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Maternal Stress and Preterm Birth

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This study examined a comprehensive array of psychosocial factors, including life events, social support, depression, pregnancy-related anxiety, perceived discrimination, and neighborhood safety in relation to preterm birth (<37 weeks) in a prospective cohort study of 1,962 pregnant women in central North Carolina between 1996 and 2000, in which 12% delivered preterm. There was an increased risk of preterm birth among women with high counts of pregnancy-related anxiety (risk ratio (RR) = 2.1, 95% confidence interval (CI): 1.5, 3.0), with life events to which the respondent assigned a negative impact weight (RR = 1.8, 95% CI: 1.2, 2.7), and with a perception of racial discrimination (RR = 1.4, 95% CI: 1.0, 2.0). Different levels of social support or depression were not associated with preterm birth. Preterm birth initiated by labor or ruptured membranes was associated with pregnancy-related anxiety among women assigning a high level of negative impact weights (RR = 3.0, 95% CI: 1.7, 5.3). The association between high levels of pregnancy-related anxiety and preterm birth was reduced when restricted to women without medical comorbidities, but the association was not eliminated. The prospective collection of multiple psychosocial measures on a large population of women indicates that a subset of these factors is associated with preterm birth.

anxiety; depression; discrimination (psychology); infant, premature; pregnancy; social support; stress, psychological

Abbreviations: CI, confidence interval; RR, risk ratio.

Preterm birth continues to have a significant emotional, social, health, and economic impact on infants and families because few risk factors and preventive measures have been identified (1, 2). Although plausible biologic pathways linking stress and preterm birth exist, the role of stress in preterm birth has not been firmly established (3–14).

In studies dating to the 1960s, psychosocial measures have been examined as possible risk factors contributing to adverse birth outcomes. Although the quality of studies has improved, evidence for such associations remains equivocal. Some studies show an increased risk of preterm birth among women experiencing a greater number of life events, increased anxiety, or increased perceived stress (15–19). Most studies have not shown a main or buffering effect of social support on preterm birth (15, 20–26). A few studies examining depression and pregnancy outcome have shown an association (27, 28) while others have not (29, 30). Little attention has been given to women's perceptions of discrimination or stress from the neighborhood and preterm birth, although Collins et al. (31) found an association between unfavorable ratings of neighborhoods and low birth weight. A few well-designed studies have examined a broader profile of psychosocial factors and preterm birth and have shown that a constellation of poor psychosocial attributes increased the risk of adverse pregnancy outcome (16–18, 32).

This study measured prospectively a wide range of psychosocial domains and examined their association with

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TABLE 1. Characteristics of all Pregnancy, Infection, and Nutrition Study-eligible and -recruited women (pregnancies beginning April 1996–August 2000)

	No. eligible (n = 3,965)	% of eligible women who were recruited (n = 2,444)	% of recruited women with complete psychosocial and outcome information (n = 1,962)
Mother's race			
African American	1,604	60	73
White	2,073	64	85
Other	284	52	79
Missing	4	100	75
Mother's education			
<12 years	775	62	72
12 years	1,114	65	78
>12 years	1,730	68	86
Missing	346	19	70
Mother's age at 24 weeks' gestation			
16–19 years	572	64	75
20–29 years	2,100	62	79
≥30 years	1,290	60	84
Missing	3	0	
Marital status			
Not married	1,973	59	74
Married	1,928	65	86
Missing	64	8	40

preterm birth. A conceptual model that included external stressors, buffers and enhancers of stress, and perceived stressors guided these examinations. Interaction terms for multiple psychosocial factors were also examined. By collecting prospective information about multiple psychosocial domains, along with a variety of potential covariates, this study expands our understanding about the psychosocial-preterm birth associations relative to previous studies of more limited scope.

MATERIALS AND METHODS

The Pregnancy, Infection, and Nutrition Study, a prospective cohort study of risk factors for preterm birth, recruited women from two prenatal clinics in central North Carolina who were between 24 and 29 weeks' gestation, beginning in August 1995. Women were excluded if they did not speak English, were under age 16 years, were carrying a multiple gestation, did not plan to deliver at the study site, or lacked telephone access. Study protocols were approved by institutional review boards at the University of North Carolina and WakeMed Hospital.

At recruitment, women signed a consent form, were required to provide genital tract specimens, and were asked to provide blood and urine and to complete several questionnaires. A psychosocial instrument was added in November 1996, and these analyses include women who completed that questionnaire through November 2000. During this period, a total of 3,965 women were eligible, 2,444 (62 percent) were recruited, and 2,029 (83 percent of recruited) completed the psychosocial questionnaire. Of these women, seven were excluded because the delivery date was missing and 60 because they represented a second pregnancy in the study, resulting in 1,962 women in the analysis. Study recruitment has been described elsewhere (33).

During clinic recruitment, women were given the self-administered, mail-back psychosocial questionnaire; 93 percent completed it between gestational weeks 24 and 30. A telephone interview administered around 29 weeks' gestation was completed by 95 percent of the women who completed the psychosocial questionnaire. Demographic characteristics and pregnancy history were assessed through the interview or from medical charts. The delivery date was obtained from hospital records.

The last menstrual period and the earliest ultrasound assessment were used to date the pregnancy. If both were available and agreed within 14 days, the last menstrual period was used. Ultrasound was used when disagreement exceeded 14 days. Among women in this analysis, 82 percent had last menstrual period and ultrasound, and for 88 percent of these, the last menstrual period was used to date the pregnancy; 8 percent had last menstrual period only; and 10 percent had ultrasound only.

Preterm birth was defined as less than 37 weeks' completed gestation, and 231 women (12 percent) delivered preterm. Study obstetricians reviewed the medical charts of

TABLE 2. Characteristics of Pregnancy, Infection, and Nutrition Study women who completed a life events questionnaire (pregnancies beginning April 1996–August 2000)

	No. (n = 1,962)	%	% preterm	Risk ratio for preterm birth	95% confidence interval
Mother's race					
African American	707	36.0	12.2	1.0	0.8, 1.3
White*	1,134	57.8	11.7	(1.0)	
Other	121	6.2	9.9	0.8	0.5, 1.5
Mother's education					
<12 years	354	18.0	11.3	0.8	0.6, 1.2
12 years*	558	28.4	14.0	(1.0)	
>12 years	1,050	53.5	10.8	0.8	0.6, 1.0
Mother's age at 24 weeks' gestation					
16–19 years	274	14.0	9.1	0.8	0.5, 1.1
20–29 years*	1,036	52.8	12.0	(1.0)	
≥30 years	652	33.2	12.6	1.1	0.8, 1.4
Parity					
0*	957	49.0	9.4	(1.0)	
1	578	29.6	14.5	1.5	1.2, 2.0
≥2	417	21.4	13.4	1.4	1.0, 2.0
Missing	10				
Marital status					
Not married*	864	55.9	11.6	(1.0)	
Married	1,096	44.1	11.9	1.0	0.8, 1.3
Missing	2				
Height					
<62 inches†	199	10.4	15.6	1.3	0.9, 1.9
62–<68 inches*	1,426	74.7	11.8	(1.0)	
≥68 inches	283	14.8	9.9	0.8	0.6, 1.2
Missing	54				

Table continues

215 women whose deliveries were preterm to assess clinical presentation, yielding 117 preterm births from spontaneous labor or ruptured membranes and 98 that were medically indicated; two charts were not located for assessment; and 14 preterm births were at other hospitals and, although the delivery date was known, charts were not accessible.

The psychosocial questionnaire included several standardized instruments plus questions used in other studies of health outcomes. Scales were categorized as measuring external stress, a buffer of stress, an enhancer of stress, or perceived stress. The Life Experiences Survey (34) was modified by combining items that distinguished husband and boyfriend and by dropping items about getting pregnant. Women were asked if they had experienced 39 life events since the start of pregnancy, and they could report two more events of their choice. If the event occurred, they were asked to weight their perception of its impact on their lives, from extremely negative (–3) to extremely positive (+3). The count of events was used to assess external stressors, while impact ratings were used to assess perception of stress.

A social support scale (35) assessed support as a buffer of stress. Measures of enhancers of stress included depression (36) and six questions about pregnancy-related anxiety taken from a prenatal inventory (37). The weighted impact of pregnancy-related anxiety items was assessed using the same approach as described for life events.

Perceptions of stress included the following: a sum of the absolute values of the woman's perception of the impact of the life events, a sum of the impact of the life events perceived as negative, a sum of the absolute value of the pregnancy-related anxiety impacts, a sum of the pregnancy-related anxiety impacts perceived as negative, the perception of racial or gender discrimination (38, 39), and perceptions of neighborhood safety (40).

When fewer than 10 percent of each set of scale items were missing, the mean value of the nonmissing items was imputed for the missing item. For all constructed scales, over 90 percent of the observations had zero or only one item missing.

Univariate distributions of each scale were examined along with a review of the literature to determine appropriate

TABLE 2. Continued

	No. (n = 1,962)	%	% preterm	Risk ratio for preterm birth	95% confidence interval
Prepregnancy body mass index					
Underweight (<19.8)	300	16.0	10.3	0.9	0.6, 1.4
Normal weight (19.8–26.0)*	936	50.0	11.1	(1.0)	
Overweight (>26.0–29.0)	200	10.7	11.5	1.0	0.7, 1.6
Obese (>29.0)	435	23.3	14.2	1.3	1.0, 1.7
Missing	91				
% of poverty index					
<100% of poverty	449	25.6	13.8	1.2	0.9, 1.6
100%–<200% of poverty	458	26.1	10.5	0.9	0.7, 1.3
≥200% of poverty*	846	48.3	11.5	(1.0)	
Missing	209				
Bacterial vaginosis infection					
No infection*	1,649	87.8	11.6	(1.0)	
Infection detected	230	12.2	12.2	1.0	0.7, 1.5
Missing	83				
Alcohol use during pregnancy					
<5 drinks/week*	1,839	99.2	11.5	(1.0)	
≥5 drinks/week	15	0.8	13.3	1.2	0.3, 4.2
Missing	108				
Smoked during months 1–6 of pregnancy					
None*	1,419	77.3	10.9	(1.0)	
1–9 cigarettes/day	244	13.3	13.9	1.3	0.9, 1.8
10–19 cigarettes/day	121	6.6	15.7	1.4	0.9, 2.2
≥20 cigarettes/day	51	2.8	13.7	1.3	0.6, 2.5
Missing	127				

* Referent.
† One inch = 2.54 cm.

categorizations, resulting in the use of quartiles and tertiles, depending on the scale. Because symptoms of depression and pregnancy may overlap (27), higher cutpoints than are customary in a nonpregnant population were used for the depression scale, with a score of ≥25 for the highest category and of 17 through <25 for the middle category.

Covariates were considered on findings in other studies of risks for preterm birth (1, 41, 42). A percent-of-poverty index was constructed using 1996 cutpoints for living in poverty in the United States (known as 100 percent of the poverty level) (43). Bacterial vaginosis was assessed using the method of Nugent et al. (44). Alcohol use (≥5 drinks per week at any time during pregnancy) and smoking during months 1–6 of pregnancy were assessed. Because these health behaviors may be in a causal pathway between stress and adverse pregnancy outcomes, they were examined separately as covariates.

Crude risk ratios and 95 percent confidence intervals were generated for individual psychosocial domains and their associations with preterm birth. Confounding by covariates for each psychosocial-preterm association was assessed, and if the association changed by 10 percent when the confounder was included, it was kept in adjusted models (45). Adjusted risk ratios were generated with log-linear modeling using the SAS GENMOD procedure (46).

We explored whether women with more than one adverse psychosocial factor were at increased risk of preterm birth by including two psychosocial measures in the model and then interaction terms. A maximum likelihood ratio test was performed to determine whether the interaction term improved the fit of the model.

Because pregnancy-related anxiety may reflect medical problems with the pregnancy, two composite dichotomous variables were constructed for 1) self-report of bleeding or being put on bed rest during the pregnancy and 2) history of preterm birth, stillbirth, or miscarriage. Women were stratified into those experiencing any versus none of each of these medical problems, and the association between pregnancy-related anxiety and preterm birth was examined in each stratum.

TABLE 3. Crude and adjusted risk ratios for psychosocial factors and preterm birth (*n* = 1,962), Pregnancy, Infection, and Nutrition Study, April 1996–August 2000

	No. of term births (*n* = 1,731)	No. of preterm births (*n* = 231)	Crude		Confounder adjustment	
			RR*	95% CI*	RR	95% CI
External stressors						
Life events, sum of total count†						
Low stress‡	430	51	(1.0)		(1.0)	
Medium-low stress	454	68	1.2	0.9, 1.7	1.2	0.9, 1.7
Medium-high stress	387	61	1.3	0.9, 1.8	1.3	0.9, 1.8
High stress	444	48	0.9	0.6, 1.3	0.9	0.6, 1.3
Buffer of stress						
Social support, sum of scale§						
High support‡	421	67	(1.0)		(1.0)	
Medium-high support	453	56	0.8	0.6, 1.1	0.8	0.5, 1.1
Medium-low support	419	47	0.7	0.5, 1.0	0.7	0.5, 1.0
Low support	429	61	0.9	0.7, 1.3	0.9	0.6, 1.3
Enhancers of stress						
Depression†						
Low count‡	995	128	(1.0)		(1.0)	
Medium count	320	42	1.0	0.7, 1.4	1.0	0.7, 1.4
High count	404	60	1.2	0.9, 1.5	1.2	0.9, 1.5
Pregnancy-related anxiety, sum of total count¶						
Low anxiety‡	616	54	(1.0)		(1.0)	
Medium anxiety	783	110	1.5	1.1, 2.1	1.5	1.1, 2.1
High anxiety	304	63	2.1	1.5, 3.0	2.1	1.5, 3.0
Perceived stressors						
Life events, sum of total impact†,#						
Low stress‡	444	50	(1.0)		(1.0)	
Medium-low stress	404	57	1.2	0.9, 1.7	1.2	0.8, 1.7
Medium-high stress	420	59	1.2	0.9, 1.7	1.2	0.8, 1.7
High stress	438	60	1.2	0.8, 1.7	1.2	0.8, 1.7

Table continues

RESULTS

Table 1 shows the characteristics of the women eligible for the Pregnancy, Infection, and Nutrition Study with pregnancies beginning April 1996–August 2000, women who were successfully recruited, and women who completed the psychosocial questionnaire. Women who were White, more educated, and married were more likely to be recruited and to complete the questionnaire. As maternal age increased, a somewhat higher percentage completed the questionnaire.

Descriptive characteristics and unadjusted risk ratios and 95 percent confidence intervals for preterm birth are presented (table 2). The study population included a large representation of African-American women, about half the subjects were nulliparous, more than half were not currently married, and there was a large representation of low income households. A slight increased risk for preterm birth occurred among women who were parous, short in stature, obese, or smokers.

Correlations between psychosocial factors were examined to see if constructs were measuring similar domains. Independent scales were not highly correlated, with Pearson's correlation coefficients ranging from 0.06 to 0.52. Table 3 presents crude and adjusted risk ratios with 95 percent confidence intervals for individual psychosocial factors and preterm birth. The total counts of life events, social support, and depression were not associated with preterm birth. Women with medium and high counts of pregnancy-related anxiety items showed an increased risk of preterm birth (risk ratio (RR) = 1.5, 95 percent confidence interval (CI): 1.1, 2.1, and RR = 2.1, 95 percent CI: 1.5, 3.0, respectively).

Among perceived stressors, the impact of all life events that occurred during pregnancy—those perceived as positive and those perceived as negative—resulted in no increased risk of preterm birth among the women in the higher stress categories. Women in the highest negative life events impact quartile had the highest risk (RR = 1.8, 95 percent CI: 1.2,

TABLE 3. Continued

	No. of term births (n = 1,731)	No. of preterm births (n = 231)	Crude		Confounder adjustment	
			RR	95% CI	RR	95% CI
Life events, sum of negative impact**						
Low stress‡	416	39	(1.0)		(1.0)	
Medium-low stress	427	58	1.4	0.9, 2.1	1.5	1.0, 2.2
Medium-high stress	461	58	1.3	0.9, 1.9	1.4	0.9, 2.1
High stress	402	71	1.8	1.2, 2.5	1.8	1.2, 2.7
Pregnancy-related anxiety, sum of total impact†,#						
Low anxiety‡	553	51	(1.0)		(1.0)	
Medium anxiety	579	70	1.3	0.9, 1.8	1.3	0.9, 1.8
High anxiety	453	92	2.0	1.4, 2.8	2.0	1.4, 2.8
Pregnancy-related anxiety, sum of negative impact†						
Low anxiety‡	443	39	(1.0)		(1.0)	
Medium anxiety	640	78	1.3	0.9, 1.9	1.4	0.9, 2.0
High anxiety	502	96	2.0	1.4, 2.8	2.0	1.4, 2.9
Perceived racial discrimination††						
No racial discrimination‡	1,206	152	(1.0)		(1.0)	
Some racial discrimination	258	27	0.8	0.6, 1.2	0.9	0.6, 1.4
Higher racial discrimination	243	46	1.4	1.0, 1.9	1.4	1.0, 2.0
Perceived gender discrimination†						
No gender discrimination‡	1,097	141	(1.0)		(1.0)	
Some gender discrimination	381	46	0.9	0.7, 1.3	0.9	0.7, 1.3
High gender discrimination	235	39	1.2	0.9, 1.7	1.2	0.9, 1.7
Perceived neighborhood safety†						
Safe neighborhood‡	653	83	(1.0)		(1.0)	
Medium safe neighborhood	356	44	1.0	0.7, 1.4	1.0	0.7, 1.4
Unsafe neighborhood	286	45	1.2	0.9, 1.7	1.2	0.9, 1.7

* RR, risk ratio; CI, confidence interval.
† Variables found to be confounders for the model: none.
‡ Referent.
§ Variables found to be confounders for the model: body mass index, poverty index.
¶ Variables found to be confounders for the model: bacterial vaginosis.
# Sum of absolute value.
** Variables found to be confounders for the model: poverty index.
†† Variables found to be confounders for the model: parity, poverty index.

2.7); however, the middle categories did not show increasing risk with increasing measures of stress.

The highest measures of the impact of pregnancy-related anxiety, both total and negative, were associated with a twofold increased risk of preterm birth. A high score on the racial discrimination scale was associated with an increased risk of preterm birth (RR = 1.4, 95 percent CI: 1.0, 2.0). Women with the highest scores for gender discrimination and perception of living in an unsafe neighborhood showed a slight, imprecise increased risk of preterm birth.

In summary, a few of the models examining the main effects of psychosocial factors on preterm birth had adjusted risk ratios of 1.8 or higher. The addition of alcohol or tobacco use to the models did not alter the association between psychosocial factors and preterm birth.

Table 4 shows that women with higher pregnancy-related anxiety impacts were at higher risk of spontaneous preterm births than of medically indicated preterm births (RR = 2.5 vs. 1.8 for total impact and RR = 3.0 vs. 1.7 for negative impact). Medically indicated preterm births had higher risk ratios for the two intermediate levels of life events with negative impacts than did spontaneous preterm birth. Other psychosocial domains showed little difference in risk for spontaneous versus medically indicated preterm births.

To examine combinations of psychosocial measures and preterm birth, we developed 11 models with two psychosocial factors in each. Based on a maximum likelihood test, none of the models with interaction terms was an improvement over models in which the two psychosocial measures were included without an interaction term (p value for χ^2 ranged from 0.2 to 0.9). In most models, the adjusted risk

TABLE 4. Adjusted risk ratios stratified by spontaneous and medically indicated preterm births for psychosocial factors and preterm birth, Pregnancy, Infection, and Nutrition Study, April 1996–August 2000*

	Spontaneous preterm births		Medically indicated preterm births	
	RR†	95% CI†	RR	95% CI
External stressors				
Life events, sum of total count				
Low stress‡	(1.0)		(1.0)	
Medium-low stress	1.2	0.7, 2.0	1.3	0.8, 2.3
Medium-high stress	1.3	0.8, 2.2	1.4	0.7, 2.4
High stress	1.0	0.6, 1.7	0.9	0.5, 1.6
Buffer of stress				
Social support, sum of scale				
High support‡	(1.0)		(1.0)	
Medium-high support	0.8	0.5, 1.4	0.6	0.3, 1.1
Medium-low support	0.6	0.3, 1.0	0.7	0.4, 1.2
Low support	1.0	0.6, 1.6	0.8	0.4, 1.4
Enhancers of stress				
Depression				
Low count‡	(1.0)		(1.0)	
Medium count	1.3	0.8, 2.0	0.7	0.4, 1.3
High count	1.2	0.8, 1.9	1.0	0.6, 1.6
Pregnancy-related anxiety, sum of total count				
Low anxiety‡	(1.0)		(1.0)	
Medium anxiety	1.8	1.1, 2.8	1.5	0.9, 2.5
High anxiety	2.6	1.5, 4.3	2.1	1.2, 3.7
Perceived stressors				
Life events, sum of total impact§				
Low stress‡	(1.0)		(1.0)	
Medium-low stress	1.5	0.9, 2.6	1.1	0.6, 1.9
Medium-high stress	1.5	0.9, 2.5	1.0	0.6, 1.7
High stress	1.6	0.9, 2.7	0.9	0.5, 1.6

Table continues

ratios were consistent with the main effects models except in the model containing the count of life events and the count of pregnancy-related anxiety levels, in which the risk ratio for the high anxiety group increased from 2.1 to 2.6 (95 percent CI: 1.7, 4.0). The model containing social support and the impact of negative life events also yielded a higher risk ratio for the highest negative impact group with an increase from 1.8 to 2.3 (95 percent CI: 1.4, 3.7).

In assessing confounding of anxiety by medical problems or adverse reproductive history, we found that women who either reported bleeding/bed rest or had any adverse reproductive history had higher risk ratios for preterm birth (ranging from 2.0 to 2.4 in high-anxiety women) than women who did not (ranging from 1.3 to 1.7 for the high-anxiety group). Although the measure of association decreased in the absence of medical comorbidities, women not experiencing these problems were still at increased risk of preterm birth if they reported high levels of pregnancy-related anxiety, though residual confounding may still be present.

DISCUSSION

The literature on psychosocial factors and birth outcomes has included a predominance of studies addressing life events and various birth outcomes, often with life event measures limited to counts. Only a few studies measured perception of stress by collecting the woman's assessment of the direction or magnitude of impact of the events (16, 47). In most studies that reported an increased risk of preterm birth among women with more life events during pregnancy, the association was modest (48, 49) and our findings are consistent with these studies, with stronger associations found among women who reported higher negative impacts from events.

TABLE 4. Continued

	Spontaneous preterm births		Medically indicated preterm births	
	RR	95% CI	RR	95% CI
Life events, sum of negative impact				
Low stress‡	(1.0)		(1.0)	
Medium-low stress	1.0	0.5, 1.8	2.9	1.5, 5.6
Medium-high stress	1.1	0.6, 2.0	2.0	1.0, 4.2
High stress	2.0	1.1, 3.4	2.0	0.9, 4.1
Pregnancy-related anxiety, sum of total impact§				
Low anxiety‡	(1.0)		(1.0)	
Medium anxiety	1.2	0.7, 2.0	1.5	0.9, 2.5
High anxiety	2.5	1.6, 3.9	1.8	1.0, 3.0
Pregnancy-related anxiety, sum of negative impact				
Low anxiety‡	(1.0)		(1.0)	
Medium anxiety	1.8	1.0, 3.2	1.2	0.7, 2.1
High anxiety	3.0	1.7, 5.3	1.7	1.0, 2.9
Perceived racial discrimination				
No racial discrimination‡	(1.0)		(1.0)	
Some racial discrimination	1.0	0.6, 1.7	0.7	0.4, 1.5
Higher racial discrimination	1.4	0.9, 2.3	1.5	0.9, 2.6
Perceived gender discrimination				
No gender discrimination‡	(1.0)		(1.0)	
Some gender discrimination	1.1	0.7, 1.7	0.8	0.5, 1.3
High gender discrimination	1.3	0.8, 2.2	1.1	0.6, 1.9
Perceived neighborhood safety				
Safe neighborhood‡	(1.0)		(1.0)	
Medium safe neighborhood	1.2	0.7, 2.0	0.7	0.4, 1.2
Unsafe neighborhood	1.4	0.8, 2.3	1.0	0.6, 1.7

* A total of 117 spontaneous preterm births, 98 medically indicated preterm births, and 1,731 term births (referent); 16 preterm births could not be classified because they did not occur at study hospitals.
† RR, risk ratio; CI, confidence interval.
‡ Referent.
§ Sum of absolute value.

Our finding that social support did not decrease the risk of preterm birth was consistent with findings from some studies (21, 50). The lack of association for depression is also consistent with other research (18, 29).

Anxiety during pregnancy and its association with adverse birth outcomes have been examined in a few studies, some of which found an association (51–53) while others did not (25, 30, 32, 47). One study found that pregnancy-related anxiety was associated with shorter gestations (19), and our analysis supports this finding. When women with a history of adverse pregnancy outcome or who reported bleeding/bed rest were excluded, the effect of anxiety was reduced but not eliminated, indicating that women who are anxious but do not have these medical conditions may be at increased risk of preterm birth. Anxiety may be linked to some general malaise that is difficult to measure but may be indicative of problems with the pregnancy. Because some of the risk may be attributable to a physiologic response to anxiety, anxiety may influence gestational age at delivery. Our data cannot directly address the direction of causality.

It has been postulated that perceptions of racial and gender discrimination and of unsafe neighborhoods and their associated stress may contribute to an increased risk of preterm birth (40, 54, 55). We found a modest but imprecise increased risk for these three measures. Alternate psychometrically validated instruments that measure perceived racism (56) may be more sensitive than the instrument used.

Although there was a somewhat stronger association between pregnancy-related anxiety and spontaneous preterm birth and between negative life events and medically indicated preterm births, the association between psychosocial factors and each of these subgroups did not differ substantially from associations seen in the aggregate. Because biomechanisms through which stress may contribute to preterm birth are not well understood, these findings neither

clearly support nor contradict the existence of distinct pathways that explain the stress-preterm birth association.

Studies that have incorporated several psychosocial domains to develop a composite psychosocial measure or that examined several factors in their models were more likely to find some association between stressors and preterm birth than were unifactorial examinations (17–19, 32). Collins et al. (26) found that women with more life events and higher quality social support showed an increased birth weight, but the interaction did not hold for women with lower numbers of life events. We examined several interaction models, and our findings indicate that this approach did not yield a substantial improvement over single scales. Other studies found no buffering effect of social support (15, 20–26). Our analyses support the general findings that social support's buffering effect is, at most, small among women with high levels of stress.

An advantage of this study was the prospective data collection during the late second or early third trimester, thus eliminating the problem of reporting being influenced by outcome. A criticism of some psychosocial-birth outcome studies has been their limited examination of confounding or effect modification (54, 57). The Pregnancy, Infection, and Nutrition Study's extensive data collection allowed examination of a wide range of covariates. We found minimal confounding, consistent with the lack of strong risk factors of preterm birth. When we examined health behaviors that might be influenced by stress and thus potentially act as intermediates on the causal pathway, we found that their inclusion did not significantly change the associations of psychosocial factors with preterm birth.

Limitations of this study must be acknowledged. The Pregnancy, Infection, and Nutrition Study recruited women from a small number of prenatal clinics before week 29 of pregnancy; therefore, women seeking no or late prenatal care were excluded. Vital records for the catchment area indicated that 2 percent of women initially seek care after 6 months of pregnancy. Among the study population, some risk factors often found in other populations were not associated with higher risk of preterm birth, including bacterial vaginosis, and only a modest increase by poverty, age, and prepregnancy body mass index. White women were at higher risk of preterm birth, and African-American women were at lower risk when compared with North Carolina population statistics, largely reflective of the populations served at participating study clinics rather than nonresponse within those clinics. The selected clinics and their clientele may account for the lack of concurrence regarding an association with preterm birth on some of these measures, and our findings may not be generalizable to other populations.

A number of measurement issues are challenges for any psychosocial-birth outcome study. A study of preterm birth has the potential for misclassification of gestational age given possible errors in reporting the last menstrual period (58). There are a wide variety of psychosocial domains and associated instruments, with no "gold standards." We generally used instruments that were validated in other studies of pregnancy or health outcomes where possible and incorporated as many psychosocial domains from our conceptual model as feasible. For the stratification by clinical presentation and the multiple psychosocial risk evaluation, the number of women in some categories was small, resulting in limited power.

Future research that incorporates multiple psychosocial domains, information about the woman's social environment, life circumstances, and resources, and possible biologic pathways through which stress operates may further our understanding of the role of stress in pregnancy.

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