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Impact of previous preterm birth and interbirth interval length on subsequent adverse birth outcomes in African American women.

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B.S., Northwestern University, 2011

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Abstract

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By Jessamyn V. Sneed

Preterm birth (PTB) complicates approximately 12% of all deliveries in the United States and, in addition to low birthweight (LBW), is classified as an adverse birth outcome due to its association with significantly higher rates of neurodevelopmental morbidity. The 2011 National Vital Statistics Report states that non-Hispanic black infants have the highest rates of preterm birth and low birthweight (16.75% and 13.33%, respectively) compared to Hispanic infants and non-Hispanic white infants in the United States. The exact cause of these increased rates of ABO in the African American community is unknown, but recent studies have implicated interbirth intervals and history of preterm birth among other variables. This study was conducted using data from the Pregnancy Risk Assessment Monitoring System, a surveillance project of the Centers for Disease Control and Prevention which collects nationwide data on maternal attitudes and experiences before, during, and after pregnancy. This cohort provided an unprecedented opportunity to study the multiplicative effect of interbirth interval (IBI) length and previous preterm birth on adverse birth outcomes. This study population consisted of 11,093 women. A forward elimination approach was used to develop logistic regression models which were used to estimate the odds of a study participant's current pregnancy being preterm or low birth weight. In addition to the two covariates of interest, thirteen predictors were included in each model: maternal BMI, race, income, marital status, age, education, history of hypertension and diabetes, recent miscarriage status, number of previous live births, smoking and drinking habits during pregnancy, and prenatal care seeking behavior. Mothers with IBIs of four years were shown to have the lowest statistically significant odds of having a subsequent PTB (aOR =0.67, $p = 0.002$) when compared to the referent group, mothers with IBIs of two years. Women with IBIs less than one year had significantly higher odds of subsequent LBW (aOR = 4.64, $p=0.028$) compared to the same reference group. African American women had statistically increased odds of having a subsequent LBW infant (aOR =1.96, $p<0.0001$) compared to White women. The results of this study, if confirmed, suggest that the ideal interbirth interval is four years.

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Introduction

Preterm birth, defined by the World Health Organization as delivery before 37 weeks' gestational age, complicates approximately 12% of all deliveries in the United States and is associated with 75% of all perinatal mortality as well as significantly higher rates of neurodevelopmental morbidity such as cerebral palsy [Goldenberg and McClure, 2010; Ananth and Vintzileos, 2006]. To be considered low birthweight, a newborn must weigh less than 2500g at birth, regardless of gestational age. Like preterm birth, low birthweight has been shown to be associated with a range of neonatal morbidities that inhibit neurodevelopment [Breslau et al, 2004]. Due to their impact on perinatal mortality and morbidity, preterm birth and low birthweight are considered to be adverse birth outcomes (ABOs). ABO rates are significantly affected by parity in that once a mother has a child with an ABO, the risk of ABO reoccurrence increases with each subsequent child [Simonsen et al., 2013; Khoury et al., 1989] Rates of adverse birth outcomes also vary significantly by race. The 2011 National Vital Statistics Report states that non-Hispanic black infants have the highest rates of preterm birth and low birthweight (16.75% and 13.33% , respectively) compared to Hispanic infants (11.66% and 7.02%, respectively) and non-Hispanic white infants (10.49% and 7.09%, respectively) [Hamilton et al., 2012]. The exact cause of these increased rates of ABO in the African American community is unknown, but recent studies have implicated interpregnancy intervals (IPIs) amongst other variables.

An interpregnancy interval is defined as the amount of time between concurrent pregnancies and is calculated as the number of months between previous delivery and subsequent conception. IPIs are crucial for maternal and child health as this time allows

for a mother to reregulate her nutrients and hormones which were altered due to childbearing and childbirth [Winkvist et al., 1992]. Zhu et al. (1999) found that IPIs lasting 18 to 23 months are associated with the lowest risks of adverse perinatal outcomes, and this interval is often used as the ideal IPI. Compared with infants conceived 18 to 23 months after a live birth, infants conceived after interpregnancy intervals of less than six months were found to have increased odds of preterm birth (OR = 1.4, 95% CI = 1.3-1.5), low birth weight (OR = 1.4, 95% CI = 1.3-1.6), and small for gestational age (OR = 1.3, 95% CI = 1.2-1.4). Infants born after interpregnancy intervals greater than 120 months also had increased odds of preterm birth (OR = 1.5, 95% CI = 1.3-1.7), low birth weight (OR = 2.0, 95% CI = 1.7-2.4), and small for gestational age (OR = 1.8, 95% CI = 1.6-2.0). African American women are 1.8 times as likely to have an IPI of less than six months compared to all women [Khoshnood et al., 1998]. Although African American women are known to have higher rates of ABO and shorter IPIs than women of other races, little work has been done to see how both these factors influence subsequent births. If previous child's preterm birth status and interpregnancy interval length are found to influence subsequent birth outcomes, then the models developed in this study could potentially be used to inform African American mothers about statistically significant risk factors that can lead to their subsequent child being born preterm (PTB) or low birth weight (LBW) and thus highlight avenues, such as exercise or earlier seeking of prenatal care, by which they can decrease their odds for these ABOs.

Nabukera et al. (2009) evaluated racial disparities in birth outcomes and IPIs among women who chose to delay initiation of childbirth. Study participants included women with two consecutive singleton births occurring in Missouri who were between

the ages of 20 and 50 at first pregnancy. Compared to Caucasian women, African American women were found to have significantly higher rates of fetal death (0.84% vs. 0.46%, $p < 0.0001$), preterm birth (13.4% vs. 7.1%, $p < 0.0001$), low birth weight (11.3% vs. 5.0%, $p < 0.0001$), and small for gestational age infants (18.6% vs. 9.1%, $p < 0.0001$). Interestingly, African American mothers were seen to have significantly longer mean IPIs (35.3 mos. \pm 30.2 vs. 29.5 mos. \pm 22.9). For both groups, mean IPI decreased with increasing age at first birth. Across IPI strata, African American women had significantly increased rates of IPI $<$ 6 months than white women; however, this association became insignificant after controlling for maternal age at first pregnancy. Though this study did help to elucidate racial disparities in rates of IPI length, it only controlled for maternal age at first birth, ignoring all other highlighted influential covariates such as maternal education status, smoking, and previous adverse birth outcomes.

In an effort to negate confounding due to socioeconomic status, Rawlings et al. (1995) studied African American and Caucasian women from military families to measure racial disparities in low birth weight and preterm birth in relation to IPI. The study population consisted of women who had two consecutive, singleton pregnancies during the study period and, due to their relation to the US armed forces, had access to free, high-quality healthcare. It was determined that PTB and LBW were most prevalent with an IPI of less than nine months in African American women (15.5%) and an IPI of less than three months (11.8%) in white women. A stepwise logistic regression was used to gauge the strength of association between prevalence of PTB and LBW and ten obstetric risk factors: maternal age less than 21 years, income, marital status, smoking status, late prenatal care, history of PTB or LBW, IPI $<$ 3 months, IPI $<$ 6 months, IPI $<$ 9

months, IPI < 12 months. Among African American women, history of PTB or LBW in the first pregnancy ($p < 0.001$) was found to be the strongest indicator of PTB and LBW in the second pregnancy, followed by an IPI of less than six months ($p = 0.004$) and an IPI of less than nine months ($p = 0.02$). Among white women, history of PTB or LBW in the first pregnancy ($p < 0.001$) was found to be the strongest indicator of PTB and LBW in the second pregnancy, followed by an IPI of less than three months ($p < 0.004$) and smoking ($p = 0.025$). It was concluded short interpregnancy intervals occur more frequently in African American women which accounts in part for the discrepancy in PTB and LBW. Though the methodology is sound, the results found in this study may not be applicable to the greater African American and Caucasian population due to its unique study population. Unrestricted access to medical services is very rare amongst the general population; therefore definitive conclusions cannot be drawn using a population with higher access to medical care and, as a result, potentially more knowledge as to the benefits of longer IPI and other means of preventing PTB and LBW. Additionally, the IPI of women in military families could be influenced by outside factors such as spousal military leave and stress. Similar to the Nabukera et al. study, this methodology measures a number of confounders, yet does not evaluate results after controlling for any of them with the exception of history of LBW and PTB.

The study of Hogue et al. (2011), who performed a qualitative analysis of published studies which examined IPI and PTB, had a three-fold aim: 1) To determine if 'short' IPI was associated with PTB and its potential causal mechanism, 2) To examine whether African American women were more likely to have a short IPI when compared to Caucasian women, and 3) To investigate whether extending IPIs to at least eighteen

months resulted in decreased racial disparities in PTB rates. It was found that, despite variation in the definition of a 'short' IPI and the gestational age of a preterm birth, the results of all studies analyzed were similar in that there was at least a 40% increased risk of subsequent preterm birth associated with IPIs of less than six months. One proposed causal hypothesis for this link between short IPI and subsequent PTB is nutritional depletion as a short IPI may not give mothers adequate time to replenish essential nutrients such as folate and iron leading to an increased risk of PTB. Hogue and colleagues additionally found that African American women are more apt to have shorter IPIs compared to Caucasian women, and are more likely to have IPIs of < 6 months or < 12 months. This increased likelihood of short IPI, combined with the association of short IPIs with increased risks of PTB, lead the authors to suggest that birth spacing interventions could help lower the risk of PTB for African American women by 8 percent and for Caucasian women by 4 percent, thus decreasing the racial gap in preterm birth rates.

Ekwo and Moawad (1998) designed a study to measure the relationship between IPI and preterm birth in black and white women. Their study was unique in that IPIs between the first-second, second-third, and third-fourth pregnancies were included in the research. Study subjects were Caucasian and African American women with complete reproductive history records who delivered singleton infants in the University of Chicago Hospital Perinatal Network between January 1988 and December 1993. Research showed that premature birth rates among blacks increased significantly from the first pregnancy (18.2%) to the second pregnancy (30.5%), but decreased for the third (24.5%) and fourth (25%) pregnancies. In comparison, PTB rates for whites did not vary by parity and

remained between 9.8% and 11.7% with the exception of that of the fourth pregnancy which was unreliable due to small sample size. There was significantly increased risk of PTB associated with an IPI less than three months; however this risk was the same for black and white women. Risk of PTB was not significantly increased in African American mothers with an IPI of less than nine months compared to African American mothers with an IPI of greater than nine months. This finding is in contrast to the Rawlings et al. (1995) study which found that IPIs of less than nine months were significantly associated with PTB in African American women. PTB rates of African American women with IPIs of less than or equal to six months were found to be significantly greater than PTB rates of African American women with IPIs greater than six months. However, logistic regression analysis showed that this association became nonsignificant when controlling for maternal race and previous preterm birth. When additionally controlling for census tract income \leq \$10,000, maternal smoking status, and late or no prenatal care, the odds of PTB for an African American mother with an IPI of less than six months is 1.67 times that of an African American mother with an IPI over six months. Ekwo and Moawad (1998), like Rawlings et al. (1995), briefly highlight the significant effect of history of preterm birth and low birth weight on ABO, yet do not directly examine the effects of this history and corresponding IPIs on ABO.

The Preterm Prediction Study was a project conducted by the Maternal-Fetal Medicine Network from 1993 to 1996 which focused on studying the demographic, behavioral, and nutritional risk factors for preterm birth in a cohort of 3,000 pregnant women. Goldenberg et al. (2003) analyzed the Preterm Prediction Study in an effort to develop a model that could predict preterm births based on maternal biological and

sociological risk factors. Surprisingly, many of the risk factors commonly associated with PTB were not associated with PTB in this study. These factors include maternal age less than 18 years, smoking, alcohol and drug use, and education. This difference is attributed to weak associations between individual factors and PTB, which in combination with the relatively small sample size, seem nonsignificant. This research also focused on the relationship between previous PTB and subsequent pregnancy outcome. Prior PTB was found to cause a 2.5 –fold increase in risk of subsequent PTB (from 8.8% to 21.7%). The influence of previous PTB was found to be time dependent in that the earlier the preterm birth occurred in the first pregnancy, the higher the risk of preterm birth happening again in the subsequent pregnancy. This study is unique in that it highlights the influence of time in the relationship between prior and subsequent preterm birth.

The majority of the studies examine the relationship between previous preterm birth and subsequent birth outcomes or interpregnancy interval length and subsequent birth outcomes, ignoring the possible multiplicative effect of the two exposures on adverse birth outcomes. From previous research, it stands to reason that a high number of African American women are at high risk of preterm birth and low birth weight because they are more likely to have preterm births and shorter interpregnancy intervals. Therefore, the outcome of this research could have a positive impact on countless future pregnancies by influencing public health interventions to decrease rates of preterm birth and increase pregnancy spacing in the African American community.

Methods

Study Population

This study was conducted using data from the Pregnancy Risk Assessment Monitoring System (PRAMS) database. Founded in 1987, PRAMS is a surveillance project of the Centers for Disease Control and Prevention (CDC) which collects data on maternal attitudes and experiences before, during, and after pregnancy from women across the nation. Each participating state conducts a stratified random sample of live births by means of a mailed questionnaire sent to women approximately 3-6 months after delivering. Although stratification variables differ across states, all oversample for low birth weight infants. Thus, analyses must be weighted to account for the different sampling proportions.

Study participants consisted of women who had a live, singleton birth between the years of 2004 and 2010, had previously delivered at least one live infant, had an interbirth interval of less than ten years, and were 18 years or older at their most recent birth. Additionally, subjects who did not provide their specific race, namely those who identified themselves as mixed race or other race, were excluded from the study. Women from the state of Vermont, North Dakota, and Massachusetts were not included in this study. The state of Vermont did not release any data on the ethnicity of their PRAMS participants and all participants from Vermont were removed from this study. North Dakota and Massachusetts did not submit any information to PRAMS during the years investigated. Based on these criteria there were 11,063 women eligible for the study.

Data Description

Two perinatal outcomes were evaluated in this study: low birth weight, characterized by birth weight below 2,500 grams (g), and preterm birth, defined as birth before 37 weeks gestational age. These outcomes are known to heavily influence infant mortality and morbidity and they are important risk factors for numerous health problems in children and adolescents [Goldenberg and McClure, 2010; Ananth and Vintzileos, 2006; Breslau et al, 2004]. PRAMS groups all its gestational age and birth weight data according to National Association for Public Health Statistics and Information Systems (NAPHSIS) standards. Hence, gestational age data was divided into four categories: moderate PTB (≤ 33 weeks), late PTB (34-36 weeks), normal gestational age (37-42 weeks), and late gestational age (≥ 43 weeks). Birth weight data ranged from 227g to 7,249g and was grouped in 250g increments. Subjects were further sorted into five groups: extreme LBW (≤ 999 g), very LBW (1,000-1,499g), moderate LBW (1,500-2,499g), normal birth weight (2,500-3,999g), and large birth weight ($\geq 4,000$ g) [Nabukera et al., 2009]. Birth spacing, one of the main confounders of interest in this study, was represented by a last live birth variable which measured the years between deliveries for each subject also known as the interbirth interval (IBI). The second confounder of interest assessed the gestational age of the child born immediately prior to the current birth and determined if the older child was born preterm.

Thirteen additional maternal reproductive risk factors were evaluated as potential confounders. Maternal race was divided into eleven different categories: African American, Alaskan native, American Indian, Caucasian (reference), Chinese, Filipino, Hawaiian, Japanese, other Asian, mixed race, and other race. These categories were

further condensed into: Alaskan Native and American Indian (AN/AI), Asian, Black, and White.. Income was grouped into three categories based loosely upon 2010 federal poverty guidelines: income \leq \$24,999, $\$25,000 \leq$ income \leq \$49,999 (reference), and income \geq \$50,000. Maternal BMI was clustered according to 2011 CDC guidelines [CDC, 2011] and were classified as: underweight (BMI $<$ 29.8), normal (reference, $19.8 \leq$ BMI \leq 26), overweight ($26 <$ BMI \leq 29), and obese (BMI $>$ 29). Maternal age was split into five NAPHISIS categories: 18-19 years of age, 20-24 years of age, 25-29 years of age (reference), 30-34 years of age, 35-39 years of age, and \geq 40 years of age. The number of children for each subject was also categorized according to NAPHISIS as one previous live birth, two previous live births (reference), three previous live births, four previous live births, five previous live births, six and seven previous live births, and eight and nine previous live births. The study population's prenatal care (PNC) seeking behavior was divided into tertiles: sought no PNC, sought PNC early (months 1-4, reference), and sought PNC late (months 5-9). The maternal education variable was stratified into three levels: low education (\leq 8 years of schooling), medium education (9-12 years of schooling, referent), and high education (\geq 13 years of schooling). Marital status, smoking habits during pregnancy, drinking habits during pregnancy, miscarriage within the last 12 months, history of diabetes, and history of hypertension were also considered as potential confounders.

Statistical Analysis

Descriptive analysis was performed to obtain distributions of key variables for the study population. A weighted forward elimination approach was used to obtain reduced logistic regression models for both outcome variables. All analyses were weighted using a weight variable provided that accounts for differential sampling, differential response rates across strata, and an additional weight to reflect the final count of live births in each stratum once all births occur during the year. All covariates in the model were evaluated at a 5% level of significance. To assess collinearity, variance inflation factors for each predictor were examined then a collinearity macro was used on the model [Kleinbaum et al. 2008, Kleinbaum et al. 2010]. No interaction terms between independent variables were included in this model because, when added to the fifteen predictors in this model, the high number of covariates caused the model to be unable to converge without the use of ridging techniques which significantly detract from the validity of the resulting odds ratios and variance estimates. Analyses were conducted using Statistical Analysis Software (SAS) Version 9.3.

Results

Descriptive statistics for the 11,063 study participants are shown in Table 1. At their time of entry into PRAMS, the majority of subjects were white (69.8%), married (69.1%), had a high level of education (57.0%), and one previous child (56.3%). Pluralities of maternal characteristics included age 25 to 29 (32.0%) and normal BMI (47.1%). Over eleven percent (11.3 %) of women included in the study bore their previous child preterm. 11.5% of women had an interpregnancy interval of one year or less, of which 0.1 % had less than one year between pregnancy, compared to 62.9% of women who waited the recommended two to four years between births[Zhu et al., 1999].

Of the over ten thousand births examined in this study, approximately 7.2% were found to be preterm and 5.0% produced low birth weight infants. As seen in Table 2, there were noticeable differences in PTB prevalence across maternal race with Blacks having the highest proportion of moderate and late PTB (3.1% and 7.2%, respectively) and Whites having the lowest proportion of moderate and late PTB (1.2% and 5.0%, respectively). Table 3 shows parallel trends in low birth weight with African Americans again having the highest rates of extreme LBW (0.8%), very LBW (0.8%), and moderate LBW (7.4%). Dissimilarly however, Whites only had the lowest prevalence of moderate LBW (3.4 %) with Asians having the lowest proportions of extreme LBW and very LBW (0.1% and 0.2%, respectively).

A logistic regression model containing interbirth interval, previous child's preterm birth status, maternal race, marital status, maternal age, miscarriage status, maternal education, number of previous live births, smoking status during pregnancy, drinking status during pregnancy, maternal history of hypertension, income, PNC seeking

behavior, maternal history of diabetes, and maternal BMI was used to model the subsequent child's preterm birth status. All covariates were evaluated at a 5% significance level. The reduced PTB model contained the following significant variables: interbirth interval, previous child's preterm birth status, , maternal age, number of previous live births, maternal history of hypertension, maternal history of diabetes, and maternal BMI (Table 4). Another logistic regression model containing the aforementioned fifteen risk factors was used to model the subsequent child's low birth weight status. Again, all covariates were evaluated at a 5% significance level. The reduced LBW model contained the following significant variables: interbirth interval, previous child's preterm birth status, maternal race, maternal age, smoking status during pregnancy, maternal history of hypertension, income, and maternal BMI (Table 5)

Table 6 shows the adjusted odds ratios calculated using the reduced logistic regression model which controlled for the two variables of interest, previous PTB status and IBI length, as well as maternal race, age, education, BMI, income, marital status, smoking and drinking habits during pregnancy, history of diabetes and hypertension, miscarriage history, PNC seeking behavior, and previous number of live births. IBI was not found to be significantly associated with PTB ($p = 0.067$) and only an IBI of four years was found to be statistically significantly different from the reference of 2 years ($p = 0.002$). The direction of the associations were as hypothesized, but all confidence intervals save that of IBI = 4 [CI: (0.35, 0.83)] included 1.0. For women whose previous child was born preterm, IBIs of one year, three years, and five years had non-significantly increased odds of subsequent PTB which were 1.35 times [CI: (0.59, 3.06)] 1.13 times [CI: (0.56, 2.82)], and 1.50 times [CI: (0.66, 3.38)] that of women whose IBI

was two years, respectively. IBIs of six to seven years [aOR = 1.41, CI: (0.64, 3.09)] and eight to nine years [aOR = 1.27, CI: (0.51, 3.21)] also had higher odds of subsequent PTB, albeit not statistically different from the referent group. Subjects with IBIs of four years were found to have similar odds of subsequent PTB compared to those whose had a two year IBI [aOR = 0.77, CI: (0.36, 1.62)]. Unfortunately, the sample size for IBIs of less than one year was too small to obtain an odds ratio for this subset of the population. For women whose previous child had a normal gestational age, those with IBIs of less than one year were found to have 1.63 times [CI: (0.33, 7.95)] higher odds of subsequent PTB, however these increased odds were not significant ($p = 0.320$). IBIs of four years [aOR = 0.50, CI: (0.30, 0.83), $p = 0.023$] and five years [aOR = 0.50, CI: (0.32, 0.79), $p=0.012$] significantly decreased the odds of subsequent PTB. The previous child's gestational age was seen to have an effect on the odds of the subsequent child's PTB status across all IBIs. Women whose previous child was born preterm had higher odds of a subsequent PTB for each IBI examined. IBIs of five years produced the largest difference in odds ratios as mothers whose previous child was preterm with an non-significant adjusted odds ratio of 1.50 [CI: (0.66, 3.38)] and mothers whose previous child had a normal gestational age had an significant adjusted odds ratio of 0.50 [CI: (0.32, 0.79), $p=0.012$]. Subjects with IBIs of three years had the smallest difference with previous PTB subjects having a non-significant adjusted odds ratio of 1.13 [CI: (0.56, 2.82)] compared to subjects without a previous PTB who had a non-significant adjusted odds ratio of 0.89 [CI: (0.55, 1.42)].

Previous PTB status, IBI length, maternal race, age, education, BMI, income, marital status, smoking and drinking habits during pregnancy, history of diabetes and

hypertension, miscarriage history, PNC seeking behavior, and previous number of live births were also controlled for when evaluating the odds of having the subsequent child being low birth weight. Unlike subsequent PTB, IBI was found to be significantly associated with subsequent LBW ($p = 0.004$), but only an IBI of less than one year was found to be statistically significantly different from the reference of 2 years. Again, the direction of the associations were as hypothesized but, except for that of IBI less than 1 [CI: (1.251, 17.214)], all confidence intervals encompassed 1.0. Women whose previous child was born preterm and had an IBI of one year were found to have higher odds of having a LBW infant [aOR = 1.90, CI: (0.81, 4.43)]; however these odds were not statistically different from the referent group (Table 7). Subjects with IBIs of three years, five years, and eight to nine years had non-significantly increased odds of subsequent LBW which were 1.76 times [CI: (0.87, 3.58)], 1.83 times [CI: (0.74, 4.53)], and 2.02 times [CI: (0.86, 4.73)] that of women whose IBI was two years, respectively. Mothers with IBIs of four years [aOR = 0.63, CI: (0.31, 1.30)] and six to seven years [aOR = 0.81, CI: (0.41, 1.61)] were found to have odds of subsequent LBW similar to the referent group. Again, the sample size for IBIs of less than one year was too small to obtain an odds ratio for this subset of the population. For women whose previous child had a normal gestational age, a non-significant change in odds of subsequent LBW was seen with women with an IBI of less than two years whose odds were 2.58 times [CI: (0.44, 15.06)] and 1.06 times [CI: (0.67, 1.67)] that of women with a two year IBI, respectively. IBI of five years [aOR = 1.32, CI: (0.74, 2.36)], six to seven years [aOR = 1.14, CI: (0.72, 1.80)], and eight to nine years [aOR = 1.54, CI: (0.88, 2.70)] were also seen to

increase odds of subsequent LBW, though these increases were determined to be statistically similar to the referent group as all the confidence intervals included 1.0.

When using the aforementioned reduced logistic regression model to analyze subsequent PTB, it was determined that maternal race alone was not a significant predictor of subsequent PTB ($p=0.510$) and no minority races were found to be statistically different from the White race. The direction of the associations were as expected, but all confidence intervals included 1.0. Regardless of the previous child's gestational age, African American women had the highest odds of having a subsequent PTB when compared to AI/AN and Asian women, using White women as a referent group (Table 8). Though higher, these odds were not statistically significantly different than that of White women ($p = 0.218$). Black women whose previous child was born preterm had 1.21 times [CI: (0.68, 2.13)] the odds of having a subsequent PTB compared to White women. Black women whose previous child had a normal gestational age had 1.35 times [CI: (0.94, 1.93)] the odds of their subsequent child being born preterm compared to White women. Across all maternal races, mothers whose previous child was born preterm had similar odds of a subsequent PTB compared to mothers whose previous child had a normal gestational age. There were no statistically significant differences, although the results were against the hypothesis of increased risk with a previous PTB. African American women had the highest odds of having a subsequent LBW infant irrespective of their previous child's preterm birth status (Table 9). Black mothers whose previous child was preterm were found to have over 200% higher odds [aOR = 2.05, CI: (1.21, 3.45), $p=0.0001$] of subsequent LBW when compared to the referent group. Black mothers whose previous child was not born preterm were also seen to have significantly

higher odds of subsequent LBW [aOR = 2.13, CI: (1.51, 3.01), $p < 0.0001$]. AI/AN women had the lowest odds of subsequent LBW of all races examined with previous PTB subjects having significantly lower odds [aOR = 0.44, CI: (0.23, 0.84), $p = 0.002$] compared to White women. AI/AN mothers with a normal previous birth had 0.74 times the odds of the subsequent ABO [CI: (0.45, 1.22)]; however these odds were not significant as the accompanying confidence interval included one. The odds of subsequent LBW were not found to be significant for Asian women with either previous preterm birth status.

Discussion

A number of women were excluded from the study because they possessed characteristics which would have biased the data. Only singleton births were included in the study because plural births have been shown to have rates of PTB and LBW in excess of 50% [Blondel and Kaminski, 2002]. Subjects under the age of 18 were also excluded from the dataset as teenage (≤ 17 years old) mothers have been found to have significantly higher rates of PTB and LBW [Fraser et al, 1995]. Women in this study had IBIs of less than ten years because IBI greater than ten years may indicate factors that would bias the study outcome such as infertility or use of assisted reproductive technologies. To be considered in this study, the subject's most current birth had to be alive at time of entry into PRAMS. This decreased the chance that any child included in this study was born very preterm or had an extremely low birthweight due to other morbidity factors.

The results of this study suggest that, regardless of the previous child's preterm birth status, women with an IBI of four years have the lowest odds for their subsequent child being preterm. These significant findings agree with the results of Zhu et al. (1999) IBIs of less than one year had the highest odds of subsequent PTB and LBW, which concurs with previous literature (Zhu et al, 1999. Hogue et al., 2011. Ekwo and Moawad, 1998.). While IBIs of less than one year were found to significantly affect the odds of having a subsequent LBW infant ($p = 0.029$), they were not deemed to significantly impact the odds of subsequent PTB ($p = 0.127$). This PTB finding agrees with Kristensen et al. (1995) who determined that the risk of a preterm second birth in women with a preterm first birth did not differ significantly. However, these authors did find that the type of preterm birth in the first pregnancy (idiopathic vs. indicated) did

affect the rates of repeated PTB and LBW infants. Though Kristensen et al. did not look at risk of PTB across various IPI lengths, their findings are still applicable as only an IBI of four years was found to be significantly associated (i.e., protective) with subsequent PTB in this study.

Much like Nabukera et al.(2008), racial disparities in ABOs were found in this study. Irrespective of the previous child's preterm birth status, African American women had the highest odds ratios [aOR = 1.25, CI: (0.93, 1.69)]for subsequent PTB; however these odds were not found to be significant ($p=0.220$). Black mothers also had the highest odds [aOR = 1.96, CI: (1.47, 2.62)] of subsequent LBW which were determined to be significant ($p<0.0001$), regardless of the previous child's gestational age. The literature has presented a number of theories as to why African American women experience higher odds of PTB and LBW, the most popular explanations being differences in socio-economic status (SES) and maternal stress. Berg et al. (2001) suggested that SES is to blame in part for racial disparities in prevalence of very low birth weight infants as African American women in their study did not report more behavioral risk factors than White women, yet had significantly higher rates of very low birth weight children. Though SES may have an impact in this study as well, it doesn't fully explain the racial disparities in odds of subsequent PTB and LBW as Alaskan Native/American Indians had the highest proportion (63.7%) of subjects reporting an income of less than \$25,000, yet they still had lower odds of subsequent PTB and LBW than African American women. Mulder et al. (2002) performed a literature review which revealed that pregnant women with high stress and anxiety levels are at increased risk for spontaneous abortion, preterm labor, and growth-retarded infants. The general stress of being pregnant in combination

with the strains of a low SES status could explain in part the higher odds for African American women. This theory could also explain the higher odds of subsequent ABOs for women whose previous child was born preterm compared to women whose previous child had a normal gestational age. It stands to reason that the stress of pregnancy may be even higher for mothers whose previous child was born preterm, especially if the previous child's gestational age led to them needing additional care in a hospital, as the mother may worry throughout her pregnancy as to the health of her subsequent child.

One of the biggest factors which influenced this study is the statistical software used to do analyses. PRAMS provided complex survey data which was analyzed with SAS software rather than statistical software specifically designed to manage complex data such as SUDAAN. Due to their different methods of variance estimation, SAS and SUDAAN produce different results when given strata with only the primary sampling unit. This variation often causes SAS to produce wider confidence intervals than would SUDAAN which could significantly impact significance levels in the study by causing confidence intervals to include 1.0 when they otherwise would not.

Another limitation of this study is its measurement of birth spacing. Ideally, rather than interbirth interval this study would use interpregnancy interval as a main predictor which would produce more detailed and informative results as IPIs are measured in months rather than years. However, creating an IPI from an IBI requires a knowledge of exact gestational age which was not available in PRAMS since it categorized all gestational age data by NAPHSIS standards. An IBI of < 1 year indicates an IPI of < 3 months if the subsequent birth was full-term but an IPI of 4-6 months if the subsequent birth was preterm. Similarly, an IBI of 1 year indicates an IPI of 3-15 months if the

subsequent birth is full-term but 5-17 months if the subsequent birth was preterm. This discrepancy may also help to explain the nonsignificant findings for short IBIs when studies of IPIs have found significant elevation of risk for PTB.

Having no interactions in either model, despite interactions existing between covariates in said model, also served as a limitation in this study because the model was less able to accurately represent the relationship between the previous PTB and IBI length and subsequent ABOs. This exclusion of interactions was necessary however as the addition of appropriate interactions to the model caused such high collinearity that the model was no longer able to converge.

Conclusion

The logistic regression models created in this study were able to describe how previous preterm birth and interbirth interval length influence subsequent ABOs. Subjects with IBIs of four years were shown to have the lowest statistically significant odds of having a subsequent PTB (aOR =0.67, CI: (0.35, 0.83), $p = 0.002$). IBIs of less than one year were shown to have the highest odds of subsequent PTB [aOR = 2.33, CI: (0.62, 8.79)]; however these odds were not found to be significant ($p=0.127$). Women with IBIs of less than one year also had significantly ($p=0.028$) increased odds of subsequent LBW [aOR = 4.64, CI: (1.25, 17.21)]. African American women were found to have the highest odds of having a subsequent PTB when compared to AI/AN, Asians, and Whites, regardless of their previous preterm birth status. However, these odds were not statistically different from the reference group, White women. Black women did have significantly higher odds of having a subsequent LBW infant [aOR =1.96, CI: (1.47, 2.62), $p<0.0001$]. The results of this study, if confirmed, suggest that the ideal IBI is 4 years.

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Tables

Table 1: Demographic characteristics of study population (n=11,063)

Variable	Frequency	Percentage	Variable	Frequency	Percentage	Variable	Frequency	Percentage
<i>Previous Child Born Preterm</i>			<i>Miscarriage within last 12 months</i>			<i>Drank During Pregnancy</i>		
Yes	1601	11.3	Yes	1558	13.2	Yes	833	8.0
No	8685	82.8	No	9290	85.2	No	9975	89.7
Missing	777	5.9	Missing	215	1.5	Missing	255	2.2
<i>Interbirth Interval (years)</i>			<i>Maternal Age (years)</i>			<i>Maternal BMI (kg/m²)</i>		
0	26	0.1	18-19	260	2.5	Underweight (<19.8)	1025	9.5
1	1366	11.4	20-24	2143	18.1	Normal (19.8-26)	5050	47.1
2	2854	27.4	25-29	2989	32.0	Overweight (>26-29)	1526	14.1
3	2244	22.7	30-34	2415	28.2	Obese (>29)	2778	24.0
4	1355	12.8	35-39	2656	15.8	Missing	684	5.2
5	922	8.5	40+	598	3.4			
6 to 7	1165	9.5	Missing	2	0.0			
8 to 9	692	5.7						
Missing	439	2.08						
<i>Maternal Race</i>			<i>Maternal Education</i>			<i>Income</i>		
American Indian/ Alaskan Native	1650	3.3	Low (0-8 years)	438	3.4	\$<24,999	3895	31.4
Asian	730	5.2	Medium (9-12 years)	4770	38.9	\$25,000 to \$49,999	2266	21.1
Black	2143	21.5	High (13+ years)	5647	57.0	≥\$50,000	4172	42.5
White	6214	69.8				Missing	730	5.1
Missing	326	0.2						
<i>Marital Status</i>			<i>No. of Previous Live Births</i>			<i>Sought Prenatal Care</i>		
Married	7384	69.1	1	5516	56.3	Early (0-5 months)	9466	89.4
Not Married	3679	30.9	2	2928	26.5	Late (6-9 months)	1070	8.1
			3 to 5	2216	15.3	No Prenatal Care Sought	140	0.9
			6 or more	313	1.6	Missing	387	1.6
			Missing	90	0.3			
<i>Maternal History of Hypertension</i>			<i>Smoked During Pregnancy</i>			<i>Maternal History of Diabetes</i>		
Yes	724	4.2	Yes	1696	13.0	Yes	446	4.3
No	10336	95.8	No	9119	84.8	No	10614	95.7
Missing	3	0.0	Missing	248	2.2	Missing	3	0.0

Table 2: Prevalence of preterm birth across racial categories (n =10,715)

	AI/AN† (%)	Asian‡ (%)	Black (%)	White (%)	Total	
Gestational Age Categories	Moderate PTB (≤ 33 weeks)	116 (2.5)	47 (1.2)	289 (3.1)	367 (1.2)	819 (1.7)
	Late PTB (34-36 weeks)	179(6.9)	91(5.4)	327(7.2)	632(5.0)	1229 (5.5)
	Normal Age (37-42 weeks)	1326 (89.3)	588 (93.2)	1523 (89.6)	5161 (93.6)	8598 (92.6)
	Late Age (≥43 weeks)	24 (1.23)	2 (0.1)	2(0.1)	41(0.3)	69 (0.2)
	Total	1650 (3.3)	730 (5.2)	2143 (21.6)	6214 (69.9)	10715 (100.0)

† AI/AN = American Indian and Alaskan Native

‡ Includes Chinese, Filipino, Hawaiian, Japanese, and other Asian

Table 3: Prevalence of low birth weight across racial categories (n =10,737)

	AI/AN† (%)	Asian‡ (%)	Black (%)	White (%)	Total
Extreme LBW (<999 g)	32 (0.5)	13 (0.1)	81 (0.8)	83 (0.2)	209 (0.3)
Very LBW (1,000 g-1,499g)	19 (0.3)	9 (0.2)	82 (0.8)	96 (0.3)	206 (0.4)
Moderate LBW (1,500g-2,499g)	198 (3.5)	165 (4.1)	622 (7.4)	996 (3.4)	1981 (4.3)
Normal (2,500g - 3,999g)	1106 (76.1)	507 (90.0)	1261 (84.8)	4363 (83.7)	7237 (84.0)
Large (≥4,000g)	295 (19.6)	36 (5.6)	97 (6.1)	676 (12.4)	1104 (10.9)
Total	1650 (3.3)	730 (5.2)	2143 (21.6)	6214 (70.0)	10737 (100.0)

† AI/AN = American Indian and Alaskan Native

‡ Includes Chinese, Filipino, Hawaiian, Japanese, and other Asian

Table 4: Significant results of the logistic regression model evaluating subsequent preterm birth ($\alpha = 5\%$). $n = 8,113$.

Variable	Estimate	Standard Error	p-value
Intercept	-3.81	0.33	<0.0001
<i>Previous Child Born Preterm</i>			
Yes	1.73	0.14	<0.0001
No	-	-	-
<i>Interbirth Interval (years)</i>			
0	0.90	0.59	0.127
1	-0.07	0.18	0.709
2	-	-	-
3	0.01	0.16	0.955
4	-0.56	0.18	0.002
5	-0.31	0.17	0.077
6 to 8	-0.07	0.19	0.690
7 to 9	0.05	0.21	0.829
<i>Maternal History of Hypertension</i>			
Yes	1.12	0.19	<0.0001
No	-	-	-
<i>Number of Previous Live Births</i>			
1	-0.30	0.14	0.035
2	-	-	-
3 to 5	-0.11	0.15	0.476
≥ 6	0.54	0.31	0.082
<i>Maternal Age (years)</i>			
18 to 19	-0.83	0.31	0.008
20 to 24	-0.21	0.16	0.199
25 to 29	-	-	-
30 to 34	0.03	0.14	0.849
35 to 39	0.34	0.14	0.017
≥ 40	0.59	0.23	0.012
<i>Maternal History of Diabetes</i>			
Yes	0.57	0.26	0.032
No	-	-	-
<i>Maternal BMI (kg/m²)</i>			
Underweight (<19.8)	0.34	0.16	0.038
Normal (19.8-26)	-	-	-
Overweight (>26-29)	-0.12	0.14	0.406
Obese (>29)	-0.17	0.11	0.141
<i>Marital Status</i>			
Married	-0.48	0.18	0.009
Not Married	-	-	-

Table 5: Significant results of the logistic regression model evaluating subsequent low birth weight ($\alpha = 5\%$). $n = 8,119$.

Variable	Estimate	Standard Error	p-value	Variable	Estimate	Standard Error	p-value
Intercept	-4.43	0.27	<0.0001	Maternal Age (years)			
Previous Child Born Preterm				18 to 19	-0.42	0.28	0.131
Yes	1.39	0.14	<0.0001	20 to 24	-0.01	0.14	0.949
No	-	-	-	25 to 29	-	-	-
Interbirth Interval (years)				30 to 34	0.07	0.13	0.579
0	1.26	0.57	0.029	35 to 39	0.24	0.15	0.099
1	-0.02	0.19	0.904	≥ 40	0.31	0.16	0.052
2	-	-	-	Maternal BMI (kg/m ²)			
3	-0.25	0.17	0.125	Underweight (<19.8)	0.58	0.15	0.000
4	-0.67	0.17	0.000	Normal (19.8-26)	-	-	-
5	0.05	0.20	0.809	Overweight (>26-29)	-0.42	0.13	0.001
6 to 8	-0.28	0.16	0.080	Obese (>29)	-0.13	0.11	0.248
7 to 9	0.20	0.19	0.303	Maternal Race			
Maternal History of Hypertension				AI/AI†	-0.56	0.14	<0.0001
Yes	1.08	0.18	<0.0001	Asian ‡	0.01	0.14	0.924
No	-	-	-	Black	0.61	0.10	<0.0001
Income				White	-	-	-
≤\$24,999	0.17	0.11	0.105	Smoke During Pregnancy			
\$25,000 to \$49,999	-	-	-	Yes	0.5614	0.18	0.002
≥\$50,000	-0.20	0.10	0.050	No	-	-	-
Sought Prenatal Care							
Early (0-5 months)	-	-	-				
Late (6-9 months)	-0.22	0.16	0.177				
No Prenatal Care Sought	0.50	0.25	0.043				

† AI/AI = American Indian and Alaskan Native

‡ Includes Chinese, Filipino, Hawaiian, Japanese, and other Asian

Table 6: Results of logistic regression analysis of interbirth interval and previous child's preterm birth status as a risk factor for preterm birth weight in current pregnancy †

		Previous PTB			No Previous PTB		
		OR	95% CI	p-value	OR	95% CI	p-value
Interbirth Interval	0	‡	‡		1.63	(0.33, 7.95)	0.320
	1	1.35	(0.59, 3.06)	<.0001	0.74	(0.48, 1.13)	0.648
	2	-	-	-	-	-	-
	3	1.13	(0.56, 2.82)	<.0001	0.89	(0.55, 1.42)	0.635
	4	0.77	(0.36, 1.62)	<.0001	0.50	(0.30, 0.83)	0.023
	5	1.50	(0.66, 3.38)	<.0001	0.50	(0.32, 0.79)	0.012
	6 to 7	1.41	(0.64, 3.09)	<.0001	0.72	(0.43, 1.23)	0.628
	8 to 9	1.27	(0.51, 3.21)	<.0001	0.92	(0.52, 1.63)	0.584

†: Controlled for previous PTB status, IBI length, maternal race, age, education, BMI, income, marital status, smoking and drinking habits during pregnancy, history of diabetes and hypertension, miscarriage history, PNC seeking behavior, and previous number of live births.

‡: Sample size too small to obtain

OR

Table 7: Results of logistic regression analysis of interbirth interval and previous child's preterm birth status as a risk factor for low birth weight in current pregnancy[†]

		Previous PTB			No Previous PTB		
		OR	95% CI	p-value	OR	95% CI	p-value
Interbirth Interval	0	‡	‡		2.58	(0.44, 15.06)	0.311
	1	1.90	(0.81, 4.43)	0.0006	1.06	(0.67, 1.67)	0.602
	2	-	-	-	-	-	-
	3	1.76	(0.87, 3.58)	<.0001	0.81	(0.49, 1.33)	0.089
	4	0.63	(0.31, 1.30)	<.0001	0.73	(0.44, 1.20)	0.025
	5	1.83	(0.74, 4.53)	0.0001	1.32	(0.74, 2.36)	0.653
	6 to 7	0.81	(0.41, 1.61)	<.0001	1.14	(0.72, 1.80)	0.858
	8 to 9	2.02	(0.86, 4.73)	<.0001	1.54	(0.88, 2.70)	0.252

[†]: Controlled for previous PTB status, IBI length, maternal race, age, education, BMI, income, marital status, smoking and drinking habits during pregnancy, history of diabetes and hypertension, miscarriage history, PNC seeking behavior, and previous number of live births.

‡: Sample size too small to obtain OR

Table 8: Results of logistic regression analysis of maternal race and previous child's preterm birth status as a risk factor for preterm birth in current pregnancy

Maternal Race		Previous PTB			No Previous PTB		
		OR	95% CI	p-value	OR	95% CI	p-value
	AI/AN†	0.55	(0.25, 1.24)	0.132	1.31	(0.88, 1.95)	0.494
	Asian ‡	0.90	(0.39, 2.07)	0.951	1.13	(0.62, 2.04)	0.817
	Black	1.21	(0.68, 2.13)	0.140	1.35	(0.94, 1.93)	0.341
	White	-	-	-	-	-	-

† AI/AN = American Indian and Alaskan Native

‡ Includes Chinese, Filipino, Hawaiian, Japanese, and other Asian

Table 9: Results of logistic regression analysis of maternal race and previous child's preterm birth status as a risk factor for low birth weight infant in current pregnancy

Maternal Race		Previous PTB			No Previous PTB		
		OR	95% CI	p-value	OR	95% CI	p-value
	AI/AN†	0.44	(0.23, 0.84)	0.002	0.74	(0.45, 1.22)	0.009
	Asian ‡	0.96	(0.42, 2.18)	0.979	1.23	(0.79, 1.92)	0.798
	Black	2.05	(1.21, 3.45)	0.000	2.13	(1.51, 3.01)	<.0001
	White	-	-	-	-	-	-

† AI/AN = American Indian and Alaskan Native

‡ Includes Chinese, Filipino, Hawaiian, Japanese, and other Asian