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Behavioral Influences on Preterm Birth: Integrated Analysis of the Pregnancy, Infection, and Nutrition Study

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Abstract

Most previous studies of preterm birth have considered risk factors in isolation rather than examining the collective impact of multiple candidate determinants. In order to examine the combined impact of a set of behavioral risk factors on the risk of preterm birth, we analyzed data collected for the Pregnancy, Infection, and Nutrition Study on a range of sociodemographic, behavioral, and related factors. Women who received prenatal care at selected clinics in central North Carolina and gave birth in the period 1995–2005 were recruited into a prospective cohort study, with 4,251 women providing the required information on risk factors and pregnancy outcome. A number of demographic and behavioral attributes were modestly associated with preterm birth, with odds ratios of 1.3–1.5, including age >35, African-American ethnicity, height of 63 inches or less, parity 2+, and delivery at the academic medical center. Despite weak associations for individual risk factors, changes in a constellation of behaviors during pregnancy predict substantial shifts in the risk of preterm birth, suggesting a reduction from 8 to 3% preterm among those with a low-risk baseline profile, and a reduction from 18 to 7% pre-term among those with a high-risk baseline profile. While inferences are limited by the incomplete range of available

predictors, uncertainty regarding whether observed associations are causal, and substantial challenges in changing component behaviors, the possibility of substantial reduction in risk merits more serious consideration of whether behavioral interventions could markedly reduce the risk of preterm birth.

Keywords

Preterm birth; Prediction models; Health behaviors

Introduction

The search for causes of preterm birth has had limited success, with no strong, modifiable determinants found thus far [1]. There are a number of powerful *predictors* of preterm birth, including multifetal gestation, prior preterm birth, African-American ethnicity, mid-pregnancy fetal fibronectin, and short cervical length [1], but other than allowing for adjustment of clinical care in anticipation of possible preterm birth, there are no direct preventive measures with the exception of progesterone injections for women with prior preterm births [2]. Smoking, low prepregnancy weight, and inadequate gestational weight gain are the only established modifiable predictors, each associated with a modestly increased risk [1, 3, 4].

The failure to identify individually strong, modifiable causes of preterm birth is not due to insufficient research, given numerous studies focused on psychosocial stress [1] and health behaviors, particularly tobacco, alcohol, and illicit drugs [4]. A number of suggestive associations have been reported for maternal prepregnancy weight, gestational weight gain, diet, stress, depression, cocaine use, and physical activity [1], but because of the challenge in accurately assessing such factors, most studies collect detailed data or analyze only one realm at a time. To address the hypothetical impact of a constellation of behaviors, an extensive analysis of a wide range of behavioral influences on preterm birth based on high quality measurements is needed.

Methods

Data Collection

The Pregnancy, Infection and Nutrition (PIN) Study recruited women from August 1995 through June 2005 under three different recruitment protocols (referred to here as PIN 1, 2, and 3) [5–7]. Exclusion criteria were similar across the three cohorts: less than age 16, non-English speaking, not planning to continue care or deliver at the recruitment hospital, carrying multiple gestations, or lacking a telephone. Exact times of recruitment and assessment varied but were sufficiently compatible for combining data across recruitment periods. The institutional review boards of the University of North Carolina School of Medicine (PIN 1, 2, and 3) and Wake Medical Center (PIN 1 only) approved the study.

A total of 5,169 pregnancies make up the combined PIN cohort, 62% of those eligible. Exclusions were made for stillbirths (N = 28), induced abortion (N = 1), spontaneous abortion (N = 3), documented congenital anomaly present at birth (N = 84), unknown birth date (N = 80), pre-existing hypertension or diabetes mellitus (N = 382), and second or third pregnancies to the same woman in the cohort (N = 340) to maintain independence of observations. The final analysis cohort included 4,251 births.

Gestational age at delivery was calculated based on the first ultrasound performed prior to 22 weeks' gestation. For women without an early ultrasound (N = 394, 9.3%), self-reported

last menstrual period was used to determine gestational age at delivery. Preterm birth was defined as a live birth before 37 completed weeks of gestation. Subtypes of preterm birth were classified by clinical presentation as preterm labor, preterm premature rupture of membranes (rupture of membranes preceding onset of uterine contractions by at least 4 h, preterm PROM), or medical indication based on chart review by a collaborating obstetrician. Gestational age at delivery was also used to categorize preterm births into early (<34 weeks) or late (34–<37 weeks).

Predictors of Preterm Birth

We selected 17 risk factors for consideration based on prior support for an association with preterm birth and availability in all three cohorts (Table 1).

Demographic Variables—Age (<25, 25–34, 35+, race (African-American, Non-African-American), and completed years of education (high school or less, more than high school) were considered. Percent poverty was based on total family income combined with the total number of adults and children relying on the income and compared to the benchmark for defining poverty level (1996 referent for PIN 1 and 2 and 2001 referent for PIN 3). The poverty value was standardized by subtracting the mean percent poverty level for the participants (305%) and dividing by the SD (238) and treated as a continuous variable in the analysis.

Other Non-Modifiable Factors—Height at the time of recruitment was dichotomized at the 25th percentile (63 inches) for analysis based on prior evidence that short stature is associated with increased risk of preterm birth [8]. Parity was categorized as nulliparous, 1 previous birth, or 2 or more previous births. Women were recruited from one of two sites; either a county health department and associated community hospital (Wake Medical Center) in Raleigh, NC, or University of North Carolina Hospital (UNC), an academic medical center in Chapel Hill, NC.

Prepregnancy Behaviors—Women reported pre-pregnancy weight which was combined with height to calculate body mass Index (BMI, kg m^{-2}), categorized based on the 2009 Institute of Medicine (IOM) Guidelines [9] as Underweight (<18.5), Normal weight (18.5–24.9), Overweight (25.0–29.9), or Obese (≥ 30.0). Women reported vitamin use prior to pregnancy. A question about regular exercise or strenuous activities was collected similarly for all three cohorts between 24 and 29 weeks' gestation. The question included an assessment of physical activity during the 3 months prior to pregnancy. More women in PIN 3 reported physical activity overall, possibly due to different formulation of the questions, so an interaction term with PIN cohort was considered in the analysis.

Pregnancy Behaviors—Maternal weight throughout the pregnancy was abstracted from the medical record and the date of the last reported weight was noted to determine gestational weight gain. Adequacy of weight gain during pregnancy was assessed by calculating a total expected weight gain for each woman based on her prepregnancy BMI and date of her last weight measurement, assuming a fixed first trimester weight gain (2 kg for Underweight, Normal, and Overweight women and 1.5 kg for Obese women), and referring to guidelines for 2nd and 3rd trimester rate of weight gain [9]. Weight gain was categorized as Inadequate, Adequate or Excessive if the ratio fell below, within, or above the BMI specific recommend range of weight gain [9]. Smoking was categorized as none, <10 cigarettes d^{-1} , or 10+ cigarettes d^{-1} . Exercise was assessed as described above for the first and second trimester of pregnancy.

Four measures of diet during the second trimester of pregnancy were considered: vitamin C, folate, fat, and total energy. Information on dietary intake was collected using the modified Block Food Frequency questionnaire [10] administered between gestational weeks 24 and 29 and reflects the previous 3 months. Folate and Vitamin C levels were categorized using the cutpoints selected for previously published analyses [11, 12], the 66th percentile ($500 \mu\text{g d}^{-1}$) for folate and the 10th percentile (67 mg d^{-1}) for Vitamin C. Fat Intake was divided into three equally sized groups using 66 and 102 g d^{-1} as cutpoints. Daily estimated energy intake was used in all models which included any dietary variable. Total energy (calories) was treated as a continuous variable centered at the mean of 2,500 calories.

Two psychosocial measures, depression and social support, were chosen for this analysis based on previous literature and their availability in all three cohorts. The Center for Epidemiological Studies-Depression (CES-D) Scale [13] was administered between 24 and 29 weeks' gestation and classified using established cutpoints [14, 15] modified for pregnancy symptoms (0–16, 17–24, 25+). The Medical Outcomes Study Social Support Survey [16] assesses the perceived availability of social support from close friends and relatives. Quartiles of the total score were used for categorization with the highest level of social support (90+) used as the referent.

Statistical Methods

To make optimal use of the available data and minimize potential biases due to item non-response, we conducted multiple imputations. Ten multiply imputed datasets were created using Markov chain Monte Carlo methods [17, 18]. The imputation model included all variables in the final analysis model plus markers of pregnancy health, use of prenatal care, maternal Hispanic ethnicity, and infant birth weight. Height, pre-pregnancy weight and total gestational weight gain were used in the imputation model as opposed to BMI and adequacy of weight gain. Preterm birth subtype, missing for 35 pregnancies, was not imputed, so these women were excluded from the subtype-specific analysis.

A logistic model was developed using all of the predictors and the outcome of preterm birth. A logistic model was fitted to each imputed dataset, and the estimates were combined using methods which incorporate the variability across the 10 imputations (PROC MIANALYZE in SAS 9.2 [19]). Rather than using model selection to include only those main effect measures that were significantly predictive of the outcome, we retained all for presentation, as the absence of an independent effect is also of interest. For preterm birth in the aggregate and the specific subtypes of preterm birth, few exposures were associated with a *P* value of less than 0.20 for interactions with site or physical activity and cohort consistently across all levels of a variable. An approximate *F* test to compare the model with all of the interaction variables to the model with none of the interaction variables yielded a *P* value of 0.96 for all preterm births and 1.0 for subtypes of preterm birth, so no interaction terms were included in subsequent models.

A generalized logistic model, which included all of the subtypes of preterm birth in a single polytomous model, was used to estimate associations within subtypes and to assess any apparent heterogeneity across subtypes. For each variable, an approximate *F* test was used to test the equality of the three estimates. A similar process was used for subtypes of preterm birth based on gestational age at delivery (early preterm births: <34 weeks, and late preterm births: 34–<37 weeks) versus term.

Risk profiles were developed to calculate the predicted probability of preterm birth, subtypes of preterm birth, and severity of preterm birth among hypothetical women with varying combinations of risk factors. Variables which showed stronger associations in the previous analysis, and were relatively common in the cohort, were chosen to define baseline risk

status at the time of recruitment: race (African-American, non-African-American), parity (nulliparous, parous), education (13+ years, 12 years), and recruitment site (Wake Medical Center, UNC Hospitals). Modifiable behaviors during pregnancy were used to define low and high risk status: exercise in the second trimester (no, yes), dietary folate intake ($<500 \mu\text{g d}^{-1}$, $>500 \mu\text{g d}^{-1}$), and dietary fat intake ($<66 \text{ g d}^{-1}$, $66+ \text{ g d}^{-1}$). Given the similarity in magnitude of risk in subsets of smokers, low risk status was defined as non-smoking while high risk was defined as any smoking. All other variables were set to the most common value in the cohort, as indicated in the table footnotes. To provide statistically stable and more credible estimates, we dichotomized most variables and considered prevalence in developing the risk profiles, with different selection of variables and scaling of variables than those used in the initial analysis. The four risk profiles, low and high baseline risk and low and high risk pregnancy behaviors, allowed us to examine the predicted effect of favorable versus unfavorable pregnancy behaviors in groups with high and low risk profiles at the time of recruitment. Linear predictors for each of the 10 imputed data sets were calculated and combined and transformed to a single predicted probability with appropriate confidence interval for each risk profile (Table 4).

Due to sizable amounts of missing data and concern about inclusion of variables on causal pathways [20], several potentially important variables were not included in the main analysis. To address restriction to those with complete data for the additional variables, a fully adjusted logistic model was developed using only the same variables as in the main analysis. Then, in this restricted subset of the population, a fully adjusted model was constructed that included the additional variables in addition to the original variables in the main analysis. We applied this approach to the assessment of bacterial vaginosis [21], vomiting due to pregnancy, vaginal bleeding, gestational diabetes, and gestational hypertension (none, isolated pregnancy induced hypertension, or preeclampsia), and pregnancy history (nulliparous, parous with a poor previous outcome, or parous without a poor previous outcome). Observations with complete data ($N = 2,028$) on all of the variables of interest for the sensitivity analysis were extracted from the imputed datasets used in the main analysis.

Results

No strong predictors of preterm birth in the aggregate were identified (Table 1), but a number of demographic and behavioral attributes were associated with odds ratios of 1.3–1.5 (Table 1): age >35 , African-American ethnicity, height of 63 inches or less, parity 2+, and delivery at the academic medical center. Among prepregnancy behaviors, only low prepregnancy BMI was associated with increased risk. Several modestly predictive behaviors during pregnancy were identified: inadequate weight gain, smoking (particularly 10+ cigarettes per day), lack of exercise in the second trimester, low dietary folate, and high dietary fat, none exceeding an odds ratio of 1.6. There was little confounding present, with adjustment slightly reducing the effect of low education, parity, and elevated BMI, and enhancing the effect of delivery hospital. Sensitivity analysis including history of previous adverse pregnancy outcomes, pregnancy symptoms and complications, and bacterial vaginosis had little impact on these results.

Consideration of preterm birth subtypes defined by clinical presentation (Table 2) yielded some suggestive differences relative to total preterm birth but limited in precision. It appears that African-American women were at greater risk for preterm PROM than the other subtypes and that parity was associated only with increased risk of preterm birth due to preterm labor. Low prepregnancy BMI was associated with increased risk of preterm birth due to preterm labor and elevated prepregnancy BMI appeared to be associated only with preterm birth associated with medical indications. Excessive gestational weight gain was

inversely related only to the risk of preterm PROM. Exercise appeared to be more strongly inversely related to preterm birth due to preterm labor than to the other subtypes. While there were a number of apparent differences across groups, the *P* values indicate how statistically unstable those differences are.

Comparison of predictors of early (<34 weeks) and late (34–<37 weeks) preterm birth (Table 3) yielded more suggestive differences than clinical presentation, mostly indicating stronger associations for earlier preterm births. This was the case for the increased risks associated with higher prepregnancy BMI, inadequate gestational weight gain, smoking 10+ cigarettes per day, high dietary fat intake, and higher depression score, as well as an anomalous inverse association for low education. A stronger association was found for late preterm births compared to early preterm births for parous women.

The impact of hypothetical changes in the constellation of modifiable behaviors (Table 4) suggests that these individually modest predictors might have a sizable aggregate impact. Among women with low baseline risk, the predicted effect of a shift from the lowest risk behavior profile (predicted probability of 3%) to the highest risk profile (predicted probability of 8%) is substantial (5% absolute risk), but with a higher baseline risk, the predicted shift is even more notable in absolute terms (from 7 to 18%, a difference of 11%). Although the absolute rates were much lower for subtypes of preterm birth defined by clinical presentation and severity, the same general pattern applied—a predicted benefit of more favorable pregnancy behaviors that was notably enhanced in absolute magnitude among those with less favorable baseline risk factor profiles.

Discussion

Despite the modest impact of individual factors on risk of preterm birth, our study suggests that they act independently, and thus may have a substantial cumulative impact. The models predict that changing a series of behaviors would, in theory, yield a substantial decrement in risk of preterm birth, most notable for those at high baseline risk due to sociodemographic characteristics, i.e., women who are poor, African-American, older, and with limited education. The assumptions underlying the quantitative estimates are clearly speculative, predicated on the validity of the model, the ability to effect such changes, and the belief that with such changes, women would experience the preterm birth risks of those who have the more favorable profile. Nonetheless, these data offer some basis to suggest that we may have more of an understanding of modifiable determinants of preterm birth than analyses of individual risk factors would suggest. If, in fact, we were to learn that changing this constellation of behaviors had a substantial causal impact on risk of preterm birth, public health policies and clinical care that promoted such lifestyle modifications would be warranted.

Others have developed multivariate predictive models of preterm birth [22–24], mostly focused on developing purely statistical prediction models which might be of use for interventions with “high risk” patients rather than for prevention. The strongest predictors in fact are non-modifiable characteristics—multiple gestation, prior preterm birth, African-American ethnicity, older age at birth, etc. The only modifiable factors that emerged as predictors with some regularity were smoking [22, 23, 25], low prepregnancy weight [26], and inadequate gestational weight gain [27, 28]. Other studies are focused on emerging clinical problems during the course of pregnancy to predict preterm birth, such as nausea and vomiting, vaginal bleeding, proteinuria, hypertension, and other signs and symptoms of concern [22, 29, 30]. The predictive power from such measures can be quite impressive as pregnancy proceeds [22], but the preventive implications are limited for biological processes that are already in progress.

We recognize inherent limitations in the inferences that can be drawn from these analyses. Like any single clinical sample, the PIN study participants reflect a particular region, medical care setting, and self-selection for participation. There were problems with missing data that in some cases precluded consideration of reasonable candidate predictors from the model and called for the indirect solution of using multiple imputation for other predictors. While multiple imputation is preferable to restricting to those with complete data or creating a stratum of those with missing information [31], uncertainty remains where the data are incomplete. The interpretation of statistical predictors as causal influences is fraught with uncertainty, and the effort to estimate the impact of changing risk factor profiles presumes all are causal. Randomized trials provide a much stronger basis for inferring causality than observational studies such as this one, and we have been reminded repeatedly that ostensibly strong and plausible risk factors identified through observational studies prove not to be effective tools for prevention when subjected to trials.

Our data provide little encouragement to look for *the cause* of preterm birth or even for individually powerful risk factors among the constellation of behaviors. While strong behavioral influences may be present but diluted through measurement error, the empirical data do not support this contention. Instead, our findings encourage consideration of multifaceted lifestyle modification to reduce the risk of preterm birth. Behavioral change of the magnitude suggested poses formidable logistical challenges, but pregnancy is a time of unusually strong health motivation and offers the hope that women might shift from a high risk to low risk profile and markedly improve the prospects for a healthy pregnancy. Preterm birth remains an extremely common adverse outcome of pregnancy, and even marginally preterm births are now known to have negative consequences [32, 33]. Randomized trials to test this hypothesis should be considered, despite the complexity and challenges of conducting such multi-faceted behavioral interventions.

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Table 1

Predictive model of preterm birth in the pregnancy, infection, and nutrition study

	N pregnancies	N preterm	Crude ^a OR	Adjusted ^{a,b} OR (95% CI)
<i>Demographic factors</i>				
Maternal age (yrs)				
<25	1,738	209	1.2	1.1 (0.9, 1.4)
25–34	2,049	217	1.0	1.0
35+	464	59	1.2	1.3 (0.9, 1.7)
Missing	0			
Race				
African American	1,447	188	1.3	1.3 (1.0, 1.6)
White/other	2,801	296	1.0	1.0
Missing	3			
Education				
12 yrs	1,786	225	1.2	1.0 (0.7, 1.2)
13+ yrs	2,450	259	1.0	1.0
Missing	15			
Percent poverty				
Mean (SD)	305% (238)	271% (226)	0.9	0.9 (0.8, 1.1)
Missing	573			
<i>Other non-modifiable factors</i>				
Height				
63 in	1,265	169	1.3	1.3 (1.0, 1.5)
>63 in	2,763	298	1.0	1.0
Missing	223			
Parity				
Nulliparous	2,063	203	1.0	1.0
One	1,298	148	1.2	1.1 (0.9, 1.4)
Two+	880	133	1.6	1.4 (1.1, 1.9)
Missing	10			
Recruitment site				
Wake	1,159	110	1.0	1.0
UNC	3,092	375	1.3	1.7 (1.3, 2.1)
Missing	0			
<i>Pre-pregnancy behaviors</i>				
BMI (kg m ⁻²)				
<18.5	234	40	1.7	1.6 (1.1, 2.3)
18.5–24.9	2,114	213	1.0	1.0
25.0–29.9	801	105	1.3	1.2 (0.9, 1.5)
30.0+	835	100	1.2	1.0 (0.7, 1.2)
Missing	267			
Exercise pre-pregnancy ^c				

	N pregnancies	N preterm	Crude ^a OR	Adjusted ^{a, b} OR (95% CI)
Yes	1,233	116	0.9	1.1 (0.8, 1.6)
No	2,245	260	1.0	1.0
Multivitamin use ^d				
Yes	1,386	135	0.9	1.0 (0.8, 1.3)
No	2,159	236	1.0	1.0
Missing	706			
<i>Pregnancy behaviors</i>				
Weight gain				
Inadequate	586	92	1.5	1.4 (1.1, 2.0)
Excessive	2,143	234	1.0	1.0 (0.8, 1.3)
Missing	561			
Smoking months 1–6				
None	2,991	304	1.0	1.0
<10 cig d ⁻¹	488	62	1.4	1.3 (1.0, 1.7)
10+ cig d ⁻¹	318	51	1.7	1.6 (1.1, 2.3)
Missing	454			
Exercise 1st trimester ^c				
Yes	798	69	0.8	0.9 (0.6, 1.4)
No	2,680	307	1.0	1.0
Exercise 2nd trimester ^c				
Yes	599	46	0.7	0.7 (0.5, 1.1)
No	2,879	330	1.0	1.0
Missing exercise ^c	773			
Total energy intake (calories d ⁻¹) ^e Mean (SD)	2,579 (1,315)	2,679 (1,343)		
Dietary vitamin C ^e (mg d ⁻¹)				
<67	216	21	1.1	1.0 (0.6, 1.5)
67	3,374	352	1.0	1.0
Dietary folate ^e (μg d ⁻¹)				
500	2,155	233	1.3	1.2 (0.9, 1.6)
>500	1,435	140	1.0	1.0
Dietary fat ^e (g d ⁻¹)				
<66	1,165	101	1.0	1.0
66–101	1,228	130	1.2	1.2 (0.9, 1.6)
102+	1,197	142	1.5	1.5 (1.0, 2.2)
Missing dietary values ^e	661			
Depression score				
<17	1,860	176	1.0	1.0
17–24	500	58	1.2	1.1 (0.8, 1.5)
25+	523	59	1.2	1.1 (0.8, 1.5)
Missing	1,368			

	N pregnancies	N preterm	Crude ^a OR	Adjusted ^{a, b} OR (95% CI)
Total social support				
<70	737	81	1.0	0.8 (0.6, 1.2)
70–81	779	75	0.9	0.8 (0.6, 1.1)
82–89	685	75	1.0	1.0 (0.7, 1.3)
90+	849	98	1.0	1.0
Missing	1,201			

CI confidence interval, *in* inches, *OR* odds ratio, *SD* standard deviation, *yrs* years

^aOR calculated in 10 imputed data sets. N = 4,251

^bAdjusted for all variables in the table. Standardized poverty and centered calories used in regression

^cNumber of missing is the same for all physical activity variables

^dMultivitamin use must have started before conception

^eDietary variables each adjusted for daily calorie intake in the crude analysis. Number of missing is the same for all dietary variables

Table 2

Predictive model of preterm birth subtypes in the pregnancy, infection, and nutrition study

	Preterm labor N = 171		PPROM N = 99		Medical indication N = 180		P for equality across subtypes
	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	
Demographic factors							
Maternal age (yrs)							
<25	83	1.3 (0.8, 1.9)	36	1.0 (0.6, 1.7)	71	1.0 (0.7, 1.5)	0.67
25–34	71	1.0	48	1.0	84	1.0	
35+	17	1.1 (0.6, 1.9)	15	1.4 (0.8, 2.7)	25	1.3 (0.8, 2.2)	0.79
Missing	0		0		0		
Race							
African American	63	0.9 (0.6, 1.4)	39	1.8 (1.1, 3.1)	68	1.4 (1.0, 2.1)	0.10
White/other	108	1.0	60	1.0	111	1.0	
Missing	0		0		1		
Education							
12 yrs	88	0.9 (0.6, 1.4)	39	0.8 (0.5, 1.4)	79	1.1 (0.7, 1.7)	0.66
13+ yrs	83	1.0	60	1.0	100	1.0	
Missing	0		0		1		
Percent poverty							
Mean (SD)	233% (200)	0.9 (0.6, 1.2)	314% (257)	1.0 (0.7, 1.3)	308% (233)	1.1 (0.9, 1.4)	0.50
Missing	31		12		27		
Other non-modifiable factors							
Height							
63 in	54	1.1 (0.8, 1.5)	34	1.2 (0.8, 1.9)	62	1.2 (0.9, 1.7)	0.77
>63 in	109	1.0	61	1.0	113	1.0	
Missing	8		4		5		
Parity							
Nulliparous	61	1.0	43	1.0	88	1.0	
One	61	1.5 (1.0, 2.2)	31	1.0 (0.6, 1.7)	43	0.8 (0.5, 1.1)	0.04
Two+	49	1.8 (1.1, 2.8)	24	1.1 (0.6, 2.1)	49	1.3 (0.8, 2.0)	0.40
Missing	0		1		0		

	Preterm labor N = 171		PPROM N = 99		Medical indication N = 180		P for equality across subtypes
	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	
Recruitment site							
Wake	45	1.0	19	1.0	37	1.0	
UNC	126	1.6 (1.1, 2.3)	80	1.9 (1.1, 3.4)	143	1.6 (1.0, 2.4)	0.80
Missing	0		0		0		
<i>Pre-pregnancy behaviors</i>							
BMI (kg m ⁻²)							
<18.5	20	2.0 (1.2, 3.4)	5	0.8 (0.3, 2.1)	9	1.2 (0.6, 2.5)	0.21
18.5–24.9	75	1.0	50	1.0	74	1.0	
25.0–29.9	31	0.9 (0.6, 1.5)	18	1.1 (0.6, 1.9)	48	1.5 (1.0, 2.3)	0.22
30.0+	36	0.9 (0.6, 1.3)	19	0.9 (0.5, 1.5)	40	1.3 (0.8, 1.9)	0.40
Missing	9		7		9		
Exercise pre-pregnancy ^b							
Yes	32	1.2 (0.7, 2.1)	27	1.1 (0.5, 2.2)	52	1.1 (0.7, 1.9)	0.97
No	97	1.0	52	1.0	87	1.0	
Multivitamin use ^c							
Yes	34	0.8 (0.5, 1.4)	37	1.3 (0.8, 2.3)	56	1.1 (0.7, 1.6)	0.42
No	86	1.0	43	1.0	88	1.0	
Missing	51		19		36		
<i>Pregnancy behaviors</i>							
Weight gain							
Inadequate	38	1.7 (1.0, 2.7)	27	1.7 (0.9, 2.9)	24	1.1 (0.6, 1.8)	0.37
Adequate	35	1.0	27	1.0	37	1.0	
Excessive	86	1.1 (0.7, 1.6)	37	0.6 (0.3, 1.0)	105	1.1 (0.7, 1.6)	0.14
Missing	12		8		14		
Smoking months 1–6							
None	101	1.0	64	1.0	118	1.0	
<10 cig d ⁻¹	24	1.3 (0.9, 2.0)	9	1.2 (0.6, 2.5)	22	1.3 (0.9, 2.0)	0.99
10+ cig d ⁻¹	20	1.3 (0.7, 2.4)	11	2.2 (1.1, 4.7)	16	1.5 (0.8, 2.8)	0.56
Missing	26		15		24		

	Preterm labor N = 171		PPROM N = 99		Medical indication N = 180		P for equality across subtypes
	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	
Exercise 1st trimester ^b							
Yes	15	0.8 (0.4, 1.6)	17	0.8 (0.4, 1.9)	36	1.3 (0.7, 2.2)	0.49
No	114	1.0	62	1.0	103	1.0	
Exercise 2nd trimester ^b							
Yes	6	0.4 (0.2, 1.0)	16	1.2 (0.6, 2.5)	23	0.8 (0.5, 1.4)	0.20
No	123	1.0	63	1.0	116	1.0	
Missing exercise ^b	42		20		41		
Total energy intake mean ^d (SD) (calories d ⁻¹)	2,770 (1,211)		2,480 (1,604)		2,662 (1,205)		
Dietary vit C ^d (mg d ⁻¹)							
<67	5	0.9 (0.4, 1.9)	8	1.2 (0.5, 2.5)	8	1.0 (0.5, 1.9)	0.88
67	117	1.0	75	1.0	132	1.0	
Dietary folate ^d (μg d ⁻¹)							
500	69	1.0 (0.5, 1.7)	61	1.8 (1.0, 3.4)	87	1.2 (0.8, 1.9)	0.27
>500	53	1.0	22	1.0	53	1.0	
Dietary fat ^d (g d ⁻¹)							
<66	28	1.0	30	1.0	36	1.0	
66–101	43	1.3 (0.8, 2.2)	30	1.0 (0.6, 1.8)	50	1.3 (0.9, 2.1)	0.77
102+	51	1.6 (0.8, 3.4)	23	0.9 (0.4, 2.0)	54	1.8 (0.9, 3.4)	0.37
Missing dietary values ^d	49		16		40		
Depression score							
<17	54	1.0	38	1.0	71	1.0	
17–24	23	1.2 (0.8, 1.9)	11	1.2 (0.6, 2.6)	21	1.0 (0.7, 1.6)	0.87
25+	21	1.1 (0.7, 1.9)	11	1.2 (0.6, 2.5)	20	1.0 (0.6, 1.6)	0.95
Missing	73		39		68		
Total social support							
<70	27	0.8 (0.4, 1.4)	15	0.8 (0.4, 1.5)	29	0.9 (0.5, 1.4)	0.96
70–81	31	0.9 (0.5, 1.5)	10	0.5 (0.3, 1.1)	31	0.9 (0.5, 1.4)	0.48
82–89	23	0.9 (0.5, 1.6)	18	0.9 (0.5, 1.7)	27	0.9 (0.6, 1.5)	1.00
90+	32	1.0	25	1.0	38	1.0	

	Preterm labor N = 171		PPROM N = 99		Medical indication N = 180		P for equality across subtypes
	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)	
Missing	58		31		55		

CI confidence interval, *in* inches, *aOR* adjusted odds ratio, *PPROM* premature preterm rupture of amniotic membranes, *SD* standard deviation, *yrs* years

^aOR calculated in 10 imputed data sets. Adjusted for all variables in the table using continuous standardized poverty and calories centered on 2,500 kcal. N = 4,216. 35 preterm births missing subtype status

^bNumber of missing is the same for all physical activity variables

^cMultivitamin use must have started before conception

^dNumber of missing is the same for all dietary variables

Table 3

Predictive model of preterm birth severity in the pregnancy, infection, and nutrition study

	Early preterm <34 weeks N = 109		Late preterm 34–36 weeks N = 376		P for equality across severity
	No. of cases	aOR ^a (95% CI)	No. of cases	aOR ^a (95% CI)	
<i>Demographic factors</i>					
Maternal age (yrs)					
<25	54	1.4 (0.8, 2.3)	155	1.0 (0.8, 1.4)	0.34
25–34	42	1.0	175	1.0	
35+	13	1.5 (0.8, 3.0)	46	1.2 (0.8, 1.7)	0.50
Missing	0		0		
Race					
African American	50	1.6 (1.0, 2.6)	138	1.2 (0.9, 1.6)	0.34
White/other	58	1.0	238	1.0	
Missing	1		0		
Education					
12 yrs	49	0.6 (0.4, 1.0)	176	1.1 (0.8, 1.4)	0.05
13+ yrs	59	1.0	200	1.0	
Missing	1		0		
Percent poverty					
Mean (SD)	241% (213)	0.8 (0.6, 1.2)	280% (230)	1.0 (0.8, 1.2)	0.46
Missing	18		56		
<i>Other non-modifiable factors</i>					
Height					
63 in	38	1.3 (0.9, 2.0)	131	1.2 (1.0, 1.6)	0.82
>63 in	66	1.0	232	1.0	
Missing	5		13		
Parity					
Nulliparous	51	1.0	152	1.0	
One	29	0.8 (0.5, 1.3)	119	1.2 (0.9, 1.6)	0.11
Two+	29	1.0 (0.6, 1.7)	104	1.6 (1.1, 2.1)	0.16
Missing	0		1		

	Early preterm <34 weeks N = 109		Late preterm 34–36 weeks N = 376		P for equality across severity
	No. of cases	aOR ^a (95% CI)	No. of cases	aOR ^a (95% CI)	
Recruitment site					
Wake	28	1.0	82	1.0	
UNC	81	1.8 (1.1, 2.9)	294	1.6 (1.2, 2.2)	0.80
Missing					
<i>Pre-pregnancy behaviors</i>					
BMI (kg m ⁻²)					
<18.5	10	1.7 (0.8, 3.5)	30	1.6 (1.0, 2.4)	0.87
18.5–24.9	40	1.0	173	1.0	
25.0–29.9	22	1.4 (0.8, 2.4)	83	1.1 (0.8, 1.5)	0.46
30.0+	27	1.4 (0.8, 2.3)	73	0.9 (0.6, 1.2)	0.14
Missing	10		17		
Exercise pre-pregnancy ^b					
Yes	23	1.3 (0.6, 2.5)	93	1.1 (0.8, 1.5)	0.74
No	55	1.0	205	1.0	
Multivitamin use ^c					
Yes	27	1.1 (0.6, 1.8)	108	1.0 (0.8, 1.4)	0.90
No	49	1.0	187	1.0	
Missing	33		81		
<i>Pregnancy behaviors</i>					
Weight gain					
Inadequate	33	2.1 (1.2, 3.8)	59	1.2 (0.9, 1.8)	0.10
Adequate	22	1.0	78	1.0	
Excessive	40	0.7 (0.4, 1.3)	194	1.1 (0.8, 1.4)	0.17
Missing	14		45		
Smoking months 1–6					
None	59	1.0	245	1.0	
<10 cig d ⁻¹	11	1.3 (0.7, 2.4)	51	1.3 (1.0, 1.7)	0.95
10+ cig d ⁻¹	17	2.6 (1.4, 5.1)	34	1.3 (0.8, 2.0)	0.06
Missing	22		46		

		Early preterm <34 weeks N = 109		Late preterm 34–36 weeks N = 376		P for equality across severity
		No. of cases	aOR ^a (95% CI)	No. of cases	aOR ^a (95% CI)	
Exercise 1st trimester ^b						
Yes		14	0.9 (0.3, 2.4)	55	0.9 (0.6, 1.4)	0.91
No		64	1.0	243	1.0	
Exercise 2nd trimester ^b						
Yes		11	1.0 (0.4, 2.4)	35	0.7 (0.4, 1.0)	0.40
No		67	1.0	263	1.0	
Missing exercise ^b		31		78		
Total energy intake mean (SD) (calories d ⁻¹) ^d		2,861 (1,353)		2,630 (1,338)		
Dietary vitamin C ^d (mg d ⁻¹)						
<67		6	1.1 (0.4, 2.9)	15	0.9 (0.6, 1.5)	0.76
67		73	1.0	279	1.0	
Dietary folate ^d (μg d ⁻¹)						
500		48	1.3 (0.6, 2.6)	185	1.2 (0.9, 1.6)	0.90
>500		31	1.0	109	1.0	
Dietary fat ^d (g d ⁻¹)						
<66		14	1.0	87	1.0	
66–101		31	1.9 (1.0, 3.6)	99	1.1 (0.8, 1.5)	0.13
102+		34	2.1 (0.8, 5.3)	108	1.4 (0.9, 2.1)	0.39
Missing dietary values ^d		30		82		
Depression score						
<17		27	1.0	149	1.0	
17–24		10	1.3 (0.7, 2.3)	48	1.1 (0.7, 1.5)	0.64
25+		16	1.6 (0.8, 2.9)	43	0.9 (0.6, 1.4)	0.16
Missing		56		136		
Total social support						
<70		16	1.0 (0.5, 2.1)	65	0.8 (0.6, 1.2)	0.63
70–81		18	1.0 (0.5, 1.9)	57	0.8 (0.5, 1.0)	0.40
82–89		15	1.1 (0.5, 2.3)	60	0.9 (0.7, 1.3)	0.66
90+		17	1.0	81	1.0	

P for equality across severity			
Early preterm <34 weeks N = 109		Late preterm 34–36 weeks N = 376	
No. of cases	aOR ^a (95%, CI)	No. of cases	aOR ^a (95%, CI)
43		113	
Missing			

CI confidence interval, *in* inches, *aOR* adjusted odds ratio, *PTL* preterm labor, *PPROM* premature preterm rupture of amniotic membranes, *SD* standard deviation, *yrs* years

^aaOR calculated in 10 imputed data sets. Adjusted for all variables in the table using continuous standardized poverty and calories centered on 2,500 kcal. N = 4,251

^bNumber of missing is the same for all physical activity variables

^cMultivitamin use must have started before conception

^dNumber of missing is the same for all dietary variables

Table 4

Estimated probability and 95% confidence interval of preterm birth for risk profiles defined by factors present at the time of recruitment and pregnancy risk behaviors

Established factors ^a	Pregnancy risk behaviors ^b	Predicted probability of preterm birth	Predicted probability of preterm birth due to preterm labor	Predicted probability of preterm birth due to PPRM	Predicted probability of preterm birth due to medical indication	Predicted probability of early preterm birth	Predicted probability of late preterm birth
Low ^c	Low ^d	3.0% (1.6%, 5.3%)	0.8% (0.0%, 1.5%)	0.7% (0.0%, 1.5%)	1.3% (0.2%, 2.4%)	0.4% (0.0%, 0.8%)	2.6% (1.0%, 4.2%)
Low	High ^e	7.9% (5.1%, 12.2%)	2.7% (0.8%, 4.7%)	1.5% (0.1%, 2.9%)	3.5% (1.1%, 6.0%)	1.4% (0.1%, 2.7%)	6.4% (3.4%, 9.4%)
High ^f	Low	7.1% (3.8%, 12.7%)	1.5% (0.0%, 3.0%)	1.9% (0.0%, 4.2%)	3.3% (0.5%, 6.3%)	0.5% (0.0%, 1.2%)	7.2% (2.9%, 11.5%)
High	High	17.7% (11.6%, 26.0%)	5.0% (1.5%, 8.6%)	3.9% (0.3%, 7.6%)	8.6% (3.0%, 14.2%)	1.9% (0.2%, 3.8%)	16.2% (9.3%, 23.1%)
Overall prevalence ^g		11.4%	4.06%	2.35%	4.27%	2.56%	8.84%

^aAll risk profiles have the following characteristics: age <35 years, 1 SD above mean poverty, height >63 in, BMI above 18.5, no exercise pre-conception and no multivitamin use

^bAll risk profiles have the following characteristics: normal or excessive pregnancy weight gain, no exercise 1st trimester, 2,500 calories d⁻¹, vitamin C intake 67 mg d⁻¹, CES-D below 17 and social support 90+

^cNot African-American, nulliparous, 13+ years education, recruited at Wake Medical Center

^dNon smoker, exercised in 2nd trimester, folate intake >500 µg d⁻¹ and fat intake <66 g d⁻¹

^eSmoker, No exercise 2nd trimester, folate intake 500 µg d⁻¹ and fat intake 66 g d⁻¹

^fAfrican-American, parous, 12 years education, recruited at UNC

^gPrevalence in cohort. Subtype of preterm birth not available for 35 births