humrep/dew106 [PubMed: 27165624]
26. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. *The Lancet*. 2014; 384(9956):1800–19. DOI: 10.1016/s0140-6736(14)61277-0
27. Roomruangwong C, Kanchanatawan B, Sirivichayakul S, Maes M. Antenatal depression and hematocrit levels as predictors of postpartum depression and anxiety symptoms. *Psychiatry Res*. 2016; 238:211–7. DOI: 10.1016/j.psychres.2016.02.039 [PubMed: 27086235]
28. Hinkle SN, Buck Louis GM, Rawal S, Zhu Y, Albert PS, Zhang C. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. *Diabetologia*. 2016; doi: 10.1007/s00125-016-4086-1
29. Temples HS, Willoughby D, Holaday B, Rogers CR, Wueste D, Bridges W, et al. Breastfeeding and Growth of Children in the Peri/postnatal Epigenetic Twins Study (PETS): Theoretical

- Epigenetic Mechanisms. *J Hum Lact.* 2016; 32(3):481–8. DOI: 10.1177/0890334416637594 [PubMed: 27009979]
30. !!! INVALID CITATION !!! (8, 15).
 31. !!! INVALID CITATION !!! (5, 16, 18)
 32. Murray L, Cooper P, Fearon P. Parenting difficulties and postnatal depression: implications for primary healthcare assessment and intervention. *Community Pract.* 2014; 87(11):34–8.
 33. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: a metaanalytic review. *Clin Psychol Rev.* 2000; 20(5):561–92. [PubMed: 10860167]
 34. Minkovitz CS, Strobino D, Scharfstein D, Hou W, Miller T, Mistry KB, et al. Maternal depressive symptoms and children's receipt of health care in the first 3 years of life. *Pediatrics.* 2005; 115(2): 306–14. DOI: 10.1542/peds.2004-0341 [PubMed: 15687437]
 35. Clifton VL. Review: Sex and the human placenta: mediating differential strategies of fetal growth and survival. *Placenta.* 2010; 31(Suppl):S33–9. DOI: 10.1016/j.placenta.2009.11.010 [PubMed: 20004469]
 36. Sandman CA, Glynn LM, Davis EP. Is there a viability-vulnerability tradeoff? Sex differences in fetal programming. *J Psychosom Res.* 2013; 75(4):327–35. DOI: 10.1016/j.jpsychores.2013.07.009 [PubMed: 24119938]
 37. Cheng TS, Loy SL, Cheung YB, Chan JK, Pang WW, Godfrey KM, et al. Sexually dimorphic response to feeding mode in the growth of infants. *Am J Clin Nutr.* 2016; 103(2):398–405. DOI: 10.3945/ajcn.115.115493 [PubMed: 26718413]
 38. Nguyen N, Gesquiere L, Alberts SC, Altmann J. Sex differences in the mother-neonate relationship in wild baboons: social, experiential and hormonal correlates. *Animal Behaviour.* 2012; 83(4): 891–903. DOI: 10.1016/j.anbehav.2012.01.003
 39. Eaton WW, Neufeld K, Chen LS, Cai G. A comparison of self-report and clinical diagnostic interviews for depression: diagnostic interview schedule and schedules for clinical assessment in neuropsychiatry in the Baltimore epidemiologic catchment area follow-up. *Arch Gen Psychiatry.* 2000; 57(3):217–22. [PubMed: 10711906]
 40. Health NYSoCM. Statewide Comprehensive Plan. 2017:2016–2020.

What is already known about this subject

- Depression is common among reproductive-aged women.
- In addition to the considerable impact of depression to the mother's health and social functioning, there is also concern that maternal depression impacts offspring development.
- Empirical evidence is inconclusive regarding the association between maternal depression and child growth.

What this study adds

- Maternal depression is differentially associated with children's growth depending upon its timing.
- Antenatal depression was associated with decreased weight- and height-for-age among singleton boys, while postnatal depression or depressive symptoms was associated with decreased height- for-age.
- This study adds empirical evidence on potential sex-specific responsiveness to maternal stress which may result in sexually dimorphic growth responses *in utero* and *ex utero*.

Table 1
Descriptive characteristics of the study population by maternal depressive symptoms, the Upstate KIDS Study

	Total			Antenatal Depression ¹		Postnatal Depressive Symptoms (Ever) ²	
	No	Yes	Ever	Yes	None	None	Ever
Total	4,394 (100.0)	4,091 (100.0)	303 (100.0)	303 (100.0)	3,970 (100.0)	424 (100.0)	
Maternal characteristics							
Maternal age at delivery, years: Mean (SD)	30.8 (6.0)	30.9 (5.9)	29.7 (6.2)	29.7 (6.2)	* 31.0 (5.9)	29.1 (6.7)	*
Maternal race (White): n (%)	3,619 (82.4)	3,363 (82.2)	256 (84.5)	256 (84.5)	* 3,298 (83.1)	321 (75.7)	*
Maternal education: n (%)					*		*
High school or less	693 (15.8)	609 (14.9)	84 (27.7)	84 (27.7)	555 (14.0)	138 (32.5)	
High school - Some college	1,329 (30.2)	1,223 (29.9)	106 (35.0)	106 (35.0)	1,183 (29.8)	146 (34.4)	
Beyond some college	2,372 (54.0)	2,259 (55.2)	113 (37.3)	113 (37.3)	2,232 (56.2)	140 (33.0)	
Marital status (Married): n (%)	3,805 (86.6)	3,568 (87.2)	237 (78.2)	237 (78.2)	* 3,483 (87.7)	322 (75.9)	*
Breastfeeding at hospital discharge: n (%)	3,477 (79.1)	3,282 (80.2)	195 (64.4)	195 (64.4)	* 3,193 (80.4)	284 (67.0)	*
Pre-pregnancy BMI: n (%)					*		*
Underweight/Normal weight	2,145 (48.8)	2,023 (49.4)	122 (40.2)	122 (40.2)	1,967 (49.6)	1768 (42.0)	
Overweight	1,102 (25.1)	1,040 (25.4)	62 (20.5)	62 (20.5)	1,006 (25.3)	96 (22.6)	
Obese	1,139 (25.9)	1,020 (24.9)	119 (39.3)	119 (39.3)	991 (25.0)	148 (34.9)	
Smoking during pregnancy: n (%)	556 (12.7)	461 (11.3)	95 (31.4)	95 (31.4)	* 450 (11.3)	106 (25.0)	*
Drinking during pregnancy: n (%)	558 (12.7)	527 (12.9)	31 (10.2)	31 (10.2)	505 (12.7)	53 (12.5)	
Infertility treatment: n (%)	1,374 (31.3)	1,301 (31.8)	73 (24.1)	73 (24.1)	* 1,266 (31.9)	108 (25.5)	*
Gestational diabetes: n (%)	450 (10.2)	412 (10.1)	38 (12.5)	38 (12.5)	399 (10.1)	51 (12.0)	
Private insurance: n (%)	3,413 (77.7)	3,218 (78.7)	195 (64.4)	195 (64.4)	* 3,165 (79.7)	248 (58.5)	*
Child characteristics							
Infant sex: n (%)							
Boy	2,268 (51.6)	2,110 (51.6)	158 (52.1)	158 (52.1)	2,033 (51.2)	235 (55.4)	
Girl	2,126 (48.4)	1,981 (48.4)	145 (47.9)	145 (47.9)	1,937 (48.8)	189 (44.6)	
Birthweight, grams: Mean (SD)	3,189 (685.1)	3,191 (682.2)	3,163 (724.4)	3,163 (724.4)	3,198 (681.2)	3,109 (716.1)	*
Gestational age, weeks: Mean (SD)	38.1 (2.4)	38.1 (2.4)	38.0 (2.5)	38.0 (2.5)	38.1 (2.4)	37.8 (2.7)	*
Plurality: n (%)							
Singleton	3,440 (78.3)	3,192 (78.0)	248 (81.8)	248 (81.8)	3,107 (78.3)	333 (78.5)	

	Total	Antenatal Depression ¹		Postnatal Depressive Symptoms (Ever) ²	
		No	Yes	None	Ever
Twin	954 (21.7)	899 (22.0)	55 (18.2)	863 (21.7)	91 (21.5)
Weight-for-age, z-score: Mean (SD) ³	0.2 (1.1)	0.2 (1.1)	0.1 (1.2)	0.2 (1.1)	0.2 (1.2)
Length or Height-for-age, z-score: Mean (SD) ³	-0.2 (1.7)	-0.2 (1.7)	-0.5 (2.0) *	-0.2 (1.7)	-0.4 (2.0)
BMI-for-age, z-score: Mean (SD) ³	0.4 (1.6)	0.4 (1.6)	0.5 (2.0)	0.4 (1.6)	0.5 (1.8)
Weight-for-length/height, z-score: Mean (SD) ³	0.4 (1.6)	0.4 (1.6)	0.5 (1.9)	0.4 (1.6)	0.5 (2.0)
Months at the last assessment: Mean (SD)	20.7 (12.6)	20.9 (12.6)	17.3 (11.9) *	20.9 (12.6)	18.8 (12.3) *

Note:

¹ . Antenatal depression was derived from the SPARCS for mothers with any in- or out-patient discharge records due to depression before the date of child delivery

² . Postnatal depressive symptoms were measured by the abridged EPDS at 4, 12, 24, and 36 months after delivery using 5 items assessing emotional experiences over the past seven days. Postnatal depressive symptoms ever were used to summary purposes only in this table as they were time-variant measures.

³ . Values at the last assessment were used to calculate means and SDs. 4. Information was missing for postnatal maternal depressive symptoms (i.e. EPDS) (n=190), self-reported antenatal depressive symptoms (n=508), breastfeeding at hospital discharge (n=46), marital status (n=155), pre-pregnancy BMI (n=8), and private insurance (n=3).

Abbreviations: Body mass index (BMI); Statewide Planning and Research Cooperative System (SPARCS); Edinburgh Postnatal Depression Scale (EPDS)

* : p<0.05.

Associations between combined depressive symptoms and depression and children's growth through 3 years, the Upstate KIDS Study

Table 2

	All participants		Singletons		Singleton boys		Singleton girls		Twins	
	b	95% CI	b	95% CI	b	95% CI	b	95% CI	b	95% CI
Antenatal depression (from both SPARCS and self-reported depressive symptoms)										
Weight-for-age	-0.13	-0.27, 0.00	-0.13	-0.28, 0.01	-0.24	-0.43, -0.05	-0.02	-0.22, 0.18	-0.23	-0.58, 0.08
Height-for-age	-0.12	-0.29, 0.04	-0.12	-0.29, 0.05	-0.26	-0.51, -0.02	0.03	-0.21, 0.26	-0.30	-0.66, 0.07
Weight-for-height	-0.05	-0.21, 0.12	-0.05	-0.21, 0.12	-0.05	-0.27, 0.17	-0.04	-0.28, 0.20	-0.15	-0.47, 0.17
BMI-for-age	-0.07	-0.22, 0.09	-0.07	-0.23, 0.09	-0.12	-0.33, 0.09	-0.01	-0.24, 0.22	-0.14	-0.44, 0.16
Postnatal depression (from both SPARCS and EPDS)										
Weight-for-age	0.04	-0.06, 0.15	0.04	-0.06, 0.15	-0.02	-0.17, 0.13	0.11	-0.04, 0.27	0.00	-0.20, 0.21
Height-for-age	-0.07	-0.22, 0.09	-0.07	-0.23, 0.09	-0.16	-0.37, 0.06	0.00	-0.23, 0.23	-0.04	-0.31, 0.23
Weight-for-height	0.13	0.00, 0.26	0.13	0.00, 0.26	0.08	-0.10, 0.26	0.21	0.01, 0.42	0.07	-0.18, 0.31
BMI-for-age	0.13	0.00, 0.26	0.13	-0.01, 0.27	0.10	-0.08, 0.28	0.19	-0.02, 0.40	0.03	-0.22, 0.29
Both antenatal and postnatal depression (Self-reported depressive symptoms, SPARCS, and EPDS)										
Weight-for-age	-0.06	-0.22, 0.10	-0.06	-0.22, 0.11	-0.26	-0.47, -0.05	0.14	-0.11, 0.39	-0.33	-0.65, -0.02
Height-for-age	-0.16	-0.35, 0.03	-0.16	-0.35, 0.03	-0.43	-0.70, -0.16	0.09	-0.17, 0.36	-0.30	-0.77, 0.17
Weight-for-height	0.10	-0.10, 0.29	0.10	-0.10, 0.30	0.05	-0.22, 0.31	0.16	-0.13, 0.45	-0.26	-0.72, 0.20
BMI-for-age	0.07	-0.12, 0.26	0.07	-0.12, 0.27	-0.02	-0.27, 0.24	0.18	-0.11, 0.46	-0.23	-0.61, 0.16

Notes: 1. Regression coefficients indicate the differences of z-scores for children's growth between whose mother with postnatal depression and those without. 2. A combined antenatal measure consisted of mothers with self-reported antenatal depressive symptoms and SPARCS data. 3. A combined postnatal measure consisted of SPARCS and EPDS. 4. Adjusted antenatal models examined the crude associations between maternal depression measures and child growth after adjusting for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, pre-pregnancy BMI, pre-pregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression. 5. Adjusted postnatal models were adjusted for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, pre-pregnancy BMI, history of smoking, history of alcohol consumption, pre-pregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression. 6. In this table, we denoted depression as present if either a diagnosis was present or the participant reported a high level of symptoms.

Abbreviations: Body mass index (BMI); Edinburgh Postnatal Depression Scale (EPDS); Statewide Planning and Research Cooperative System (SPARCS)

Table 3
Associations between antenatal depression and children’s growth through 3 years, the Upstate KIDS Study

	All participants		Singletons		Singleton boys		Singleton girls		Twins	
	b	95% CI	b	95% CI	b	95% CI	b	95% CI	b	95% CI
Self-reported antenatal depressive symptoms: Birth certificate										
Weight-for-age	-0.15	-0.36, 0.06	-0.15	-0.36, 0.07	-0.16	-0.47, 0.15	-0.13	-0.43, 0.17	-0.22	-0.59, 0.15
Height-for-age	-0.05	-0.28, 0.19	-0.04	-0.28, 0.20	-0.06	-0.43, 0.31	-0.01	-0.32, 0.29	-0.05	-0.58, 0.48
Weight-for-height	-0.20	-0.44, 0.04	-0.21	-0.45, 0.04	-0.16	-0.50, 0.18	-0.25	-0.60, 0.09	-0.29	-0.71, 0.13
BMI-for-age	-0.20	-0.43, 0.04	-0.20	-0.44, 0.05	-0.19	-0.52, 0.14	-0.20	-0.54, 0.15	-0.25	-0.65, 0.14
Antenatal depression: SPARCS										
Weight-for-age	-0.09	-0.25, 0.07	-0.09	-0.26, 0.07	-0.27	-0.48, -0.06	0.07	-0.18, 0.31	-0.28	-0.63, 0.08
Height-for-age	-0.16	-0.35, 0.04	-0.16	-0.35, 0.04	-0.42	-0.69, -0.14	0.07	-0.21, 0.34	-0.35	-0.81, 0.11
Weight-for-height	0.06	-0.13, 0.25	0.06	-0.13, 0.25	0.03	-0.23, 0.28	0.09	-0.19, 0.38	-0.10	-0.56, 0.35
BMI-for-age	0.03	-0.16, 0.21	0.03	-0.16, 0.22	-0.06	-0.31, 0.19	0.11	-0.17, 0.38	-0.11	-0.52, 0.31

Notes: 1. Regression coefficients indicate the differences of z-scores for children’s growth between children whose mother had postnatal depression and children without. 2. Mothers with self-reported antenatal depressive symptoms were categorized as whose answer includes ‘moderately depressed’, ‘very depressed’, and ‘very depressed and had to get help’ from self-reported maternal depression during pregnancy on the NYS birth certificate. 3. Antenatal depression was derived from the SPARCS for mothers with any in- or out-patient discharge records due to depression before the date of child delivery. 4. Adjusted model examined the crude associations between maternal depression measures and child growth after adjusting for a priori selected confounders, such as maternal age, race, education, marital status, infertility treatment, health insurance status, pre-pregnancy BMI.

Abbreviations: Body mass index (BMI); Statewide Planning and Research Cooperative System (SPARCS)

Associations between postnatal depression and children’s growth through 3 years, the Upstate KIDS Study

Table 4

	All participants		Singletons		Singleton boys		Singleton girls		Twins	
	b	95% CI	b	95% CI	b	95% CI	b	95% CI	b	95% CI
Severe postnatal depressive symptoms: EPDS										
Weight-for-age	-0.03	-0.16, 0.10	-0.04	-0.17, 0.10	-0.08	-0.25, 0.10	0.01	-0.19, 0.21	0.01	-0.21, 0.22
Height-for-age	-0.11	-0.30, 0.08	-0.11	-0.31, 0.08	-0.03	-0.28, 0.22	-0.22	-0.53, 0.08	-0.05	-0.33, 0.24
Weight-for-height	0.06	-0.11, 0.23	0.06	-0.11, 0.23	-0.11	-0.32, 0.11	0.27	0.01, 0.54	0.04	-0.27, 0.36
BMI-for-age	0.04	-0.13, 0.20	0.04	-0.13, 0.21	-0.10	-0.30, 0.11	0.21	-0.07, 0.49	0.04	-0.27, 0.34
Postnatal depression: SPARCS										
Weight-for-age	0.08	-0.07, 0.23	0.08	-0.07, 0.24	0.05	-0.16, 0.27	0.13	-0.09, 0.34	-0.07	-0.48, 0.35
Height-for-age	-0.04	-0.25, 0.17	-0.04	-0.25, 0.17	-0.22	-0.52, 0.08	0.14	-0.14, 0.42	0.00	-0.52, 0.52
Weight-for-height	0.14	-0.04, 0.32	0.14	-0.04, 0.32	0.24	-0.01, 0.49	0.06	-0.18, 0.30	0.01	-0.46, 0.48
BMI-for-age	0.16	-0.03, 0.35	0.16	-0.03, 0.35	0.26	-0.03, 0.55	0.09	-0.15, 0.32	-0.04	-0.48, 0.39

Notes: 1. Regression coefficients indicate the differences of z-scores for children’s growth between whose mother with postnatal depression and those without. 2. Severe postnatal depressive symptoms were measured by the abridged EPDS at 4, 12, 24, and 36 months after delivery using 5 items assessing emotional experiences over the past seven days. 3. Postnatal depression was derived from the SPARCS for mothers with any in- or out-patient discharge records due to depression after the date of child delivery. 4. Adjusted model examined the crude associations between maternal depression measures and child growth after adjusting for a priori selected confounders, such as maternal age, race, education, marital status, history of smoking, history of alcohol consumption, infertility treatment, health insurance status, pre-pregnancy BMI, pre-pregnancy or gestational diabetes, gestational hypertension, breastfeeding status at hospital discharge, and antenatal depression.

Abbreviations: Body mass index (BMI); Edinburgh Postnatal Depression Scale (EPDS); Statewide Planning and Research Cooperative System (SPARCS)