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# Prepregnancy Depressive Symptoms and Preterm Birth in the Black Women's Health Study

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## Abstract

**PURPOSE—**To examine the association between prepregnancy depressive symptoms and preterm birth.

**METHODS—**The present study is a prospective investigation of prepregnancy depressive symptoms—measured by the Center for Epidemiologic Studies Depression Scale (CES-D)—and risk of preterm birth reported in the Black Women's Health Study. With data on 2,627 singleton births (175 spontaneous and 163 medically-indicated preterm births and 2,289 term births), we used generalized estimating equation models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) adjusted for potential confounders.

**RESULTS—**Relative to mothers with CES-D scores <16, the multivariable ORs of spontaneous preterm birth for mothers with CES-D scores of 16-22, 23-32, and ≥33 were 1.17 (95% CI=0.78-1.80), 1.20 (95% CI=0.69-2.10), and 2.00 (95% CI=0.94-4.25), respectively (P-trend=0.09). There was little evidence of an association between prepregnancy depressive symptoms and medically-indicated preterm birth.

**CONCLUSIONS—**Our data provide some evidence of an increased risk of spontaneous preterm birth among women with high prepregnancy depressive symptoms.

### Keywords

African Americans; depression; premature birth



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**Conflicts of Interest:** None

## Introduction

Preterm birth, which affects approximately one in eight births, is the leading cause of neonatal disability and mortality in the United States (1-[3]). The risk of preterm birth is twice as high among Blacks as among Whites (3-[5]). The disparity in preterm birth is not fully explained by established risk factors such as history of preterm birth, intrauterine infections, single marital status, and low socioeconomic status (6).

Some studies have suggested that depressive symptoms may be more prevalent among Blacks than other racial groups (7-[9]). However, others have found no increased prevalence of major depressive disorder among Blacks independent of socioeconomic position (10,[11]). The association between depressive symptoms and preterm birth has been examined in 13 studies (12-[24]). Five found positive associations with preterm birth (12-[16]) and one found a two-fold increased risk of spontaneous preterm labor that was not statistically significant (17). All previous studies except one (24) measured depressive symptoms during pregnancy. The single study that examined the relation between preconception depressive symptoms and preterm birth found no association of preterm birth with retrospectively assessed depressive symptoms (24). Only two studies (12,[13]) included more than 100 Black women with preterm births. Since Black women are more likely to give birth preterm and may have a higher prevalence of depressive symptoms, it is of interest to assess associations of depressive symptoms with preterm birth in this population group separately.

An association between depressive symptoms and spontaneous preterm birth may be due to deleterious effects of maternal stress. Black women are more likely than White women in the U.S. to be exposed to chronic and acute environmental stressors associated with discrimination and socioeconomic disadvantage (25). High concentrations of the stress-responsive hormone, cerebrospinal corticotrophin-releasing hormone (CRH), have been linked with melancholic depression in pregnant (26) and non-pregnant (27,[28]) individuals. In turn, a history of depression before pregnancy may predict higher CRH levels during pregnancy (29). Increased concentrations of placental CRH are associated with higher risk of spontaneous preterm birth (30-[32]) but it is unknown whether this association is causal (33). Thus, prepregnancy depression may influence the hypothalamic-pituitary-adrenal-placental axis during pregnancy to raise the risk of spontaneous preterm delivery. In addition, there may be as yet unknown mechanisms at work related to the presence of underlying depression that could affect risk of spontaneous or medically induced preterm birth.

Most studies to date used instruments that had limited ability to separate symptoms of depression from some of the experiences of pregnancy (e.g. fatigue, changes in sleep or appetite patterns) (12). As a result, some of the pregnant women could have been misclassified as depressed. An appreciable proportion of women with prepregnancy depression will go on to have depressive symptoms during pregnancy (34). Therefore, there is value in examining how depressive symptoms measured before pregnancy affects birth outcomes. Public health organizations such as the Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists have recommended examining women's preconception health in relation to obstetric outcomes (35,[36]). We did so in the present study by prospectively examining the association between depressive symptoms measured before pregnancy with both spontaneous and medically-indicated preterm birth among Black women in the United States.

## Methods

### Study population and data collection

The Black Women's Health Study (BWHS) is a large prospective cohort study of determinants of health and illness among Black women in the United States (37). In 1995, the study enrolled

women aged 21 to 69 years who completed health questionnaires mailed to subscribers of *Essence*, a general magazine marketed to Black women. Other enrollees were family and friends of early participants or members of selected Black professional organizations. The 59,000 participants with valid addresses have been followed through biennial questionnaires. In each of the follow-up cycles through 2003, questionnaires were completed by an average of 80% of the cohort (37-[39]). Of these participants, 8,697 reported having a singleton birth, of which 15.0% were preterm. The study was approved by the Institutional Review Board of Boston University Medical Center.

## Assessment of depressive symptoms

The Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item psychiatric instrument (40), was included in the 1999 BWHS follow-up questionnaire. The CES-D was designed to identify symptoms of depression in community settings, not to impart a diagnosis of clinical depression. The use of the CES-D in community settings has been shown to be reliable and valid (40-[42]), including among Black women (42,[43]). A confirmatory factor analysis showed that the four-factor structures of the CES-D (i.e. depressed, somatic, positive, and interpersonal) fit the BWHS data well (44).

Participants were asked to report the frequency of various emotions felt during the past week using the following four categories: “0–rarely or none of the time (less than 1 day)”, “1–some or little of the time (1-2 days)”, “2–occasionally or a moderate amount of time (3-4 days)”, “3–most or all of the time (5-7 days).” These frequencies were applied to each of the 20 items such as “I felt depressed,” “My sleep was restless,” “I thought my life had been a failure,” and “I was happy” to create scores ranging from 0 to 60. The cutoff score of ≥16 is commonly used to indicate the presence of depressive symptoms (40). In the present study, the CES-D scores were categorized into four levels (<16, 16-22, 23-32, and ≥33). A cut point of 23 was used in a community-based validation study to distinguish “probable” from “possible” cases of depression (45). A higher cut point of ≥33 was used in a study conducted among pregnant Black women in Baltimore, Maryland (12).

## Assessment of preterm birth

On each biennial questionnaire, women were asked if they had given birth to a liveborn or stillborn singleton child in the previous two years. A total of 2,682 singleton births were reported in the 2001 and 2003 questionnaires by women who were less than 45 years of age at delivery who had completed the CES-D in 1999. Mothers were asked if they had been told by the doctor that the baby was born at least three weeks early and if so, how early. Those who reported a birth at least three weeks early were further asked whether the birth was due to any of the following three reasons: labor began early for no known reason; membranes ruptured early and baby was delivered to prevent infection; or labor was induced or had a caesarian section because of a medical indication. We defined preterm birth as a birth three or more weeks early. We classified 175 preterm births as spontaneous (premature labor for no known reason or early rupture of membranes) and 163 preterm births as medically-indicated (medical induction or caesarian section), although we acknowledge that some caesarian sections may have followed preterm labor. We excluded 26 preterm births that could not be classified as spontaneous or medically-indicated because the mothers reported both reasons for the preterm birth. We also excluded 29 births of mothers who reported on the 1999 questionnaire that they were taking antidepressant medications at least three days a week because the medications may have altered their symptoms and their responses to the CES-D in 1999. Our final analytic population consisted of 2,627 births.

We validated the BWHS classification of preterm birth (born ≥3 weeks early) and the reason for this outcome (spontaneous or medically-indicated) against records in two small validation

studies. In one study, medical records confirmed the outcome for 92% of 25 women who reported a preterm birth and confirmed the stated reason for 87% of the 23 women who truly had a preterm birth (38,[39]). In the second study, preterm birth cases reported by women who delivered in Massachusetts were compared with birth certificates from the Massachusetts Department of Public Health birth registry. Preterm birth was confirmed for 21 of 23 (91%) participants overall (11 of 12 participants who reported spontaneous preterm birth and 10 of 11 who reported medically indicated preterm birth). The proportion of preterm births according to level of education in this cohort fit well with national statistics. In the BWHS, 93% of the mothers had at least 13 years of education. The proportion of preterm birth in the present data was 14.6% among women who had completed 13-15 years of education and 11.9% among women who had completed 16 years or more, compared to corresponding national data among Black women showing 14.5 and 12.8%, respectively (25).

## Covariates

Reproductive and demographic variables were selected *a priori* as potential confounders. Maternal age (≤29, 30–34, 35–39, ≥40 years) was the participant's age at the time of delivery. The following covariates were chosen to avoid adjusting for factors that may be on the causal pathway: years of completed education, ascertained in 1995 (≤12, 13–15, 16, ≥17), mother herself born preterm (no, yes), ascertained in 1997, marital status in 1999 (married or living as married, divorced/separated/widowed, single), body mass index ($kg/m^2$) in 1999 (<20, 20-24, 25-29, ≥30) (46), cigarette smoking status in 1999 (current, past, never), and parity in 1999 (nulliparous, parous). We also adjusted for histories of any thyroid condition (e.g. hypothyroidism) (no, yes), prepregnancy or gestational hypertension (no, yes), and prepregnancy or gestational diabetes (no, yes), prior to the index pregnancy. While household income may be a confounder, we did not control for it because income was assessed on the 2003 questionnaire rather than before the occurrence of the births. However, we note that adjustment for this variable resulted in little change in the effect estimates.

## Statistical analyses

Chi-square tests were used in descriptive analyses to compare CES-D score categories by maternal demographic and reproductive characteristics. Age-adjusted and multivariable generalized estimating equation (GEE) models (47) were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between prepregnancy depressive symptoms and preterm birth. Multivariable models were adjusted for covariates listed above. To maximize power, we used indicator terms to model missing covariate values. Effect estimates from this missing indicator method were compared to estimates based on the complete case approach and multiple imputation. Overall, we found that our estimates from the missing indicator method were similar to those from the other two methods of handling missing values.

GEE models were used to adjust for correlations of more than one birth from the same mother. Of 2,627 births in the analytic sample, 208 (7.9%) were second births to the same mother. The procedure was executed using SAS PROC GENMOD with the "logit link" function, an exchangeable working correlation structure, and an empirical variance estimator (47).

We conducted subgroup analyses among nulliparous women and among women with no history of hypertension, diabetes, or thyroid conditions. We conducted these sensitivity analyses to examine the possible influence of residual confounding by adverse pregnancy outcomes (e.g. previous preterm birth which could be a common cause of depression and subsequent preterm birth) or by comorbidities (hypertension, diabetes, thyroid conditions). Residual confounding from previous adverse birth outcomes would have been absent among nulliparous women, and residual confounding from maternal health conditions would have

been reduced among women free of hypertension, diabetes, and thyroid disorders. All analyses were conducted in SAS version 9.1 (48).

## Results

Among the 2,627 births, the maternal CES-D score was ≥16 for 25.9%, ≥23 for 11.0%, and ≥33 for 2.9%. The mean CES-D score was 11.4 (SD= 8.7). Mothers who were less educated, single, overweight or obese, cigarette smokers, parous, born preterm, or had lower household income were more likely to report depressive symptoms (Table 1).

For spontaneous preterm birth, the multivariable ORs for mothers with CES-D scores of 16-22, 23-32, and ≥33 relative to <16 were 1.17 (95% CI=0.78-1.80), 1.20 (95% CI=0.69-2.10), and 2.00 (95% CI=0.94-4.25), respectively (*p* trend=0.09), after controlling for risk factors for preterm birth and comorbid conditions (Model 3 in Table 2). When we collapsed the two upper CES-D categories, the OR for CES-D ≥23 relative to <16 was 1.40 (95% CI=0.88-2.24) (*p* trend=0.14).

For medically-indicated preterm birth, the multivariable ORs for mothers with CES-D scores of 16-22, 23-32, and ≥33 relative to <16 were 0.89 (95% CI=0.55-1.42), 0.94 (95% CI=0.52-1.70), and 1.41 (95% CI=0.61-3.27), respectively (*p* trend=0.85), after controlling for risk factors for preterm birth and comorbid conditions (Model 3 in Table 2). The OR for CES-D ≥23 relative to <16 was 1.05 (95% CI=0.64-1.74) (*p* trend=0.99). Given that we observed little evidence of an association with medically-indicated preterm birth, all subsequent analyses were restricted to spontaneous preterm births.

The adjusted OR for spontaneous preterm birth comparing CES-D ≥23 with <16 was stronger among the 1,506 women who had not previously given birth (OR=1.81, 95% CI=1.03-3.20; *p* trend= 0.08) (Table 3). Among women without any comorbid factors (hypertension, diabetes, or thyroid conditions), the adjusted OR was also stronger (OR=1.51, 95% CI=0.89-2.58; *p* trend= 0.19) for CES-D ≥23 relative to <16.

## Discussion

In this cohort of U.S. Black women, we found some suggestive evidence of a positive association between prepregnancy depressive symptoms and spontaneous preterm birth. Women with CES-D scores of 33 or higher had two times the odds of spontaneous preterm birth of women with CES-D scores less than 16, although the finding was not statistically significant after adjustment for maternal demographic, reproductive, and comorbid factors. The positive association persisted among nulliparous women. We found no evidence of an association between depressive symptoms and medically-indicated preterm birth after adjustment for confounders.

Given that hypertension, diabetes, and thyroid conditions have been associated with depression (49-[51]) and preterm birth (24,[52]-[56]) in the literature, there may have been some residual confounding by these factors. We found that the effect estimates were slightly larger among women who had no comorbid conditions. Likewise, the association between depressive symptoms and spontaneous preterm birth strengthened after restricting our analyses to nulliparous women. These findings suggest that uncontrolled confounding by factors associated with previous pregnancies or with comorbid chronic illnesses may have attenuated our overall results rather than produced a spurious positive association.

Thirteen previous studies have assessed the risk of preterm birth in relation to depression during pregnancy using a variety of instruments to assess depression: the CES-D (12,[13],[21],[22],[24]), Edinburgh Postnatal Depression Scale (17), Beck Inventory Depression (BDI) (15,[19]),

Structured Clinical Interview for DSM Disorders (SCID) (16), Primary Care Evaluation of Mental Disorders (PRIME-MD) (18), Abbreviated Scale for the Assessment of Psychosocial Status in Pregnancy (14,[20]), and the General Health Questionnaire (GHQ) (23). In all studies except one (17), the instruments may have had limited ability to distinguish symptoms of depression from some of the experiences of pregnancy (e.g. fatigue, changes in sleep or appetite patterns), resulting in some misclassification of pregnant women as depressed. However, studies have implemented other methods in efforts to circumvent this issue, such as increasing symptom cutoff levels (12,[22]). In the eight studies that made a distinction between spontaneous and indicated preterm births (12,[14],[17]-[21],[23]), depression during pregnancy was associated with an increased risk of spontaneous preterm birth (12), spontaneous and indicated preterm birth combined (14), and a two-fold increased risk of spontaneous preterm labor that was not statistically significant (17). In the five studies that did not assess spontaneous and medically-indicated preterm birth separately (13,[15],[16],[22],[24]), three found positive associations (13,[15],[16]). The study by Orr et al. (12), which only enrolled Black women, is most comparable to ours because the investigators assessed spontaneous preterm birth and measured depressive symptoms with the 20-item CES-D scale. Using the upper 10% of CES-D scores (cutpoint = 33) to define depressive symptoms, Orr et al. reported an adjusted odds ratio of 1.96 (95% CI: 1.04, 3.72), which is comparable to our estimate of 2.00 using the same cutpoint for high prepregnancy depressive symptoms. The only prior study of prepregnancy depression (24) assessed depressive symptoms after participants had given birth using the short-form version of the CES-D with a cutpoint of ≥10 to indicate presence of symptoms. The odds ratio for preterm birth overall in that study was 1.21 (95% CI 0.71, 2.08). Our estimate comparing CES-D score ≥16 to <16 in relation to spontaneous preterm birth was similar, 1.26 (95% CI: 0.89, 1.79).

To our knowledge, our study is the first to prospectively examine prepregnancy depressive symptomatology in relation to preterm birth. Recall bias was avoided because women were unaware of their future pregnancy outcomes at the time they completed the CES-D instrument. Although we had limited power to estimate the effect of having CES-D scores ≥33, our sample size was larger than previous studies on depression and preterm birth. We assessed spontaneous and medically-indicated preterm births separately because they may have different etiologies (6) and we controlled for several important potentially confounding variables.

A limitation of our study is that we had only one measurement of depressive symptoms, before the index pregnancy. We had no information on depressive symptoms during the pregnancy. Given the transient nature of depression, multiple measurements would have been a more robust approach to capture either lifetime depressive symptoms or psychologic state just prior to, or in the early stages of, the index pregnancy. Furthermore, the gold standard for determination of depression is clinical interview, which was not feasible in this large cohort. Misclassification of the exposure would have generally biased the effect estimates toward unity. In our study, depressive symptoms were measured in 1999, two to four years prior to the birth outcome. A study by Cohen et al (34) found that 43% of pregnant women with histories of major depression had a relapse of major depression during pregnancy.

Another limitation of our study is the self-report of gestational age which could be subject to non-differential misclassification. However, the BWHS validation results and the similarity between BWHS and national preterm birth estimates among Black women suggest that our definition of preterm birth is consistent with the usual clinical definition (<37 weeks gestation). Self-report of the type of preterm birth, spontaneous or medically indicated, would also have been subject to error. Given the available data, we were unable to assess the role of stress, personality, or coping. Finally, because the study included few women who had not graduated from high school, our results may not be generalizable to Black women with low levels of education.

Our results, although not statistically significant, indicate some suggestive evidence of a positive association between prepregnancy depressive symptoms and spontaneous preterm birth. Studies that measure depression both before conception and during pregnancy could increase our understanding of whether and how the timing of depression influences the risk of preterm birth. Moreover, studies conducted among ethnically diverse populations are needed to determine whether maternal depression contributes to the racial disparity of preterm birth in the United States.

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## References

1. Goldenberg RL. The management of preterm labor. Obstet Gynecol 2002;100:1020–37. [PubMed: 12423870]
2. Green NS, Damus K, Simpson JL, et al. Research agenda for preterm birth: recommendations from the March of Dimes. Am J Obstet Gynecol 2005;193:626–35. [PubMed: 16150253]
3. Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2003. Natl Vital Stat Rep 2005;54:1–116.
4. Blackmore CA, Savitz DA, Edwards LJ, et al. Racial differences in the patterns of preterm delivery in central North Carolina, USA. Paediatr Perinat Epidemiol 1995;9:281–95. [PubMed: 7479277]
5. Ananth CV, Misra DP, Demissie K, et al. Rates of preterm delivery among Black women and White women in the United States over two decades: an age-period-cohort analysis. Am J Epidemiol 2001;154:657–65. [PubMed: 11581100]
6. Berkowitz GS, Blackmore-Prince C, Lapinski RH, et al. Risk factors for preterm birth subtypes. Epidemiology 1998;9:279–85. [PubMed: 9583419]
7. Jones-Webb RJ, Snowden LR. Symptoms of depression among blacks and whites. Am J Public Health 1993;83:240–4. [PubMed: 8427330]
8. Gazmararian JA, James SA, Lepkowski JM. Depression in black and white women. The role of marriage and socioeconomic status. Ann Epidemiol 1995;5:455–63. [PubMed: 8680608]
9. Orr ST, Blazer DG, James SA. Racial disparities in elevated prenatal depressive symptoms among black and white women in eastern north Carolina. Ann Epidemiol 2006;16:463–8. [PubMed: 16257228]
10. Williams DR, Gonzalez HM, Neighbors H, et al. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: results from the National Survey of American Life. Arch Gen Psychiatry 2007;64:305–15. [PubMed: 17339519]
11. Breslau J, Aguilar-Gaxiola S, Kendler KS, et al. Specifying race-ethnic differences in risk for psychiatric disorder in a USA national sample. Psychol Med 2006;36:57–68. [PubMed: 16202191]
12. Orr ST, James SA, Blackmore Prince C. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. Am J Epidemiol 2002;156:797–802. [PubMed: 12396996]
13. Li D, Liu L, Odouli R. Presence of depressive symptoms during early pregnancy and the risk of preterm delivery: a prospective cohort study. Hum Reprod 2009;24:146–53. [PubMed: 18948314]
14. Neggers Y, Goldenberg R, Cliver S, et al. The relationship between psychosocial profile, health practices, and pregnancy outcomes. Acta Obstet Gynecol Scand 2006;85:277–85. [PubMed: 16553174]
15. Steer RA, Scholl TO, Hediger ML, et al. Self-reported depression and negative pregnancy outcomes. J Clin Epidemiol 1992;45:1093–9. [PubMed: 1474405]

16. Field T, Diego M, Hernandez-Reif M, et al. Depressed pregnant black women have a greater incidence of prematurity and low birthweight outcomes. Infant Behav Dev 2009;32:10–6. [PubMed: 19004502]
17. Dayan J, Creveuil C, Herlicoviez M, et al. Role of anxiety and depression in the onset of spontaneous preterm labor. Am J Epidemiol 2002;155:293–301. [PubMed: 11836191]
18. Andersson L, Sundstrom-Poromaa I, Wulff M, et al. Neonatal outcome following maternal antenatal depression and anxiety: a population-based study. Am J Epidemiol 2004;159:872–81. [PubMed: 15105180]
19. Chung TK, Lau TK, Yip AS, et al. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med 2001;63:830–4. [PubMed: 11573032]
20. Copper RL, Goldenberg RL, Das A, et al. The preterm prediction study: maternal stress is associated with spontaneous preterm birth at less than thirty-five weeks' gestation. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 1996;175:1286–92. [PubMed: 8942502]
21. Dole N, Savitz DA, Siega-Riz AM, et al. Psychosocial factors and preterm birth among African American and White women in central North Carolina. Am J Public Health 2004;94:1358–65. [PubMed: 15284044]
22. Messer LC, Dole N, Kaufman JS, et al. Pregnancy intendedness, maternal psychosocial factors and preterm birth. Matern Child Health J 2005;9:403–12. [PubMed: 16249944]
23. Perkin MR, Bland JM, Peacock JL, et al. The effect of anxiety and depression during pregnancy on obstetric complications. Br J Obstet Gynaecol 1993;100:629–34. [PubMed: 8369244]
24. Haas JS, Fuentes-Afflick E, Stewart AL, et al. Prepregnancy health status and the risk of preterm delivery. Arch Pediatr Adolesc Med 2005;159:58–63. [PubMed: 15630059]
25. Committee on Understanding Premature Birth and Assuring Healthy Outcomes, Board on Health Sciences Policy. Preterm Birth: Causes, Consequences, and Prevention. Washington, D.C.: The National Academie Press; 2007.
26. Rich-Edwards JW, Mohllajee AP, Kleinman K, et al. Elevated mid-pregnancy corticotropin-releasing hormone is associated with prenatal, but not postpartum, maternal depression. J Clin Endocrinol Metab. 2008 In press.
27. Arborelius L, Owens MJ, Plotsky PM, et al. The role of corticotropin-releasing factor in depression and anxiety disorders. J Endocrinol 1999;160:1–12. [PubMed: 9854171]
28. Kasckow JW, Baker D, Geracioti TD Jr. Corticotropin-releasing hormone in depression and post-traumatic stress disorder. Peptides 2001;22:845–51. [PubMed: 11337099]
29. Mohllajee, AP. The relation of pre-pregnancy depression with corticotropin-releasing hormone levels during pregnancy. Presented at Presented at the Society for Pediatric and Perinatal Epidemiologic Research Conference; Boston, Massachusetts. June 2007;
30. Sandman CA, Wadhwa PD, Chicz-DeMet A, et al. Maternal stress, HPA activity, and fetal/infant outcome. Ann N Y Acad Sci 1997;814:266–75. [PubMed: 9160976]
31. Holzman C, Jetton J, Siler-Khodr T, et al. Second trimester corticotropin-releasing hormone levels in relation to preterm delivery and ethnicity. Obstet Gynecol 2001;97:657–63. [PubMed: 11339911]
32. McLean M, Smith R. Corticotrophin-releasing hormone and human parturition. Reproduction 2001;121:493–501. [PubMed: 11277868]
33. Moawad AH, Goldenberg RL, Mercer B, et al. The Preterm Prediction Study: the value of serum alkaline phosphatase, alpha-fetoprotein, plasma corticotropin-releasing hormone, and other serum markers for the prediction of spontaneous preterm birth. Am J Obstet Gynecol 2002;186:990–6. [PubMed: 12015526]
34. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. Jama 2006;295:499–507. [PubMed: 16449615]
35. Johnson K, Posner SF, Biermann J, et al. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. MMWR Recomm Rep 2006;55:1–23. [PubMed: 16617292]
36. ACOG Committee Opinion number 313, September 2005. The importance of preconception care in the continuum of women's health care. Obstet Gynecol 2005;106:665–6. [PubMed: 16135611]

37. Rosenberg L, Adams-Campbell L, Palmer JR. The Black Women's Health Study: a follow-up study for causes and preventions of illness. J Am Med Womens Assoc 1995;50:56–8. [PubMed: 7722208]
38. Rosenberg L, Palmer JR, Wise LA, et al. Perceptions of racial discrimination and the risk of preterm birth. Epidemiology 2002;13:646–52. [PubMed: 12410005]
39. Rosenberg L, Wise LA, Palmer JR. Hair-relaxer use and risk of preterm birth among African-American women. Ethn Dis 2005;15:768–72. [PubMed: 16259506]
40. Radloff L. The CES-D scale: a self-reported depression scale for research in the general population. Applied Psychological Measurement 1977;1:385–401.
41. Roberts RE. Reliability of the CES-D Scale in different ethnic contexts. Psychiatry Res 1980;2:125–34. [PubMed: 6932058]
42. Callahan CM, W F. The effects of gender and race on the measurement properties of the CES-D in older adults. Medical Care 1994;1994:341–56. [PubMed: 8139299]
43. Nguyen HT, Kitner-Triolo M, Evans MK, et al. Factorial invariance of the CES-D in low socioeconomic status African Americans compared with a nationally representative sample. Psychiatry Res 2004;126:177–87. [PubMed: 15123397]
44. Williams CD, Taylor TR, Makambi K, et al. CES-D four-factor structure is confirmed, but not invariant, in a large cohort of African American women. Psychiatry Res 2007;150:173–80. [PubMed: 17291596]
45. Husaini BA, Neff JA, Harrington JB, Hughes MD, Stone RH. Depression in rural communities: validating the CES-D Scale. Journal of Community Pyschology 1980;8:20–7.
46. WHO Expert Committee. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995;854:1–452. [PubMed: 8594834]
47. Horton NJ, Lipsitz SR. Review of software to fit generalized estimating equestion (GEE) regression models. The American statistician 1999;53:160–9.
48. SAS Institute Inc. SAS/STAT User's Guide. Cary, NC: SAS Institute Inc; 2003.
49. Chapman DP, Perry GS, Strine TW. The vital link between chronic disease and depressive disorders. Prev Chronic Dis 2005;2:A14. [PubMed: 15670467]
50. Kirkegaard C, Faber J. The role of thyroid hormones in depression. Eur J Endocrinol 1998;138:1–9. [PubMed: 9461307]
51. Horwitz SM, Briggs-Gowan MJ, Storfer-Isser A, et al. Prevalence, correlates, and persistence of maternal depression. J Womens Health (Larchmt) 2007;16:678–91. [PubMed: 17627403]
52. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol 2005;105:239–45. [PubMed: 15684146]
53. Hedderson MM, Ferrara A, Sacks DA. Gestational diabetes mellitus and lesser degrees of pregnancy hyperglycemia: association with increased risk of spontaneous preterm birth. Obstet Gynecol 2003;102:850–6. [PubMed: 14551018]
54. Rosenberg TJ, Garbers S, Lipkind H, et al. Maternal obesity and diabetes as risk factors for adverse pregnancy outcomes: differences among 4 racial/ethnic groups. Am J Public Health 2005;95:1545–51. [PubMed: 16118366]
55. Ehrenthal DB, Jurkovitz C, Hoffman M, et al. A population study of the contribution of medical comorbidity to the risk of prematurity in blacks. Am J Obstet Gynecol 2007;197:409 e1–6. [PubMed: 17904981]
56. Sibai BM, Caritis SN, Hauth JC, et al. Preterm delivery in women with pregestational diabetes mellitus or chronic hypertension relative to women with uncomplicated pregnancies. The National institute of Child health and Human Development Maternal- Fetal Medicine Units Network. Am J Obstet Gynecol 2000;183:1520–4. [PubMed: 11120521]


## Acronyms

| | |
|---|---|
| CES-D | Center for Epidemiologic Studies Depression Scale |
| BWHS | The Black Women's Health Study |
| OR | Odds ratio |

| | |
|---|---|
| CI | confidence interval |

## Table 1

Distribution of maternal demographic and reproductive characteristics by CES-D score for 2,627 births, Black Women's Health Study*

| | CES-D < 16 | CES-D 16-22 | CES-D ≥ 23 | |
|---|---|---|---|---|
| **Characteristic (units)** | **N (%)** | **N (%)** | **N (%)** | **$\chi^2$ p-value** |
| No. of births | 1946 | 391 | 290 | |
| No. of mothers | 1776 | 369 | 274 | |
| Age at delivery (years) | | | | |
| 24-29 | 303 (15.6) | 90 (23.0) | 58 (20.0) | 0.003 |
| 30-34 | 902 (46.4) | 170 (43.5) | 145 (50.0) | |
| 35-39 | 609 (31.3) | 110 (28.1) | 71 (24.5) | |
| 40-44 | 132 (6.8) | 21 (5.4) | 16 (5.5) | |
| Completed education (years) | | | | |
| ≤ 12 | 89 (4.6) | 29 (7.4) | 30 (10.3) | <0.001 |
| 13-15 | 592 (30.4) | 159 (40.7) | 119 (41.0) | |
| 16 | 684 (35.2) | 113 (28.9) | 79 (27.2) | |
| ≥ 17 | 569 (29.2) | 87 (22.3) | 59 (20.3) | |
| Missing | 12 (0.6) | 3 (0.8) | 3 (1.0) | |
| Marital status | | | | |
| Married or living as married | 1388 (71.3) | 218 (55.8) | 148 (51.0) | <0.001 |
| Divorced/separated/widowed | 110 (5.7) | 35 (9.0) | 33 (11.4) | |
| Single | 423 (21.7) | 132 (33.8) | 101 (34.8) | |
| Missing | 25 (1.3) | 6 (1.5) | 8 (2.8) | |
| Body mass index (kg/m$^2$) | | | | |
| < 20 | 115 (5.9) | 16 (4.1) | 13 (4.5) | <0.001 |
| 20-24 | 732 (37.6) | 116 (29.7) | 81 (27.9) | |
| 25-29 | 604 (31.0) | 125 (32.0) | 87 (30.0) | |
| ≥ 30 | 486 (25.0) | 130 (33.3) | 106 (36.6) | |
| Missing | 9 (0.5) | 4 (1.0) | 3 (1.0) | |
| Smoking status | | | | |
| Current | 108 (5.6) | 23 (5.9) | 33 (11.4) | <0.001 |
| Past | 157 (8.1) | 48 (12.3) | 33 (11.4) | |
| Never | 1679 (86.3) | 320 (81.8) | 224 (77.2) | |
| Missing | 2 (0.1) | 0 (0.0) | 0 (0.0) | |
| Parity | | | | |
| Nulliparous | 1230 (63.2) | 231 (59.1) | 147 (50.7) | 0.001 |
| Parous | 713 (36.6) | 159 (40.7) | 143 (49.3) | |
| Missing | 3 (0.2) | 1 (0.3) | 0 (0.0) | |
| Mother herself born preterm | | | | |
| Yes | 135 (6.9) | 23 (5.9) | 37 (12.8) | 0.002 |
| No | 1210 (62.2) | 232 (59.3) | 160 (55.2) | |
| Not sure/unknown | 601 (30.9) | 136 (34.8) | 93 (32.1) | |

[*] Education was ascertained in 1995, mother herself born preterm was ascertained in 1997, and all other characteristics were measured in 1999.

**Table 2**

Odds ratios and 95% confidence intervals for spontaneous and medically-indicated preterm birth in relation to prepregnancy CES-D score*, Black Women's Health Study, 1999–2003

| | | | Model 1 † | | | Model 2 ‡ | | | Model 3 § | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Term | Preterm (%) | Odds ratio | 95% confidence interval | *p*# | Odds ratio | 95% confidence interval | *p*# | Odds ratio | 95% confidence interval | *p*# |
| Spontaneous preterm birth | | | | | | | | | | | |
| CES-D scores | (n=2289) | (n=175) | | | | | | | | | |
| < 16 | 1707 | 121 (6.6) | 1.00 | Referent | | 1.00 | Referent | | 1.00 | Referent | |
| 16-22 | 338 | 29 (7.9) | 1.16 | 0.74, 1.80 | | 1.18 | 0.77, 1.81 | | 1.17 | 0.78, 1.80 | |
| 23-32 | 184 | 16 (8.0) | 1.20 | 0.70, 2.07 | | 1.23 | 0.71, 2.15 | | 1.20 | 0.69, 2.10 | |
| ≥ 33 | 60 | 9 (13.0) | 2.17 | 1.05, 4.49 | 0.08 | 2.03 | 0.96, 4.30 | 0.08 | 2.00 | 0.94, 4.25 | 0.09 |
| CES-D score 23 | 244 | 25 (9.3) | 1.44 | 0.92, 2.28 | 0.11 | 1.43 | 0.90, 2.28 | 0.12 | 1.40 | 0.88, 2.24 | 0.14 |
| CES-D score 16 | 582 | 54 (8.5) | 1.28 | 0.91, 1.80 | | 1.28 | 0.91, 1.81 | | 1.26 | 0.89, 1.79 | |
| Medically-indicated preterm birth | | | | | | | | | | | |
| CES-D scores | (n=2289) | (n=163) | | | | | | | | | |
| < 16 | 1707 | 118 (6.5) | 1.00 | Referent | | 1.00 | Referent | | 1.00 | Referent | |
| 16-22 | 338 | 24 (6.6) | 1.02 | 0.64, 1.63 | | 0.90 | 0.57, 1.44 | | 0.89 | 0.55, 1.42 | |
| 23-32 | 184 | 14 (7.1) | 1.13 | 0.64, 2.02 | | 0.97 | 0.54, 1.75 | | 0.94 | 0.52, 1.70 | |
| ≥ 33 | 60 | 7 (10.5) | 1.72 | 0.78, 3.83 | 0.26 | 1.46 | 0.64, 3.36 | 0.74 | 1.41 | 0.61, 3.27 | 0.85 |
| CES-D score 23 | 244 | 21 (7.9) | 1.28 | 0.79, 2.07 | 0.35 | 1.09 | 0.66, 1.80 | 0.89 | 1.05 | 0.64, 1.74 | 0.99 |
| CES-D score ≥ 16 | 582 | 45 (7.2) | 1.14 | 0.80, 1.63 | | 0.98 | 0.68, 1.42 | | 0.96 | 0.66, 1.39 | |

*CES-D score category <16 is the referent category for all analyses.

†Adjusted for age at delivery.

‡Adjusted for age at delivery, marital status, education, body mass index, cigarette smoking, parity, and mother born preterm.

§Adjusted for age at delivery, marital status, education, body mass index, cigarette smoking, parity, mother born preterm, and any comorbid condition (diabetes, hypertension, or thyroid conditions).

#*p*-value for test of linear trend for CES-D score exposure with 4-categories (< 16, 16-22, 23-32, ≥ 33) and for CES-D score exposure with 3-categories (< 16, 16-22, ≥23).

**Table 3**

Adjusted* odds ratios and 95% confidence intervals for spontaneous preterm birth in relation to prepregnancy CES-D score among nulliparous women and women without selected comorbid factors, Black Women's Health Study, 1999–2003

| | CES-D < 16 | | | CES-D 16-22 | | | | CES-D ≥ 23 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Maternal characteristics** | **Term** | **Preterm** | **Odds ratio** | **Term** | **Preterm** | **Odds ratio** | **95% confidence interval** | **Term** | **Preterm** | **Odds ratio** | **95% confidence interval** | ***p* value, test for trend** |
| Nulliparous | 1072 | 82 | Referent | 200 | 15 | 0.97 | 0.54, 1.74 | 119 | 18 | 1.81 | 1.03, 3.20 | 0.08 |
| Comorbid factors | | | | | | | | | | | | |
| No hypertension | 1494 | 101 | Referent | 295 | 21 | 1.03 | 0.63, 1.68 | 199 | 20 | 1.49 | 0.88, 2.50 | 0.19 |
| No diabetes | 1640 | 116 | Referent | 323 | 26 | 1.12 | 0.71, 1.76 | 230 | 23 | 1.42 | 0.87, 2.30 | 0.16 |
| No thyroid conditions | 1703 | 121 | Referent | 337 | 29 | 1.18 | 0.77, 1.81 | 240 | 25 | 1.45 | 0.91, 2.31 | 0.11 |
| No comorbidity † | 1442 | 97 | Referent | 280 | 19 | 1.00 | 0.60, 1.68 | 188 | 19 | 1.51 | 0.89, 2.58 | 0.19 |

*Adjusted for age at delivery, marital status, education, body mass index, cigarette smoking, parity, and mother born preterm.

†Women without hypertension, diabetes, or thyroid conditions.