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Sarah Haight Date

The Relationship Between Short Interpregnancy Intervals and

Adverse Pregnancy Outcomes by Maternal Age in the United States, 2013-2015

By

Sarah Haight

Master of Public Health

Epidemiology

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

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2017

Abstract

The Relationship Between Short Interpregnancy Intervals and Adverse Pregnancy Outcomes by Maternal Age in the United States, 2013-2015

By Sarah Haight

Objective: To examine the association between interpregnancy interval (IPI) and adverse pregnancy outcomes by maternal age (15-39) to U.S. mothers on their 2nd – 4th live birth.

Methods: Publically available birth certificate data and multivariable modified Poisson regression were utilized to assess risk of preterm birth (PTB), defined as <37 weeks' gestation, and severe maternal morbidity (having any of the following conditions: gestational hypertension, gestational diabetes, maternal transfusion, perineal laceration, ruptured uterus, and unplanned hysterectomy) by length of IPI (0-23 months from last live birth to conception of next pregnancy) for 1,460,135 U.S. singleton births from 2013-2015.

Results: Compared to 18-23 month IPIs, overall adjusted risk ratios (aRR) for PTB for 12-17, 6-11, and <6 month IPIs were 1.04 (95% Confidence Interval (CI): 1.02, 1.06), 1.17 (95% CI: 1.15, 1.19) and 1.55 (95% CI: 1.52, 1.58), respectively. Across single years of maternal age, PTB risk was elevated for IPIs <6 months (aRR range: 1.28-1.75). There was also elevated PTB risk for IPIs 6-11 months among ages 19-34 (aRR range: 1.10-1.27) but not among ages 35 and older. There was a protective association of maternal morbidity with 6-17 month IPIs among ages 20-37 (aRR range: 0.81-0.95) and with <6 month IPIs for ages 20-28 (aRR range: 0.88-0.93).

Conclusions: All mothers may be advised to avoid a <6 month IPI to protect the next child from PTB risk. However, for women older than 35, when compared to an IPI of 18-23 months, an IPI of 12-17 months may not increase PTB risk, but may reduce maternal morbidity risk.

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List of Abbreviations

IPI	Interpregnancy Interval
LARC	Long-acting Reversible Contraceptives
LMP	Last Menstrual Period
NCHS	National Center for Health Statistics
PTB	Preterm Birth
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organization
WIC	The Special Supplement Nutrition Program for Women, Infants, and Children

CHAPTER I. BACKGROUND

The World Health Organization (WHO) recommends that individuals and couples making choices regarding pregnancy timing consider health risks, benefits, age, fecundity, fertility aspirations, access to health services, child-rearing support, social and economic circumstances, and personal preferences (1). In general, after a live birth, the WHO recommends waiting at least 24 months to reduce the risk of adverse maternal, perinatal, and infant outcomes before conceiving (1). This recommended length of time avoids the range of intervals associated with the highest risk of poor pregnancy outcomes and is consistent with the WHO/UNICEF (United Nations International Children's Emergency Fund) recommendation of breastfeeding for at least two years (1).

Preterm Birth and Interpregnancy Interval

The length of time before conceiving again after a live birth is more commonly referred to as the interpregnancy interval (IPI). In the current study, this interval is defined as the number of months between the previous live birth and the conception of the subsequent pregnancy (2). Short IPIs, defined as less than 18 months, and long IPIs, defined as greater than 47 months, are associated with adverse neonatal and maternal birth outcomes such as low birthweight, small for gestational age, preterm birth, and maternal morbidities and mortalities (3-8). These associations prompted the formation of the aforementioned WHO guidelines.

The main causal mechanism for the short IPI and preterm birth association is the lack of recovery time between births. After delivery, a woman’s uterus takes time to return to its normal state and repair the inflammation caused by the

previous pregnancy. Mothers experience a depletion of essential vitamins, minerals, and amino acids towards the end of pregnancy and into the following months. As a result of the lack of nutrients, decreased blood volume, and reduced uterine blood flow, women looking to deliver soon thereafter may experience preterm birth, defined as infants born at less than 37 completed gestational weeks (9).

Preterm birth is a pressing public health issue because despite the recent improvements in health outcomes for preterm births, these infants still experience higher rates of infant mortality and neonatal morbidities (10). Preterm infants exhibit higher prevalence of temperature instability, respiratory distress, apnea, hypoglycemia, seizures, jaundice, kernicterus, feeding difficulties, periventricular leucomalacia, and re-hospitalizations. As preterm infants grow and develop, they also exhibit a higher prevalence of minor neuro-motor dysfunctions, poor coordination, anxiety, depression, cognitive dysfunctions regarding attention, visual processing, academic progress, and executive function; many of these issues may continue into adolescence and early adulthood (10).

Women with a short IPI compared to women with a 'healthy' IPI of 18-23 months were found to be at a substantially higher risk of preterm birth (4, 11-13). Smith et al. (2003) found this to be the case even amongst women who had a first term live birth, controlling for maternal age, marital status, height, socioeconomic deprivation category, smoking, the previous baby's birthweight, and previous cesarean section (12). Zhu et al. (2005) focused on the association between IPI and preterm birth, stratified by maternal age, and still found a statistically significant J-shaped association pattern within all age groups, suggesting that the association

was not confounded by maternal age (13). However, maternal age in this study was grouped and differences in risk between single years of maternal age were not addressed. These studies suggest that the association between IPI and risk of preterm birth is most likely not due to residual confounding. This view is not universally accepted, however.

Maternal Morbidity and Interpregnancy Interval

In addition to preterm birth, short IPIs pose a unique risk to maternal morbidity, an association that has not been widely studied (14). Maternal morbidity, which include any combination of gestational hypertension, gestational diabetes, maternal transfusion, perineal laceration, ruptured uterus, unplanned hysterectomy or admission to intensive care, can be another result of a mother not having the time to recover from the physiological stress imposed by the previous pregnancy (9, 15, 16). She may have a depletion of maternal nutrient stores and anemia, which in turn, may result in premature rupture of membranes and puerperal endometritis (17, 18). Just a few studies have found women with short IPIs to be at a higher risk of multiple maternal morbidities (3, 19). In 2012, Wendt et al. performed a meta-analysis on the association between IPIs and poor outcomes and reported a lack of high quality, non-observational studies that appropriately controlled for many potential confounders. The researchers found very little research focused on the impact of IPI length on maternal nutrition, morbidity, and mortality such that they performed a meta-analysis only on the association of short IPIs with infant outcomes. They found a statistically significant association of short IPIs with extreme (less than 6 months gestation) and moderate (6-11 months

gestation) preterm birth, low birthweight, stillbirth (fetal loss at 20 weeks of gestation or later), and early neonatal death (death within one week of birth) (7). This meta-analysis highlights the lack of research focused on maternal outcomes.

Sociodemographic Risk Factors

Many sociodemographic factors are associated with IPI length and risk of adverse outcomes including but not limited to maternal age, marital status, education, race and ethnicity, parity, paternity, and parental socioeconomic status. Women with short IPIs are more likely to have more demographic, obstetric, and health service risk factors than women with intervals of 18-59 months (11). These risk factors include, but are not limited to, young age, high parity, unfavorable outcomes of previous pregnancies, lower education, minority race, and tobacco use (13, 20-22).

One sociodemographic factor in particular, race and ethnicity, has been widely studied. Disparities in pregnancy outcomes by race have been attributed to wide differences in socioeconomic status and access to preventive health care (22-25). An early study by Rawlings et al. (1995) discovered a significant difference in risk of preterm birth between intervals less than 6 months and intervals greater than 6 months, but only amongst black mothers. The authors concluded that the strong association between prevalence of preterm delivery and interval length could be largely accounted for by the greater frequency of these outcomes amongst black infants (23). Ekow and Moawad (1998) took this conclusion a step further and concluded no significant association between interval and adverse outcomes and that the difference in rates of preterm birth between black and white mothers was

not due to length of interval, but rather to factors associated with race, many of which are difficult to control for (21).

Opposing Opinions

To account for the association between sociodemographic risk factors and the likelihood of both a short interval and adverse outcomes, many previous studies have adjusted for the aforementioned risk factors. After doing so, many found the relationship between IPI and adverse outcomes to persist (26-28).

Despite these findings, IPI is not universally accepted as an independent risk factor of preterm birth and maternal morbidity. Recent studies have concluded that the variation in birth outcomes might be better explained by risk factors that vary between women, but typically persist between pregnancies, like genetic predisposition, lifestyle, or social conditions (29). To test whether the widely studied association between IPI and adverse outcomes is a matter of confounding, some groups utilized case-crossover studies, and therefore, had each mother serve as her own control. This type of study allowed the researchers to control for genetics, early life exposures, socioeconomic status, and education without actually needing to quantify or categorize these characteristics (29, 30). The results of these studies contested much of the previous literature regarding the relationship between IPI and adverse outcomes and concluded that the harmful effect of very short intervals on adverse outcomes is present, but significantly less than the earlier studies had concluded (6, 27). In particular, Koullali, et al. (2016) found a differentiation between women with previous uncomplicated pregnancies and women with previous complicated pregnancies. They recommended that women

with a history of uncomplicated pregnancies should base their birth spacing decisions on personal desires before obstetric concerns as interval does not have a significant association with adverse outcomes (27).

In a more recent paper, Hanley et al. (2017) used a case-crossover analysis of longitudinally linked records to conclude that previous evidence of increased risk of preterm birth after a short IPI was a result of poor study design and analyses of cross sectional data (30). In an editorial response to this article, Klebanoff (2017) agreed with Hanley (2017), arguing that all studies concluding the harmful effect of short IPI overestimated the association (31). Klebanoff (2017) noted that future research should confirm whether short IPIs affect subsequent pregnancy outcome in women whose initial pregnancy ended before term and whether the effect of short IPIs vary with delivery route (31). The current analysis goes beyond previous research by using a very large sample size to assess the competing risks of maternal age and IPI (6, 27).

Maternal Age

Even fewer studies have addressed how the relationship between short IPI and adverse pregnancy outcomes varies across maternal age, particularly for women in the United States (32). While previous studies have controlled for age, there are no specific guidelines in place given the age of the mother at the beginning of the interval. The current study strives to address the need for a public health message that has yet to be nailed down - given age at delivery, should a woman maintain the suggested interval of 18-23 months or should she shorten that interval to avoid conceiving at an advanced age? Analysis of this relationship is now

possible because IPI became nationally available beginning with the 2003 version of the U.S. Standard Certificate of Birth. Analysts reported that short IPIs (i.e., less than 6 months, 6–11 months, and 12–17 months) were more common among mothers aged 35 and over (5.7%, 16.3%, and 22.1%, respectively) than among mothers who were under age 20 at their previous birth (5.1%, 8.8%, and 8.4%, respectively) (2). Given that approximately half of mothers in their mid-thirties and older have short IPIs, it is important to understand whether they are making healthy choices.

The current study addresses the question of whether older women face greater risk of adverse outcomes from shorter IPIs or from older maternal age. If it is discovered that there is an ideal IPI by maternal age, public health professionals can better advise older women planning to conceive. For example, physicians could be advised to suggest LARC methods of birth control after delivery, to prolong the interval, and in turn, reduce the rates of preterm birth and maternal morbidity.

CHAPTER II. EXTENDED METHODS

Data Source and Study Population

Data were obtained from public use natality files for all U.S. births from 2013-2015. Specific variables regarding IPI became nationally available beginning with the 2003 version of the U.S. Standard Certificate of Birth (33). Therefore, the study population from which participants were drawn includes all women in states (plus the District of Columbia) that had implemented the U.S. 2003 Standard Certificate of Live Birth by 2013 (41 states), 2014 (47 states), or 2015 (48 states) (34-36). In 2015, births using the 2003 version of the birth certificate represented approximately 96.5% of all live births in the United States (35). Natality files include information on maternal demographics, maternal and infant clinical characteristics as well as pregnancy outcomes. This study was exempt from IRB approval as it employed secondary analysis of pre-existing publicly available de-identified data.

Interpregnancy Interval

The IPI was defined as the interval between previous delivery and subsequent conception. Months since last live birth and months since last other pregnancy outcome were collected, separately, on the 2003 version of the birth certificate. Birth intervals are computed for all births of second or higher order from the infant's date of birth (month and year) and the date of the last live birth (month and year). This information is collected directly from the medical record using the facility worksheet (34-36). IPI was calculated by first converting the months since last live birth to weeks (assuming 4.5 weeks per month), imputing a

randomly selected number of weeks (0-3, uniform distribution), and adding that to each 4.5-week month in order to account for variability of number of weeks within a given month. Second, the gestational age of the pregnancy in weeks (see below for details) was then subtracted from the weeks since last live birth to estimate IPI in weeks. Third, IPI in weeks was converted to IPI in months by dividing by 4.5 weeks, in order to be consistent with how IPI since last live birth has been categorized in previous literature (37).

Preterm Birth

One of our adverse outcomes of interest was preterm birth (PTB). PTB was defined as any birth occurring before the 37th completed week of pregnancy, which is consistent with the ICD-9 and ICD-10 definitions (38). Gestational age for PTB determination was obtained from the obstetric estimate as entered by the birth attendant using the maternal obstetric admission history and physical form (39). In 2014, the National Center for Health Statistics (NCHS) transitioned to using the obstetric estimate as the standard, primary measure of gestational age based on validity studies; however it is also available for analysis on 2013 births because 90% of births in 2013 had the obstetric estimate reported in addition to the last menstrual period (LMP) based measure (39). This preterm birth variable was modeled as a dichotomous outcome.

Maternal Morbidity

The other adverse outcome of interest was maternal morbidity. Six morbidity items are separately identified with checkboxes allowing for the reporting of more than one morbidity as well as 'none.' This information is typically

collected directly from the medical record using the facility worksheet (34-36). Maternal morbidity was defined as any combination of gestational hypertension (elevation of blood pressure above normal for age, gender, and physiological conditions diagnosed during pregnancy), gestational diabetes (glucose intolerance requiring treatment diagnosed during pregnancy), maternal transfusion (infusion of whole blood or packed red blood cells associated with labor and delivery), perineal laceration (laceration extending through the perineal skin, vaginal mucosa, perineal body and partially or completely through the anal sphincter or rectal mucosa), ruptured uterus (tearing of the uterine wall), unplanned hysterectomy (surgical removal of the uterus that was not planned prior to the admission) or admission to intensive care (any admission, planned or unplanned of the mother to a facility/unit designated as providing intensive care) (33). Maternal morbidity was recorded by the birth attendant onto the birth certificate using: the delivery record, physician delivery or operative notes; and intake and output forms (33). For 2013 births, we used the individual maternal morbidity items, gestational diabetes, and gestational hypertension to create a composite variable indicating whether at least one maternal morbidity was recorded on the birth certificate. For 2014 and 2015 births, the composite maternal morbidity variable created by the NCHS, gestational diabetes, and gestational hypertension were used to create the maternal morbidity composite variable. This composite variable was determined based on the same individual maternal morbidity items as 2013 with the exception of unplanned operation (34-36). If a mother had at least one of the following, gestational hypertension, gestational diabetes, one of the maternal morbidity single items, or

the maternal morbidity composite item, then she was considered to be positive for maternal morbidity. This composite variable was modeled as a dichotomous outcome.

Maternal Age

In order to assess risk of adverse outcomes by maternal age at the previous delivery, we conducted a back calculation using the maternal age noted on the subsequent birth certificate. According to the data file user guides, if the entered age was deemed implausible (<8 or >65 years) then it was assigned to the mean age of mothers based on data from a previous year within the same race, Hispanic origin, and total birth order. Furthermore, extreme values of age were grouped, 9-11 years are collapsed into "12 years and under" and 50-64 years were collapsed into the category of "50-54 years" (34-36). Since the publicly available birth certificate data files disclose only single year of maternal age, simply subtracting the interval since last live birth from the maternal age ignored the variability within a single year of age (e.g., 30 years and 1 week old versus 30 years and 50 weeks old). Maternal age, gestational age, and a random number generator were utilized to calculate the maternal age at the beginning of the IPI. If a woman was less than 35 at the subsequent delivery, her age in years was converted to her age in weeks and a random number of weeks (0-52, uniform distribution) was added; then the interval since last live birth was subtracted from this age in weeks. Under the assumption that older women may feel a particular urgency to conceive, resulting in earlier conceptions within their single year of age, if a woman was aged 35 years or older at the subsequent delivery, her age in years was converted to her age in weeks and a

random number of weeks was added, but these weeks were restricted to those corresponding to the first half of the year (0-26, uniform distribution). For all women, the interval since last live birth was then subtracted from her newly calculated age in weeks, and this was then converted back into years by rounding down to the nearest birthday. This calculated age, which was based on maternal age at the beginning of the IPI, was the maternal age used for our analysis. In order to address the non-linear relationship between maternal age and our outcomes, the calculated age value was squared; both age and age squared were included as continuous variables in the modeling process.

Race/Ethnicity

Race and ethnicity are reported separately on the birth certificate (34-36). If a woman indicated that she was Mexican, Mexican American, Chicana, Puerto Rican, Cuban, South American, or another Hispanic ethnicity group she was categorized as Hispanic. There are 15 race categories collected on the birth certificate – if a woman indicated she was not Hispanic then she was categorized by her race. This analysis was then restricted to only Hispanic, non-Hispanic Black, and non-Hispanic White women. Race and ethnicity categories were modeled nominally.

Education

Women were instructed to check the box that describes the highest degree or level of school completed at time of delivery (34-36). Maternal education was reduced to four nominal categories. Education levels of 8th grade or less, 9th through 12th grade with no diploma, and high school graduate or GED completed was categorized as "High School Degree or Less." Some College credit, but not a degree

was categorized as "Some College." Associate's degree (AA, AS), Bachelor's degree (BA, AB, BS) were categorized as "College Degree." Master's degree (MA, MS) and Doctorate (PhD, EdD) or Professional degrees (DVM, LLB, JD) were categorized as "Post-College Degree." Education categories were modeled nominally.

Marital Status

Marital status is denoted as either unmarried or married. This is an imputed value on the birth certificate data – if marital status was unknown and the father's age known then the mother was considered married; if marital status was unknown and the father's age was unknown, then the mother was considered unmarried (34-36). Marital status was modeled as a dichotomous variable.

WIC

Information on receipt of WIC (The Special Supplement Nutrition Program for Women, Infants, and Children) food for the mother during pregnancy is available for all states implementing the 2003 revision of the birth certificate (34-36). The WIC program is run by the U.S. Department of Agriculture to help low-income pregnant women and their infants and children receive proper nutrition. For this analysis it is used as a measure of SES and kept dichotomous as noted on the birth certificate. WIC status was modeled as a dichotomous variable.

Pre-Pregnancy Smoking

Information on smoking before pregnancy is available for the revised reporting area except for Hawaii (34-36). The question asks for the number of cigarettes smoked for the three months before pregnancy. If the mother reports, on average, smoking at least one cigarette daily for this time period, she is classified as

a pre-pregnancy smoker (34-36). Pre-pregnancy smoking was modeled as a dichotomous variable.

Pre-Pregnancy BMI

Body mass index (BMI) is available from all states implementing the 2003 revision of the birth certificate. It is calculated as mother's pre-pregnancy weight (lb.) divided by mother's height (in.) squared and multiplied times 703. The range of accepted weight values is 50-400 lbs. and height values is 1 – 8 feet and 1 – 11 inches; all other values are edited to "not stated" (34-36). For the current analysis BMI was categorized as follows, Underweight (<18.5), Normal (18.5-24.9), Overweight (25.0 -29.9), Obese (35.0-39.9), and Extremely Obese (>40.0). Pre-pregnancy BMI was depicted as a categorized variable in Table 1 but otherwise modeled as a continuous variable.

Parity

Parity was determined based on the specified live-birth order and indicates what number the present birth represents with respect to previous live births. This value is determined by the birth attendant using values obtained from the mother, number of previous live births now living and number of previous live births now dead (34-36). Parity was modeled as a continuous variable.

Previous PTB, Pre-Pregnancy Hypertension, and Pre-Pregnancy Diabetes

Previous PTB, pre-pregnancy hypertension, and pre-pregnancy diabetes are available on all births as they were on the 1989 revision of the birth certificate. Previous preterm birth was kept dichotomous as denoted on the birth certificate. Pre-pregnancy hypertension and pre-pregnancy diabetes were combined into one

composite variable indicating whether the mother had either pre-pregnancy hypertension or diabetes, or both. Previous preterm birth was modeled as a dichotomous variable in the models for preterm birth. Pre-pregnancy hypertension and pre-pregnancy diabetes were modeled as a composite dichotomous variable in the models for maternal morbidity.

Plurality

Plurality is classified as single, twin, triplet, and higher order birth with a continuous number. This information is obtained from the medical record using the facility worksheet. Records for which the plurality was unknown were imputed as singletons (34-36). This variable was used for exclusion criteria to include only singleton births.

We did not consider clinical characteristics of the current pregnancy (e.g., pregnancy induced hypertension, smoking during pregnancy, gestational diabetes) as potential confounders as these conditions could have been caused by length of preceding IPI and adjusting for them could have introduced bias (40).

Study Restrictions

This analysis used specific exclusion criteria to minimize residual and unknown confounding. Singleton live births of at least 21 weeks gestation to non-Hispanic White, non-Hispanic Black, and Hispanic women who were aged 15-39 at the start of their 0-23 month IPI were included. These women were excluded from the analysis for the following reasons: women younger than 15 or older than 39 at the start of the interval, to avoid further unmeasured confounding from very young or advanced maternal age (n=21,172); women on their fifth or higher birth, to avoid

unmeasured confounding associated with higher birth orders (n=543,016), women with a history of termination, miscarriage, or stillbirth, to avoid misclassification of IPI from a pregnancy loss between a previous live birth and subsequent live birth artificially lengthening the IPI (N=1,693,215), and women with IPIs of 24 months or greater, to avoid unmeasured confounding from the association between extended intervals, underlying infertility, and adverse pregnancy outcomes (n=2,179,266). Women were considered to have had a termination, miscarriage, or stillbirth if their live birth order was not equal to their total birth order, if she indicated that she had 1 or more terminations, or if her interval since last live birth was not equal to her interval since last pregnancy. Furthermore, IPI was necessary for this analysis so women with no information on IPI a woman was excluded because the current birth was her first delivery (n=4,387,137), the data were missing (n=523,726), or gestational age and IPI were illogical (n=9,479). Illogical values were those that indicated a live birth of less than 21 weeks gestation or intervals between deliveries that were shorter than gestational age.

Descriptive Analysis Methods

A descriptive analysis was performed on demographic and clinical variables, stratified by maternal age at beginning of the IPI (Table 1). The 1,460,135 births were split into four categories of maternal age, each representing approximately 25% of the data. Maternal education was grouped to four nominal categories. IPI was modeled as a nominal variable and classified as less than 6 months, 6-11 months, 12-17 months, and 18-23 months. Women with the IPI length of 18-23 months were selected as the "ideal" IPI or the reference group based on literature

indicating that mothers with this IPI had the lowest risk of adverse events (13, 37). In order to assess the generalizability of our data set after exclusions, we compared the prevalence of the outcomes in our analysis dataset to the full dataset (prior to exclusions). We then performed a univariate analysis of BMI to check for outliers and found none, a result of the weight and height bounds on the birth certificate.

Modeling Methods

Initially, unadjusted and adjusted logistic regression was performed to produce odds ratios for our outcomes of interest for all ages and stratified by single year of maternal age. Then, modified Poisson regression was used to estimate risk ratios because the estimated odds ratio derived from logistic regression could overestimate the risk ratio given that PTB was not a rare event (<10% risk in all subgroups) (41). Unadjusted modified Poisson regressions were run to estimate the overall association between IPI and adverse outcomes (PTB and maternal morbidity) as well as the association stratified by single year of maternal age. Adjusted modified Poisson regressions were then used to estimate the overall association between IPI and PTB as well as the association stratified by single year of maternal age, adjusting for maternal age, maternal age^2, maternal race/ethnicity, maternal education, marital status, WIC receipt, previous PTB, pre-pregnancy smoking status, parity, and pre-pregnancy BMI.

Similar adjusted modified Poisson regression analyses were conducted to estimate the association between IPI and maternal morbidity for women overall as well as the association stratified by single year of maternal. These models were adjusted for the same set of covariates as the PTB models, except that pre-

pregnancy hypertension and pre-pregnancy diabetes were included as covariates instead of previous PTB. We then compared our results from logistic regression to our results from modified Poisson regression. Adjusted results from modified Poisson were graphed for both outcomes.

Software

We used SAS 9.4 statistical software to conduct all analyses.

CHAPTER III. MANUSCRIPT

Introduction

A growing number of women in the United States wish to delay childbearing until later in life, but increased maternal age and giving birth shortly after a previous pregnancy present competing risks. After a live birth, the World Health Organization (WHO) recommends waiting 18-23 months before conceiving again to reduce the risk of adverse maternal, perinatal, and infant outcomes (1). This recommendation stems from the multitude of research focused on interpregnancy interval (IPI) and preterm birth (PTB) and a small number of studies focused on IPI and maternal morbidity (6, 7, 29, 37).

Women who have shorter IPIs (generally defined as <18 months) are also more likely to have other risk indicators for PTB and maternal morbidity, such as black race, older maternal age, and lower socioeconomic status (31, 42-44). There is a lack of recent, national data on this topic for the United States. More specifically, only a few studies have examined how the relationship between short IPI and these health outcomes varies across maternal age, particularly for women in the United States (32, 45). These studies have concluded that short IPI and older maternal age were independent risk factors for adverse perinatal outcomes and that the effect of short IPI varies across maternal age categories (32, 45).

Analyses of short IPI and pregnancy outcomes among U.S. women on a national level are now possible because interval information became nationally available beginning with the 2003 revision of the U.S. birth certificate. The objective of the current study was to estimate the association between short IPIs and adverse

pregnancy outcomes across maternal age, focusing on PTB, a major cause of infant mortality and morbidity, and maternal morbidity. By examining these associations across maternal age, our analysis can help inform advice for older women whether to decrease their IPIs to avoid having a pregnancy at an older age (which can increase the risk of adverse pregnancy outcomes) or to achieve an 18-23 month interval (the current ideal across all maternal ages). If the association between short IPIs and pregnancy outcomes varies across maternal age, public health professionals, clinicians, and women can be better informed as to when it is healthy to begin a new pregnancy after giving birth, an increasingly important topic as women continue to delay childbearing to older ages.

Materials and Methods

Data Source and Study Population

Data were obtained from public use natality files for all U.S. births from 2013-2015. Specific variables regarding IPI became nationally available beginning with the 2003 version of the U.S. Standard Certificate of Birth (33). Therefore, the study population from which participants were drawn includes all women in states (plus the District of Columbia) that had implemented the U.S. 2003 Standard Certificate of Live Birth by 2013 (41 states), 2014 (47 states), or 2015 (48 states) (34-36). In 2015, births using the 2003 version of the birth certificate represented approximately 96.5% of all live births in the United States. Natality files include information on maternal demographics, maternal and infant clinical characteristics,

and pregnancy outcomes. This study was exempt from IRB approval as it employed secondary analysis of pre-existing publicly available de-identified data.

Interpregnancy Interval

The IPI was defined as the interval between previous delivery and subsequent conception. Months since last live birth and months since last other pregnancy outcome were collected, separately, on the 2003 version of the birth certificate. IPI was calculated by first converting the months since last live birth to weeks (assuming 4.5 weeks per month), imputing a randomly selected number of weeks (0-3, uniform distribution), and adding that to each 4.5-week month in order to account for variability of number of weeks within a given month. Second, the gestational age of the pregnancy in weeks (see below for details) was then subtracted from the weeks since last live birth to estimate IPI in weeks. Third, IPI in weeks was converted to IPI in months by dividing by 4.5 weeks, in order to be consistent with how IPI since last live birth has been categorized in previous literature (37).

Preterm Birth

One of our adverse outcomes of interest was preterm birth (PTB). PTB was defined as any birth occurring before the 37th completed week of pregnancy, which is consistent with the ICD-9 and ICD-10 definitions (38). Gestational age for PTB determination was obtained from the obstetric estimate as entered by the birth attendant using the maternal obstetric admission history and physical form (39). In 2014, the National Center for Health Statistics (NCHS) transitioned to using the obstetric estimate as the standard, primary measure of gestational age based on

validity studies; however it is also available for analysis on 2013 births because 90% of births in 2013 had the obstetric estimate reported in addition to the last menstrual period (LMP) based measure (39).

Maternal Morbidity

The other adverse outcome of interest was maternal morbidity. Maternal morbidity was defined as any combination of gestational hypertension (elevation of blood pressure above normal for age, gender, and physiological conditions diagnosed during pregnancy), gestational diabetes (glucose intolerance requiring treatment diagnosed during pregnancy), maternal transfusion (infusion of whole blood or packed red blood cells associated with labor and delivery), perineal laceration (laceration extending through the perineal skin, vaginal mucosa, perineal body and partially or completely through the anal sphincter or rectal mucosa), ruptured uterus (tearing of the uterine wall), unplanned hysterectomy (surgical removal of the uterus that was not planned prior to the admission) or admission to intensive care (any admission, planned or unplanned of the mother to a facility/unit designated as providing intensive care) (33). Maternal morbidity was recorded by the birth attendant onto the birth certificate using: the delivery record; physician delivery or operative notes; and intake and output forms (33). For 2013 births, we used the individual maternal morbidity items to create a composite variable indicating whether at least one maternal morbidity was recorded on the birth certificate. For 2014 and 2015 births, a composite maternal morbidity variable created by the NCHS was used for our analysis. This composite variable was

determined based on the same individual maternal morbidity items as 2013 with the exception of unplanned operation (34-36).

Maternal Age

In order to assess risk of adverse outcomes by maternal age at the previous delivery, we conducted a back calculation using the maternal age noted on the subsequent birth certificate. Since the publicly available birth certificate data files disclose only single year of maternal age, simply subtracting the interval since last live birth from the maternal age ignored the variability within a single year of age (e.g., 30 years and 1 week old versus 30 years and 50 weeks old). Maternal age, gestational age, and a random number generator were utilized to calculate the maternal age at the beginning of the IPI. If a woman was less than 35 at the subsequent delivery, her age in years was converted to her age in weeks and a random number of weeks (0-52, uniform distribution) was added; then the interval since last live birth was subtracted from this age in weeks. Under the assumption that older women may feel a particular urgency to conceive, resulting in earlier conceptions within their single year of age, if a woman was aged 35 years or older at the subsequent delivery, her age in years was converted to her age in weeks and a random number of weeks was added, but these weeks were restricted to those corresponding to the first half of the year (0-26, uniform distribution). For each woman, the interval since last live birth was then subtracted from her newly calculated age in weeks, and this was then converted back into years by rounding down to the nearest birthday. This calculated age, which was based on maternal age at the beginning of the IPI, was the maternal age used for our analysis.

Other Covariates

Potential confounders included the following demographic and clinical characteristics available from the birth certificate that were self-reported by the mother: race and ethnicity; highest level or degree of school completed at the time of delivery; marital status; receipt of the food from the Special Supplemental Nutrition Program for Women, Infants, and Children for herself during the pregnancy; pre-pregnancy smoking (at least one cigarette a day on average for the three months before pregnancy began); and pre-pregnancy body mass index (BMI, kg/m^2) as calculated with height and weight entered by the mother (33).

Potential confounders also included the following variables entered by the birth attendant using the prenatal care record, the labor and delivery nursing admission triage form, or the admission history and physical: parity (total number of previous live births), history of other pregnancy outcomes (spontaneous or induced losses or ectopic pregnancies), previous PTB, pre-pregnancy hypertension (elevated blood pressure above normal for age, gender, and physiological conditions diagnosed prior to onset of pregnancy), and pre-pregnancy diabetes (glucose intolerance requiring treatment diagnosed prior to onset of pregnancy) (33).

We did not consider clinical characteristics of the current pregnancy (e.g., pregnancy induced hypertension, smoking during pregnancy, gestational diabetes) as potential confounders as these conditions could have been caused by length of preceding IPI and adjusting for them could have introduced bias (40).

Study Restrictions

This analysis used specific exclusion criteria to minimize residual and unknown confounding. Singleton live births of at least 21 weeks gestation to non-Hispanic White, non-Hispanic Black, and Hispanic women who were aged 15-39 at the start of their 0-23 month IPI were included. These women were excluded from the analysis for the following reasons: women younger than 15 or older than 39 at the start of the interval, to avoid further unmeasured confounding from very young or advanced maternal age (n=21,172); women on their fifth or higher birth, to avoid unmeasured confounding associated with higher birth orders (n=543,016); women with a history of any termination, miscarriage, or stillbirth, to avoid misclassification from a pregnancy loss between a previous live birth and subsequent live birth artificially lengthening the IPI (n=1,693,215); and women with IPIs of 24 months or greater, to avoid unmeasured confounding from the association between extended intervals, underlying infertility, and adverse pregnancy outcomes (n=2,179,266). Furthermore, IPI was necessary for this analysis so women with no information on IPI were excluded if the current birth was her first delivery (n=4,387,137), the data were missing (n=523,726), or gestational age and IPI were illogical (n=9,479). Illogical values were those that indicated a live birth of less than 21 weeks gestation or an interval between deliveries that was shorter than gestational age.

Descriptive Analysis Methods

A descriptive analysis was performed on demographic and clinical variables, stratified by maternal age at beginning of the IPI (Table 1). The 1,460,135 births

were split into four categories of maternal age, each representing approximately 25% of the data. Women who indicated that they were of Mexican, Puerto Rican, Cuban, South American, or other Hispanic ethnicity were categorized as Hispanic. Women who indicated that they were non-Hispanic Black or non-Hispanic White were categorized as such. Maternal education was collapsed into four categories. IPI was modeled as a nominal variable and classified as less than 6 months, 6-11 months, 12-17 months, and 18-23 months. Women with the IPI length of 18-23 months were selected as the "ideal" IPI or the reference group based on literature indicating that mothers with this IPI had the lowest risk of adverse events (13, 37).

Modeling Methods

Modified Poisson regression was used to estimate risk ratios because the estimated odds ratio derived from logistic regression could overestimate the risk ratio given that PTB was not a rare event (<10% risk in all subgroups) (41). Unadjusted modified Poisson regressions were run to estimate the overall association between IPI and adverse outcomes (PTB and maternal morbidity) as well as the association stratified by single year of maternal age. Adjusted modified Poisson regressions were then used to estimate the overall association between IPI and PTB as well as the association stratified by single year of maternal age, adjusting for maternal age, maternal age^2, maternal race/ethnicity, maternal education, marital status, WIC receipt, previous PTB, pre-pregnancy smoking status, parity, and pre-pregnancy BMI. Due to the non-linear relationship between IPI and our outcomes, we included a quadratic term for maternal age in our regression models.

Similar adjusted modified Poisson regression were conducted to estimate the association between IPI and maternal morbidity for women overall as well as the association stratified by single year of maternal. These models were adjusted for the same set of covariates as the PTB models, except that pre-pregnancy hypertension and pre-pregnancy diabetes were included as covariates instead of previous PTB.

Software

We used SAS 9.4 statistical software to conduct all analyses.

Results

This analysis assessed 1,460,135 singleton live births of at least 21 weeks gestation to non-Hispanic White, non-Hispanic Black, and Hispanic women aged 15-39 at the start of their 0-23 month IPI. Maternal demographic and clinical characteristics were associated with maternal age group. The 15-21 age group had the largest proportions of non-Hispanic Black and Hispanic mothers (32.5% and 21.8%, respectively), and higher proportions of unmarried, less educated, WIC receiving, and pre-pregnancy smoking women (Table 1). The proportion of women with these characteristics decreased with increasing maternal age.

The distribution of IPI length, PTB, and maternal morbidity also varied across maternal age. The 15-21 age group had the highest prevalence of short IPIs (<6 months) and the 30-39 age group had the lowest prevalence (Table 1). The 15-21 age group had the highest prevalence of PTB and the lowest prevalence of

maternal morbidity, the 26-29 age group had the lowest prevalence of PTB, and the 30-39 age group had the highest prevalence of maternal morbidity.

There was a significant difference in risk of PTB by IPI length and across maternal age. Compared to an IPI 18-23 months, short IPI was moderately associated with PTB (adjusted relative risk aRR: 1.55, 95% CI: 1.52, 1.58), while IPI 6-11 months had a smaller, but still significant, association with PTB (aRR: 1.17, 95% CI: 1.15, 1.19), and IPI 12-17 months had a near null, but still significant, association with PTB (aRR: 1.04, 95% CI: 1.02, 1.06). Modified Poisson regression produced age-specific adjusted risk ratios as seen in Figure 1 for ages 19-39. Short IPI was associated with PTB with significant risk ratios ranging from 1.28-1.75 across all ages. IPI 6-11 months was associated with PTB with significant ratios ranging from 1.10–1.27, mostly for ages 19-29. IPI 12-17 months showed significant risk ratios for PTB only for ages 19 (aRR: 1.10) and 22 (aRR: 1.09). Crude and adjusted risk ratios for PTB by maternal age, along with 95% confidence intervals, are presented in Tables 3 and 4.

There was a significant association between IPI and risk of maternal morbidity. In comparison to IPI 18-23 months, all shortened IPI lengths showed a moderate protective association on the risk of maternal morbidity: short IPI (aRR: 0.93, 95% CI: 0.91, 0.94), IPI 6-11 months (aRR: 0.92, 95% CI: 0.91, 0.94), and IPI 12-17 months (aRR: 0.95, 95% CI: 0.94, 0.97). Protective associations were observed for select ages across the entire age range where models converged (ages 20-39) for the IPI 6-11 and 12-17 month categories (Figure 2). Short IPI was associated with reduced risk of maternal morbidity only for select ages of women

within the younger age range (21-28). Crude and adjusted risk ratios by maternal age, along with 95% confidence intervals, are presented in Tables 5 and 6.

Discussion

The average age of women at first birth has risen over the past forty years and is expected to continue to rise, reflecting a shift in women's desires to no longer conceive at a young age and potentially, increasing access to effective contraception (46, 47). The current investigation aimed to evaluate whether older women should be advised to decrease their IPI to avoid risks associated with older age or maintain an "ideal" 18-23 month IPI despite reaching an at-risk age for comorbidity and pregnancy complications.

After controlling for potential confounders, there was increased risk of PTB with IPI of length 12-17 months compared to IPI 18-23 months for ages 19 and 22. For IPI of length 6-11 months among mostly 19-29 year olds, a significant increase in risk of PTB was observed. We also found evidence of an increased risk of PTB with IPIs of lengths less than 6 months across all ages. These results suggest that younger mothers (<30 years old) looking to have another baby would reduce their likelihood of experiencing a PTB by waiting at least 12 months from the time of their last live birth before conceiving again but not longer than 24 months as IPIs >23 months were not included in this analysis, but rather substantial literature shows the nadir of risk at the 18-23 month IPI (13, 37). Older mothers (30-39 years old) wishing to have another baby would also reduce the likelihood of PTB by waiting 12-23 months before conceiving; however, this IPI length potentially brings with it

the additional risk of increasing maternal morbidity. An IPI <18 months is associated with a 0-15% reduction in risk of maternal morbidity, depending on maternal age and IPI length, compared to an IPI 18-23 month. This lower risk may be due to the increasing risk of maternal morbidity with increasing age (48-50). Findings from our study show that shorter IPIs are protective against maternal morbidity compared to IPIs 18-23 month because mothers of the same age at their previous delivery who have shorter IPIs are younger at their subsequent delivery than are mothers with longer IPIs.

These results are consistent with substantial research indicating that short IPIs (<18 months) present an increased risk of PTB (32, 37). Our study's results showed a smaller magnitude of increased risk of PTB for all shortened IPIs compared to other studies, but an emphasis still remains on the significantly increased risk of PTB with the short IPI (<6 months) (13). The association of IPI with maternal morbidity has not been widely studied, and the published studies are smaller sample size and of poor quality (7). Some studies have found significant adverse associations between long IPIs (>59 months) and maternal morbidity, but little evidence exists for an association between short IPI and maternal morbidity (3, 7, 51). Our analysis mirrors this prior research in that an increased risk of maternal morbidity for shorter IPIs was not observed; however, a slight 'protective' association between short IPI and maternal morbidity was seen.

These results differ from those of Hanley (2017) who used a case-crossover analysis of longitudinally linked records to conclude that previous evidence of increased risk of PTB after a short IPI was a result of poor study design and analyses

of cross sectional data (30). In an editorial response to this article, Klebanoff (2017) agreed with Hanley (2017), arguing that older studies concluding the harmful effect of short IPIs overestimate the association (31). However, other case-crossover studies have reported statistically significant increases in risk of PTB for IPIs shorter than 18-23 months (6, 27). All of these case-crossover studies show reduced time-invariant confounding when using a within-woman analysis compared to a between-woman analysis. However, these studies are answering a different research question than this analysis, that is, is IPI associated with PTB risk only among women who had an adverse outcome in one, but not the other of their second and third pregnancies and whose two IPIs were different from each other (31). This is only a small fraction of the population, and these findings may not apply to all women.

A limitation of the current study was the inability to assess maternal morbidity and obstetric complications during previous pregnancies and events that occurred during the IPI. Controlling for the existence of any previous PTB and restricting the study to women with no previous pregnancy losses or terminations attempted to address confounding and the potential misclassification of IPI. However, these exclusions limit the generalizability of the current results to lower-risk mothers than women overall. There is a potential for residual confounding from variables not available on birth certificate data. Additionally, a validation study conducted in two states found that maternal morbidity variables collected on the birth certificate may be an underestimate of true maternal morbidity, but sensitivity and specificity on a national level have not been assessed (52). Because

this analysis only utilizes data from those states that have implemented the 2003 revision of the birth certificate, it is not nationally representative.

However, despite these limitations, the current analysis goes beyond previous research by using a very large sample size based on more than 90% of relevant U.S. births in 2013-2015 to assess the competing risks of maternal age and IPI on PTB and maternal morbidity. All mothers may be advised to avoid a <6 month IPI to protect their next child from PTB risk. However, for women older than 35, when compared to an IPI of 18-23 months, an IPI of 12-17 months may not increase PTB risk, but may reduce maternal morbidity risk because of younger age at next delivery.

CHAPTER IV. PUBLIC HEALTH IMPLICATIONS AND FUTURE DIRECTIONS

Public Health Implications

Results from the current study revealed that low-risk mothers, aged 28 or older, who wish to conceive again may be advised to wait at least 5 months, but that additional waiting may incrementally increase their chances of experiencing morbidity, while not greatly decreasing the risk of PTB. While more research is needed, this suggestion may play a role in clinician family planning guidance and methodology. If a woman aged 28 or older is considering conceiving, particularly more than once, she may be advised by her clinician to wait only a few months to maximize both her health and the health of her next child. This information is important to both the clinician and the patient because much of the current literature states 24 months as ideal, but this interval does not necessarily take into account the competing risk of increasing maternal age. Bigelow et al. (2015) created an evidence-based guide for clinicians based on numerous IPI studies. They maintained that women should exhibit an 18-23 month interval after a live birth, a suggestion that does not specifically account for advanced maternal age. The authors concluded that more research is needed to assess the recommended IPI following various other pregnancy outcomes as well as for women who delay initiation of childbearing (14).

IPI is potentially modifiable by public health intervention, such as universal access to effective postpartum contraception, and thus was our exposure of interest. Contraceptive choices may depend on maternal age and personal needs. Younger mothers may benefit from a long-acting reversible contraceptive (LARC) method

which will increase their ability to postpone pregnancy to an ideal 18-23 months or longer, depending on their personal situation. Older mothers may seek out a shorter term contraceptive method, such as oral contraceptives.

Future Directions

Well-designed studies to-date have focused on low-risk mothers. For example, the current research study was limited to women with no history of pregnancy loss and no indication of previous pregnancy complications, with the exception of preterm births. Further research is needed to tailor physician family planning advice to specific women's needs. This research should utilize large sample sizes, varying study designs to investigate different pregnancy outcomes with a focus on high-risk populations and intervals after non-live births. Quality longitudinal studies properly controlling for all of the hypothesized confounders would help to clarify this association between interval and adverse outcomes. Furthermore, these studies need to focus their investigation not only on maternal morbidity and mortality, but also on other infant and maternal outcomes such as psychological health, development and nutrition.

Research on differences in IPI and adverse outcomes between Black and White mothers has been researched, with many authors concluding large differences in the likelihood of short IPI and adverse pregnancy outcomes (5, 21-23, 25). Black mothers are approximately twice as likely as White mothers to have preterm infants (21, 53). Some studies attribute this difference to the fact that Black women are more likely to exhibit short IPIs than White women (5, 22, 23, 25). Others concluded that the difference in preterm rates and likelihood of exhibiting a

short IPI for Black mothers compared to White mothers leads to a spurious association (21). An exploration of the unique experiences and associated risk factors in minority race women could contribute valuable insight into family planning guidance for these populations. For example, studies should have adequate sample size to estimate risks and benefits for other minority groups.

Just as the unique experiences of minority race women may shape the likelihood of various outcomes, low SES women face a unique set of challenges that also play a role in the IPI – pregnancy outcome relationship. These women may lack the education and resources to receive family planning advice and methods, and for this reason, public health implications must be tailored to a low-resource population.

While some of the literature focuses on post-abortion intervals, much more is needed to further investigate the effect of stillbirths, miscarriages, and terminations on the likelihood of short interval length and adverse pregnancy outcomes. Holmlund et al. (2016) concluded that amongst women who had had an induced abortion, a short IPI seemed to contribute to higher risk for preeclampsia and maternal care (54). Shachar et al. (2016) found a short IPI after a pregnancy termination to be associated with reduced odds for PTB (6). Wong et al. (2014) concluded that adverse pregnancy outcomes were not associated with a very short IPI after a prior pregnancy loss and that an IPI $\leq$ 3 months is not associated with a lower rate of live subsequent birth and appears to be comparable to those with an IPI > 3 months (55). All of the aforementioned authors concluded that further work is needed on the risk of adverse outcomes associated with short IPIs after various

pregnancy outcomes (6, 54, 55). These types of birth outcomes can drastically alter the likelihood of IPI lengths in a way that varies from woman to woman. Some women may wish to conceive right away after a non-live birth outcome, while others wait longer than the advised length of time. This type of research would need to consider this dichotomy, and therefore, could be quite complicated.

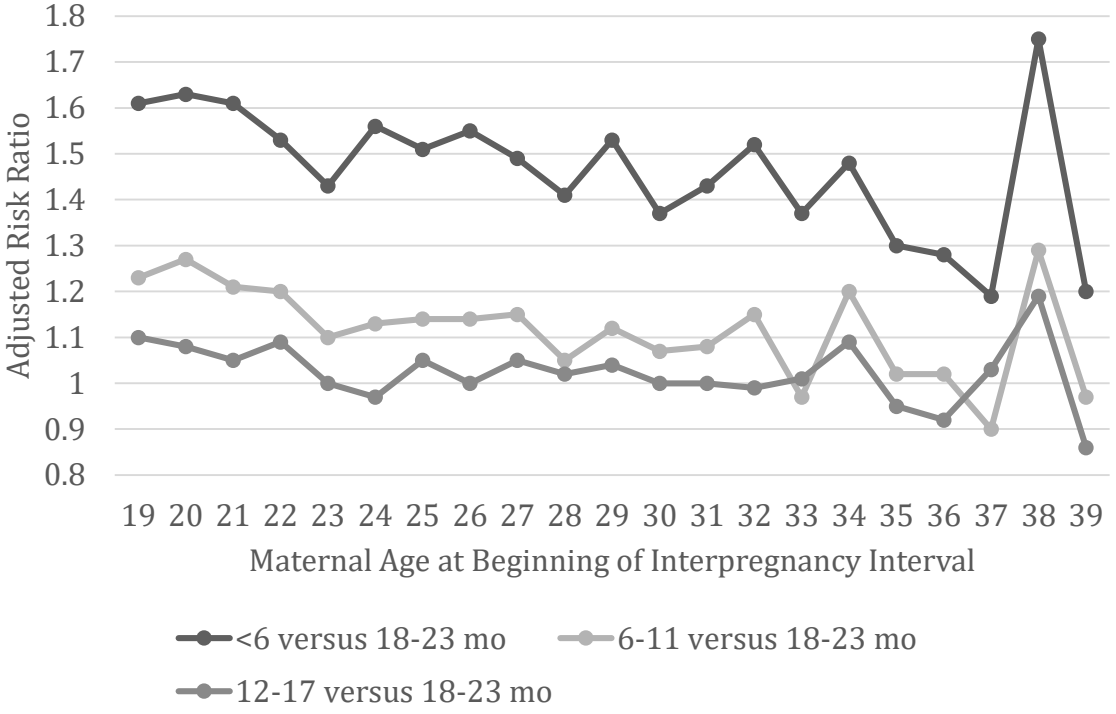
CHAPTER V. TABLES AND FIGURES

Table 1. Characteristics of the Study Population by Maternal Age at Beginning of Interpregnancy Interval[a] (N= 1,460,135)

	15-21 (n = 386,533)		22-25 (n=362,651)		26-29 (n=362,933)		30-39 (n=348,018)	
Characteristics	N	N (%)	N	N (%)	N	N(%)	N	N(%)
Maternal Race/Ethnicity	384,572		360,338		360,290		344,127	
non-Hisp. white		175,476(45.6)		218,667 (60.7)		261,447 (72.6)		252,860 (73.5)
non-Hisp. black		125,139(32.5)		80,988 (22.5)		53,168 (14.8)		48,081 (14.0)
Hispanic[b]		83,957(21.8)		60,683 (16.8)		45,675 (12.7)		43,186 (12.6)
Marital Status	386,533		362,651		362,933		348,018	
Married		127,240 (32.9)		226,188 (62.4)		300,110 (82.7)		304,904 (87.6)
Unmarried		259,293 (67.1)		136,463 (37.6)		62,823 (17.3)		43,114 (12.4)
Maternal Educ.	383,155		359,332		359,601		343,614	
≤ High School		292,342 (76.3)		166,195 (46.3)		82,546 (23.0)		55,524 (16.2)
Some College		76,985 (20.1)		96,109 (26.7)		63,745 (17.7)		43,469 (12.7)
College Degree		13,461 (3.5)		88,185 (24.5)		155,872 (43.3)		145,871 (42.5)
Post-Grad Degree		367 (0.1)		8,843 (2.5)		57,438 (16.0)		98,750 (28.7)
WIC Receipt [c]	379,208		355,094		355,375		340,589	
Yes		261,030 (68.8)		180,253 (50.8)		97,626 (27.5)		68,348 (20.1)
No		118,178 (31.2)		174,841 (49.2)		257,749 (72.5)		272,241 (79.9)
Pre-preg. BMI[d]	372,791		350,413		351,304		335,621	
Underweight		20,261 (5.4)		12,933 (3.7)		9,845 (2.8)		7,764 (2.3)
Normal		163,056 (43.7)		151,679 (43.3)		172,483 (49.1)		167,952 (50.0)
Overweight		93,045 (25.2)		89,850 (25.6)		89,242 (25.4)		86,503 (25.8)
Obese		79,713 (21.4)		77,923 (22.2)		65,611 (18.7)		60,647 (18.1)
Morbidly Obese		15,716 (4.2)		18,028 (5.1)		14,123 (4.0)		12,755 (3.8)
Pre-preg. Smoking[e]	376,717		353,578		353,950		339,629	
Smoker		58,775 (15.6)		38,923 (11.0)		18,274 (5.2)		10,767 (3.2)
Non-Smoker		317,942 (84.4)		314,655 (89.0)		335,676 (94.8)		328,862 (96.8)
Parity	386,257		362,357		362,653		347,737	
2nd Live Birth		271,978 (70.4)		196,167 (54.1)		213,747 (58.9)		200,328 (57.6)
3rd Live Birth		91,501 (23.7)		113,794 (31.4)		97,839 (27.0)		93,822 (26.9)
4th Live Birth		22,778 (5.9)		52,396 (14.5)		51,067 (14.1)		53,587 (15.4)
IPI[a]	386,533		362,651		362,933		348,018	
<6 Mo.		70,589 (18.3)		51,404 (14.2)		32,576 (9.0)		28,308 (8.1)
6-11 Mo.		114,442 (29.6)		104,303 (28.8)		93,284 (25.7)		90,841 (26.1)
12-17 Mo		116,389 (30.1)		120,074 (33.1)		136,972 (37.5)		134,057 (38.5)
18-23 Mo.		84,113 (22.0)		86,870 (24.0)		101,101 (27.9)		94,812 (27.2)
Previous PTB[f]	385,957		362,221		362,933		347,740	
Yes		15,452 (4.0)		13,360 (3.7)		11,649 (3.2)		11,347(3.3)
No		370,505 (96.0)		348,861 (96.3)		350,979 (96.8)		336,393(96.7)
PTB[f]	386,533		362,651		362,933		348,018	
Preterm		33,554 (8.7)		24,182 (6.7)		18,684 (5.2)		18,740 (5.4)
Term		352,979 (91.3)		338,469 (93.3)		344,249 (94.9)		329,278 (94.6)
Maternal Morbidity[g]	385,898		362,138		362,449		347,418	
Yes		20,189 (5.2)		24,707 (6.8)		28,332 (7.8)		33,409 (9.6)
No		365,709 (94.8)		337,431 (93.2)		334,117 (92.2)		314,009 (90.4)

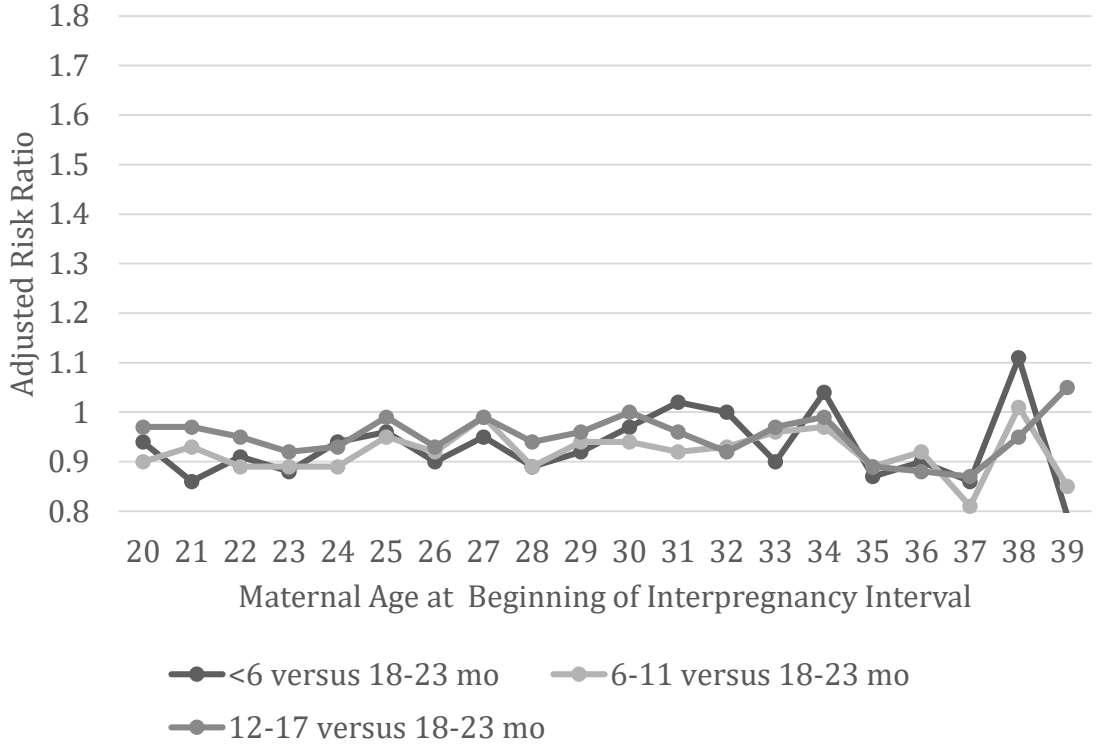
[a] Interpregnancy Interval, the number of months between previous birth and subsequent conception
[b] Includes all persons of Hispanic origin of any race
[c] Receipt of food from the Special Supplemental Nutrition Program for Women, Infants, and Children for herself during pregnancy
[d] Pre-Pregnancy Body Mass Index
[e] Mothers who smoked on average, at least one cigarette daily for the three months before pregnancy
[f] Preterm Birth, defined as infants born at less than 37 completed gestational weeks
[g] Includes any combination of maternal transfusion, perennial lacerations, ruptured uterus, unplanned hysterectomy, admission to intensive care, gestational diabetes, and gestational hypertension

Figure 1. Preterm Birth (PTB) and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Adjusted[a]



[a]Adjusted for age, age^2, race, highest level of education, marital status, WIC receipt, previous preterm birth, pre-pregnancy smoking status, parity, and pre-pregnancy BMI

Figure 2. Maternal Morbidity and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Adjusted[a]



[a]Adjusted for age, age^2, race, highest level of education, marital status, WIC receipt, previous hypertension/diabetes, pre-pregnancy smoking status, parity, and pre-pregnancy BMI

Table 3. Preterm Birth (PTB) and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Unadjusted

		18-23 month IPI (ref)	<6 month IPI		6-11 month IPI		12-17 months IPI	
Age	N	% PTB	% PTB	RR(95% CI)	% PTB	RR(95% CI)	% PTB	RR(95% CI)
All	1,460,135	5.4	10.5	**1.96(1.92,1.99)**	6.9	**1.28(1.26,1.31)**	5.6	**1.05(1.03,1.06)**
15	6,095	8.1	16.2	**2.00(1.60,2.50)**	11.1	**1.37(1.11,1.68)**	8.7	1.07(0.86,1.33)
16	16,132	7.8	15.2	**1.96(1.70,2.25)**	10.9	**1.41(1.23,1.61)**	9.3	**1.19(1.04,1.37)**
17	33,782	7.2	13.0	**1.81(1.63,2.00)**	9.6	**1.34(1.21,1.48)**	8.2	**1.14(1.03,1.27)**
18	59,232	7.4	12.7	**1.70(1.57,1.84)**	9.8	**1.31(1.22,1.42)**	7.9	1.06(0.98,1.15)
19	83,725	5.4	10.5	**1.69(1.58,1.81)**	6.9	**1.26(1.18,1.35)**	5.6	**1.11(1.03,1.19)**
20	93,596	7.1	12.0	**1.70(1.59,1.81)**	8.9	**1.28(1.20,1.36)**	7.9	1.06(0.99,1.13)
21	93,971	6.8	11.6	**1.76(1.64,1.88)**	8.7	**1.25(1.17,1.34)**	7.2	1.04(0.98,1.12)
22	92,677	6.5	11.4	**1.75(1.63,1.88)**	8.1	**1.25(1.17,1.34)**	6.8	**1.09(1.02,1.17)**
23	90,190	6.1	10.6	**1.70(1.58,1.83)**	7.6	**1.19(1.11,1.27)**	6.6	1.02(0.95,1.09)
24	89,444	6.0	10.2	**1.92(1.78,2.07)**	7.1	**1.22(1.13,1.31)**	6.1	1.00(0.93,1.08)
25	90,340	5.4	10.3	**1.98(1.83,2.15)**	6.5	**1.28(1.19,1.38)**	5.4	1.07(0.99,1.15)
26	91,941	4.8	9.5	**2.03(1.87,2.21)**	6.2	**1.24(1.15,1.34)**	5.1	1.01(0.93,1.08)
27	92,625	4.7	9.5	**1.99(1.82,2.17)**	5.8	**1.27(1.18,1.37)**	4.7	1.05(0.97,1.13)
28	91,257	4.4	8.8	**1.90(1.73,2.09)**	5.6	**1.18(1.09,1.27)**	4.7	1.01(0.94,1.09)
29	87,110	4.5	8.5	**2.05(1.86,2.26)**	5.2	**1.25(1.15,1.36)**	4.5	1.04(0.96,1.12)
30	78,639	4.2	8.6	**1.97(1.78,2.18)**	5.3	**1.20(1.10,1.31)**	4.4	1.01(0.93,1.09)
31	68,081	4.3	8.6	**1.96(1.76,2.19)**	5.2	**1.21(1.11,1.33)**	4.4	1.01(0.93,1.10)
32	62,220	4.5	8.8	**1.98(1.76,2.22)**	5.5	**1.27(1.16,1.40)**	4.6	1.01(0.92,1.10)
33	47,921	4.3	8.5	**1.67(1.47,1.91)**	5.5	1.06(0.95,1.17)	4.4	1.03(0.93,1.14)
34	31,506	5.2	8.6	**1.95(1.68,2.28)**	5.4	**1.33(1.17,1.52)**	5.3	1.09(0.96,1.23)
35	22,522	4.7	9.2	**1.54(1.29,1.83)**	6.3	1.07(0.93,1.24)	5.1	0.92(0.80,1.05)
36	15,837	5.8	8.9	**1.56(1.28,1.90)**	6.2	1.09(0.92,1.30)	5.3	0.97(0.82,1.14)
37	10,550	6.0	9.3	**1.45(1.14,1.84)**	6.6	0.99(0.81,1.21)	5.8	1.00(0.83,1.21)
38	6,706	6.7	9.7	**1.74(1.31,2.31)**	6.6	1.19(0.92,1.54)	6.7	1.07(0.83,1.37)
39	4,036	6.3	10.9	1.31(0.94,1.83)	7.5	1.01(0.75,1.35)	6.7	0.86(0.64,1.15)

Bold indicates significance at the 95% confidence level

Table 4. Preterm Birth (PTB) and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Adjusted[a]

		18-23 month IPI (ref)	**<6 months IPI**		**6-11 month IPI**		**12-17 month IPI**	
Age	N	% PTB	% PTB	aRR (95% CI)	% PTB	aRR (95% CI)	% PTB	aRR (95% CI)
All	1,348,396	5.4	10.5	**1.55(1.52,1.58)**	6.9	**1.17(1.15,1.19)**	5.6	**1.04(1.02,1.06)**
19	77,441	7.1	12.0	**1.61(1.50,1.72)**	8.9	**1.23(1.15,1.32)**	7.9	**1.10(1.03,1.18)**
20	86,383	6.8	11.6	**1.63(1.52,1.75)**	8.7	**1.27(1.19,1.36)**	7.2	1.08(1.00,1.15)
21	86,670	6.5	11.4	**1.61(1.50,1.73)**	8.1	**1.21(1.13,1.30)**	6.8	1.05(0.98,1.13)
22	85,661	6.1	10.6	**1.53(1.41,1.64)**	7.6	**1.20(1.11,1.28)**	6.6	**1.09(1.02,1.17)**
23	83,171	6.0	10.2	**1.43(1.32,1.54)**	7.1	**1.10(1.02,1.18)**	6.1	1.00(0.93,1.07)
24	82,726	5.4	10.3	**1.56(1.44,1.69)**	6.5	**1.13(1.05,1.21)**	5.4	0.97(0.90,1.05)
25	83,495	4.8	9.5	**1.51(1.38,1.65)**	6.2	**1.14(1.06,1.23)**	5.1	1.05(0.97,1.13)
26	85,153	4.7	9.5	**1.55(1.42,1.69)**	5.8	**1.14(1.05,1.23)**	4.7	1.00(0.93,1.08)
27	85,715	4.4	8.8	**1.49(1.36,1.64)**	5.6	**1.15(1.06,1.24)**	4.7	1.05(0.97,1.13)
28	84,441	4.5	8.5	**1.41(1.27,1.55)**	5.2	1.05(0.97,1.14)	4.5	1.02(0.94,1.10)
29	80,501	4.2	8.6	**1.53(1.38,1.70)**	5.3	**1.12(1.03,1.22)**	4.4	1.04(0.96,1.12)
30	72,626	4.4	8.6	**1.37(1.23,1.54)**	5.2	1.07(0.98,1.17)	4.4	1.00(0.92,1.08)
31	62,791	4.5	8.8	**1.43(1.27,1.61)**	5.5	1.08(0.99,1.19)	4.6	1.00(0.92,1.10)
32	57,121	4.3	8.5	**1.52(1.35,1.73)**	5.5	**1.15(1.04,1.27)**	4.4	0.99(0.90,1.08)
33	44,019	5.2	8.6	**1.37(1.19,1.57)**	5.4	0.97(0.87,1.08)	5.3	1.01(0.91,1.12)
34	28,823	4.7	9.2	**1.48(1.26,1.74)**	6.3	**1.20(1.05,1.37)**	5.1	1.09(0.96,1.24)
35	20,523	5.8	8.9	**1.30(1.08,1.56)**	6.2	1.02(0.88,1.19)	5.3	0.95(0.82,1.10)
36	14,465	6.0	9.3	**1.28(1.04,1.58)**	6.6	1.02(0.86,1.22)	5.8	0.92(0.77,1.09)
37	9,565	6.7	9.7	1.19(0.92,1.53)	6.6	0.93(0.75,1.15)	6.7	1.03(0.84,1.26)
38	6,058	6.3	10.9	**1.75(1.28,2.39)**	7.5	1.29(0.98,1.70)	6.7	1.19(0.91,1.56)
39	3,628	8.5	11.1	1.20(0.84,1.72)	8.6	0.97(0.71,1.33)	7.3	0.86(0.63,1.18)

Bold indicates significance at the 95% confidence level

Ages 15-18 did not converge with modified Poisson Regression

[a] Adjusted for age, age^2, race, highest level of education, marital status, WIC receipt, previous preterm birth, pre-pregnancy smoking status, parity, and pre-pregnancy BMI

Table 5. Maternal Morbidity and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Unadjusted

		18-23 month IPI (ref)	<6 month IPI		6-11 month IPI		12-17 month IPI	
Age	N	% Morb	% Morb	RR(95% CI)	% Morb	RR(95% CI)	% Morb	RR(95% CI)
All	1,457,903	7.6	7.3	**0.96(0.94,0.98)**	7.2	**0.95(0.93,0.96)**	7.3	**0.96(0.95,0.98)**
15	6,086	5.6	4.9	0.87(0.61,1.24)	4.2	0.75(0.56,1.02)	4.3	0.76(0.57,1.02)
16	16,096	4.5	3.5	**0.77(0.60,0.99)**	4.1	0.91(0.75,1.11)	4.1	0.91(0.75,1.11)
17	33,725	4.9	4.6	0.94(0.81,1.09)	4.1	**0.84(0.73,0.97)**	4.6	0.95(0.83,1.08)
18	59,136	5.2	4.7	0.91(0.82,1.02)	4.6	**0.89(0.80,0.98)**	4.7	0.92(0.83,1.01)
19	83,595	5.5	4.8	**0.86(0.78,0.94)**	5.0	**0.90(0.83,0.98)**	5.4	0.97(0.90,1.05)
20	93,429	5.9	5.3	**0.91(0.84,0.99)**	5.2	**0.88(0.82,0.95)**	5.7	0.97(0.90,1.04)
21	93,831	6.1	5.3	**0.87(0.80,0.95)**	5.6	**0.93(0.86,1.00)**	6.0	0.98(0.91,1.05)
22	92,523	6.6	6.1	0.92(0.85,1.00)	6.0	**0.90(0.84,0.97)**	6.3	0.95(0.89,1.02)
23	90,066	7.2	6.7	0.94(0.86,1.01)	6.5	**0.90(0.84,0.96)**	6.5	**0.91(0.86,0.97)**
24	89,317	7.4	7.4	1.00(0.93,1.08)	6.7	**0.92(0.86,0.98)**	6.8	**0.93(0.87,0.99)**
25	90,232	7.4	8.0	1.08(1.00,1.17)	7.3	0.98(0.92,1.05)	7.3	0.99(0.93,1.05)
26	91,819	7.8	7.9	1.02(0.94,1.10)	7.5	0.96(0.90,1.02)	7.2	**0.93(0.87,0.98)**
27	92,494	7.6	8.8	**1.16(1.07,1.26)**	7.9	1.05(0.99,1.12)	7.5	0.99(0.94,1.05)
28	91,141	8.0	9.1	**1.15(1.06,1.24)**	7.8	0.97(0.92,1.04)	7.6	0.96(0.90,1.01)
29	86,995	8.2	9.7	**1.18(1.09,1.29)**	8.4	1.03(0.97,1.09)	7.8	0.96(0.91,1.01)
30	78,510	8.4	10.4	**1.24(1.14,1.35)**	8.6	1.02(0.96,1.09)	8.5	1.01(0.96,1.07)
31	67,977	8.7	11.3	**1.31(1.20,1.43)**	8.8	1.01(0.95,1.08)	8.3	0.96(0.90,1.02)
32	62,108	8.9	11.6	**1.30(1.18,1.42)**	9.3	1.04(0.97,1.11)	8.3	**0.93(0.87,0.99)**
33	47,825	9.7	11.0	**1.14(1.02,1.27)**	10.1	1.05(0.97,1.13)	9.4	0.97(0.90,1.04)
34	31,449	10.1	13.4	**1.32(1.18,1.49)**	10.9	1.08(0.98,1.18)	10.0	0.99(0.91,1.08)
35	22,490	11.7	12.8	1.10(0.96,1.26)	11.1	0.96(0.86,1.06)	10.4	**0.89(0.81,0.98)**
36	15,815	11.7	14.0	**1.20(1.03,1.40)**	12.2	1.05(0.93,1.18)	10.7	0.92(0.82,1.03)
37	10,523	13.7	14.7	1.07(0.90,1.28)	12.2	0.89(0.77,1.02)	11.8	**0.87(0.76,0.99)**
38	6,691	12.1	16.5	**1.36(1.10,1.68)**	13.1	1.08(0.90,1.30)	11.9	0.99(0.83,1.17)
39	4,030	14.6	14.0	0.96(0.74,1.27)	12.9	0.88(0.71,1.11)	15.4	1.06(0.86,1.30)

Bold indicates significance at the 95% confidence level

Table 6. Maternal Morbidity and Interpregnancy Interval (IPI) by Maternal Age at Beginning of Interval, Adjusted[a]

		18-23 month IPI (ref)	<6 month IPI		6-11 month IPI		12-17 month IPI	
Age	N	% Morb	% Morb	aRR (95% CI)	% Morb	aRR (95% CI)	% Morb	aRR (95% CI)
All	1,346,192	7.6	7.3	**0.93(0.91,0.94)**	7.2	**0.92(0.91,0.94)**	7.3	**0.95(0.94, 0.97)**
20	86,313	5.9	5.3	0.94(0.86,1.02)	5.2	**0.90(0.84,0.98)**	5.7	0.97(0.90,1.05)
21	86,616	6.1	5.3	**0.86(0.78,0.93)**	5.6	0.93(0.86,1.00)	6.0	0.97(0.91,1.05)
22	85,566	6.6	6.1	**0.91(0.83,0.99)**	6.0	**0.89(0.83,0.96)**	6.3	0.95(0.88,1.02)
23	83,111	7.2	6.7	**0.88(0.81,0.96)**	6.5	**0.89(0.83,0.95)**	6.5	**0.92(0.86,0.98)**
24	82,656	7.4	7.4	0.94(0.87,1.02)	6.7	**0.89(0.83,0.95)**	6.8	**0.93(0.87,0.99)**
25	83,433	7.4	8.0	0.96(0.89,1.05)	7.3	0.95(0.88,1.01)	7.3	0.99(0.94,1.06)
26	85,084	7.8	7.9	**0.90(0.83,0.98)**	7.5	**0.92(0.86,0.98)**	7.2	**0.93(0.88,0.99)**
27	85,629	7.6	8.8	0.95(0.87,1.04)	7.9	0.99(0.93,1.05)	7.5	0.99(0.94,1.05)
28	84,373	8.0	9.1	**0.89(0.82,0.97)**	7.8	**0.89(0.84,0.95)**	7.6	0.94(0.89,1.00)
29	80,431	8.2	9.7	0.92(0.84,1.01)	8.4	0.94(0.88,1.00)	7.8	0.96(0.91,1.02)
30	72,540	8.4	10.4	0.97(0.88,1.06)	8.6	0.94(0.88,1.00)	8.5	1.00(0.94,1.06)
31	62,719	8.7	11.3	1.02(0.93,1.12)	8.8	**0.92(0.86,0.98)**	8.3	0.96(0.90,1.02)
32	57,041	8.9	11.6	1.00(0.90,1.10)	9.3	**0.93(0.86,0.99)**	**8.3**	**0.92(0.86,0.98)**
33	43,956	9.7	11.0	0.90(0.80,1.00)	10.1	0.96(0.88,1.03)	9.4	0.97(0.90,1.05)
34	28,780	10.1	13.4	1.04(0.92,1.18)	10.9	0.97(0.88,1.07)	10.0	0.99(0.90,1.07)
35	20,506	11.7	12.8	0.87(0.76,1.00)	11.1	**0.89(0.80,0.98)**	**10.4**	**0.89(0.81,0.98)**
36	14,448	11.7	14.0	0.90(0.77,1.05)	12.2	0.92(0.82,1.04)	**10.7**	**0.88(0.78,0.99)**
37	9,547	13.7	14.7	0.86(0.71,1.03)	12.2	**0.81(0.70,0.94)**	**11.8**	**0.87(0.76,0.99)**
38	6,048	12.1	16.5	1.11(0.89,1.39)	13.1	1.01(0.84,1.22)	11.9	0.95(0.79,1.14)
39	3,625	14.6	14.0	0.79(0.60,1.06)	12.9	0.85(0.68,1.08)	15.4	1.05(0.85,1.30)

Bold indicates significance at the 95% confidence level

Ages 15-19 did not converge with modified Poisson Regression

[a]Adjusted for age, age^2, race, highest level of education, marital status, WIC receipt, previous hypertension/diabetes, pre-pregnancy smoking status, parity, and pre-pregnancy BMI

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