Fall 2010

Occupation and injuries: risk factors for preterm delivery

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OCCUPATION AND INJURIES: RISK FACTORS FOR PRETERM DELIVERY

by

Karisa Kay Harland

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Epidemiology
in the Graduate College of
The University of Iowa

December 2010

Thesis Supervisor: Professor Audrey F. Saftlas

ABSTRACT

Preterm delivery (PTD) is a leading cause of infant death, and surviving infants are at risk for poor health. Data from the Iowa Health in Pregnancy Study, a case-control study of maternal stress on risk of PTD and small for gestational age (SGA) deliveries were used to address three aims: 1) develop a method to correct for error in ultrasound measurement among suspected SGA infants, 2) estimate the association of occupational stress on risk of PTD, and 3) examine injury-related risk factors for PTD.

Estimates of gestational age using ultrasound can be biased if the fetus is growth-restricted, yielding underestimates due to the small stature of the fetus. Multivariate linear regression modeling was used to estimate and correct for this bias among subjects with a suspected SGA infant who 1) began prenatal care in the first trimester, 2) reported a last menstrual period and 3) had an ultrasound examination between 7-21 weeks. To correct for this bias, an average of 1.5 weeks was added to the ultrasound gestational age. Following the correction, the proportion of PTD cases decreased from 29.1% to 26.5% while SGA cases increased from 23.7% to 31.3%.

Using this PTD classification, occupational physical and psychosocial stressors were studied. Continuous employment over the first 20 weeks of pregnancy was associated with a 30% increased risk of PTD versus not working. Working women reporting highly repetitive tasks (aOR=1.47(1.10-1.98)) or inadequate breaks (aOR=1.67(1.03-2.73)) were at increased risk of PTD. Working women who reported high lifting in the home had double the risk of PTD.

Over 5% of control subjects reported an injury during pregnancy, and injured women tended to be younger, unmarried, less educated, and have lower incomes. Women with injuries involving >1 body part (aOR=2.50(1.14-5.49)), or injuries to the abdomen and other regions of the body (OR=1.75(0.59-5.23)) were at increased risk of PTD.

Our findings provide a statistical approach to assess and correct for underestimates of ultrasound gestational age in case-control studies of PTD and SGA. The analyses of occupational exposures and injury during pregnancy indicate the need for studies that incorporate specific and standardized assessments of these exposures.

Abstract Approved: ______________________________
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CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

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has been approved by the Examining Committee
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ACKNOWLEDGMENTS

First, I would like to thank my mentor and thesis advisor, Dr. Audrey F. Saftlas for nurturing my young epidemiologic career with invaluable teaching, advising and experiences I will never forget. To Dr. Corinne Peek-Asa, thank you for reminding me of my abilities and helping me see the light at the end of the tunnel. To Dr. Anne B. Wallis, my gratitude for being my confidant when the process seemed impossible. I want to thank all members of my thesis committee for their technical advice and continued support throughout this process. A special thanks to my friend and colleague Dr. Jennifer Makelarski for being there through it all. Last but not least, I want to thank those most important to me: my husband, Ryan and children, Brock and Katelyn for supporting me with smiles, giggles and hugs; my parents, Tom & Karen Hobbs, who taught me the value of hard work and the desire to go after what you want; my sister, Jenny Hobbs, for endless hours of babysitting so I could accomplish this goal and Michele Galvan for always listening when I needed a friend.

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LIST OF ABBREVIATIONS

LMP	Last menstrual period
PTD	Preterm delivery
SGA	Small for gestational age
IHIPS	Iowa Health in Pregnancy Study
CRH	Corticotrophin-releasing hormones
ACOG	American Congress of Obstetrics and Gynecology
US	United States

CHAPTER I

SELECTED OCCUPATIONAL AND INJURY EXPOSURES AND RISK OF PRETERM DELIVERY

Public Health and Clinical Significance of Preterm Delivery

Preterm delivery (PTD), defined as delivery before 37 completed weeks of gestation, is the second leading cause of infant death in the United States (1), and accounts for 36.5% of all infant deaths (2, 3). In 2008, 12.3 percent of all live births were preterm; this equates to a preterm infant being born every minute (4, 5). The rate of preterm delivery in the United States has continued to grow despite efforts to identify risk factors and preventive interventions. The increase in the rate of PTD is not only due to the rise in the number of multiple births because the rate of singleton preterm births has also increased by 14% since 1990 (6). The adverse effects of preterm delivery are enduring, contributing to almost half of birth related childhood morbidity (7) including greater risk of respiratory distress, inability to control blood sugar levels, hearing or sight impairment, and neurological disorders (2, 8). Half of pediatric neurodevelopmental disabilities are due to prematurity (2). Of particular clinical concern are births before 32-34 gestational weeks, these contribute the highest proportion of infant deaths and long term morbidity. An infant born extremely preterm (<28 weeks) is 170 times more likely to die than a term infant (6). Late preterm infants (34-36 weeks) also suffer substantially increased risks of respiratory distress, hypoglycemia, and hypothermia (9). In 2001, $5.8 billion was spent on treating preterm or low birth weight infants during just the first year of life with an average cost of $15,000-$65,000 per infant (10). Only half of these health care costs were paid by private health insurance with Medicaid and private payment covering the additional half (10).

Epidemiology of Preterm Delivery

PTD is a multi-factorial condition without a single root cause. A previous preterm delivery is the strongest predictor of a subsequent preterm delivery with an over five-fold increased odds of PTD; additional factors include maternal infection, multiples, the extremes of maternal age and African-American race, less formal education, short cervical length, cervical incompetence, and maternal smoking (2, 7, 11-15).

The etiology of PTD is not well understood. PTD is often classified into three subtypes; 1) spontaneous onset of preterm labor, 2) preterm premature rupture of membranes (PPROM) prior to the onset of labor, and 3) medically-induced preterm birth. Common risk factors for the three subtypes of preterm delivery include previous preterm delivery, African American maternal race, and inadequate prenatal care (16, 17). Women with spontaneous onset of preterm delivery, including spontaneous labor or rupture of membranes, are more likely to have low pre-pregnancy body mass, be less than 18 years of age, maternal infection, cervical incompetence and participate in unhealthy behaviors such as smoking (2, 16, 18, 19). Medically induced PTD is more likely due to maternal conditions such as hypertension and antepartum bleeding as well as fetal conditions such as intrauterine growth restriction and developmental anomalies (2, 16, 19).

In recent years, the identification of preterm risks associated with a woman's own intrauterine experiences has been established. If a woman herself was born preterm she is at over a 50% increased risk of delivering a preterm infant (20). Women with a family history (mother, full sister or maternal half-sister) of PTD are 40-60% more likely to deliver a preterm infant compared to women whose mother, full or half sister had delivered a term infant (14). A partner's history of preterm delivery with another woman did not increase PTD risk but a previous preterm delivery by the mother, regardless of whether it was the same or different partner, increased the risk of PTD, suggesting a maternal genetic component to PTD (14).

The determination of gestational age to classify PTD

Several methods for determining gestational age at delivery have been used in research and surveillance. Historically, pregnancy dating has been based on a woman's last menstrual period (LMP). The LMP, based on maternal self-report, can overestimate gestational age if non-menstrual vaginal bleeding is mistaken for a menstrual period or can underestimate gestation age in women with an ovulation cycle longer than 28 days leading to misclassification (21). LMP dating is also prone to digit preferences for the 15th day of the month and days that are a multiple of five (22). Lastly, women at high risk of a poor pregnancy outcome (younger age, less educated, uninsured, with little or no prenatal care) are also reported to have less accurate recall of LMP dating (23-25). To improve on LMP-based gestational age estimates, the United States birth certificate added the clinical estimate of gestational age in 1989. The clinical estimate of gestational age considers all available prenatal and neonatal information to provide a more accurate estimation of gestational age; however the actual source of the measurement is not recorded on the birth certificate. It is possible that postnatal knowledge of birth weight could affect the clinical estimate: lighter infants are more likely to be classified as preterm and heavier infants are more likely to be classified as term when dating is based on the clinical estimate rather than a reliable LMP date (26-29).

Gestational age dating by ultrasound is widely used in studies of risk factors for preterm delivery. Gestational age dating by ultrasound is based on the key assumption that fetal growth is relatively uniform early in gestation (30-32). In normally grown fetuses, ultrasound dating before 21 weeks gestation is viewed as the most accurate source of dating (22, 33, 34). However, several studies report that reliance on ultrasound dating of fetuses with growth restriction in the mid-2nd trimester is likely to underestimate gestational age compared to dating based on reliable 1st trimester LMP dates (33, 35, 36). As such, infants that are small for gestational age (SGA) may be classified on a second trimester ultrasound as a 'younger' or less mature fetus and assigned an erroneously late due date (33, 34, 36). In this instance, ultrasound dating provides the infant with an erroneously younger gestational age, increasing the likelihood that the birth will be classified as preterm rather than SGA. Such misclassification may be less likely to occur with ultrasound performed in the first trimester (36). In a clinical trial of women with reliable LMP dates and an ultrasound gestational age estimate at 15 weeks, Waldenstrom et al (37) found that the use of ultrasound gestational dating, instead of LMP, underestimated the incidence of SGA by 26%. Over a five-year period, physician preferences for ultrasound gestational age dating over reliable LMP dating in one hospital system led to a decrease in the average gestational age at delivery (39.2 versus 38.2 completed weeks) resulting in a 6% increase in the rate of PTD and a 4% decrease in SGA deliveries (38). Given that the perinatal mortality rate among SGA infants is 10 to 20 times that of normally grown fetuses (39) and that preterm delivery contributes to almost one-third of infant mortality, being able to correctly classify gestational age at delivery, either by ultrasound or LMP, is essential.

Finally, US fetal growth curves for identifying SGA are based on LMP estimates of gestational age at delivery, not on ultrasound estimates of gestational age (40, 41). Use of ultrasound estimates of gestational age at delivery in place of LMP dating decreasing the likelihood of SGA identification due to the ultrasound systematic error to date small fetus' as 'younger' (42, 43). Some authors have attributed this tendency of 'younger' dating by ultrasound to prolonged menstrual cycles (44). Our analysis presented in Chapter II, however, suggests there is a systematic under-estimation of gestational age based on ultrasound examinations among infants who are suspected to be small for gestational age, resulting in an overestimation of preterm birth and an underestimation of small for gestational age rates.

The physiology of stress and PTD

The relationship between stress and preterm delivery has not been firmly established. Previous research has shown that life stress or stress due to pregnancy complications may put women at an increased risk of preterm delivery (45). Few studies to date, however, have examined the effects of occupational physical and psychological stress on PTD risk while simultaneously controlling for life and pregnancy-related stress.

In general, stress to a human, regardless of the source, stimulates an increased release of corticotrophin releasing hormone (CRH) by the hypothalamus. The release of CRH results in increased plasma circulation of CRH and plasma cortisol. The increased cortisol inhibits immune responses, reproduction through sub-fertility and miscarriage, and growth (46).

There are three key physiological mechanisms of stress that could influence the risk of preterm delivery (Figure 1.0). First, both physical and psychological strains have been shown to trigger an individual physiological stress response resulting in an increase in CRH (45, 47, 48). During pregnancy maternal stress stimulates the placenta and fetal membranes to release CRH into maternal and fetal circulation (49, 50). Over the course of pregnancy the levels of CRH naturally increase as the pregnancy progresses; these increasing levels of CRH, either from pregnancy progression or maternal stress induced, may signal to the fetus that birth is near, directly or indirectly through their interaction with oxytocin and prostaglandins. Approaching parturition, circulating CRH interacts with oxytocin and prostaglandins in maintenance of uterine contractions (51). Therefore stress may lead to the initiation of preterm uterine contractions and maintain these contractions through the release of CRH and its interaction with oxytocin and prostaglandins.

Secondly, physical strain can trigger an individual's physiological stress response resulting in the release of CRH and cortisol, immune suppression and increased risk of maternal infection and/or inflammation (48, 51). Maternal inflammation and infectious processes are associated with increased risk of preterm premature rupture of membranes (51) and uterine irritability; both of which can cause cervical dilatation and uterine activity that leads to PTD.

Lastly, strenuous activity of short duration reduces blood volume to the placenta and fetus causing fetal distress (49, 52). This may trigger the onset of labor or encourage medical intervention to relieve fetal distress, increasing the likelihood of spontaneous or medically induced preterm delivery.

Occupational exposures and risk of PTD

Standing and PTD

Large prospective studies and reviews have found an association between standing and preterm delivery while less methodologically sound studies are unable to detect such a relationship due to limitations such as small sample size and poor measurement of exposure. The definition of standing has varied across studies including a minimum time of 4-8 hours per day to a vague definition such as “prolonged” standing making conclusions about the risk of standing on preterm delivery difficult.

Standing during pregnancy has been associated with a 20-200% increased risk of PTD (53-57). A review by Ahlborg et al (58) found that pregnant women who stood for at least 5 hours per day were more likely to have a preterm delivery than those in sedentary jobs. In a large prospective cohort study, Launer et al (52) reported that women who stand at work versus those in sedentary jobs were at increased risk of PTD.

Other studies have shown no increased risk of PTD with standing. In a cross-sectional study of Mexican pregnant workers, Ceron-Mierles et al (59) found that the average length of time standing at work was 4 hours but there was no association between standing and PTD. Pompelli et al (12) determined that women in their nested case-control study who stood at least 30 hours per week were not at an increased risk of PTD. The proposed research utilizes data from a population-based case-control study of PTD that is adequately powered to examine standing during pregnancy as a risk factor.

Heavy lifting and PTD

The literature on heavy lifting and risk of PTD has been mixed. The definition of “heavy” has varied across studies, with definitions cited in terms of 15 or greater pounds or the number of times per week that anything considered “heavy” was lifted, regardless of weight.

In general, heavy lifting has been associated with an increased risk of preterm delivery but most results have not been statistically significant. Cohort (12, 60, 61) and cross-sectional (62, 63) studies that examined lifting in the first or second trimester have found a 14% to 49% increased risk of preterm delivery: however, just one study of over 15,000 births found the risk to be significant (62). Case-control studies by Berkowitz (64) and Saurel-Cubizolles (56) found no increased risk of preterm delivery with heavy lifting.

Psychological Work Stress and PTD

The definition of psychological work stress varies. Much of the literature has used the Karasek Job Content Questionnaire (65) as the measure of occupational psychological demand while others have used Mamelle's occupational fatigue index (66) to measure this construct. Often in research of psychological work stress, authors have used job title linked with the O*Net (67) database to estimate the level of occupational stress. The O*Net database provides comprehensive details on key elements of jobs and can be easily linked to job title if one of several recognized job coding systems (e.g. Standard Occupational Classification, etc) corresponds to the job title.

Although convenient and cost-effective, use of job title as a proxy for psychological stress does not account for individual variation in responses to stress at work. Studies that have assessed psychological job stress using job title as a proxy for self-reported experience have identified psychological stress as a risk factor for PTD but all results have been non-significant due to small sample sizes (68).

Women working in high strain jobs, defined by Karasek as jobs with a high level of demand but little control over the work process, are shown to experience a 30-40% increased risk of PTD (59, 69, 70). A study by Escriba-Aguir et al (71) found that women working for more than the first 3 months of pregnancy in jobs with high psychological demand, a subscale of the Karasek job strain construct, had a 46% increased chance of PTD. Previous research has not taken into account a subject's general disposition or pregnancy-related distress when measuring work-related mental stress, therefore previous results may not be approximating just work mental stress but general stress during pregnancy.

A self-report of occupational psychological stress, as compared to job title as a surrogate, is a better measurement of actual stress response. Hobel et al (72) found that it was not a specific event that increased a woman's risk of preterm delivery but her stress response to that event that was associated with increased risk; therefore maternal self-report may account for within job variability of psychological stress that a job title proxy cannot.

Maternal injury and PTD

Unintentional injury is the leading cause of death in women of reproductive age in the United States. From 2002-2005, there were almost 500 injury-related deaths to Iowa women aged 18-45 years (73). Given the special medical management considerations of injured pregnant women and the large number of injuries sustained by women of reproductive age it is important to understand the risks associated with injury in a population based sample of pregnant women, as explored in Chapter IV.

Pregnant women who are admitted for trauma during pregnancy are more likely to deliver preterm (74) regardless of the severity of injury (75). In addition, those considered 'non-injured' after examination are also at increased risk of PTD (76). Previous research on maternal prenatal injury has focused only on women requiring medical attention (74-76) or secondary analysis of hospital discharge injury codes (74) therefore the characteristics of injuries among pregnant women who do not seek medical care is not well documented. Among medical-care seeking injured pregnant women, more than half of fetal losses are due to a minor injury (77); therefore it is important to study injuries in a population based sample of pregnant women that do not require admittance as these "minor" injuries may affect the health of the unborn fetus.

Among non-pregnant women, falls and motor-vehicle accidents are the leading causes of non-fatal injury in the United States (73), so it is of no surprise that these are also the leading mechanisms of injury among pregnant women. Motor vehicle accidents are the leading mechanism of injury among pregnant women who report for medical care (78). The blunt abdominal trauma that may occur during a motor vehicle accident can lead to placental abruption or uterine rupture resulting in fetal distress or demise (79). It is estimated that there are three times more fetal deaths as infant deaths due to maternal motor vehicle accidents (79) which underlines the public health importance and need to understand the risk factors for maternal/fetal injury to guide development of effective prevention strategies for these injuries. Non-severely injured pregnant women may be at an increased risk of abruption, which may be subclinical and therefore not identified at the time of the injury, but still lead to an increased risk of a negative pregnancy outcome such as preterm delivery or fetal death (76, 78, 79). Prenatal programs to educate women on the proper placement of a seatbelt during pregnancy may prevent almost half of fetal losses in motor vehicle crashes (79). Klinich et al (79) found that 29% of women who were properly restrained had adverse fetal outcome while 50% and 80% of those that were improperly restrained or unrestrained, respectively, had adverse fetal outcomes.

Falls are the second leading mechanism of injury in pregnant women (74-76). Falls resulting in more severe injury and admission have been linked to poor outcomes, such as fetal death and prematurity (74). In the only population-based study of falls, Dunning et al (80) found increased risk among women who were less than 24 years of age, had less than 12 years of education and in their sixth through eighth month of pregnancy. The mechanisms associated with falls in this population based sample included stairs and slippery surfaces. The most commonly reported injuries were bruises and sprains/strains.

The lack of population based studies of injury risk during pregnancy hinders the ability to create evidence based prevention and education resources on this important public health topic. As well, the current estimates of injuries during pregnancy are likely underestimates as the majority include only medically treated injuries. Chapter IV identifies individual and environmental risk factors associated with injury among controls in a population-based case control study.

Iowa Health in Pregnancy Study

The Iowa Health in Pregnancy Study (IHIPS) is a population-based case-control study of the effect of intimate partner violence and maternal stress on the risk of preterm delivery and small-for-gestational-age among 2,709 live births to Iowa residents over the period, 2002-2005. The target population of IHIPS included all residents of Polk, Johnson, Scott and Black Hawk counties who delivered a singleton live birth in Iowa over the period from May 1, 2002 through June 30, 2005. Electronic Iowa birth certificates served as the sampling frame for the study. All residents who delivered a singleton preterm or SGA infant, based on birth certificate data, were selected for study participation. Potential control subjects delivered full-term singleton infants, and were randomly selected after frequency matching on county of residence. Excluded from the study were women under 18 years of age at the time of delivery, women with type-1 or type-2 diabetes mellitus, systemic lupus, or chronic renal disease, women who do not speak English, and those with multiple fetus pregnancies (e.g., twins). Women with the previously mentioned chronic conditions and multiple fetuses are more likely to have adverse pregnancy outcomes; therefore, they were not included in the study.

All women selected from the birth certificates were contacted by mail with a study introductory letter. The Iowa birth certificate does not provide parental telephone numbers; thus, intensive staff efforts were required to identify a potential subject's telephone number; a specific study introductory letter was sent to a women based on her telephone number availability. Women with a telephone number were contacted two weeks following the introductory letter to introduce the study procedures and complete informed consent. At least 10 call attempts was made to each subject at different times of the day over different days of the week before a subject was considered unable to be reached by phone. Subjects who consented completed eligibility screening, a 45-minute telephone interview, and signed and returned a prenatal and labor/delivery medical record release.

Using standardized scripts and questionnaires, interviewers collected data that covered many areas related to the risk of preterm delivery: demographic, socioeconomic, lifestyle characteristics, health and occupational histories as well as types of stress, including life, relationship and occupational stress.

Of the 7202 potential births selected from the birth certificate, 4250 (59.0%) could be reached by phone. Of these, 19.7% (N=836) refused to participate and 12.9% (N=548) were ineligible for study participation. Over 94.5% (N=2709) of the 2866 eligible to participate completed the telephone interview. The response rate for IHIPS was 45.2% and the participation rate was 76.6% (81). Signed prenatal and labor/delivery medical record releases were received from over 90% of interviewed cases and controls.

There are several advantages to using the IHIPS database to study these research questions. IHIPS is uniquely able to assess several types of stressors, presenting an outstanding opportunity to study occupational stress while controlling for other types of maternal stress. In addition, IHIPS is a population-based case-control study that will allow for a description of injuries in non-medically treated pregnant women. Lastly, the IHIPS data set includes sources of gestational age dating by early ultrasound and last menstrual period among a case-control population making it an exceptional dataset for studying the issue of gestational age dating. IHIPS is a relatively large population-based study, well powered for these research questions, and allows for accurate definition of gestational age at delivery based on medical record abstractions of ultrasound dating, and self-reported last menstrual period.

Goal and Significance

The long term goal of this project is to reduce the occurrence of preterm delivery. As a step towards this goal, the dissertation analyses will examine the association of occupational physical and psychological stress and maternal injury with PTD risk using a rigorous classification of gestational age at delivery that reduces the bias inherent in use of ultrasound gestational age dating in women with a suspected small for gestational age infant. Ultimately, better understanding of the effects of these stressors on risk of preterm delivery will lead to interventions that reduce the prevalence of preterm delivery.

Approach

The aims of this dissertation are three-fold:

1. To determine an ultrasound gestational age correction method to apply to subjects that are selected from the birth certificate as a suspected fetal growth restricted with a first trimester-reported last menstrual period and ultrasound between 7 and 20 weeks gestation.

2. To determine if maternal physical work characteristics and psychological job stress increases a woman's risk of preterm delivery.

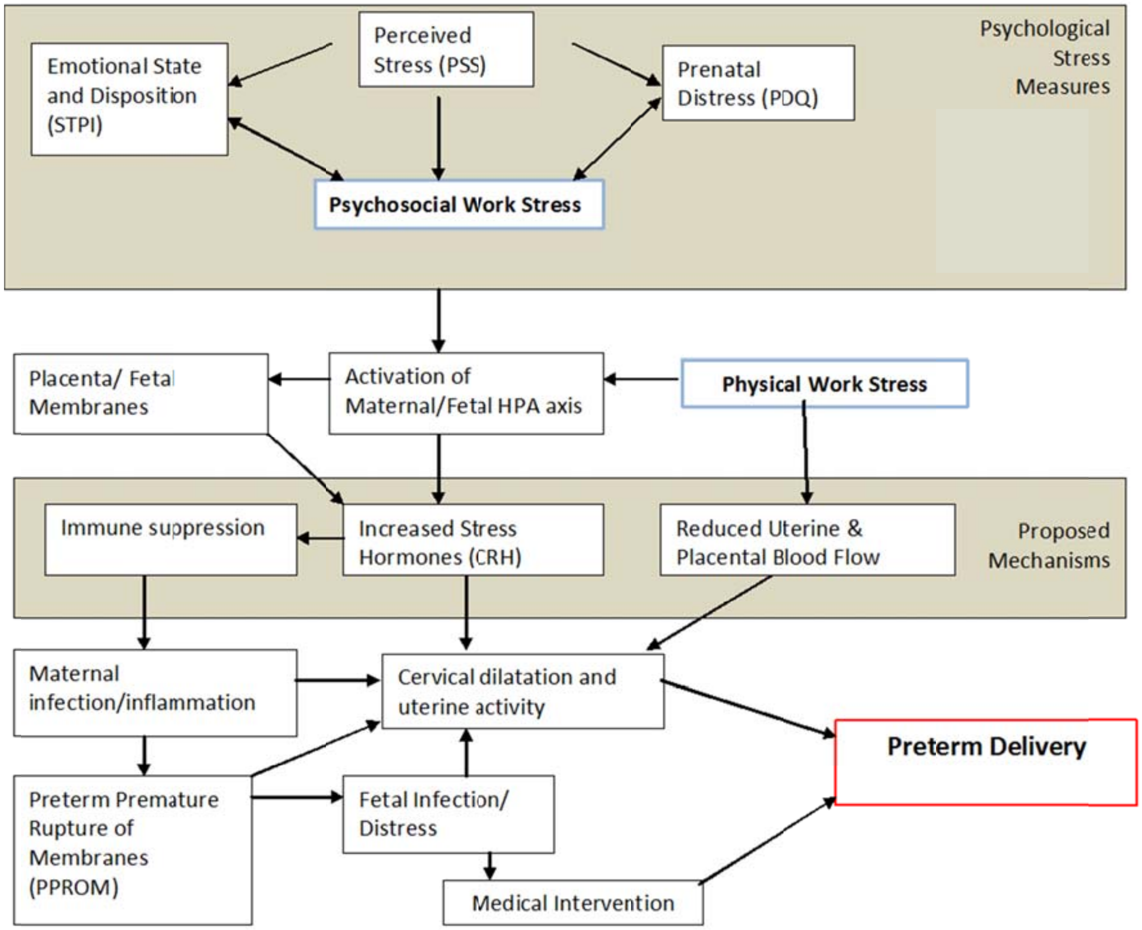
3. To determine if maternal prenatal injury increases a woman's risk of preterm delivery.

Multivariate linear regression is used to determine the ultrasound gestational age correction for subjects selected as small for gestational age from the birth certificate with a 1st trimester reported last menstrual period and ultrasound between 7 and 20 weeks.

To estimate the risks associated with occupational exposures during pregnancy, data from IHIPS were used to measure the frequency and duration of physical work load as well as the occupational mental stress felt by women who worked continuously during the first 20 weeks of pregnancy while controlling for important covariates using logistic regression analysis.

IHIPS data are also used to describe the types of injuries among controls in this population and to estimate the crude risk of preterm delivery associated with maternal injury.

Figure 1.1 Biological mechanisms for the relationship between work physical and psychological stress and PTD.



CHAPTER II

GESTATIONAL AGE DATING: BEING SMALL CAN MAKE A BIG DIFFERENCE

Summary of findings

Purpose**:** Recommended algorithms for gestational age dating by ultrasound are based on studies of low-risk women with regular and reliable last menstrual periods. Application of these guidelines among infants with suspected fetal growth restriction is likely to underestimate their gestational age because they are small. We developed a statistical approach to adjust for errors in dating by an ultrasound at ≤ 20 weeks among subjects selected as potential small for gestational age (SGA) cases for a case-control study.

Methods**:** The analysis includes subjects from a case-control study of preterm delivery and SGA who began prenatal care in the first trimester, had a valid LMP date and an ultrasound between 7-20 weeks (N=1135). In clinical practice, when LMP and ultrasound disagree by >7 days at <14 week ultrasound or >10 days at 14-20 week ultrasound, a subject's dating is based on ultrasound rather than LMP. This algorithm was applied and the proportion with LMP dating re-assigned to ultrasound dating was calculated by selected case (SGA or preterm) or control status. Confounding and interaction between maternal characteristics and risk of reassignment were explored. Multi-variable linear regression was used to develop models that correct ultrasound gestational age dating for subjects with suspected SGA.

Results**:** Subjects selected as SGA had a mean of 5.5 days difference between LMP and ultrasound. Controls and preterms had a mean difference of 1.1 and -0.2 days, respectively. Controls/preterms had 20.2% of LMP dates reassigned to ultrasound while 31.6% of SGA infants were reassigned. Over 87% of SGA infants were reassigned when their LMP dating was greater than their ultrasound dating. For all SGA selected infants, an average of a 1.5-week correction in ultrasound dating was needed. This correction

differs by maternal age, vaginal bleeding in the first trimester, and smoking in 1st or 2nd trimester.

Conclusion**:** Ultrasound underestimates the gestational age of infants pre-designated from the birth certificate as SGA. The authors have developed an approach for correcting ultrasound dating in infants selected as SGA in a case-control population that may be applied to other case-control studies of SGA.

Introduction

Accurate gestational age dating of pregnancies is vital to public health surveillance and research investigating causes of small for gestational age (SGA) and preterm deliveries (PTD). Errors in estimating gestational age can result in misclassification of these adverse birth outcomes.

Several methods are available for dating a fetus in-utero but each has strengths and weaknesses. The most widely available approach is a woman's self-reported date of the last menstrual period (LMP), defined as the first day of the last menstrual period before conception. The accuracy of gestational age dating based on LMP has been questioned. The major shortcomings of dating by LMP include mistaking vaginal bleeding early in pregnancy as a menstrual period, inaccurate recall of the LMP date, and menstrual cycles longer (or shorter) than the 28 days assumed in calculating gestational age (82-84). Ultrasound dating at or before 20 weeks gestation has been considered a more accurate source of dating, particularly when performed in early pregnancy (22, 85, 86).

In normally grown fetuses, ultrasound dating has been shown to be more accurate than the LMP (22, 33, 34); however, few studies to our knowledge have assessed the validity of ultrasound dating in women with growth restricted babies. Fetal ultrasound dating assumes that fetal growth is relatively uniform early in gestation (30, 31); however, this may be untrue, particularly in the growth restricted fetus (87, 88). Several studies report that reliance on 1st or 2nd trimester ultrasound dating of fetuses with growth restriction is more likely to underestimate gestational age than when dating is based on reliable LMPs reported during the first trimester of prenatal care (33, 35, 36). Consequently, complete reliance on ultrasound dating of growth restricted fetuses could ultimately lead to an overestimation of the PTD rate and an underestimation of the rate of SGA deliveries. This error is due to fetal growth restriction being misclassified by ultrasound as a 'younger' fetus rather than a fetus with growth restriction (33, 34, 36). In a clinical trial of gestational age dating of infants by LMP or ultrasound at 15 weeks, Waldenstrom et al (37) found that the use of ultrasound dating, instead of LMP, reduced the rate of SGA infants by 26%.

The serial ultrasound studies used to establish gestational age dating rules and guidelines have typically included low-risk women with very reliable LMPs. Thus, the validity of these guidelines is less likely to hold up when applied to high risk obstetric populations. Of note, in case-control studies of preterm or small for gestational age deliveries, the study populations include much higher proportions of high-risk women with adverse pregnancy outcomes and unreliable LMP dates than the study populations used to develop the ultrasound dating guidelines, putting the application of these algorithms in question. The consequence is increased misclassification of gestational age, which will ultimately impact the validity of study findings and the risk of type 1 and type 2 errors.

The objective of this paper is to test the hypothesis that infants with suspected SGA are systematically dated 'younger' by ultrasound than by LMP, and to develop a statistical approach to correct for such errors in gestational age dating. For this purpose, we analyze data from a large population-based case-control study of preterm delivery and small for gestational age births and compare gestational age dating based on LMPs reported during the first trimester of pregnancy versus dating based on a first ultrasound exam performed between 7 and 20 weeks of gestation.

Methods

We analyzed data from the Iowa Health in Pregnancy Study (IHIPS) to compare gestational age dating by LMP and an ultrasound conducted between 7 and 20 completed weeks. The American Congress of Obstetrics and Gynecology (ACOG) guideline for gestational age dating by ultrasound and LMP were used as a standard for acceptable agreement between the two dating sources.

Study design

IHIPS is a population-based case-control study conducted to determine the influence of intimate partner violence and maternal stress on preterm delivery (PTD) and small for gestational age (SGA) outcomes among live births to Iowa residents living in four counties over the period May 1, 2002 through June 30, 2005. Electronic Iowa birth certificates served as the sampling frame for the study.

All Iowa residents of the study counties who delivered a singleton preterm or SGA infant, based on birth certificate data, were selected for study participation. Gestational age at delivery was based on the date of the LMP or clinical estimate as recorded on the birth record. Preterm delivery was defined as birth before 37 weeks of pregnancy. SGA was classified as the lowest tenth percentile of birth weight for gestational age at delivery using the algorithm developed by Alexander et al which was based on United States births from January 1, 1994 through December 31, 1996 (89)(89). Potential control subjects delivered normally grown or term singleton infants, and were randomly selected after frequency matching on the distribution of county of residence among cases. Excluded from IHIPS were women under 18 years of age at the time of delivery, women with type-1 or type-2 diabetes mellitus, systemic lupus, or chronic renal disease, women who do not speak English, and those with multiple fetus pregnancies (e.g., twins).

All women selected from the birth certificates were contacted by mail with a study introductory letter. Following intensive staff efforts to trace potential subjects' telephone numbers, women with identified telephone numbers were contacted to introduce the study procedures and complete informed consent. Study participation consisted of a brief eligibility screening, a 45-minute telephone interview, and provision of a signed medical record release allowing the research team access to their prenatal and hospital delivery records.

Of the 7202 potential births selected from the birth data, 4250 (59.0%) could be reached by phone. Of these, 19.7% (N=836) refused to participate and 12.9% (N=548) were ineligible for study participation. Over 94.5% (N=2709) of the 2866 eligible to participate completed the telephone interview. The response rate for IHIPS was 45.2% and the participation rate was 76.6% (81). Signed prenatal and labor/delivery medical record releases were received from over 90% of interviewed cases and controls.

Data collection

Information ascertained from the postpartum interview included demographic and lifestyle characteristics as well as medical and pregnancy history. Trained medical record abstractors extracted data on LMP, earliest ultrasound exam dating and estimated gestational age from the subject's prenatal, and labor/delivery medical record.

All study protocols and informed consent procedures were approved by the University of Iowa Institutional Review Board.

Analysis population

To address our study objective, we restricted our analyses to subjects who met each of the following inclusion criteria: participants completed the telephone interview, returned a signed medical release form, and began prenatal care in the first trimester (months 1-3), had a non-missing LMP, and received a prenatal ultrasound between 7 and 20 completed weeks, as estimated by ultrasound. Early prenatal care is associated with better recall of LMP and access to an early ultrasound, thus all subjects had to have initiated prenatal care before the 14th gestational week. If the LMP date was missing from the medical chart it was substituted from the birth certificate, if available. Subjects who had an ultrasound exam before 7 weeks were excluded from the analysis as these ultrasounds measure only the yolk sac, a highly unreliable parameter compared to biparietal diameter, which is first visible by 7 weeks (32). A total of 1135 subjects met inclusion criteria for the study analysis: 493 met birth certificate criteria for SGA; 256 met birth certificate criteria for PTD, and 386 were selected as control subjects.

Covariates

We focused on several maternal demographic and pregnancy factors collected during the interview that could be associated with LMP and ultrasound dating. The following were recorded as reported during the interview: maternal age at delivery (<20, 20-24, 25, 29, 30-34, 35+), race and Hispanic origin (non-Hispanic white, non-Hispanic black, Hispanic, Asian, Mixed race and other), maternal education (≤ high school, some college, college graduate, graduate degree), maternal smoking during the 1st or 2nd trimester, and use of peri-concenceptual or pregnancy prenatal vitamins. First trimester vaginal bleeding was based on data from the interview or recorded in the medical chart. Pregnancy intention and the excitement about pregnancy once a subject found out she was pregnant was examined using questions from the Pregnancy Risk Assessment Monitoring System 2000-2003 Core Questionnaire. (http://www.cdc.gov/prams/Questionnaire.htm). Fertility techniques used to conceive the index pregnancy were asked only of the subjects with intended pregnancies. Household and individual incomes were categorized based on the distribution in IHIPS control subjects.

Statistical analysis

To identify differences between subjects included in our analysis versus those excluded we compared reproductive and demographic characteristics. Chi-square tests for categorical variables were used to identify significant differences between the groups. Students t-tests were used to compare continuous variables including age at delivery, pre-pregnancy body mass index, household and subject income. Demographic and reproductive characteristics were examined if they had previously been associated with timing of the beginning of prenatal care, receiving a prenatal ultrasound examination before 21 weeks, or the reliability of LMP dating.

To determine if maternal and pregnancy characteristics affect the likelihood of ultrasound dating replacing LMP dating, we examined differences by initial case control status. Characteristics were examined if they had been previously linked in the literature to the reliability of LMP reporting, likelihood of receiving an ultrasound before 21 weeks and associated with beginning prenatal care in the first trimester.

To compare gestational age dating by LMP and ultrasound, we calculated the discrepancy (in days) between LMP and ultrasound gestational age at the time of ultrasound. The LMP was used as the referent for the computation of days difference (i.e., LMP gestational age estimate – ultrasound gestational age estimate). This discrepancy will hereafter be referred to as ‘days difference.’ A positive day difference represents an LMP estimate that dated the fetus as ‘older’ than the corresponding ultrasound estimate; a negative day difference represents an LMP estimate that dated the fetus as ‘younger’ than the corresponding ultrasound estimate. We examined the distribution of the days difference variable stratified by initial case-control status using measures of central tendency (mean, median, standard deviation), and in graphical form for clarity. The Students t-test was used to compare the mean day difference by initial case-control status.

To determine the proportion of reassignment from LMP to ultrasound dating the ACOG gestational age dating guidelines were applied to the study sample. Among women who have an ultrasound before 14 completed weeks of gestation, ACOG recommends use of the ultrasound estimate of gestational age when the LMP and the ultrasound estimates differ by more than 7 days. Among women who have had an ultrasound between 14 and 20 weeks, ACOG recommends use of the ultrasound estimate when the LMP and the ultrasound dating differ by more than 10 days (90).

To measure and evaluate the extent of any differences between gestational ages as estimated by the two methods, we compared and plotted the ultrasound estimate of gestational age versus the LMP estimate of gestational age at the time of the ultrasound exam, using the ACOG dating guidelines as the standard for acceptable agreement between the two estimates.

To establish if an ultrasound gestational age correction was needed and if so, how much of a correction, linear regression modeling was conducted with ultrasound gestational age as estimated by ultrasound as the independent variable and LMP gestational age at time of ultrasound as the dependent variable. Maternal characteristics associated with reassignment of LMP dating based on ACOG guidelines were modeled as potential interaction and confounding variables. These covariates were first tested for interaction with gestational age as estimated by ultrasound if there was biological plausibility to support the analysis (i.e., maternal age, smoking during 1^{st} or 2^{nd} trimester, and 1^{st} trimester vaginal bleeding). Interaction and confounding were considered if a chi-square p-value was less than 0.10 or previous research had established an association. A statistically significant interaction was determined when the slopes of the values within a variable were significantly different from each other. The intercept value for the final multivariate linear models was used as the initial gestational age correction value added to (or subtracted from) the ultrasound estimate of gestational age, and then adjusted, as appropriate, for the different levels of the relevant interacting and confounding variables. The classifications of preterm delivery and small for gestational age by initial case-control status from birth certificate data were compared to the classification of preterm delivery and SGA based on ACOG guideline following ultrasound dating correction from the linear regression modeling. SGA was classified using the nomogram by Alexander (89).

The data analysis for this paper was generated using SAS® software, Version 9.2 of the SAS System for Microsoft, SAS Institute Inc., Cary, NC, USA.

Results

The IHIPS sample consisted of 2709 subjects who completed the telephone interview: 1135 met inclusion criteria for this analysis. Overall, the included women tended to be older, more educated, and had higher incomes than the other IHIPS subjects (Table 1). Among subjects with an initial status of SGA, those included had a lower pre-pregnancy body mass index, a higher proportion of intended pregnancies, were less likely to have used fertility interventions to conceive, were more likely to use prenatal or multi-vitamins during the peri-conceptional period and were less likely to smoke during or before pregnancy than SGA subjects who did not meet inclusion criteria. Among control subjects, those included in the analysis were less likely to smoke, less likely to conceive using fertility treatment, more likely to take prenatal vitamins during pregnancy, and had a higher proportion of intended pregnancies. The PTD subjects meeting inclusion criteria were more likely to be pregnant for the first time and nulliparious than those excluded. The distribution of the number of days difference between the LMP and the ultrasound estimates of gestational age is displayed in Figure 1.1. The mean day difference for controls and PTDs were similar: 1.1 and -0.2 days respectively ($p=0.1404$) while the mean day difference for SGA subjects was 5.5 days: significantly higher than those of the controls and PTDs ($p=<0.0001$). The increased day difference in SGA subjects, as compared to controls and preterms, is consistently seen at all ultrasound gestational ages (Figure 1.2), further reinforcing the hypothesis that ultrasound systematically dates the SGA subjects 'younger' than their LMP due to their small size. Given the similarities in day difference between LMP and ultrasound dating for control and preterm subjects, these groups were combined for all further analyses.

As show in Figure 1.3, the SGA distribution of days difference between LMP and ultrasound gestational age estimates is heavily weighted towards a positive day difference regardless of the gestational age at the time of ultrasound. As many as 39.2% of SGA subjects requiring gestational age reassignment have LMP dating that is 'older' than their ultrasound dating. In contrast, the controls and PTDs with dating replacement are more evenly distributed on both sides of reassignment.

Application of the ACOG guidelines demonstrates the direction and extent of dating differences between the LMP and ultrasound in control/PTDs and SGA subjects (Figure 1.4). Over 79% (N=512) of control and PTD subjects' LMP dating fall within the ACOG guidelines of ±7-10 days and would not have their LMP gestational age replaced by ultrasound. Among the control/PTD subjects that have their LMP gestational age reassigned to the ultrasound dating (N=130), 56.1% (N=73) have LMP gestational ages that exceeds their ultrasound gestational age and 43.8% (N=57) have LMP gestational ages dated earlier than those estimated by ultrasound. In contrast, this relatively even distribution of reassignment is not seen in SGA subjects. Overall 31.6% (N=156) of SGA subjects have their LMP dating replaced by ultrasound. Of the 131 that are reclassified, 87.1% (N=136) are reassigned to an ultrasound gestational age estimate that dates the pregnancy as 'younger' than the LMP.

Several maternal characteristics are associated with LMP reassignment to ultrasound dating in SGAs, whereas there are few such associations among controls and PTDs (Table 1.2). Among controls and PTDs, use of prenatal vitamins is the only variable associated with reclassification of LMP gestational age to ultrasound gestational age: non-users of prenatal vitamins were more likely to be reassigned to a 'younger' ultrasound estimate of gestational age than users. SGA selected subjects with reassignment of gestational age are more likely to be young, less educated, to have smoked during the first or second trimester of pregnancy, have lower household income, and are less likely to take vitamins during the peri-conceptional period.

To correct for the systematic error in ultrasound dating of SGA subjects, we constructed four (4) linear regression models to assess the relationship between LMP gestational age at the time of ultrasound (outcome) and the gestational age as estimated by ultrasound (predictor) (Table 1.3). Variables associated with reassignment, as identified in Table 1.2 and previous research, were examined as potential effect modifiers and confounders. The variables modeled included maternal age at delivery (<25, 25-29, 30+), smoked during the first or second trimester (yes/no) and first trimester vaginal bleeding (yes/no).

Table 1.3 shows the correction factors estimated from the four linear regression models:

Model 1. A main effects model with maternal age (p=0.0214), first or second trimester smoking (p=0.1974), and first trimester vaginal bleeding (p=0.9466),

Model 2. An interaction model examining effect modification of smoking during the first or second trimester with gestational age as estimated by ultrasound (p=0.0012), while controlling for maternal age at delivery (p=0.0376) and first trimester vaginal bleeding (p=0.9367),

Model 3. An interaction model examining effect modification of first trimester vaginal bleeding with gestational age as estimated by ultrasound (p=0.0857), controlling for first or second trimester smoking (p=0.1932) and maternal age at delivery (p=0.0195), and

Model 4. A model with two interactions: the interaction between first trimester vaginal bleeding and ultrasound estimated gestational age (p=0.0646), the interaction between smoking and ultrasound gestational age (p=0.0010), controlling for maternal age at delivery (p=0.0356).

A statistically significant interaction term is interpreted as slopes of the interaction variables being significantly different from one. For example, in the bleeding interaction model (Model 3), the subjects with vaginal bleeding require a correction increase of 0.02 weeks for each week of gestational age at ultrasound, while the non-bleeders have a correction decrease of 0.05 weeks for each week of the gestational age at ultrasound.

The gestational age correction estimates varied by model and the inclusion of confounders and interaction terms. On average, without controlling for confounding variables or interaction terms, the correction factor to the ultrasound gestational age was 1.5 weeks (data not shown). Regardless of the linear regression model used, the ultrasound gestational age correction decreased as the subject's age increased. Non-smokers without first trimester vaginal bleeding required the largest correction factor in each model, except the main effects model (Model 1), regardless of maternal age.

The main effects model (Model 1) calculated the largest correction for the ultrasound dating discrepancy with a mean day difference between the adjusted ultrasound gestational age and LMP gestational age at the time of ultrasound being -6.1 days, which is significantly different than the day difference of PTDs and controls (p=<.0001). The smoking interaction model and the vaginal bleeding interaction model revealed mean day differences of -2.4 (p-value = <.0001), and -2.7 (p-value = <.0001) days, respectively. The model with both the smoking and vaginal bleeding interactions yielded a mean day difference of -2.8 days, which is not significantly different than the day difference in controls and PTDs (p-value = <.0001).

After applying correction factors to the ultrasound gestational ages there is an increase in deliveries classified as SGA and a decrease among those categorized as PTD (Table 1.4). The linear regression models resulted in at least a 13.5%, and as much as a 17.0%, increase in SGA deliveries while decreasing the proportion of PTDs by 9.9% to 13.3% compared to dating by uncorrected ultrasound before 21 weeks.

Discussion

Our analysis suggests that in case-control studies of PTD and SGA, traditional gestational age dating algorithms will over-estimate the number of preterm deliveries while under-estimating SGA for subjects with suspected fetal growth restriction. In this paper, we developed a correction to account for the error in estimated ultrasound gestational age among infants with suspected SGA. This is comparable with the work of Yang et al (91) who found that use of ultrasound dating over LMP dating leads to underestimates of fetal gestational age and hence, overestimates the preterm delivery rate.

It has been suggested that the increase in preterm deliveries and decrease in SGA infants could largely be due to reliance on ultrasound over LMP for gestational age dating (38). Our analysis further supports this hypothesis and advances the research in this area by developing a statistical approach to correct for the systematic error of ultrasound measuring fetal growth restriction as a 'younger' fetus.

The characteristics associated with use of ultrasound dating over LMP dating in our population are similar to those of other studies comparing preterm delivery and SGA classification based on gestational age dating by LMP and ultrasound. Women with an ultrasound before 21 weeks are more likely to be older, more educated, use vitamins pre-conception and to have a higher household income (32, 42, 92). The characteristic differences of women not likely to have an ultrasound before 20 weeks versus the base population limits the use of our ultrasound dating corrections, however the method developed to formulate the dating correction may be used in any population that has a self-reported LMP and ultrasound examination taken between 7 and 20 completed weeks.

Consistent across all models is the reduction in the dating correction as a woman's age at delivery increases. This is not unexpected as older age at conception often leads to earlier ultrasound due to an increased risk of pregnancy difficulties. In addition, older women may be more likely to have a planned pregnancy and therefore a more certain LMP date. Previous studies have also reported closer agreement between LMP and ultrasound dating in women aged 30 years and old (25, 31). As in previous research, our findings demonstrate that women with higher education, and planned pregnancies have higher agreement between LMP and ultrasound dating (31, 34, 93).

Our study findings further support the hypothesis that ultrasound may erroneously date a growth restricted fetus as a 'younger' fetal age, even when performed in the first trimester. In our study population, women with suspected SGA required, on average, at least a 1.5 week ultrasound dating correction. This is what one would expect given that SGA fetus' are physically small and ultrasound measurement of the fetus will date it as "younger" that its actual age. This limitation in using ultrasound dating before 21 weeks among women with suspected fetal growth restriction is supported by other studies, which have found that low birth weight infants (<2500 grams), or those that had a small crown-rump length measured in the first trimester, are consistently dated 'older' by LMP than ultrasound (31, 33, 92, 94). Mercer et al (94) found that infants dated 8-10 days 'younger' by ultrasound than LMP were two to three times more likely to be SGA than other infants. In addition, Morin (33)(33) found the proportion of low birth weight infants increased as the positive day difference between LMP and ultrasound gestational age dating increased. Our study is the first to address this potential bias directly by developing a statistical approach to correct for the systematic ultrasound gestational age dating error in infants with suspected fetal growth restriction.

As in our findings, it has been established that women who smoke during pregnancy are at greater risk of growth restriction and a positive day discrepancy between LMP and ultrasound dating. Previously, small crown-rump length in a first trimester ultrasound and greater positive inconsistency in LMP and ultrasound dating have been associated with an infant being SGA at delivery (25, 92).

The days difference in dating was most notable in subjects with earlier (<18 weeks) ultrasounds, regardless of their initial case status. It is conceivable that women with an uncertain LMP, or first trimester vaginal bleeding are more likely to have an early ultrasound to verify dating or viability of pregnancy. In our analysis, first trimester vaginal bleeding was not associated with having a first trimester ultrasound (data not shown), calling into question the validity of the LMP dating. Previous literature has documented preferential LMP dating for the 15^{th} day of the month; given this, an analysis was completed to determine if subjects within the sample had an inclination to report the 15^{th} day of the month; a preference was not seen (data not shown).

With the ultrasound dating correction, the proportion of SGA deliveries increased and that for PTD deliveries decreased. This is what one would expect as the gestational age is increased following ultrasound gestational age dating correction and some birth weights once considered 'normal' at an earlier gestational age fall into in the lowest 10th percentile of birth weight for gestational age. In a clinical trial of women with regular menstrual cycles and reliable LMP dating, the incidence of SGA diagnosis decreased almost a third using dating by an ultrasound at 15 weeks instead of LMP dating (37). Waldenstrom et al (37) concluded that the change in incidence was due to use of ultrasound dating over LMP dating methods, as the true rate of SGA was unlikely to have changed. We found a smaller proportion of subjects re-classified as SGA (7.2%-20.1%) then previous studies, however, as in other studies, the re-classification was due to ultrasound dating a fetus 'younger' than with LMP dating.

This analysis is subject to some limitations. The certainty of a woman's LMP date and length of menstrual cycle was not ascertained. Women's menstrual cycles sometimes vary from the 28-32 days used in pregnancy dating assumptions, and often have a later time ovulation (44). A longer cycle could account for a positive day difference between LMP and ultrasound but since this association was found only in subjects with an initial status of SGA and there is no reason to believe that control/PTD subjects would have shorter cycles than SGA subjects. Thus, this cannot account for the results found here. In addition, case-control study designs have the potential for recall bias. Of note, the proportion of subjects reporting first trimester vaginal bleeding did not differ by initial status. Subjects with suspected SGA were more likely to report smoking than control or preterm subjects, but given that smoking is a fundamental cause of fetal growth restriction the differences in proportions are likely to be due to the disease process and not recall bias. Ultrasound estimates of gestational age and LMP data were recorded from the subject's prenatal or labor and delivery medical record and therefore this information was collected before the pregnancy outcome was known and not subject to bias.

This study is the first to propose a method to correct for the ultrasound misclassification of gestational age in infants with suspected fetal growth restriction using LMP as the gold standard. Our findings provide strong evidence to support that reliance on ultrasound before 21 weeks alone, particularly among infants with suspected fetal growth restriction, increases the likelihood of misclassifying small for gestational age and preterm outcomes.

Table 1.1 Maternal and pregnancy characteristics for subjects with a 1st trimester LMP and ultrasound between 7 and 20 weeks (inclusion criteria) versus those that do not meet criteria by initial case-control status, Iowa Health in Pregnancy Study (IHIPS), 2002-2005 (N=2709).

		Control		*PTD*		*SGA*	
Maternal Characteristic	*All subjects N = 2709 N(Col %)*	*Included N=386 N (Col %)*	*Excluded N=525 N (Col %)*	*Included N=256 N (Col %)*	*Excluded N=397 N (Col %)*	*Included N=493 N (Col %)*	*Excluded N=652 N (Col %)*
Maternal Age							
Mean(std. dev)	28.3(5.4)	29.5(4.9)	28.5(5.4)[1]	29.2(5.7)	28.6(5.7)	28.0(5.2)	27.3(5.4)[1]
<20	148(5.5)	11 (2.9)	25 (4.8)	17 (6.6)	20 (5.0)	24 (4.9)	51 (7.8)
20-24	548(20.2)	55 (14.3)	109 (20.8)	40 (15.6)	88 (22.2)	100 (20.3)	156 (23.9)
25-29	906(33.4)	135 (35.0)	173 (33.0)	76 (29.7)	102 (25.7)	193 (39.2)	227 (34.8)
30-34	737(27.2)	122 (31.6)	144 (27.4)	75 (29.3)	130 (32.8)	119 (24.1)	147 (22.6)
35+	370(13.7)	63 (16.3)	74 (14.1)	48 (18.8)	57 (14.4)	57 (11.6)	71 (10.9)
	p-value	*0.0471*		*0.1130*		*0.1227*	
Maternal race							
White	2336(86.2)	342 (88.6)	458 (87.2)	235 (91.8)	347 (87.4)	420 (85.2)	534 (81.9)
Black	139(5.1)	16 (4.2)	26 (5.0)	9 (3.5)	20 (5.0)	18 (3.7)	50 (7.7)
Hisp/Latino	58(2.1)	5 (1.3)	17 (3.2)	5 (2.0)	8 (2.0)	11 (2.2)	12 (1.8)
Asian	93(3.4)	11 (2.9)	10 (1.9)	5 (2.0)	7 (1.8)	29 (5.9)	31 (4.8)
Mixed Race	72(2.7)	10 (2.6)	13 (2.5)	1 (0.4)	14 (3.5)	13 (2.6)	21 (3.2)
Other	11(0.4)	2 (0.5)	1 (0.2)				
	p-value	*0.3649*		*0.1230*		*0.1252*	
Maternal education							
≤ High School	536(19.8)	48 (12.4)	85 (16.2)	39 (15.2)	87 (21.9)	101 (20.5)	176 (27.0)
Some college	880(32.5)	108 (28.0)	186 (35.4)	88 (34.4)	131 (33.0)	152 (30.8)	215 (33.0)
College grad	898(33.1)	158 (40.9)	180 (34.3)	79 (30.9)	137 (34.5)	166 (33.7)	178 (27.3)
Grad degree	395(14.6)	72 (18.7)	74 (14.1)	50 (19.5)	42 (10.6)	74 (15.0)	83 (12.7)
	p-value	*0.0093*		*0.0043*		*0.0172*	

Table 1.1 continued…

Pre-pregnancy BMI							
Mean(std. dev)	25.0(5.9)	25.2(5.6)	25.4(5.7)	25.3(5.8)	25.6(6.0)	24.4(6.3)	24.6(5.8)
<25.0	1637(60.4)	222 (57.5)	297 (56.6)	145 (56.6)	228 (57.4)	340 (69.0)	405 (62.1)
25-29.9	582(21.5)	100 (25.9)	131 (25.0)	64 (25.0)	79 (19.9)	77 (15.6)	131 (20.1)
30+	473(17.5)	62 (16.1)	92 (17.5)	46 (18.0)	87 (21.9)	74 (15.0)	112 (17.2)
Missing	17 (0.6)	2 (0.5)	5 (1.0)	1 (0.4)	3 (0.8)	2 (0.4)	4 (0.6)
	p-value	*0.8224*		*0.2175*		*0.0517*	
Infant birth weight (grams)							
Mean(std. dev)	2993(677)	3249(639)	3310(633)	2808(657)	2878(712)	2821(638)	2850(607)
<2500 grams	465(17.2)	32 (8.3)	40 (7.6)	65 (25.4)	97 (24.4)	98 (19.9)	133 (20.4)
2500-2999	920(33.9)	88 (22.8)	105 (20.0)	97 (37.9)	131 (33.0)	209 (42.4)	289 (44.3)
3000-3499	767(28.3)	120 (31.1)	185 (35.3)	65 (25.4)	107 (27.0)	137 (27.8)	152 (23.3)
3500-3999	392(14.5)	102 (26.4)	137 (26.1)	21 (8.2)	43 (10.8)	32 (6.5)	57 (8.7)
4000+	165(6.1)	44 (11.4)	58 (11.1)	8 (3.1)	19 (4.8)	14 (2.8)	21 (3.2)
	p-value	*0.7125*		*0.4926*		*0.3468*	
Infant Sex							
Male	1378(50.9)	180 (46.6)	265 (50.5)	140 (54.7)	202 (50.9)	248 (50.3)	343 (52.6)
Female	1331(49.1)	206 (53.4)	260 (49.5)	116 (45.3)	195 (49.1)	245 (49.7)	309 (47.4)
	p-value	*0.2514*		*0.3418*		*0.440*	
Smoked before pregnancy							
Yes	732(27.0)	76 (19.7)	123 (23.4)	58 (22.7)	96 (24.2)	147 (29.8)	232 (35.6)
No	1977(73.0)	310 (80.3)	402 (76.6)	198 (77.3)	301 (75.8)	346 (70.2)	420 (64.4)
	p-value	*0.1771*		*0.6540*		*0.0401*	
Smoked during pregnancy							
1st or 2nd tri	589(21.7)	59 (15.3)	99 (18.9)	46 (18.0)	74 (18.6)	123 (25.0)	188 (28.8)
Not at all	2120(78.3)	327 (84.7)	426 (81.1)	76 (26.7)	136 (34.3)	370 (75.1)	464 (71.2)
	p-value	*0.1594*		*0.8289*		*0.1433*	

Table 1.1 continued…

Alcohol use 1st trimester													
Yes	963(35.5)	139	(36.0)	196	(37.3)	76	(29.7)	136	(34.3)	195	(39.6)	221	(33.9)
No	1742(64.3)	246	(63.7)	327	(62.3)	180	(70.3)	261	(65.7)	298	(60.5)	430	(66.0)
Missing	4(0.1)	1	(0.3)	2	(0.4)	0		0				1	(0.1)
	p-value		*0.6719*				*0.2234*				*0.0509*		
Pregnancy intention													
Then or sooner	1632(60.2)	258	(66.8)	294	(56.0)	165	(64.5)	242	(61.0)	307	(62.3)	366	(56.1)
Wanted later	649(23.9)	76	(19.7)	150	(28.6)	51	(19.9)	92	(23.2)	120	(24.3)	159	(24.4)
Did not want	218(8.1)	25	(6.5)	40	(7.6)	21	(8.2)	35	(8.8)	38	(7.7)	59	(9.1)
Didn't care	208(7.7)	26	(6.7)	41	(7.8)	19	(7.4)	28	(7.1)	28	(5.7)	66	(10.1)
Missing	2(0.1)	1	(0.3)	0		0		0		0		2	(0.3)
	p-value		*0.0069*				*0.7640*				*0.0307*		
Pregnancy excitement once found out pregnant													
Excited	2101(77.6)	314	(81.4)	403	(76.8)	204	(79.7)	307	(77.3)	382	(77.5)	490	(75.2)
Okay	374(13.8)	47	(12.2)	77	(14.7)	34	(13.3)	56	(14.1)	64	(13.0)	96	(14.7)
Not sure	186(6.9)	18	(4.7)	34	(6.5)	17	(6.6)	27	(6.8)	40	(8.1)	50	(7.7)
Didn't want	42(1.5)	5	(1.3)	11	(2.1)	1	(0.4)	5	(1.3)	6	(1.2)	14	(2.2)
Missing	6(0.2)	2	(0.5)	0		0		2	(0.5)	1	(0.2)	2	(0.3)
	p-value		*0.2812*				*0.5985*				*0.6650*		
Gravidity													
1	1103(40.7)	154	(39.9)	192	(36.6)	118	(46.1)	140	(35.3)	211	(42.8)	288	(44.2)
2	754(27.8)	99	(25.7)	151	(28.8)	72	(28.1)	110	(27.7)	139	(28.2)	183	(28.1)
3+	848(31.3)	132	(34.2)	181	(34.5)	65	(25.4)	146	(36.8)	143	(29.0)	181	(27.8)
Missing	4(0.2)	1	0.3	1	0.2	1	0.4	1	0.3	0		0	
	p-value		*0.4871*				*0.0043*				*0.8707*		

Table 1.1 continued…

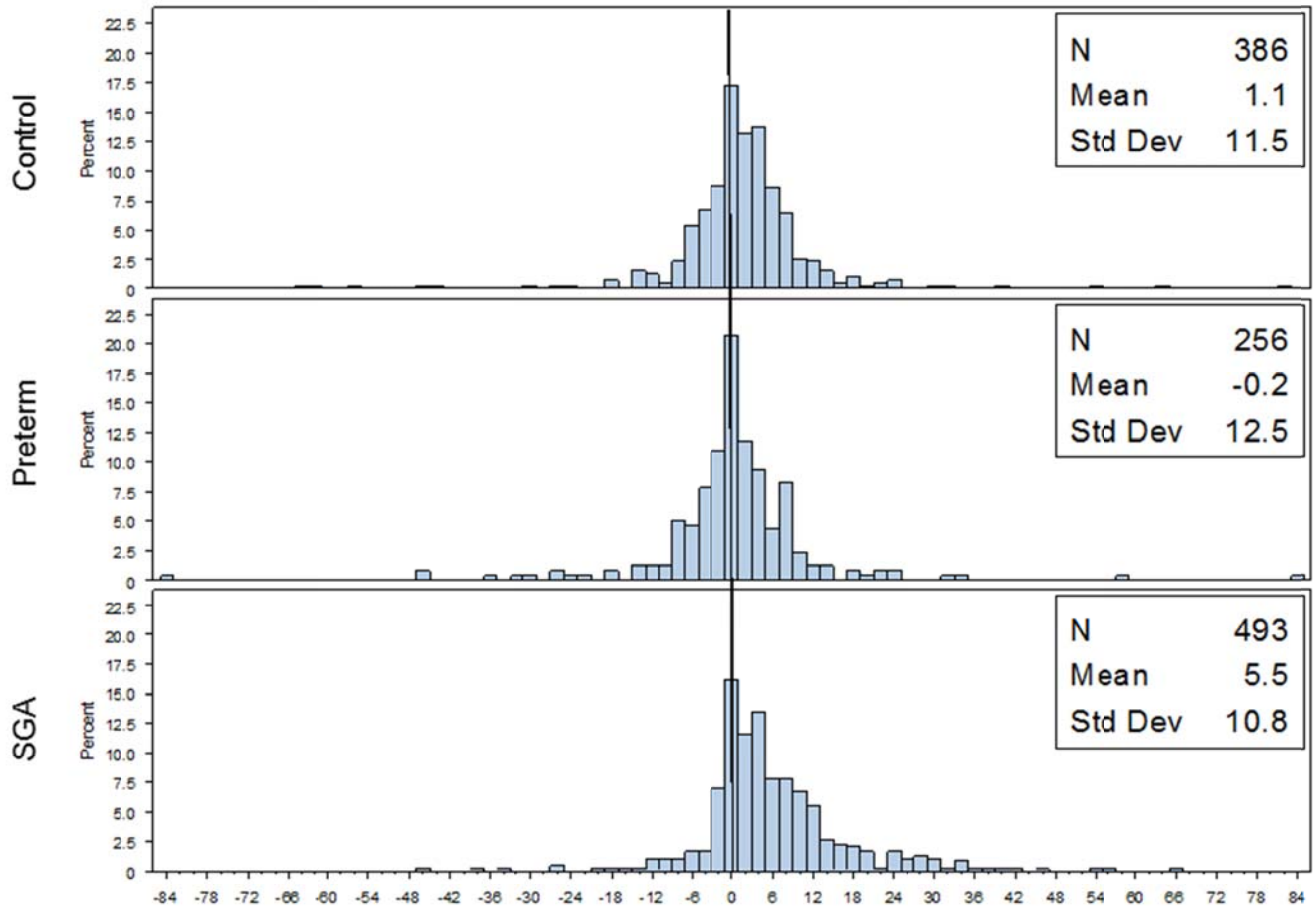
Parity													
Nulliparious	1228(45.3)	186	(48.2)	232	(44.2)	133	(52.0)	171	(43.1)	224	(45.4)	333	(51.1)
1	865(31.9)	119	(30.8)	170	(32.4)	77	(30.1)	132	(33.3)	162	(32.9)	186	(28.5)
2+	613(22.7)	80	(20.7)	122	(23.2)	46	(18.0)	93	(23.4)	107	(21.7)	133	(20.4)
Missing	3(0.1)	1	(0.3)	1	(0.2)	0		1	(0.3)	0		0	
	p-value		*0.4546*				*0.0707*				*0.1499*		
1st trimester vaginal bleeding reported by interview or medical chart													
Yes	595(22.0)	72	(18.7)	92	(17.5)	69	(27.0)	113	(28.5)	99	(20.1)	150	(23.0)
No	2114 (78.0)	314	(81.4)	433	(82.5)	187	(73.1)	284	(71.5)	394	(79.9)	502	(77.0)
	p-value		*0.6612*				*0.6743*				*0.2348*		
Fertility used to conceive index pregnancy													
Yes	152(5.6)	16	(4.2)	24	(4.6)	16	(6.3)	26	(6.6)	26	(5.3)	44	(6.8)
No	1481(54.7)	242	(62.7)	271	(51.6)	149	(58.2)	216	(54.4)	281	(57.0)	322	(49.4)
Unintended pregnancy	1073(39.6)	127	(32.9)	230	(43.8)	91	(35.6)	155	(39.0)	186	(37.7)	284	(43.6)
Missing	3(0.1)	1	(0.3)	0		0		0		0		2	(0.3)
	p-value		*0.0029*				*0.6289*				*0.0406*		
Household income ($)													
Mean (std dev)	$62,278 (47,672)	$69,081 (43,826)		$61,078 (40,649)[1]		$64,897 (45,842)		$67,615 (64,989)		$61,735 (44,493)		$55,749 (45,157)[1]	
0-31,000	644(23.8)	76	(19.7)	119	(22.7)	50	(19.5)	80	(20.2)	110	(22.3)	209	(32.1)
31,001-56,000	633(23.3)	92	(23.8)	122	(23.2)	58	(22.7)	94	(23.7)	122	(24.8)	145	(22.2)
56,001-80,000	648(23.9)	103	(26.7)	127	(24.2)	71	(27.7)	95	(23.9)	119	(24.1)	133	(20.4)
80,001+	620(22.9)	106	(27.5)	122	(23.2)	65	(25.0)	12	(25.7)	105	(21.3)	121	(18.6)
Missing	164(6.1)	9	(2.3)	35	(6.7)	13	(5.1)	26	(6.6)	37	(7.5)	44	(6.8)
	p-value		*0.4520*				*0.8069*				*0.0043*		

Table 1.1 continued…

Subject income ($)													
Mean (std dev)	$20,653 (20,652)	$24,737 (21,502)		$20,694 (20,896)[1]		$22,857 (19,310)		$22,585 (22,878)		$22,092 (20,173)		$20,173 (18,490)	
0-5,000	685(25.3)	86	(22.3)	153	(29.1)	60	(23.4)	97	(24.4)	125	(25.4)	164	(25.2)
5,001-19,000	660(24.4)	81	(21.0)	124	(23.6)	50	(19.5)	107	(27.0)	112	(22.7)	186	(28.5)
19,001-33,000	649(24.0)	104	(26.9)	117	(22.3)	74	(28.9)	84	(21.2)	122	(24.8)	148	(22.7)
33,001+	644(23.8)	107	(27.7)	121	(23.1)	62	(24.2)	101	(25.4)	121	(24.5)	132	(20.3)
Missing	71(2.5)	8	(2.1)	10	(1.9)	10	(3.9)	8	(2.0)	13	(2.6)	22	)3.4)
	p-value	*0.0349*				*0.0561*				*0.0909*			
Peri-conceptional prenatal or multi-vitamin													
Yes	1589(58.6)	238	(61.7)	300	(57.1)	165	(64.5)	241	(60.7)	301	(61.1)	344	(52.8)
No	1119(41.3)	148	(38.3)	225	(42.9)	91	(35.6)	155	(39.0)	192	(38.9)	308	(47.2)
Missing	1(0.1)					0		1	(0.3)				
	p-value	*0.1708*				*0.4720*				*0.0051*			
Prenatal vitamins during pregnancy													
Yes	2552(94.2)	372	(96.4)	490	(93.3)	241	(94.1)	372	(93.7)	468	(94.9)	609	(93.4)
No	157(5.8)	14	(3.6)	35	(6.7)	15	(5.9)	25	(6.3)	25	(5.1)	43	(6.6)
	p-value	*0.0445*				*0.8198*				*0.2799*			
Any employment during pregnancy													
Yes	2124(78.4)	308	(79.8)	399	(76.0)	209	(81.6)	316	(79.6)	388	(78.7)	504	(77.3)
No	542(20.0)	70	(18.1)	111	(21.1)	42	(16.4)	76	(19.1)	105	(21.3)	138	(21.2)
Missing	43(1.6)	8	(2.0)	15	(2.8)	5	(2.0)	5	(1.3)			10	(1.5)
	p-value	*0.4941*				*0.2807*				*0.0687*			

[1] T-test p-value < 0.05 for comparison with values in control subjects

Figure 1.2 Distribution of days difference between LMP gestational age at ultrasound and the gestational age as estimated by ultrasound by selected case status, Iowa, 2002-2005 (N=1135)



Comparison of means (ttest p-value):

Ctrl vs PTD: 0.1404 Ctrl vs SGA: <.0001 PTD vs SGA: <.0001

Figure 1.3 Distribution of days difference between gestational age as estimated by ultrasound and LMP gestational age by selected case control status and gestational age as estimated by ultrasound (N=1135)

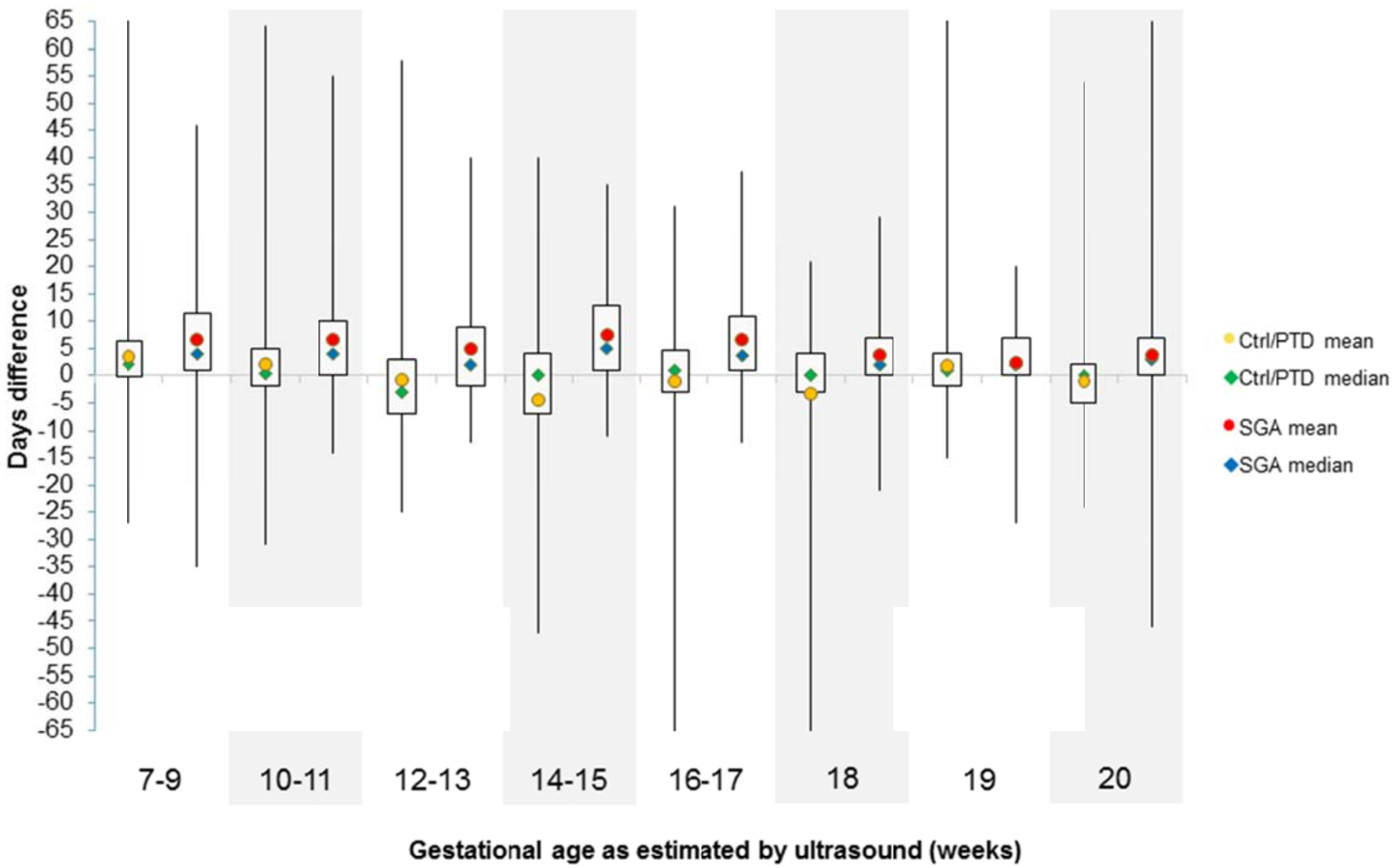


Figure 1.4 Distribution of reassignment of LMP to ultrasound dating by selected case status, and ultrasound estimated gestational age, Iowa, 2002-2005 (N=1135)

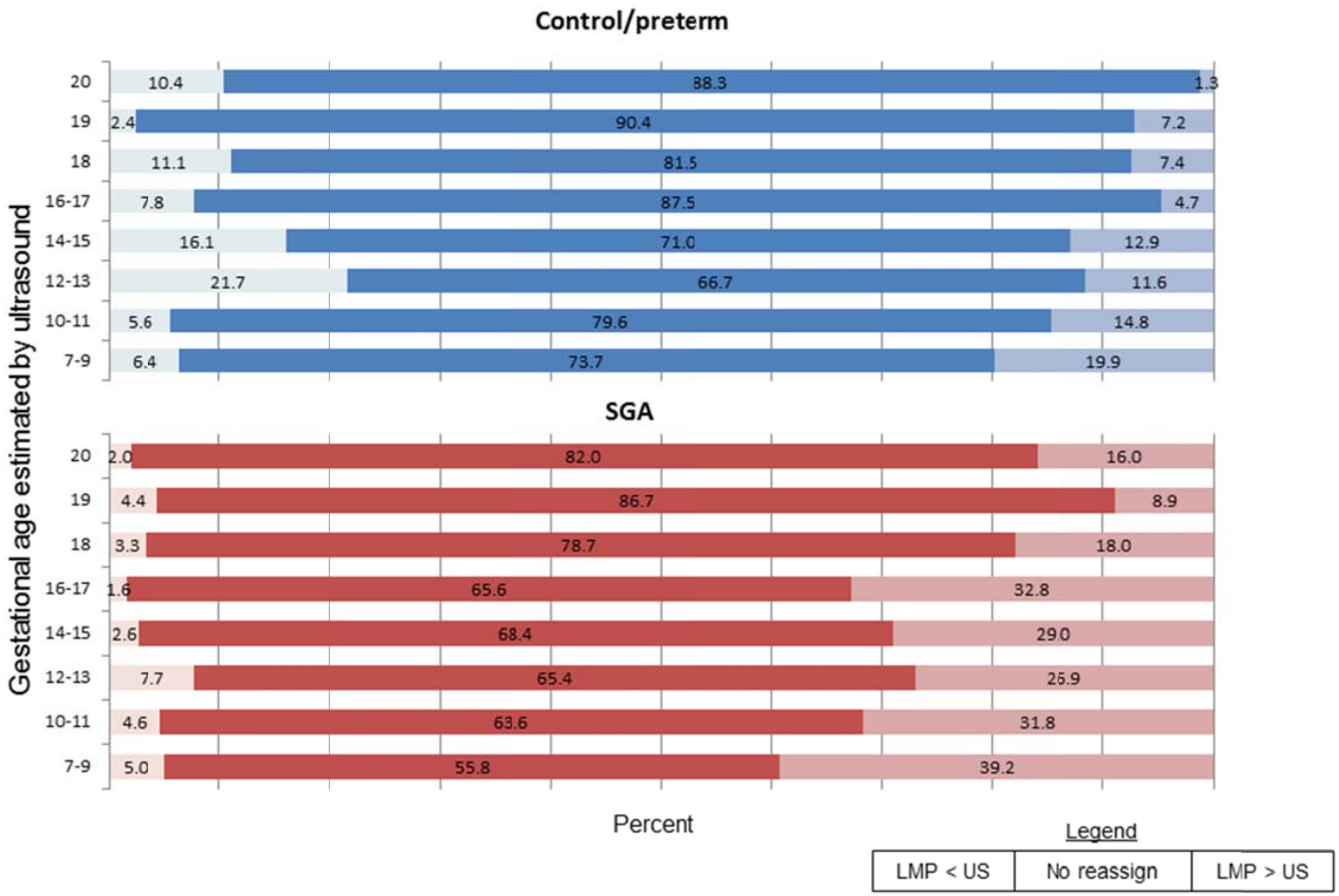


Figure 1.5 Distribution of gestational age as estimated by ultrasound and LMP gestational age at time of ultrasound, by selected case-control status and application of the ACOG guidelines, Iowa, 2002-2005 (N=1135).

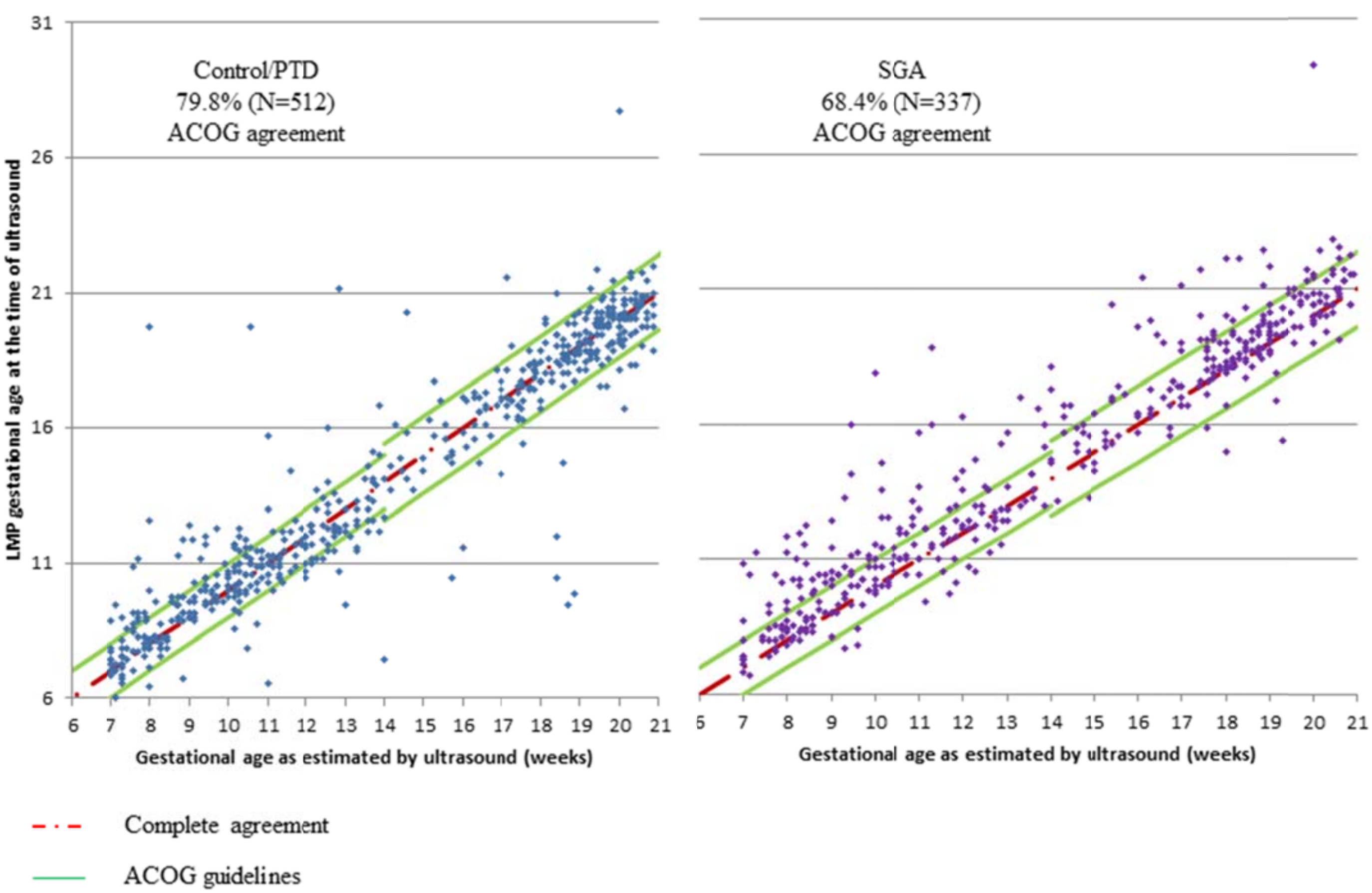


Table 1.2 Maternal and pregnancy characteristics associated with reassignment of gestational age dating from LMP to ultrasound, according to ACOG guidelines[1], by initial case-control status, Iowa, 2002-2005 (N=1135).

	Control/Preterm (N=642)			*SGA (N=493)*		
Maternal Characteristic	*Reassigned: LMP GA < US GA N=57 (n, row%)*	*No reassignment N=512 (n, row%)*	*Reassigned: LMP GA > US GA N=73 (n, row%)*	*Reassigned: LMP GA < US GA N=20 (n, row%)*	*No reassignment N=337 (n, row%)*	*Reassigned: LMP GA > US GA N=136 (n, row%)*
Maternal age						
Mean (Std. dev)	30.1(5.9)	29.3(5.4)	28.8(4.5)	27.6(5.1)	28.5(5.1)	26.8(5.4)[1]
<20	4 (14.3)	22 (78.6)	2 (7.1)	1 (4.2)	12 (50.0)	11 (45.8)
20-24	5 (5.3)	82 (86.3)	8 (8.4)	5 (5.0)	59 (59.0)	36 (36.0)
25-29	18 (8.5)	160 (75.8)	33 (15.6)	5 (2.6)	133 (68.9)	55 (28.5)
30-34	15 (7.6)	162 (82.2)	20 (10.2)	8 (6.7)	91 (76.5)	20 (16.8)
35+	15 (26.3)	86 (16.8)	10 (13.7)	1 (1.8)	42 (73.7)	14 (24.6)
p-value	*0.2245*	*referent*	*0.2026*	*0.4418*	*Referent*	*0.0056*
Maternal race						
White	46 (8.0)	464 (80.4)	67 (11.6)	17 (4.1)	286 (68.1)	117 (27.9)
Non-White	11 (16.9)	48 (73.9)	6 (9.2)	3 (4.1)	51 (69.9)	19 (26.0)
p-value	*0.0197*	*Referent*	*0.7496*	*0.9871*	*Referent*	*0.7472*
Maternal education						
< College grad	25 (8.8)	228 (80.6)	30 (10.6)	14 (5.5)	148 (58.5)	91 (36.0)
College grad	19 (8.0)	189 (79.8)	29 (12.2)	5 (3.0)	131 (78.9)	30 (18.1)
Graduate degree	13 (22.8)	95 (77.9)	14 (11.5)	1 (1.4)	58 (78.4)	15 (20.3)
p-value	*0.7140*	*Referent*	*0.8522*	*0.0643*	*Referent*	*<.0001*

Table 1.2 continued…

Pre-pregnancy BMI						
Mean (Std. dev)	25.0(4.6)	25.4(6.0)	24.8(4.4)	23.7(4.6)	24.2(6.1)	25.0(7.0)
<25.0	33 (9.0)	297 (80.9)	37 (10.1)	15 (4.4)	240 (70.6)	85 (25.0)
25-29.9	15 (9.2)	124 (75.6)	25 (15.2)	2 (2.6)	47 (61.0)	28 (36.4)
30+	9 (8.3)	88 (81.5)	11 (10.2)	3 (4.1)	48 (64.9)	23 (31.1)
Missing	0	3 (100.0)	0	0	2 (100.0)	05 (5.1)
p-value	*0.9283*	*Referent*	*0.1944*	*0.8791*	*Referent*	*0.1217*
Infant birth weight						
Mean (Std. dev)	3116(715)	3086(687)	3115(709)	2721(652)	2821(639)	2839(634)
<2500 grams	10 (10.3)	78 (80.4)	9 (9.3)	5 (5.1)	66 (67.4)	27 (27.6)
2500-2999	16 (8.7)	149 (80.5)	20 (10.8)	8 (3.8)	144 (68.9)	57 (27.3)
3000-3499	13 (7.0)	149 (80.5)	23 (12.4)	6 (4.4)	94 (68.6)	37 (27.0)
3500-3999	14 (11.4)	95 (77.2)	14 (11.4)	0	21 (65.6)	11 (34.4)
4000+	4 (7.7)	41 (78.8)	7 (13.5)	1 (7.1)	10 (71.4)	3 (21.4)
p-value	*0.7470*	*Referent*	*0.9436*	*0.7669*	*Referent*	*0.9471*
Infant Sex						
Male	29 (9.1)	249 (77.8)	42 (13.1)	12 (4.8)	181 (73.0)	55 (22.2)
Female	28 (8.7)	263 (81.7)	31 (9.6)	8 (3.3)	156 (63.7)	81 (33.0)
p-value	*0.7478*	*Referent*	*0.1547*	*0.5834*	*Referent*	*0.0090*
Smoked during pregnancy						
1st or 2nd tri	10 (9.5)	83 (79.1)	12 (11.4)	6 (4.9)	71 (57.7)	46 (37.4)
Not at all	47 (8.8)	429 (79.9)	61 (11.4)	14 (3.8)	266 (71.9)	90 (24.3)
p-value	*0.7963*	*Referent*	*0.9607*	*0.3454*	*Referent*	*0.0036*
Pregnancy intention						
Then or sooner	35 (8.3)	337 (79.7)	51 (12.1)	8 (2.6)	224 (73.0)	75 (24.4)
Wanted later	12 (9.5)	101 (79.5)	14 (11.0)	6 (5.0)	77 (64.2)	37 (30.8)
Did not want	3 (6.5)	04 (87.0)	3 (6.5)	2 (5.3)	21 (55.3)	15 (39.5)
Didn't care	7 (15.6)	33 (73.3)	5 (11.1)	4 (14.3)	15 (53.6)	9 (32.1)
p-value	*0.3737*	*Referent*	*0.7119*	*0.0096*	*Referent*	*0.0875*

Table 1.2 continued…

How felt about pregnancy once found out pregnant												
Excited	47	(9.1)	410	(79.2)	61	(11.8)	11	(2.9)	274	(71.7)	97	(25.4)
Okay	8	(9.9)	64	(79.0)	9	(11.1)	6	(9.4)	38	(59.4)	20	(31.3)
Not sure	1	(2.9)	31	(88.6)	3	(8.6)	3	(7.5)	22	(55.0)	15	(37.5)
Didn't want	1	(16.7)	5	(83.3)	0		0		3	(50.0)	3	(50.0)
Missing	0		1	(100.0)	0		0		0		1	(100.0)
p-value	*0.6954*		*Referent*		*0.8499*		*0.0277*		*Referent*		*0.0758*	
Gravidity												
1	27	(47.4)	212	(41.4)	33	(45.2)	6	(2.8)	146	(69.2)	59	(28.0)
2	17	(9.9)	133	(77.8)	21	(12.3)	5	(3.6)	94	(67.6)	40	(28.8)
3+	13	(6.6)	165	(83.8)	19	(9.6)	9	(6.3)	97	(67.8)	37	(25.9)
Missing	0		2	100.0	0		0		0		0	
p-value	*0.3380*		*Referent*		*0.5528*		*0.2842*		*Referent*		*0.9212*	
Parity												
Nulliparious	36	(11.3)	250	(78.4)	33	(10.3)	4	(1.8)	162	(72.3)	58	(25.9)
1	14	(7.1)	161	(82.1)	21	(10.7)	10	(6.2)	103	(63.6)	49	(30.3)
2+	7	(5.6)	100	(79.4)	19	(15.1)	6	(5.6)	72	(67.3)	29	(27.1)
p-value	*0.1158*		*Referent*		*0.4397*		*0.0474*		*Referent*		*0.4691*	
1st tri vaginal bleeding reported by interview or medical chart												
Yes	12	(8.5)	111	(78.7)	18	(12.8)	3	(3.0)	65	(65.7)	31	(31.3)
No	45	(9.0)	401	(80.0)	55	(11.0)	17	(4.3)	272	(69.0)	105	(26.7)
p-value	*0.9131*		*Referent*		*0.5659*		*0.6352*		*Referent*		*0.3908*	
Fertility techniques used to conceive index pregnancy												
Yes	3	(9.4)	26	(81.3)	3	(9.4)	0		23	(88.5)	3	(11.5)
No	32	(8.2)	311	(79.5)	48	(12.3)	8	(2.9)	201	(71.5)	72	(25.6)
Unintended preg	22	(10.1)	174	(79.8)	22	(10.1)	12	(6.5)	113	(60.8)	61	(32.8)
Missing	0		1	(100.0)	0		0		0		0	
p-value	*0.7790*		*Referent*		*0.7177*		*0.0410*		*Referent*		*0.0193*	

Table 1.2 continued…

Household income ($)						
Mean (Std. dev)	$74,650(62,083)	$65,991(42,683)	$64,715(43,083)	$42,237(20,497)[1]	$66,421(46,937)	$52,559(38,173)[1]
0-31,000	10 (7.9)	100 (79.4)	16 (12.7)	7 (6.4)	60 (54.6)	43 (39.1)
31,001-56,000	13 (8.7)	120 (80.0)	17 (11.3)	9 (7.4)	88 (72.1)	25 (20.5)
56,001-80,000	16 (9.2)	137 (78.7)	21 (12.1)	2 (1.7)	85 (71.4)	32 (26.9)
80,001+	17 (10.0)	135 (79.4)	18 (10.6)	1 (1.0)	83 (79.1)	21 (20.0)
Missing	1 (4.6)	20 (90.8)	1 (4.6)	1 (2.7)	21 (56.8)	15 (40.5)
p-value	*0.9513*	*Referent*	*0.9596*	*0.0168*	*Referent*	*0.0020*
Subject income ($)						
Mean (Std. dev)	$23,912(16,902)	$24,071(20,832)	$19,699(19,298)[1]	$21,223(14,732)	$23,728(22,489)	$18,115(17,329)[1]
0-5,000	8 (5.5)	117 (80.1)	21 (14.4)	4 (3.2)	81 (64.8)	40 (32.0)
5,001-19,000	16 (12.2)	97 (74.1)	18 (13.7)	5 (4.5)	71 (63.4)	36 (32.1)
19,001-33,000	19 (10.7)	139 (78.1)	20 (27.4)	6 (4.9)	84 (68.9)	32 (26.2)
33,001+	14 (8.3)	142 (84.0)	13 (7.7)	5 (4.1)	93 (76.9)	23 (19.0)
Missing	0	17 (94.4)	1 (5.6)	0	8 (61.5)	5 (38.5)
p-value	*0.1973*	*Referent*	*0.2312*	*0.9224*	*Referent*	*0.0733*
Peri-conceptual multi- or prenatal vitamins						
Yes	32 (7.9)	327 (81.1)	44 (10.9)	17 (4.4)	270 (69.6)	101 (26.0)
No	25 (10.5)	185 (77.4)	29 (12.1)	3 (2.9)	67 (63.8)	35 (33.3)
p-value	*0.2515*	*Referent*	*0.5510*	*0.5932*	*Referent*	*0.0124*
Prenatal vitamins during pregnancy						
Yes	55 (9.0)	492 (80.3)	66 (10.8)	9 (3.0)	220 (73.1)	72 (23.9)
No	2 (6.9)	20 (69.0)	7 (24.1)	11 (5.7)	117 (60.9)	64 (33.3)
p-value	*0.8826*	*Referent*	*0.0304*	*0.0661*	*Referent*	*0.7449*
Any employment during pregnancy						
Yes	46 (8.9)	412 (79.7)	59 (11.4)	17 (3.6)	322 (68.8)	129 (27.6)
No	10 (8.9)	88 (78.6)	14 (12.5)	3 (12.0)	15 (60.0)	7 (28.0)
Missing	1 (7.7)	12 (92.3)	0	0	0	0
p-value	*0.9931*	*referent*	*0.4569*	*0.0362*	*Referent*	*0.1612*

[1] T-test p-value < 0.05 for comparison with values in subjects with no reassignment.

Table 1.3 Adjustment to ultrasound gestational age at delivery, in weeks, by multivariate linear regression modeling of 1st trimester reported LMP gestational age at time of ultrasound versus gestational age as estimated by ultrasound before 21 weeks (US GA), SGA initial status, Iowa, 2002-2005. (N= 493)

		Multivariate linear models			
	N	*Model 1: Main effects*[1]	*Model 2: Smoking interaction*[2]	*Model 3: Bleeding interaction*[3]	*Model 4: Smoking & Bleeding interaction*[4]
Age at delivery < 25					
Non-smokers with vaginal bleeding	12	1.89	2.25 - (0.07 x US GA)	1.23 + (0.02 x US GA)	1.55 - (0.01 x US GA)
Non-smokers with no vaginal bleeding	53	1.88	2.23 - (0.07 x US GA)	2.07 - (0.05 x US GA)	2.45 - (0.08 x US GA)
Smokers with vaginal bleeding	9	2.11	0.87 + (0.05 x US GA)	1.45 + (0.02 x US GA)	0.14 + (0.11 x US GA)
Smokers with no vaginal bleeding	50	2.09	0.85 + (0.05 x US GA)	2.29 - (0.05 x US GA)	1.04 + (0.04 x US GA)
Age at delivery 25-29					
Non-smokers with vaginal bleeding	40	1.72	2.13 - (0.07 x US GA)	1.04 + (0.02 x US GA)	1.41 - (0.01 x US GA)
Non-smokers with no vaginal bleeding	110	1.71	2.12 - (0.07 x US GA)	1.89 - (0.05 x US GA)	2.31 - (0.08 x US GA)
Smokers with vaginal bleeding	7	1.94	0.75 + (0.05 x US GA)	1.26 + (0.02 x US GA)	0.01 + (0.11 x US GA)
Smokers with no vaginal bleeding	36	1.93	0.74 + (0.05 x US GA)	2.11 - (0.05 x US GA)	0.91 + (0.04 x US GA)
Age at delivery 30+					
Non-smokers with vaginal bleeding	26	1.39	1.81 - (0.07 x US GA)	0.72 + (0.02 x US GA)	1.10 - (0.01 x US GA)
Non-smokers with no vaginal bleeding	129	1.38	1.79 - (0.07 x US GA)	1.57 - (0.05 x US GA)	2.00 - (0.08 x US GA)
Smokers with vaginal bleeding	5	1.61	0.43 + (0.05 x US GA)	0.94 + (0.02 x US GA)	-0.31 + (0.11 x US GA)
Smokers with no vaginal bleeding	16	1.60	0.41 + (0.05 x US GA)	1.78 - (0.05 x US GA)	0.59 + (0.04 x US GA)

[1] LMP GA at ultrasound = GA estimate by ultrasound + 1st/2nd tri smoking (p=0.1974) + 1st tri vaginal bleeding (p=0.9466) + age at delivery(p=0.0214)

[2] LMP GA at ultrasound = GA estimate by ultrasound + 1st/2nd tri smoking (p=0.0081) + 1st tri vaginal bleeding (p=0.9367) + age at delivery(p=0.0376) + (1st/2nd trimester smoking*GA estimated by ultrasound) (p=0.0012)

[3] LMP GA at ultrasound = GA estimate by ultrasound + 1st/2nd tri smoking (p=0.1932) + 1st tri vaginal bleeding (p=0.1097) + age at delivery(p=0.0195) + (1st tri vaginal bleeding*GA estimated by ultrasound) (p=0.0857)

[4] LMP GA at ultrasound = GA estimate by ultrasound + 1st/2nd tri smoking (p=0.0068) + 1st tri vaginal bleeding (p=0.0858) + age at delivery(p=0.0356) + (1st tri vaginal bleeding*GA estimated by ultrasound) (p=0.0646) + (1st/2nd trimester smoking*GA estimated by ultrasound) (p=0.0010)

Table 1.4 Comparison of initial case-control status based on birth certificate data and final case-control status using six algorithms for gestational age dating. (N=1135)

	Final Status				
Initial status	*Control Only*	*PTD case*	*SGA case*	*PTD + SGA*	*Total*
Ultrasound before 21 weeks					
Control	281	14	91	0	386
PTD	32	200	6	18	256
SGA	212	13	171	3	399
PTD & SGA	9	67	2	16	94
Total	534	294	270	37	
ACOG[1] guideline					
Control	284	11	91	0	386
PTD	30	20	4	20	256
SGA	208	9	179	3	399
PTD & SGA	10	65	2	17	94
Total	532	287	276	40	
Main effects with ACOG guideline applied					
Control[2]	284	11	91	0	386
PTD[2]	30	201	4	21	256
SGA	174	6	219	0	399
PTD & SGA	25	34	16	19	94
Total	513	252	330	40	
Smoking int with ACOG guideline applied					
Control [2]	284	11	91	0	386
PTD[2]	30	201	4	20	256
SGA	181	6	212	0	399
PTD & SGA	23	44	9	18	94
Total	518	262	316	39	
Bleeding int with ACOG guideline applied					
Control[2]	284	11	91	0	386
PTD[2]	30	201	4	20	256
SGA	180	6	213	0	399
PTD & SGA	23	42	11	18	94
Total	517	260	319	39	
Smoking and bleeding int with ACOG guideline applied					
Control[2]	284	11	91	0	386
PTD[2]	30	201	4	20	256
SGA	180	6	213	0	399
PTD & SGA	23	44	9	18	94
Total	517	262	317	39	

[1] The American Congress of Obstetrics and Gynecology (ACOG) recommends that if an ultrasound is done before 14 weeks use LMP dating unless there is greater than 7 days difference between ultrasound and LMP. If the ultrasound is from 14-20weeks then a discrepancy of 10 days is allowed.

[2] Controls and PTDs in these models are all dated by ACOG guidelines

CHAPTER III

DOES WORKING DURING THE FIRST HALF OF PREGNANCY, AND THE CHARACTERISTICS OF THAT WORK, INCREASE PRETERM DELIVERY RISK?

Summary of findings

Purpose**:** Previous research on occupational lifting, standing and psychological stress during pregnancy has failed to control for off the job physical activity and general disposition of the subject. In this analysis, we investigate the effect of physical and psychological work stress during the first 20 weeks of pregnancy on the risk of preterm delivery while controlling for these important covariates.

Methods**:** This case-control study interviewed women postpartum who were residents of four Iowa counties on their work status during pregnancy. Among women who worked continuously during the first 20 weeks of pregnancy we examined lifting greater than 20 pounds, standing and standing in one position and psychological work stress. Hospital delivery and prenatal medical records were abstracted to classify gestational age at delivery: preterm delivery was classified as less than 37 weeks (N=762) and control subjects delivered at ≥ 37 weeks (N=1564). Adjusted odds ratios (aORs) were estimated using logistic regression analysis.

Results**:** Pregnant women who worked continuously during the first 20 weeks of pregnancy had a 30% (aOR=1.30; 95% CI 1.00-1.69) increased risk of preterm delivery compared to women who did not work at all during pregnancy. Among women who worked, increased risk of preterm delivery was associated with reporting a high degree of repetitive tasks (aOR=1.47;95% CI 1.10-1.98), and strongly disagreeing with having adequate breaks (aOR=1.67; 95% CI 1.03-2.73). The risks associated with repetitive tasks and inadequate break times were even stronger when examining spontaneous preterm deliveries. Women who were continuously employed and lifted greater than 20

pounds in their home for greater than 120 minutes were over twice as likely to deliver a preterm infant than those who did not lift in their home (OR=2.32; 95% CI 1.15-4.65). Conclusion**:** These findings provide evidence of an increased risk of preterm delivery with working continuously during the first 20 weeks of pregnancy and the potentially detrimental effects of psychological work stress, such as repetitive tasks and inadequate breaks. Lifting away from work, but not at work, was associated with increased risk of preterm delivery. Further research needs to discern how the type and setting (home versus work) of lifting impacts the risk of preterm delivery.

Introduction

Preterm delivery (PTD) is a leading cause of infant death in industrialized countries (1, 53, 95). In 2006, 12.8 percent of all live births in the United States were preterm (96). The adverse effects of preterm delivery are enduring, contributing to almost half of birth related childhood morbidity (7), including greater risk of illness, disability, and neurological disorders (8). The rate of preterm delivery in the United States continues to grow despite efforts to identify risk factors and preventive interventions. Maternal risk factors for preterm delivery include African-American race, the extremes of maternal age, a previous preterm delivery as well as pre-existing medical and adverse social conditions (7, 97).

Previous studies have investigated the occupational risks of preterm delivery including standing (12, 52-57), heavy lifting (12, 53, 62, 98), and psychological work stress (59, 69-71); however the results have been inconsistent.

Standing

Several studies, regardless of study design, have found a 30% to 170% increased risk of preterm delivery with standing at least three (3) hours per day at work compared to standing less than three hours per day or no standing while at work (52, 54-57, 62, 66, 99, 100). Among cohort studies examining the effect of standing on preterm delivery, those with a large sample (> 700 subjects) who inquired about standing during the 2nd

trimester of pregnancy were more likely to find a significantly increased risk (52, 54, 57, 100); among studies that asked about standing during the first trimester of pregnancy an increased risk was also found, although not significant (12, 60, 61). A potential 10% decreased risk of preterm delivery with standing was found in a small number of studies (12, 101, 102); two of these studies determined preterm delivery with less precise measures of gestational age at delivery (101, 102) and none of the three examined the inter-dependent effects of other work exposures on standing (12, 101, 102).

Heavy lifting

The literature on heavy lifting and risk of preterm delivery has been mixed. The definition of "heavy" has varied across studies with heavy being defined as 15 or greater pounds, times per week lifting (regardless of weight) or simply lifting anything (yes/no) at work. The use of different definitions of heavy lifting prevented Bonzini et al (99) from creating a pooled risk estimate in their systematic review of occupational lifting and risk of preterm delivery. In general, studies report a 30-50% increased risk of preterm delivery with lifting at work but only McDonald et al (62) found the results to be significant. In a cross sectional study of more than 22,000 women, McDonald (62) found a 25% significantly increased risk of preterm delivery with lifting heavy objects more than 15 minutes per day at work: the risk estimate is very similar to those of other studies and the large sample size provided the statistical power needed to find significance.

Psychological work stress

The definition of psychological work stress varies; much of the literature has used the Karasek Job Content Questionnaire (65) as the measure of occupational psychological demand while other research has used Mamelle's occupational fatigue index (66) to measure this construct. Often in research of psychological work stress, authors use job title linked with the O*Net (67) database to determine the level of mental occupational stress. The O*Net database provides comprehensive details on key elements of jobs and can be easily linked to job title if one of several recognized job coding systems (DOT, SOC, etc) corresponds to the job title. Although convenient and cost-effective, use of job title as a proxy for psychological stress does not account for individual variation and response to stress at work. Studies that have assessed psychological job stress using job title as a proxy for self-reported experience have been able to demonstrate psychological work stress as a risk factor for PTD but all results have been non-significant due to small sample sizes (68). When asked directly, women working in high strain jobs, defined by Karasek as jobs with a high level of demand but little control over the work process, are at a 30-46% increased risk of PTD (59, 69-71). Finally, few studies have controlled for pregnancy-specific stress or a subject's general disposition when studying the effect of mental work stress on risk of preterm delivery.

Biological mechanism of physical and psychological stress causing preterm delivery

The initiation of labor involves a complex interaction between maternal, placental, and fetal tissues that is not fully understood. It has been proposed that placental corticotrophin-releasing hormones (CRH) may be one of the primary endocrine mediators of spontaneous labor (103). CRH released from the hypothalamus plays a central role in the physiologic response to stress. The relationship between elevated concentrations of CRH to stressors and psychological distress on one hand and maternal CRH on the other hand is unclear (95). During pregnancy, CRH is not only released by the hypothalamus in response to stressors (as in the non-pregnant state) but also by the placenta and fetal membranes. CRH has been found to be elevated in women who present with preterm labor suggesting that CRH may relate to length of gestation directly through its release by maternal/fetal membranes to initiate labor or indirectly through a hypothalamic physiological stress response that also affects the maternal and fetal membranes.

The objective of this analysis is to determine the overall effect of work on preterm delivery risk while considering a large number of potentially confounding factors including prenatal stress, maternal demographic, lifestyle, personality and pregnancy characteristics. In addition, we are the first to report on the cumulative effect of physical and psychological occupational demands on the risk of preterm delivery while controlling for off the job physical activity and a subject's general disposition.

Materials and Methods

We used data from the Iowa Health in Pregnancy Study to examine occupational risk factors for preterm delivery among women who worked continuously during the first 20 weeks of pregnancy.

Iowa Health in Pregnancy Study (IHIPS)

IHIPS is a population-based case-control study designed to determine the influence of intimate partner violence and maternal stress on risk of preterm delivery (PTD) and small for gestational age (SGA) outcomes among Iowa residents of four counties who delivered a live birth from May 1, 2002 through June 30, 2005. Electronic Iowa birth certificates served as the sampling frame for the study.

All Iowa residents of the study counties who delivered a singleton preterm infant, based on birth certificate data, were selected for study participation. A potential preterm subject was selected if the gestational age at delivery, estimated by the last menstrual period or clinical estimate on the birth certificate, was less than 37 weeks. Potential control subjects were those delivering an infant that was born at 37 weeks or more. Excluded from IHIPS were women under 18 years of age at the time of delivery, women with type-1 or type-2 diabetes mellitus, systemic lupus, or chronic renal disease, women who do not speak English, and those with multiple fetus pregnancies (e.g., twins).
All women selected from the birth certificates were mailed a study introductory letter. Women with a telephone number were contacted to introduce the study procedures and complete informed consent. Study participation consisted of a brief eligibility screening, a 45-minute telephone interview, and provision of a signed medical record release form allowing the research team access to their prenatal and hospital delivery records.

Of the 7202 potential births selected from the birth certificate, 4250 (59.0%) could be reached by phone. Of these, 19.7% (N=836) refused to participate and 12.9% (N=548) were ineligible for study participation. Just under 95% (N=2709) of the 2866 eligible to participate completed the telephone interview. The response rate for IHIPS was 45.2% and the participation rate was 76.6% (81). Over 90% of interviewed case and control subjects provided signed medical record release forms enabling review of their prenatal and labor/delivery records. The average time between delivery and postpartum interview was 51 weeks for controls and 49 weeks for preterm deliveries.

Data collection

Information ascertained from the interview included demographic and lifestyle characteristics as well as medical and pregnancy history. Detailed pregnancy occupational histories were recorded during the interview including the hours worked per week by trimester, minutes per day lifting greater than 20 pounds, hours per day on their feet and standing in one position, as well as psychological work stress. Physical activity outside of work focused on leisure time physical activity (exercise), minutes per day lifting 20 pounds, and time spent caring for children less than 5 years old in home. To determine gestational age at delivery, trained medical record abstractors extracted the following information from prenatal and hospital delivery records: date of last menstrual period, date of earliest ultrasound, and estimated ultrasound gestational age.

All study protocols and informed consent procedures were approved by the University of Iowa Institutional Review Board.

Definition of preterm delivery

To classify preterm delivery, gestational age at delivery was determined following the methodology of Harland et al (2010). In short, the assumption of dating by ultrasound measurement is that fetal growth early in pregnancy is relatively uniform, this may not be valid in fetuses that are small for gestational age as an ultrasound will measure them ‘younger’ due to their small stature. If a subject was selected as a potential small for gestational age case, had a first trimester reported last menstrual period and ultrasound examination between 7 and 21 weeks, then linear regression modeling was used to estimate an adjustment (in weeks) to be made to the ultrasound estimated gestational age. The ultrasound gestational age adjustment differed by maternal age, smoking status in the first or second trimester and vaginal bleeding during the first trimester of pregnancy. Following ultrasound gestational age adjustment, the American Congress of Obstetrics and Gynecology (90) guideline was applied: the last menstrual period (LMP) gestational age was assigned unless it differed by more than 7 days with the gestational age estimate from a first trimester ultrasound (<14 weeks) or by greater than 10 days from an ultrasound administered between 14 and 20 weeks gestation. If an ultrasound before 21 weeks was not available, the LMP gestational age at delivery was used if agreement was within 7 days of the clinical estimate of gestational age from the birth certificate. If the LMP gestational age was more than 7 days different, the clinical estimate of gestational age was assigned.

Preterm delivery (PTD) was defined as birth before 37 weeks of pregnancy. Risks for spontaneous versus induced preterm delivery differ therefore preterm delivery was sub classified to conduct separate analysis. A spontaneous preterm delivery was defined as premature rupture of membranes or premature labor, as recorded on the medical record abstraction, without record of induction by artificial rupture of membranes or use of a ripening agent to induce labor. Subjects without a medical record abstraction (N=135) were excluded from analyses of preterm delivery subtypes.

Control Selection

Controls were selected from the birth certificate as singleton term deliveries and were frequency matched on the maternal county of residence. For the analysis of preterm delivery, controls subjects delivered at 37 or more weeks including 2.9% (N=45) that were term but small for gestational age. Delivery gestational age was determined by ACOG guidelines as stated above.

Definition of work

Working during pregnancy was defined as being continuously employed during the first 20 weeks of pregnancy. Because the exposures that occurred in the first 20 weeks are likely to pre-date pregnancy complications that might affect gestational length, the data from the first 20 weeks represent our primary time period of interest. Women who worked for only a portion of the first 20 weeks are likely to have pre-existing conditions that increase their risk for preterm delivery resulting in limited work; therefore these subjects were excluded from this analysis. To determine if a subject met the continuously employed criteria, interview data were examined for months during pregnancy worked, date quit working before delivery, and the gestational age when they stopped working. If a subject was employed through the 20^{th} week of pregnancy they were considered as working and eligible for this analysis.

Maternal physical work load was estimated using questions regarding the frequency and duration of standing, standing in one place without much movement, and lifting greater than 20 pounds while at work. Standing in one position without much movement (none, 1-3 hours/day, 4+ hours/day), and minutes per day lifting greater than 20 pounds (None, 1-9 min/day, 10-29 min/day, 30-179 min/day, 180+ min/day) were created from the continuous variables of length of time standing, or lifting based on the distribution in control subjects.

To estimate work psychological stress a series of six questions was asked. The first reported degree of repetitive tasks (low, moderate, high) with the remainder describing control over the amount and pace of work, control over how well they did their job, the perception of adequate breaks and whether work conditions were hot, cold or humid using a 5-level likert scale (strongly agree, agree, neutral, disagree, strongly disagree).

Covariates

Pertinent maternal demographic or lifestyle characteristics and pregnancy histories were considered as potential covariates in the relationship between preterm delivery and work during pregnancy. Maternal age at delivery was calculated by taking the date of delivery minus the maternal birth date reported during postpartum interview. The categorization of maternal age (18-19, 20-24, 25-29, 30-34, 35+) was based on previous research showing increased risk of preterm delivery with the extremes of maternal age. Other variables include maternal race (non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander and other), education (less than or equal to high school, some college, college graduate-bachelor degree, masters or professional degree), pre-pregnancy body mass index (<18.5, 18.5-24.9, 25-29.9, 30+), gravidity, and parity. If a subject reported she had previously delivered an infant before 37 weeks then she was considered to have had a previous preterm delivery. Subjects without a previous preterm delivery were divided into two sub-groups: those that had a previous delivery but it was not preterm and those with no previous deliveries (nulliparious). A subject was considered to be born low birth weight herself if her self-reported birth weight was less than 2500 grams and considered to be born preterm if she reported being born more than three (3) weeks earlier.

Analysis

To identify maternal demographic and lifestyle risk factors for preterm delivery we compared these characteristics by case-control status regardless of work status. For categorical variables, a simple chi-square test was used to determine differences. Continuous variables were compared using the Student's t-test. Logistic regression was used to calculate unadjusted odds ratios for risk of preterm delivery by maternal demographic and lifestyle factors.

To determine if maternal, pregnancy and lifestyle characteristics affect the likelihood of working continuously during the first 20 weeks of pregnancy versus not working at all during pregnancy we compared the characteristics of control subjects by work status. Chi-square tests and the Student's t-test were used to determine differences in categorical and continuous variables, respectively.

To examine work characteristics that may increase the risk of preterm delivery, frequency distributions and crude odds ratios were calculated. Odds ratios and their 95% confidence intervals were estimated from beta coefficients and standard errors calculated by logistic regression analysis. Given that subjects who worked only part of the first 20 weeks of pregnancy were at greatest risk of delivering preterm, and were more likely to quit working due to doctor recommendation for bed rest or to reduce activity (data not shown) these subjects (N=176) were excluded from all analysis.

To investigate the effect of anxiety, pregnancy-related distress, and chronic perceived stress on the relationship between work characteristics and preterm delivery these stressors were measured using validated psychological measures. The modified version for retrospective reporting, of the 10-item State Anxiety subscale of the State-Trait Personality Inventory was used to measure the acute and on-going anxiety experienced by subjects throughout pregnancy (104). The Perceived Stress Scale measured chronic perceived stress during pregnancy and has been used successfully in pregnant women (105). The Pregnancy Distress Questionnaire measured the level of pregnancy related distress felt by subjects throughout pregnancy (106). The categorization of these scales is based on the distribution in control subjects.

Multivariate Logistic Regression

All demographic, lifestyle and anxiety or perceived stress variables associated with the risk of preterm delivery or working continuously during the first 20 weeks of pregnancy were entered as covariates in the logistic regression analysis of preterm delivery and working continuously during the first 20 weeks of pregnancy. In addition, the length of time between delivery and interview, in continuous weeks, was examined as a potential covariate. Covariates were withdrawn one by one and were removed from the model if the change in the odds ratio for worked continuously during the first 20 weeks of pregnancy (yes, not at all during pregnancy) was less than 10%.

To assess the influence of selected occupational factors on risk of preterm delivery among subjects who worked continuously during the first 20 weeks of pregnancy a single multivariate logistic model was constructed. Standing in one position without much movement, minutes per day lifting greater than 20 pounds, reported degree of repetitive tasks and perceived adequacy of breaks were modeled together to determine their independent effects on preterm delivery risk. The categories of 30-59 and 60-179 minutes/day lifting were combined because they had similar crude risk estimates for preterm delivery. Covariates considered for the logistic regression model were associated with risk of preterm delivery, being continuously employed during the first 20 weeks of pregnancy, or showed such associations in the literature. These analyses were completed for all preterm deliveries and for the preterm delivery subtypes of induced or spontaneous onset of preterm delivery.

The data analysis was generated using SAS® software, Version 9.2 of the SAS System for Microsoft, SAS Institute Inc., Cary, NC, USA.

Results

Several maternal demographic, lifestyle and pregnancy characteristics are associated with an unadjusted increased risk of preterm delivery. (Table 2.1) Subjects younger than 25 or older than 29 years of age at delivery were at 30-60% increased risk of preterm delivery. Those with a pre-pregnancy body mass index (BMI) of 30 or more had a 35% increased risk of preterm delivery compared to subjects with a normal BMI. Subjects who had a prior preterm delivery were at 3-fold increased risk of delivery preterm compared to those with a previous non-preterm delivery. Nulliparious subjects were one and one-half times more likely to deliver a preterm infant than subjects who had previously delivered a non-preterm infant. Subjects who themselves were born low birth weight or preterm were at increased risk of a preterm delivery compared to subjects that were not low birth weight or born preterm. Subjects lifting greater than 20 pounds at home for greater than two hours per day were over twice as likely to deliver an infant preterm compared to subjects who did not lift at home. Subjects employed at any time during pregnancy had a 27% increased risk of delivering preterm compared to those who did not work at any time during pregnancy. Asian or Pacific Islanders had half the risks of preterm delivery as white, non-Hispanic subjects. In addition, subjects who drank alcohol at any time during pregnancy were at a decreased risk of preterm delivery compared to non-drinkers. A high degree of perceived stress, prenatal distress and state anxiety was associated with increased risk of preterm delivery (data not shown).

Variables found to be significantly associated with working continuously during the first 20 weeks of pregnancy were included in the full logistic model for risk of preterm delivery and its subtypes. These variables included maternal age at delivery, education, white race, alcohol use during pregnancy, household income, previous preterm delivery, and mother's own low birth weight status, lifting greater than 20 pounds in the home, state anxiety, and perceived stress.

Of the occupational conditions present during the first 20 weeks of pregnancy, a high degree of repetitive tasks, and inadequate breaks was significantly associated with unadjusted preterm delivery risk. (Table 2.2) Subjects who reported conducting a high degree of repetitive tasks at work had a nearly 40% increased risk of delivering preterm than those who reported a low degree of repetition in their work. In addition, subjects who strongly disagreed with having adequate break time at work were at greater than 50% increased risk preterm delivery than those who strongly agreed they had adequate breaks at work. Preterm and control subjects worked similar hours per week, and little difference was seen in the amount of time spent standing at work. There was a suggested increased risk, although not statically significant, of delivering preterm if a subject stands in one position without much movement for four or more hours per day compared to those who did not stand in one position at work. Compared to women who did not lift greater than 20 pounds at work, those that lifted for 30 to 179 minutes per day were at decreased risk of delivering an infant preterm; although it is suggested that subjects that lifted greater than 180 minutes per day may be at increased risk of preterm delivery. Among women who worked continuously during the first 20 weeks of pregnancy, those that lifted over 20 pounds at home for greater than 120 minutes per day were at a two-fold increased risk of delivering preterm compared to those that did not lift in the home.

As shown in Table 2.3, work exposures tended to be more strongly associated with spontaneous preterm delivery than with overall preterm delivery risk after controlling for potential covariates. Compared to subjects who did not work at all during pregnancy, women who worked throughout the first 20 weeks of pregnancy had a 30% increased risk of delivering an infant preterm after adjusting for off the job physical activity, pregnancy history, and maternal demographic and lifestyle characteristics. Among working women those reporting a high degree of repetitive tasks were 47% more likely to deliver a preterm infant, and 55% more likely to have a spontaneous preterm delivery after controlling for covariates and other work exposures than those with a low degree of repetition. Those who strongly disagreed with having adequate breaks were 1.67 times more likely to deliver a preterm infant and the increased risk of having a spontaneous preterm delivery was almost 2-fold compared to women with adequate breaks. Subjects that worked and reported lifting greater than 20 pounds 30-179 minutes per day had almost half the risk (OR=0.57; 95% CI 0.38-0.87) of delivering preterm as the working women who did no lifting. Subjects that delivered preterm by induction had no increased risk of preterm delivery associated with working or work characteristics (data not shown).

Discussion

Subjects working continuously during the first 20 weeks of pregnancy who reported highly repetitive tasks and inadequate break times were at increased risk of preterm delivery, with stronger associations among those with spontaneous preterm delivery. Working women who lifted greater than 20 pounds at home for more than two hours per day were also at increased risk of preterm delivery.

Many of the classic risk factors for preterm delivery are present in our analysis while other risk factors may not be apparent due to selection bias. Younger and older maternal age at delivery, prior delivering of a preterm infant, and mother themselves born low birth weight or preterm were associated with increased risk of preterm delivery in our study and previous research (7, 15, 97). In this analysis it was found that non-White race decreased the risk of preterm delivery while having a household income of greater than $30,000 (US) may increase the risk of preterm delivery. These unexpected associations may be due to selection bias. Study staff was more likely to be able to contact and consent women who were older, more educated, and have higher household incomes than the women who were not contacted therefore the women at highest risk of preterm delivery may not have been interviewed. Although the study was completed in 2002 through 2005 the use of cellular phones was on the rise and the number of land lines available for staff to contact was decreasing.

IHIPS women were more likely to work outside the home than women nationally with over 78% of women employed at some time during pregnancy. In 2003, 67% of first time expectant mothers in the United States were employed outside the home during pregnancy (107) while approximately 70% of women in the U.S. labor force had at least one child in the home under the age of 18 (108).

The effects of work characteristics on risk of preterm delivery are similar in our analysis to the results of previous research. The number of hours worked per week did not affect the risk of preterm delivery as has been documented in previous cohort (11, 12, 102) and cross-sectional studies (54, 56, 59, 101, 109, 110) although previous case-control studies (55, 56, 111) have found a 33-60% increase risk of preterm delivery with increased working hours. Luke et al (55) studied women employed as nurses during pregnancy limiting its generalizability to population based studies such as IHIPS and the study by Saurel-Cubizolles (56) took place throughout Europe where working conditions may differ from those of our population in Iowa.

The influence of occupational lifting on risk of preterm delivery has been difficult to discern given differences in measurement of lifting. In several studies (12, 61-63, 111) a suggested non-significant 14-50% increased risk of preterm delivery with occupational lifting has been seen, as is estimated in IHIPS (23%). Of note, this analysis found a protective effect (aOR=0.57 for all preterm, 0.49 for spontaneous preterm) of lifting 20 pounds for 30-179 minutes per day at work. This protective effect may be partly explained by an exercise type effect. Lifting may be beneficial at this moderate amount, similar to moderate exercise, as it may reduce the levels of hypothalamic, pituitary and placental hormones which are thought to trigger labor (61, 112, 113).

Work psychological stress has been associated with preterm delivery in several studies. Repetitive tasks have been found to increase the risk of preterm delivery by 25% (114). Newman et al (100) measured mental stress at work as repetitive tasks and finding work boring; nulliparious subjects that reported mental stress were 1.49 times more likely to have a spontaneous preterm delivery than those subjects without mental stress. This is similar to the adjusted odds of 1.55 we found for spontaneous preterm delivery. The biological mechanism for how repetitive tasks may increase preterm delivery is not well understood. Subject that have reported being able to take a break at work when feeling fatigued have been shown to be less likely to deliver an infant preterm (11). This is consistent with our result that shows an increased risk of preterm delivery (OR 1.92; 95% CI 1.09-3.56) when a subject felt she had inadequate breaks at work.

In any study of occupational risk factors the influence of the healthy worker effect must be considered. By limiting the analysis of occupational characteristics to only women who worked continuously during the first 20 weeks of pregnancy it is likely we are only measuring the effect of these exposures in ‘healthy workers’. Therefore, the estimated risks are likely to be underestimates of the effects of repetitive tasks and adequate breaks in all women that work at any time during pregnancy.

As in every case-control study there is risk of recall bias. When asked postpartum, cases may be more likely to recall stressful and physically demanding work during pregnancy when looking to answer the question of why they had a preterm delivery. In IHIPS, subjects were asked to generalize lifting, standing in one place or mental stress at work across their entire pregnancy reducing the ability to identify a time when exposure reduction may be most critical to prevent preterm delivery. In addition, if a woman is asked to generalize lifting, standing or mental stress over her entire pregnancy it is realistic to hypothesize she may think about her most recent experiences at work: if work modifications were implemented to reduce her physical demands late in pregnancy it is likely she would underestimate her total exposure and therefore reduce the ability to detect any risk for preterm delivery. Lindbohm et al (115) found that subjects self-report of occupational physical demand were more likely an underestimate of the direct observations made by researchers therefore the lack of increased risk with prolonged standing and heavy lifting may be due to under-reporting of exposure.

This analysis has several strengths including controlling for a subject's general anxious or perceived stress state while asking about her perceptions of physical or mental stress at work. Controlling for a woman's general disposition allows for more close approximation of the risk of preterm delivery attributed to work-related stress versus general stress. In addition, IHIPS allowed for the estimate of occupational risks associated with subtypes of preterm delivery, specifically finding an increased risk with spontaneous preterm delivery compared to all preterm deliveries. Lastly, subjects were asked about their perceived work-related stress and the experience of feeling stressed may actually be more closely related to having a shorter pregnancy than experiencing a certain event such as lifting or standing. Hedegaard (116) found that it was not the event a woman experienced but rather her stress response to the event that was associated with preterm labor.

In conclusion, a moderate amount of lifting at work may reduce a woman's risk of delivering preterm while there is a suggested increased risk with prolonged standing in one position at work. Programs to reduce the perception of repetitive tasks and increase breaks during pregnancy may decrease the likelihood of a preterm delivery. Lifting greater than 20 pounds at work did not show an increased risk of preterm delivery but this same lifting at home was associated with increased risk: future studies need to discern if it is the lifting or the setting in which the lifting occurs that increases preterm delivery risk. In addition, future research should attempt to prospectively collect data on work related exposures with validation by direct researcher observation to reduce the risk of recall bias that is inherent to retrospectively collected data.

Table 2.1 Maternal demographic and established risk factors for preterm delivery, Iowa Health in Pregnancy Study, 2002-2005 (N=2326).

Maternal Characteristic	*All N(Col %)*	*Control (N=1564) (n, col%)*	*PTD (N=762) (n, col%)*	*Crude OR (95% CI)*
Maternal Age				
Mean	28.4(5.4)	28.2(5.3)	28.6(5.7)	
p-value		*0.0846*		
18-19	121 (5.2)	78 (5.0)	43 (5.6)	1.44(0.96-2.15)
20-24	470 (20.2)	313 (20.0)	157 (20.6)	1.31(1.02-1.68)
25-29	779 (33.5)	563 (36.0)	216 (28.4)	1.0(ref)
30-34	635 (27.3)	411 (26.3)	224 (29.4)	1.42(1.13-1.78)
35+	321 (13.8)	199 (12.7)	122 (16.0)	1.60(1.21-2.10)
p-value		*0.0041*		
Maternal Race/Ethnicity				
White, non-Hispanic	2007 (86.3)	1333 (85.2)	674 (88.5)	1.0(ref)
Black, non-Hispanic	121 (5.2)	85 (5.4)	36 (4.7)	0.84(0.56-1.25)
Hispanic	49 (2.1)	35 (2.2)	14 (1.8)	0.79(0.42-1.48)
Asian/Pacific Islander	78 (3.4)	62 (4.0)	16 (2.1)	0.51(0.29-0.89)
Other[1]	71 (3.0)	49 (3.2)	22 (2.9)	0.89(0.53-1.48)
p-value		*0.1404*		
Maternal Education				
<= High school	446 (19.2)	296 (18.9)	150 (19.7)	1.03(0.80-1.32)
Some college	756 (32.5)	506 (32.4)	250 (32.8)	1.00(0.81-1.24)
College grad (bachelors)	772 (33.2)	517 (33.0)	255 (33.5)	1.0(ref)
Master or Prof	352 (15.1)	245 (15.7)	107 (14.0)	0.89(0.67-1.16)
p-value		*0.7760*		

Table 2.1 continued…

Pre-pregnancy BMI							
Mean	28.4	(5.4)	25.0	(5.8)	25.6	(6.0)	
p-value				*0.0219*			
<18.5	147	(6.3)	98	(6.3)	49	(6.4)	1.13(0.78-1.62)
18.5-24.9	1244	(53.5)	862	(55.1)	382	(50.1)	1.0(ref)
25-29.9	510	(21.9)	338	(21.6)	172	(22.6)	1.15(0.92-1.43)
30+	425	(18.3)	266	(17.0)	159	(20.9)	1.35(1.07-1.70)
p-value				*0.0788*			
Smoked at any time during pregnancy							
Yes	490	(21.1)	327	(20.9)	163	(21.4)	1.03(0.83-1.27)
No	1836	(78.9)	1237	(79.1)	599	(78.6)	1.0(ref)
p-value				*0.7886*			
Drank alcohol at any time during pregnancy							
Yes	832	(35.8)	582	(37.2)	250	(32.8)	0.83(0.69-0.99)
No	1487	(63.9)	979	(62.6)	508	(66.7)	1.0(ref)
Missing	7	(0.3)	3	(0.2)	4	(0.5)	
p-value				*0.0428*			
Gravidity							
1	764	(32.8)	522	(33.4)	242	(31.7)	1.0(ref)
2	671	(28.8)	438	(28.0)	233	(30.6)	1.15(0.92-1.43)
3	464	(20.0)	327	(20.9)	137	(18.0)	0.90(0.70-1.16)
4	224	(9.6)	147	(9.4)	77	(10.1)	1.13(0.83-1.55)
5	113	(4.9)	71	(4.5)	42	(5.5)	1.28(0.85-1.92)
6+	90	(3.9)	59	(3.8)	31	(4.1)	1.13(0.72-1.80)
p-value				*0.3961*			

Table 2.1 continued…

Parity							
Nulliparious	1029	(44.2)	680	(43.5)	349	(45.8)	1.0(ref)
1	769	(33.1)	522	(33.4)	247	(32.4)	0.92(0.76-1.13)
2	369	(15.9)	256	(16.4)	113	(14.8)	0.86(0.67-1.11)
3	110	(4.7)	77	(4.9)	33	(4.4)	0.84(0.54-1.28)
4+	49	(2.1)	29	(1.8)	20	(2.6)	1.34(0.75-2.41)
p-value				*0.5000*			
Fertility technology used to conceive index pregnancy							
Yes	135	(5.8)	83	(5.3)	52	(6.8)	1.29(0.89-1.85)
No	1266	(54.4)	851	(54.4)	415	(54.5)	1.0(ref)
Un-intended pregnancy	923	(39.7)	628	(40.2)	295	(38.7)	0.96(0.80-1.16)
Missing	2	(0.1)	2	(0.1)	0		
p-value				*0.3169*			
Household income ($)							
Mean	62,939	(47,985)	63,007	(49,476)	62,812	(44,799)	
p-value							
0-31,000	533	(22.9)	372	(23.8)	161	(21.1)	1.0(ref)
31,001-56,000	550	(23.6)	368	(23.5)	182	(23.9)	1.14(0.88-1.48)
56,001-80,000	565	(24.3)	365	(23.4)	200	(26.2)	1.27(0.98-1.63)
80,001+	546	(23.5)	371	(23.7)	175	(23.0)	1.09(0.84-1.41)
Missing	132	(5.7)	88	(5.6)	44	(5.8)	
p-value				*0.3187*			
Subject income ($)							
Mean	22,045	(20,927)	21,866	(20,977)	22,415	(20,833)	
p-value				*0.5580*			
0-5,000	579	(24.9)	391	(25.0)	188	(24.7)	1.0(ref)
5,001-19,000	566	(24.3)	386	(24.7)	180	(23.6)	0.97(0.76-1.24)
19,001-33,000	567	(24.4)	382	(24.4)	185	(24.3)	1.01(0.79-1.29)
33,001+	561	(24.1)	373	(23.8)	188	(24.7)	1.05(0.82-1.34)
Missing	53	(2.3)	32	(2.1)	21	(2.7)	

Table 2.1 continued…

p-value					*0.9442*			
Previous PTD								
Yes	254	(10.9)	120	(7.7)		134	(17.6)	3.06(2.31-4.05)
No	1043	(44.9)	764	(48.8)		279	(36.6)	1.0(ref)
Nulliparious	1029	(44.2)	680	(43.5)		349	(45.8)	1.41(1.16-1.70)
p-value					*<.0001*			
Subject low birth weight								
Yes	206	(8.9)	116	(7.4)		90	(11.8)	1.70(1.26-2.25)
No	2101	(90.3)	1437	(91.9)		664	(87.1)	1.0(ref)
Missing	19	(0.8)	11	(0.7)		8	(1.1)	
p-value					*0.0004*			
Subject born preterm								
Yes	170	(7.3)	100	(6.4)		70	(9.2)	1.49(1.08-2.05)
No	2140	(92.0)	1455	(93.0)		685	(89.9)	1.0(ref)
Missing	16	(0.7)	9	(0.6)		7	(0.9)	
p-value					*0.0142*			
Lifted > 20 lbs away from work								
No lifting	1314	(56.5)	871	(55.7)		443	(58.1)	1.0(ref)
1-10 min/day	314	(13.5)	227	(14.5)		87	(11.4)	0.75(0.57-0.99)
11-30 min/day	312	(13.4)	218	(13.9)		94	(12.4)	0.85(0.65-1.11)
31-60 min/day	213	(9.2)	147	(9.4)		66	(8.7)	0.88(0.65-1.21)
61-120 min/day	110	(4.7)	71	(4.6)		39	(5.1)	1.08(0.72-1.62)
121+ min/day	59	(2.5)	27	(1.7)		32	(4.2)	2.33(1.38-3.94)
Missing	4	(0.2)	3	(0.2)		1	(0.1)	
p-value					*0.0027*			

Table 2.1 continued…

Cared for kids less than 5 years old in their home							
Did not care for kids	1200	(51.5)	794	(50.8)	406	(53.3)	1.0(ref)
1-45 hrs/week	261	(11.2)	180	(11.5)	81	(10.6)	0.88(0.66-1.17)
46-60 hrs/week	318	(13.7)	213	(13.6)	105	(13.8)	0.96(0.74-1.25)
61-90 hrs/week	379	(16.3)	266	(17.0)	113	(14.8)	0.83(0.65-1.07)
91+ hrs/week	167	(7.2)	110	(7.0)	57	(7.5)	1.01(0.72-1.43)
Missing	1	(0.1)	1	(0.1)	0		
p-value				*0.6226*			
Leisure time physical activity (at least 10 minutes per week)							
None	622	(26.8)	406	(26.0)	216	(28.3)	1.0(ref)
10-60 min/week	454	(19.5)	313	(20.0)	141	(18.5)	0.85(0.65-1.10)
61-120 min/week	482	(20.7)	316	(20.2)	166	(21.8)	0.99(0.77-1.27)
121-200 min/week	351	(15.1)	248	(15.9)	103	(13.5)	0.78(0.59-1.04)
>200 min/week	412	(17.7)	279	(17.8)	133	(17.5)	0.90(0.69-1.17)
Missing	5	(0.2)	2	(0.1)	3	(0.4)	
p-value				*0.3785*			
Employed at any time during pregnancy							
Yes	1833	(78.8)	1214	(77.6)	619	(81.2)	1.27(1.02-1.58)
No	463	(19.9)	330	(21.1)	133	(17.5)	1.0(ref)
Missing	30	(1.3)	20	(1.3)	10	(1.3)	
p-value				*0.0388*			
Employed during the first 20 weeks of pregnancy							
Not at all	463	(19.9)	330	(21.1)	133	(17.5)	1.0(ref)
Part of the 20 weeks	176	(7.6)	107	(6.8)	69	(9.1)	1.60(1.11-2.30)
All of the 20 weeks	1648	(70.9)	110	(70.5)	545	(71.5)	1.23(0.98-1.53)
After 20 weeks only	8	(0.3)	4	(0.3)	4	(0.5)	2.48(0.61-10.07)
Missing	31	(1.3)	20	(1.3)	11	(1.4)	
p-value				*0.0483*			

Table 2.2 Characteristics of work and off the job physical activity among women who worked continuously during the first 20 weeks of pregnancy and risk of preterm delivery, Iowa Health in Pregnancy Study, 2002-2005 (N=1648).

Work Characteristic	*Control (N=1103) (n, col%)*		*PTD (N=545) (n, col%)*		*Crude OR (95% CI)*
Hours per week					
First trimester (<14 weeks)					
Mean (std. dev)	37.5	(10.4)	37.6	(10.2)	
p-value		*0.8150*			
≤ 20	113	(10.2)	53	(9.7)	0.91(0.64-1.30)
21-30	123	(11.2)	55	(10.1)	0.87(0.62-1.23)
31-40	626	(56.8)	322	(59.1)	1.0(ref)
41+	241	(21.8)	115	(21.1)	0.93(0.72-1.20)
p-value		*0.8217*			
Second trimester (14-20 wks only)					
Mean (std. dev)	36.9	(10.7)	36.5	(10.9)	
p-value		*0.5171*			
≤ 20	125	(11.3)	66	(12.1)	1.07(0.77-1.48)
21-30	128	(11.6)	66	(12.1)	1.04(0.75-1.44)
31-40	628	(57.0)	311	(57.1)	1.0(ref)
41+	222	(20.1)	102	(18.7)	0.93(0.71-1.22)
p-value		*0.8872*			
Standing while at work					
Hours per day on feet					
No standing	508	(46.1)	252	(46.3)	1.0(ref)
1-6	362	(32.8)	174	(31.9)	0.97(0.77-1.23)
>6	233	(21.1)	119	(21.8)	1.03(0.79-1.35)
p-value		*0.9147*			
Hours per day standing among those who stood					
Mean (std. dev)	6.1	(5.9)	5.7	(2.5)	
p-value		*0.1071*			
Standing in one position at work					
No standing in one position	859	(77.9)	422	(77.4)	1.0(ref)
1 hour/day	107	(9.7)	50	(9.2)	0.95(0.67-1.36)
2-3 hours/day	66	(6.0)	31	(5.7)	0.96(0.51-1.49)
4+ hours/day	71	(6.4)	42	(7.7)	1.20(0.81-1.79)
p-value		*0.7947*			
Hours per day standing in one position among those who stood					
Mean (std. dev)	1.1	(2.0)	1.3	(2.2)	
p-value		*0.4124*			

Table 2.2 continued…

Lifted 20+ lbs at work					
No lifting	799	(72.4)	418	(76.7)	1.0(ref)
1-9 mins/day	61	(5.5)	22	(4.0)	0.69(0.42-1.14)
10-29 mins/day	73	(6.6)	45	(8.3)	1.18(0.80-1.74)
30-59 mins/day	65	(5.9)	16	(2.9)	0.47(0.27-0.82)
60-179 mins/day	73	(6.6)	26	(4.8)	0.68(0.43-1.08)
180+ mins/day	28	(2.5)	18	(3.3)	1.23(0.67-2.25)
Missing	4	(0.5)	0		
p-value		*0.0217*			
Minutes/day lifted among those that lifted					
Mean (Std. dev)	52.9	(77.3)	61.6	(91.2)	
p-value		0.3023			
Psychological job demands throughout pregnancy					
Degree of repetitive tasks					
Low	407	(36.9)	185	(34.0)	1.0(ref)
Moderate	418	(37.9)	186	(34.1)	0.98(0.77-1.25)
High	278	(25.2)	174	(31.9)	1.38(1.07-1.78)
p-value		*0.0157*			
Control amount of work					
Strongly disagree	57	(5.2)	32	(5.9)	1.12(0.70-1.80)
Disagree	167	(15.1)	71	(13.0)	0.85(0.61-1.19)
Neutral	118	(10.7)	66	(12.1)	1.12(0.79-1.59)
Agree	421	(38.2)	206	(37.8)	0.98(0.76-1.25)
Strongly agree	340	(30.8)	170	(31.2)	1.0(ref)
p-value		*0.7095*			
Control how well did job					
Strongly disagree	6	(0.5)	1	(0.2)	0.33(0.04-2.79)
Disagree	24	(2.2)	17	(3.1)	1.42(0.75-2.69)
Neutral	46	(4.2)	25	(4.6)	1.09(0.66-1.81)
Agree	466	(42.2)	222	(40.7)	0.95(0.77-1.18)
Strongly agree	561	(50.9)	280	(51.4)	1.0(ref)
p-value		*0.5940*			
Control pace of work					
Strongly disagree	62	(5.6)	36	(6.6)	1.09(0.70-1.72)
Disagree	179	(16.2)	104	(19.1)	1.09(0.80-1.49)
Neutral	113	(10.2)	51	(9.4)	0.85(0.58-1.25)
Agree	444	(40.3)	192	(35.2)	0.81(0.63-1.05)
Strongly agree	305	(27.7)	162	(29.7)	1.0(ref)
p-value		*0.2352*			

Table 2.2 continued…

Adequate break time at work					
Strongly disagree	54	(4.9)	40	(7.3)	1.52(0.99-2.35)
Disagree	119	(10.8)	54	(9.9)	0.93(0.65-1.33)
Neutral	79	(7.2)	38	(7.0)	0.99(0.65-1.50)
Agree	329	(29.8)	159	(29.2)	0.99(0.78-1.26)
Strongly agree	522	(47.3)	254	(46.6)	1.0(ref)
p-value		*0.3797*			
Worked in hot, cold, wet or humid conditions					
Strongly disagree	527	(47.8)	271	(49.7)	1.0(ref)
Disagree	383	(34.7)	167	(30.6)	0.85(0.67-1.07)
Neutral	67	(6.1)	37	(6.8)	1.07(0.70-1.65)
Agree	84	(7.6)	43	(7.9)	1.00(0.67-1.48)
Strongly agree	42	(3.8)	27	(5.0)	1.25(0.75-2.07)
p-value		*0.4656*			
Physical activity outside of work					
Lifted < 20 lbs away from work					
No lifting	637	(57.7)	330	(60.6)	1.0(ref)
1-10 min/day	150	(13.6)	59	(10.8)	0.76(0.55-1.06)
11-30 min/day	149	(13.5)	67	(12.3)	0.87(0.63-1.19)
31-60 min/day	106	(9.6)	46	(8.4)	0.84(0.58-1.21)
61-120 min/day	46	(4.2)	25	(4.6)	1.05(0.63-1.74)
121+ min/day	15	(1.4)	18	(3.3)	2.32(1.15-4.65)
p-value		*0.0582*			
Cared for kids less than 5 years old in their home					
Did not care for kids	632	(57.3)	330	(60.6)	1.0(ref)
1-45 hrs/week	142	(12.9)	61	(11.2)	0.82(0.59-1.14)
46-60 hrs/week	176	(16.0)	88	(16.1)	0.96(0.72-1.28)
61-90 hrs/week	123	(11.2)	53	(9.7)	0.83(0.58-1.17)
91+ hrs/week	29	(2.6)	13	(2.4)	0.86(0.44-1.67)
p-value		*0.6834*			
Leisure time physical activity at least 10 min/week					
None	270	(24.5)	143	(26.3)	1.0(ref)
10-60 min/week	229	(20.8)	108	(19.8)	0.89(0.66-1.21)
61-120 min/week	221	(20.0)	131	(24.0)	1.12(0.83-1.51)
121-200 min/week	177	(16.0)	71	(13.0)	0.76(0.54-1.07)
>200 min/week	205	(18.6)	91	(16.7)	0.84(0.61-1.15)
Missing	1	(0.1)	1	(0.2)	
p-value		*0.1792*			

Table 2.3. Odds ratio and 95% confidence intervals for risk of preterm delivery-all types, and spontaneous preterm deliveries only, Iowa Health in Pregnancy Study, 2002-2005.

	All Preterm Deliveries						*Spontaneous PTD's*			
	Control (N=1433)		*All Preterm (N=678)*		*Crude OR (95% CI)*	*aOR (95% CI)*	*Spont. PTD (N=396)*		*Crude OR (95% CI)*	*aOR (95% CI)*
	N	*%*	*N*	*%*			*N*	*%*		
Continuous employed during the first 20 weeks of pregnancy										
Yes	1103	(70.5)	545	(71.5)	1.23 (0.98-1.53)	1.30 (1.00-1.69)[1]	318	(80.3)	1.24 (0.94-1.63)	1.28 (0.92-1.78)[3]
No	330	(21.1)	133	(17.5)	1.0(ref)	1.0(ref)	78	(19.7)	1.0(ref)	1.0(ref)
Work activities for those continuously employed										
Standing in one position										
None	859	(77.9)	422	(77.4)	1.0(ref)	1.0(ref)	245	(77.0)	1.0(ref)	1.0(ref)
1-3 hrs/day	173	(15.7)	81	(14.9)	0.95 (0.71-1.27)	0.96 (0.69-1.34)[2]	50	(15.7)	1.01 (0.72-1.43)	1.12 (0.76-1.65)[4]
4+ hrs/day	71	(6.4)	42	(7.7)	1.20 (0.81-1.79)	1.19 (0.75-1.88)[2]	23	(7.3)	1.14 (0.70-1.86)	1.13 (0.64-2.02)[4]
Lifting greater than 20 lbs										
None	799	(72.4)	418	(76.7)	1.0(ref)	1.0(ref)	240	(75.5)	1.0(ref)	1.0(ref)
1-9 min/day	61	(5.5)	22	(4.0)	0.69 (0.42-1.14)	0.75 (0.43-1.30)[2]	16	(5.0)	0.87 (0.49-1.54)	0.99 (0.53-1.84)[4]
10-29 min/day	73	(6.6)	45	(8.3)	1.18 (0.80-1.74)	1.05 (0.69-1.62)[2]	30	(9.4)	1.37 (0.87-2.14)	1.27 (0.77-2.07)[4]
30-179 min/day	138	(12.6)	42	(7.7)	0.58 (0.67-2.25)	0.57 (0.38-0.87)[2]	21	(6.6)	0.51 (0.31-0.82)	0.49 (0.29-0.82)[4]
180+ min/day	28	(2.5)	18	(3.3)	1.23 (0.67-2.25)	1.01 (0.50-2.02)[2]	11	(3.5)	1.31 (0.64-2.67)	1.35 (0.61-2.98)[4]

Table 2.3 continued…

Adequate break time										
Strongly Agree	54	(4.9)	40	(7.3)	1.0(ref)	1.0(ref)	141	(44.3)	1.0(ref)	1.0(ref)
Agree	329	(29.8)	159	(29.2)	0.99 (0.78-1.26)	1.08 (0.83-1.41)[2]	99	(31.1)	1.11 (0.83-1.49)	1.23 (0.89-1.68)[4]
Neutral	79	(7.2)	38	(7.0)	0.99 (0.65-1.50)	1.11 (0.70-1.75)[2]	21	(6.6)	0.98 (0.59-1.65)	1.01 (0.58-1.76)[4]
Disagree	119	(10.8)	54	(9.9)	0.93 (0.65-1.33)	0.94 (0.64-1.40)[2]	31	(9.8)	0.96 (0.62-1.49)	0.94 (0.58-1.53)[4]
Strongly Disagree	54	(4.9)	40	(7.3)	1.52 (0.99-2.35)	1.67 (1.03-2.73)[2]	26	(8.2)	1.78 (1.08-2.95)	1.92 (1.09-3.56)[4]
Repetitive tasks										
Low degree	407	(36.9)	185	(33.9)	1.0(ref)	1.0(ref)	112	(35.2)	1.0(ref)	1.0(ref)
Moderate degree	418	(37.9)	186	(34.1)	0.98 (0.77-1.25)	0.99 (0.76-1.30)[2]	104	(32.7)	0.90 (0.67-1.22)	0.96 (0.69-1.33)[4]
High degree	278	(25.2)	174	(31.9)	1.38 (1.07-1.78)	1.47 (1.10-1.98)[2]	102	(32.1)	1.33 (0.98-1.82)	1.55 (1.09-2.21)[4]

[1] adjusted for maternal age at delivery , white race , previously delivering a preterm infant , any alcohol use during pregnancy , pre-pregnancy BMI , subject born low birth weight, lifting greater than 20 lbs away from work, State Anxiety, Perceived Stress, household income, maternal education

[2] All preterm deliveries adjusted for maternal age at delivery, white race, previously delivering a preterm infant , any alcohol use during pregnancy , subject born low birth weight, lifting greater than 20 lbs away from work , leisure time physical activity, State Anxiety ,Perceived Stress , NUPDQ, household income, maternal education and other work variables in the table

[3] adjusted for maternal age at delivery , white race, previously delivering a preterm infant , any alcohol use during pregnancy , subject born low birth weight, lifting greater than 20 lbs away from work, State Anxiety, Perceived Stress, household income, maternal education

[4] Spontaneous preterm deliveries adjusted for maternal age at delivery , white race, previously delivering a preterm infant , any alcohol use during pregnancy , subject born low birth weight, State Anxiety ,Perceived Stress , household income, maternal education and other work variables in the table

CHAPTER IV

INJURIES DURING PREGNANCY AND RISK OF PRETERM DELIVERY

Summary of findings

Purpose: The prevalence of injuries during pregnancy is largely underestimated as previous research has focused on more severe injuries resulting in emergency department visits and hospitalizations. Little is known about the frequency, severity and causes of injuries in a population-based sample of pregnant women and the potential effect of these injuries on risk of preterm delivery.

Methods: A case-control study of women from four Iowa counties interviewed postpartum about injuries sustained during pregnancy. Maternal, pregnancy, and environmental characteristics associated with an injury during pregnancy in control subjects were examined to estimate population based risk factors for injury. To examine the risk of preterm delivery, we investigated the overall risk of injury and the month of pregnancy it occurred, if medical attention was sought, the mechanism of injury, and the number and location of bodily injuries that occurred. Unadjusted and adjusted odds of injury and preterm delivery were calculated using logistic regression.

Results: Women at increased risk for injury during pregnancy were 20-24 years old, less than college educated, with no partner or cohabitating with a partner, were more likely to smoke during pregnancy, had an unintended pregnancy, lived at or just above the poverty level and report intimate partner violence compared to women who were uninjured. Presence of an injury during pregnancy was not a risk factor for preterm delivery although there is suggested increased risk with an injury that involves falling from a height (OR 1.53; 95% CI 0.64-3.65), two or more body parts being injured (OR 2.04; 95% CI 0.99-4.20) or if the abdomen and other parts of the body (OR 1.75; 95% CI 0.59-5.25) are injured in the same incident. After controlling for a previous preterm delivery, partner status, and poverty threshold, women who had two or more body parts injured in

a single incident were 2.50 (95% CI 1.14-5.49) more like to deliver a preterm infant than women with no reported injury.

Conclusion: Pregnant women who are considered 'high-risk' for many pregnancy-related complications are also at increased risk of injury during pregnancy. The mechanism of injury and location of the injury are vital in understanding the risk of preterm delivery. Further investigation is needed of the environment in which these women live, and not just their individual characteristics, that may increase the risk of injury.

Introduction

Traumatic injuries during pregnancy are the leading non-obstetric cause of maternal death (117, 118). Over 6% of all pregnancies are complicated by injuries and trauma in pregnancy remains a common cause of fetal death. Over a 3-year period, Weiss et al (119) estimated that 5.4 per 1000 fetal deaths were due to maternal injury.

The scope of non-fatal maternal injury during pregnancy is difficult to estimate because less severe injuries do not require medical care and go unreported. In 2002, it was estimated that there were 4.1 injury hospitalizations per 1000 deliveries with over one-third of these resulting in a delivery (120). Pregnant women with a traumatic injury requiring delivery are more likely to suffer from a myriad of pregnancy-related complications (e.g., placental abruption, uterine rupture, fetal death); furthermore, even those not delivered at trauma hospitalization are more likely to deliver preterm and are at increased risk of placental abruption and maternal demise (74). In addition, those admitted for trauma during pregnancy and considered 'non-injured' after examination are at increased of preterm delivery (76). More than half of fetal losses among injured pregnant women have been associated with a 'minor' injury (77).

The leading mechanisms of injury during pregnancy are motor vehicle crashes and falls (78, 80, 119, 120). Among women who delivered during an injury hospitalization, falls were the most common mechanism of injury while the largest proportion of women who were non-delivered were admitted following a motor vehicle collision (74, 120). Blunt abdominal trauma resulting from contact of the pregnant abdomen with the steering wheel during a motor vehicle crash is associated with increased risk of placental abruption and uterine rupture (79). Non-severely injured pregnant women are also at increased risk of placental abruption, although it is speculated that the abruption may be sub-clinical at the time of injury and go unidentified until after discharge (76, 78, 79).

It is notable that almost three times as many fetal deaths are attributed to motor vehicle crashes than deaths to infants under the age of one (79). Many of these fetal deaths may have been avoided with maternal education on the proper use and placement of restraints during pregnancy. Despite evidence showing that properly restrained women have one-fourth to half the risk of poor pregnancy outcome as those who are improperly restrained or unrestrained (79), less than half of pregnant women report receiving prenatal counseling on proper seat belt placement during pregnancy (121).

Maternal falls have also been linked to fetal death and prematurity (74). Sperry et al (76) found that women who experienced trauma in pregnancy but did not deliver at the trauma admission were more likely to deliver a preterm infant if the injury was the result of fall rather than a vehicle crash. In the only population-based study of falls during pregnancy, Dunning et al (80) reported that nearly 30% of women fell during pregnancy and one in ten experienced more than one fall during pregnancy. The situations most likely to lead to a fall during pregnancy include maneuvering stairs, slippery floors, hurrying or carrying an object or child (80).

Maternal trauma-related deaths and hospitalizations are only the “tip of the iceberg” of the number of injuries that are likely to occur to women during pregnancy. In this analysis we sought to describe the characteristics of control women who reported any type of injury during pregnancy in a case-control study of the effect of intimate partner violence and maternal stress on risk of preterm delivery. We also estimated the risk of preterm delivery associated with the occurrence of injury and by the mechanism, timing during pregnancy, number and location of body region(s) injured.

Methods

The occurrence and risks associated with maternal prenatal injury were examined using data collected during the Iowa Health in Pregnancy Study (IHIPS). IHIPS is a population-based case-controls study of the effect of intimate partner violence and maternal stress on the risk of preterm delivery and small for gestational age outcomes. All women who delivered a live birth in Johnson, Polk, Black Hawk and Scott counties in Iowa served as the sampling frame for the study. Women were selected from the electronic Iowa birth certificate if either the last menstrual period or the clinical estimate of gestational age indicated the infant was born preterm (before 37 weeks). Controls were term infants (≥37 weeks) frequency matched on county of residence. After selection from the birth certificate, extensive telephone number tracing was completed and a study introductory letter explaining study procedures were mailed to potential subjects. Subjects with a telephone number were called within two weeks following the letter mailing to explain study procedures and obtain verbal informed consent. Consenting subjects were screened for eligibility. Eligible women were asked to respond to a 45-minute telephone interview and provide signed consent for review of their prenatal, labor, and delivery medical records.

Of 7202 births selected from the birth certificate, 4250 (59.0%) could be reached by phone. Of these, 19.7% (N=836) refused to be screened for eligibility; of those screened 12.9% (N=548) were ineligible. Over 94.5% (N=2709) of the 2866 eligible to participate completed the telephone interview. After adjusting for those that were ineligible, the response rate for IHIPS was 45.2% and the participation rate was 76.6%

(81). Signed prenatal, labor and delivery medical record releases were received from over 90% of interviewed cases and controls.

Information collected from the interview included report of any prenatal injury, the mechanism and timing of the injury, as well as part(s) of the body injured. Each subject was asked "Did you have any serious accidents or injuries during your pregnancy?" If an injury was reported then the month of gestation when the injury occurred, how the injury happened and the part(s) of the body injured was collected. In addition, each injured subject was asked if she felt the injury had affected the health of her baby and whether she sought medical care for the injury. The mechanism of injury was classified using external causation codes (E-codes) from the International Classification of Diseases, ninth version, Clinical Modification.

To classify an infant as preterm (< 37 weeks at delivery), the method developed by Harland et al (2010) was used. Briefly, the assumption of dating by ultrasound measurement is that fetal growth early in pregnancy is relatively uniform, this may not be valid in fetus' that are small for gestational age as an ultrasound will measure them 'younger' due to their small stature. Therefore if a subject was selected for IHIPS as delivering a suspected small infant, an adjustment (in weeks) was made to the ultrasound estimated gestational age. This adjustment differed by maternal age, smoking status in the first or second trimester and vaginal bleeding during the first trimester of pregnancy. Following ultrasound gestational age adjustment, the American Congress of Obstetrics and Gynecology guideline (90) was applied: gestational age at delivery estimated by the last menstrual period (LMP) was assigned unless it disagreed by greater than 7 days with a first trimester ultrasound (<14 weeks) or greater than 10 days for an ultrasound between 14 and 20 weeks gestation. If an ultrasound before 21 weeks was not available, the LMP gestational age at delivery was used unless it disagreed by greater than 7 days with the clinical estimate of gestational age from the birth certificate than the clinical estimate of gestational age was assigned. Preterm delivery (PTD) was defined as birth before 37 weeks of pregnancy. Controls subjects were those who delivered at term (37 or more weeks) including 2.9% (N=45) that were term but small for gestational age.

To adjust for the inherent bias of preterm subjects having a shorter length of gestation and therefore less time to be injured, the analysis of injury and risk of preterm delivery was restricted to only those preterm cases and controls who were injured in months one through eight or not injured at any time during pregnancy.

Covariates

Pertinent maternal demographic and lifestyle characteristics and pregnancy histories were considered as potential risk factors for injury reported during pregnancy. Maternal age at delivery was calculated by taking the date of delivery minus the maternal birth date reported during interview. The categorization of maternal age (18-19, 20-24, 25-29, 30-34, 35+) was based on previous research showing increased risk of preterm delivery with the extremes of maternal age. Other variables include maternal race (non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander and other), education (less than or equal to high school, some college, college graduate-bachelor degree, masters or professional degree), pre-pregnancy body mass index (<18.5, 18.5-24.9, 25-29.9, 30+), gravidity, and parity. Each subject was asked to report her partner status during her pregnancy: a subject was considered to not have a partner if the relationship had lasted less than four weeks during pregnancy. Pregnancy intention and excitement following conception were measured using questions from the Pregnancy Risk Assessment Monitoring System 2000-2003 Core Questionnaire (http://www.cdc.gov/prams/Questionnaire.htm). Household and subject incomes were categorized based on the distribution in controls. We calculated poverty level based on the 2004 Federal Poverty thresholds and guidelines determined by the Agency for Healthcare Research and Quality: poor or near poor (<125% of the federal poverty level), low income (125-199% of poverty level), middle income (200-399% of the poverty level) and high income (≥400% of the poverty level). This measure accounts for not only household income but the number of individuals living within the home. Continuous variables such as time spent heavy lifting at home, caring for children less than five years old in the home, and leisure time physical activity were categorized based on the distribution in controls. Intimate partner violence by a current or former partner was measured using the Abuse Assessment Screen (122) and the Women's Experience with Battering scale (123).

Analysis

To identify maternal demographic, and lifestyle characteristics associated with preterm delivery, chi-square tests were used to assess categorical variables and the Student's t-test for continuous variables. Crude odds ratios of preterm delivery were calculated to estimate the effect sizes in association with these characteristics.

To examine risk factors for injury during pregnancy among a population-based sample of women, characteristics of control subjects were compared by injury status. Again chi-square tests were used for categorical variables and the Student's t-test was used for continuous variables. Unadjusted odds of injury were estimated by maternal characteristics for those with a cell size greater than or equal to five.

To estimate the overall risk of injury and describe the mechanism, timing during pregnancy, and body location(s) of injuries with risk of preterm delivery, injury characteristics were compared by preterm case-control status. Chi-square tests were used to determine difference in proportions by case-control status. Adjusted and crude odds ratios estimating the association of injury with risk of preterm delivery were also calculated if all cell sizes in the analysis were greater than or equal to five.

Results

Maternal pregnancy history, demographic and lifestyle characteristics are associated with increased risk of preterm delivery (Table 2.1). Subjects that were younger than 25 or older than 29 years old were more likely to delivery preterm than women 25-29 years of age. Being of Asian or Pacific Islander race decreased a woman's risk of preterm delivery (OR=0.51 95% CI=0.29-0.89) compared to women who were white. Having a body mass index that was 30 or greater increased a woman's risk of preterm delivery by 35% compared to a woman with a normal body mass index. Subjects who drank alcohol at any time during pregnancy were 17% less likely to deliver preterm than subjects who did not drink during pregnancy. Among multiparious women, those who had previously delivered a preterm infant were over three times (OR=3.06 95% CI=2.31-4.05) more likely to deliver a preterm infant than women who had previously delivered a non-preterm infant. Nulliparious women were 41% more likely to deliver a preterm infant than multiparious women with no history of preterm delivery. If a subject herself was born low birth weight (<2500 grams) or preterm she was over 45% more likely to deliver a preterm infant.

The odds of injury varied substantially by several maternal and pregnancy characteristics (Table 3.1). Injured women were significantly more likely to be 20-24 years old, non-white, have less than a college degree, and smoke during pregnancy. Women who wanted to be pregnant later were 2.5 times as likely to be injured as women with planned pregnancies. In addition, those that were okay about being pregnant following conception were 83% more likely to be injured than those excited about their pregnancy. Subjects without a partner and women cohabitating with a partner were 2.71 and 1.98 times more likely to be injured than women married to their partners, respectively. Household income over $31,000 (US) was associated with decreased risk of injury. A suggested dose-response relationship is seen with individual subject income:

as income increases the risk of injury decreases (test for trend p-value = 0.1624). A similar association of increased risk was observed according to poverty level classification with subjects living in poor or near poor conditions at 2.5-fold greater risk of injury than high income women. There is suggested increased risk of injury when a woman lifted 20 pounds 1-10 minutes per day at home. Women who experienced any type of intimate partner violence (battering, physical or sexual) were 1.89 times more likely to report an injury during pregnancy than women who did not experience this violence.

There is suggested increased risk of preterm delivery by several injury characteristics (Table 3.2). Women who were injured in the second trimester were more likely to deliver preterm than those injured in the first trimester or during months seven and eight. Although those that sought medical care were not more likely to deliver preterm, among those that did seek care, those who went to a hospital or emergency room were more likely to deliver preterm than uninjured women. Falls were the most frequently reported mechanism of injury followed by motor vehicle crashes. There is a suggested increased risk of preterm delivery following a fall from a height compared to women who did not report an injury during pregnancy. Injuries to the abdomen alone or the abdomen with other locations are at 1.23 and 1.75 suggested increased risk of preterm delivery, respectively, than women reporting no injuries. Of note, those reporting two or more body parts injured in the same incident were twice (OR = 2.04; 95% CI 0.99-4.20) as likely to delivery preterm as those reporting no injury during pregnancy. After controlling for age at delivery, previous preterm delivery, partner status, and poverty threshold women reporting injuries two or more parts of their body were 2.50 (95% CI 1.14-5.49) times more likely to deliver preterm as women who reported no injuries during pregnancy.

Discussion

Subjects that report having two or more body parts injured in one incident are twice as likely to deliver preterm than women reporting no injures, after controlling for previous preterm delivery, poverty threshold and partner status. There is a suggested increased risk of preterm delivery following an injury that involved falling from a height, and having the abdomen injured. The inability to find significant results is likely to do a lack of power to detect a difference given the relatively small number of injured subjects (N = 125).

Although many studies have examined injury during pregnancy (74-77, 124), ours is the first to describe the epidemiology of injuries in a population based sample of pregnant women. Over 5% of control women reported an injury during pregnancy, a prevalence similar to many other diseases of pregnancy (e.g., pre-eclampsia, gestational diabetes) and many of the risk factors are similar. Risk factors for reporting an injury during pregnancy include younger age, lower education, smoking at any time during pregnancy, having an unintended pregnancy, and lower household income. Targeting this population for injury prevention during pregnancy would reduce the impact of these injuries.

Consistent with previous literature, we found that women with less education, younger, and not married are more likely to be injured during pregnancy (80, 125). We are the first to report on the association of pregnancy intention and pregnancy excitement following conception on risk of injury. A high risk of injury was associated with reporting intimate partner violence during pregnancy. In this analysis we are unable to determine if the injury reported is a result of an act of violence but it suggests that women who present with an injury should be screened for intimate partner violence.

Previous research of prenatal injury has put great effort into examining individual exposures and characteristics but little attention has been paid to the environment in which these individuals live. The poverty threshold is a measure of income and number of individuals in the home, a potentially better indicator of living conditions. This analysis is the first to report that living in poor or near poor circumstances is associated with substantially increased risk of injury during pregnancy. This result suggests further investigation into the environment of women at high-risk of injury is warranted and a better understanding of this environment may lead to wide-spread prevention strategies that do not place a large burden on the individual.

As found previously, the leading mechanisms of injury were falls and transportation-related (74-76, 125). The likelihood of a fall during pregnancy should be discussed during prenatal care given the shift in the center of gravidity as the abdomen extends beyond the pelvis and the decreased postural stability associated with pregnancy progression (126, 127). In addition, increased counseling in proper restraint use during pregnancy may not decrease a women's risk of being involved in a motor vehicle crash but it can reduce the severity of injury to her and her unborn child.

Our analysis did not find increased risk of preterm delivery associated with a reported injury in the first eight months of pregnancy although there was suggested increased risk (OR = 1.21; 95% CI 0.74-1.98) with an injury that was followed by a hospital or emergency room visit. Among women not delivered at an injury hospitalization, El Kady (74) found a 20% increased risk of preterm delivery. Previous studies of injury hospitalizations have found stronger associations (60-270%) between prenatal injury and preterm delivery likely due to increased injury severity leading to hospitalization (74, 75).

Injury to the abdomen has previously been associated with injury severity and increased risk of a negative pregnancy outcome as is found in our analysis. Women reporting an injury to the abdomen are more likely to have a severe injury (75, 117) resulting in delivery at injury hospitalization, and maternal or fetal death (117, 120). We found an increased risk of preterm delivery with an abdominal injury alone or in concert with other bodily injuries. This analysis is the first to report on the association between number of body parts injured and risk of preterm delivery. The greater than 2.5-fold increased risk of preterm delivery is similar to the estimates of El Kady (74) and Schiff (75) that looked at the association of injury hospitalizations and preterm delivery, the number of body parts injured is suggestive of more extensive injuries as may be seen in these hospitalizations.

Limitations to this study include possible recall bias, participation bias and the inability to classify the severity of injuries. Validated measures of injury severity, such as the Injury Severity Score, has shown an association between increasing score and adverse pregnancy outcome (118); although the severity proxy measure of number of body regions injured implies increased risk of preterm delivery with more regions injured. If recall bias were present, one would hypothesize that preterm subjects would be more likely to report an injury during pregnancy but prevalence of reported injuries did not differ by case-control status. In addition, as time passes, both preterm and control subjects may be less likely to recall less severe injuries and therefore this analysis may tend to include the more severe injuries. This is suggested by the proportion of injured subjects that sought medical care following their injury. Subjects who participated in the study were more likely to be white, have higher education and higher household income than those that did not participate. Even in this more socially advantaged group, the risk of injury in pregnancy was still associated with being young, less educated with less household income. Thus, the risk of injury among those that did not participate may be even more pronounced, which would lead to underestimation of injury during pregnancy.

Strengths of the research presented here include the analysis of a population-based sample of pregnant women to describe injuries during pregnancy and the ability to estimate the risk of preterm delivery following a reported injury. We were able to describe a high risk population, both by their individual characteristics and the environment in which they live, where maternal education on the risk of injury and preventive services should be targeted. In addition, validated measures of intimate partner violence, and pregnancy intention were used to measure risk factors for injury during pregnancy.

In conclusion, pregnant women are at high risk of injury but little population based research is available to identify those at increased risk of injury and should be targeted for education and prevention services. In addition, there is no research on the living conditions and environments where injured pregnant women reside aside from our finding on the decreased risk with higher proportion above the poverty level. Further population based research is needed to identify environmental, as well as individual, risk factors associated with injury during pregnancy to build evidence based maternal education and prevention services.

Table 3.1 Maternal and pregnancy characteristics of control subjects by injury status during pregnancy, Iowa Health in Pregnancy Study, 2002-2005 (N=1564).

	Injured at any time during pregnancy				
Maternal /Pregnancy Characteristics	*No (N=1477) N (Col %)*		*Yes (N=86) N (Col %)*		*Crude OR (95% CI)*
Maternal Age					
Mean (std. dev)	28.3	(5.3)	26.6	(5.6)	
p-value	*0.0033*				
18-19	73	(4.9)	5	(5.8)	1.42(0.53-3.80)
20-24	281	(19.0)	31	(36.1)	2.28(1.33-3.91)
25-29	537	(36.4)	26	(30.2)	1.0(ref)
30-34	397	(26.9)	14	(16.3)	0.73(0.38-1.41)
35+	189	(12.8)	10	(11.6)	1.09(0.52-2.31)
p-value	*0.0026*				
Maternal race/ethnicity					
White, non-Hispanic	1265	(85.7)	67	(77.9)	1.0(ref)
Black, non-Hispanic	78	(5.3)	7	(8.1)	1.75(0.89-3.46)
Hispanic	33	(2.2)	2	(2.3)	Unable to Calc
Asian/Pacific Islander	58	(3.9)	4	(4.7)	Unable to Calc
Other[1]	43	(2.9)	6	(7.0)	2.83(1.37-5.85)
p-value	*0.1856*				
Maternal Education					
<= High school	270	(18.3)	26	(30.2)	2.67(1.44-4.96)
Some college	475	(32.1)	30	(34.9)	1.75(0.96-3.18)
College grad	499	(33.8)	18	(20.9)	1.0(ref)
Master or Prof	233	(15.8)	12	(14.0)	1.43(0.68-3.01)
p-value	*0.0144*				
Marital Status					
Married	1168	(79.1)	56	(65.1)	1.0(ref)
Not married, living together	137	(9.2)	13	(15.1)	1.98(1.06-3.71)
Not married, not living together	50	(3.4)	3	(3.5)	Unable to Calc
No partner	77	(5.2)	10	(11.6)	2.71(1.33-5.52)
Missing	45	(3.1)	4	(4.7)	
p-value	*0.0114*				
Pre-pregnancy BMI					
Mean (std. dev)	24.9	(5.9)	24.9	(5.8)	
p-value	*0.1565*				
<18.5	95	(6.4)	3	(3.5)	Unable to Calc
18.5-24.9	819	(55.5)	43	(50.0)	1.0(ref)
25-29.9	316	(21.4)	22	(25.6)	1.33(0.78-2.25)
30+	247	(16.7)	18	(20.9)	1.39(0.79-2.45)

Table 3.1 continued…

p-value		*0.3813*			
Smoked at any time during pregnancy					
Yes	300	(20.3)	27	(31.4)	1.80(1.12-2.88)
No	1177	(79.7)	59	(68.6)	1.0(ref)
p-value		*0.0140*			
Drank alcohol at any time during pregnancy					
Yes	549	(37.2)	33	(38.4)	1.05(0.67-1.64)
No	925	(62.6)	53	(61.6)	1.0(ref)
Missing	3	(0.2)			
p-value		*0.8337*			
Gravidity					
1	488	(33.1)	34	(39.5)	1.0(ref)
2	417	(28.2)	21	(24.4)	0.72(0.41-1.27)
3	310	(21.0)	17	(19.8)	0.79(0.43-1.43)
4	139	(9.4)	7	(8.1)	0.72(0.31-1.67)
5	68	(4.6)	3	(3.5)	0.63(0.19-2.12)
6+	55	(3.7)	4	(4.7)	1.04(0.36-3.05)
p-value		*0.8415*			
Parity					
Nulliparious	640	(43.3)	40	(46.5)	1.0(ref)
1	497	(33.7)	25	(29.1)	0.81(0.48-1.35)
2	241	(16.3)	15	(17.4)	1.00(0.54-1.84)
3	72	(4.9)	4	(4.7)	0.89(0.31-2.56)
4+	27	(1.8)	2	(2.3)	1.19(0.27-5.16)
p-value		*0.9276*			
Pregnancy intention					
Conception or sooner	898	(60.8)	35	(40.7)	1.0(ref)
Wanted later	356	(24.1)	35	(40.7)	2.52(1.55-4.09)
Did not want	110	(7.5)	7	(8.1)	1.63(0.71-3.76)
Didn't care	111	(7.5)	9	(10.5)	2.08(0.97-4.44)
Missing	2	0.1	0		
p-value		*0.0038*			
Pregnancy excitement following conception					
Excited	1158	(78.4)	58	(67.5)	1.0(ref)
Okay	196	(13.3)	18	(20.9)	1.83(1.06-3.18)
Not sure	93	(6.3)	7	(8.1)	1.50(0.67-3.39)
Didn't want	27	(1.8)	2	(2.3)	Unable to Calc
Missing	3	(0.2)	1	(1.2)	
p-value		*0.0450*			

Table 3.1 continued…

Household income ($)					
Mean (std. dev)	63,490	(49,502)	54,878	(48,765)	
p-value					
0-31,000	340	(23.0)	31	(36.0)	1.0(ref)
31,001-56,000	351	(23.8)	17	(19.8)	0.53(0.29-0.98)
56,001-80,000	348	(23.6)	17	(19.8)	0.54(0.29-0.99)
80,001+	356	(24.1)	15	(17.4)	0.46(0.25-0.87)
Missing	82	(5.5)	6	(7.0)	
p-value		*0.0371*			
Subject income ($)					
Mean (std. dev)	22,100	(22,165)	18,085	(17,201)	
p-value		*0.0418*			
0-5,000	365	(24.7)	25	(29.1)	1.0(ref)
5,001-19,000	362	(24.5)	24	(27.9)	0.98(0.54-1.73)
19,001-33,000	362	(24.5)	20	(23.2)	0.81(0.44-1.48)
33,001+	357	(24.2)	16	(18.6)	0.66(0.34-1.25)
Missing	31	(2.1)	1	(1.2)	
p-value		*0.5558*			
Poverty Threshold					
Poor/Near Poor	207	(14.0)	20	(23.2)	2.55(1.34-4.83)
Low income	181	(12.3)	11	(12.8)	1.60(0.75-3.41)
Medium income	480	(32.5)	29	(33.7)	1.59(0.89-2.85)
High income	527	(35.7)	20	(23.2)	1.0(ref)
Missing	82	(5.5)	6	(7.1)	
p-value		*0.0365*			
Previous preterm delivery					
Yes	114	(7.7)	6	(7.0)	0.95(0.39-2.30)
No	723	(49.0)	40	(46.5)	1.0(ref)
Nulliparious	640	(43.3)	40	(46.5)	1.13(0.72-1.77)
p-value		*0.8411*			
Lifted > 20 lbs at home					
No lifting	824	(55.8)	47	(54.7)	1.0(ref)
1-10 min/day	209	(14.2)	18	(20.9)	1.51(0.86-2.65)
11-30 min/day	210	(14.2)	8	(9.3)	0.67(0.31-1.44)
31-60 min/day	137	(9.3)	9	(10.5)	1.15(0.55-2.40)
61-120 min/day	67	(4.5)	4	(4.6)	Unable to Calc
121+ min/day	27	(1.8)	0		Unable to Calc
Missing	3	(0.2)			
p-value		*0.3380*			

Table 3.1 continued…

Cared for kids less than 5 years old in their home					
Did not care for kids	752	(50.9)	42	(48.8)	1.0(ref)
1-45 hrs/week	166	(11.2)	14	(16.3)	1.51(0.81-2.83)
46-60 hrs/week	204	(13.8)	9	(10.5)	0.79(0.38-1.65)
61-90 hrs/week	248	(16.8)	17	(19.8)	1.23(0.69-2.20)
91+ hrs/week	106	(7.2)	4	(4.6)	Unable to Calc
Missing	1	(0.1)			
p-value		*0.4498*			
Leisure-time physical activity (at least 10 min/week)					
None	386	(26.1)	20	(23.2)	1.0(ref)
10-60 min/week	296	(20.0)	17	(19.8)	1.11(0.57-2.15)
61-120 min/week	296	(20.0)	19	(22.1)	1.24(0.65-2.36)
121-200 min/week	233	(15.8)	15	(17.4)	1.24(0.62-2.47)
>200 min/week	265	(18.0)	14	(16.3)	1.02(0.51-2.06)
Missing	1	(0.1)	1	(1.2)	
p-value		*0.9517*			
Any intimate partner violence					
Yes	117	(7.9)	12	(14.0)	1.89(1.00-3.57)
No	1360	(92.1)	74	(86.0)	1.0(ref)
p-value		*0.0481*			

Table 3.2 Characteristics of injuries reported through the eighth month of pregnancy and risk of preterm delivery, Iowa Health in Pregnancy Study, 2002-2005 (N=2317).

Injury Characteristic	*Control (N=1556) (n, col%)*		*PTD (N=761) (n, col%)*		*Crude OR (95% CI)*
Injured at any time during pregnancy					
Yes	78	(5.0)	38	(5.0)	1.00(0.67-1.48)
No	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	1	(0.1)	0		
p-value		*0.9813*			
Month of Pregnancy Injured					
Months 1 - 3	15	(1.0)	7	(0.9)	0.95(0.39-2.35)
Months 4 -6	35	(2.3)	23	(3.0)	1.34(0.79-2.29)
Months 7 - 8	27	(1.7)	8	(1.1)	0.61(0.27-1.34)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	2	(0.1)	1	(0.0)	
p-value		*0.4216*			
Seen by doctor for injury					
Yes	64	(4.1)	31	(4.1)	0.99(0.64-1.53)
No	13	(0.8)	7	(0.9)	1.10(0.44-2.77)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	2	(0.1)	0		
p-value		*0.9784*			
Went to hospital or ER for injury					
Yes	44	(2.9)	26	(3.4)	1.21(0.74-1.98)
No	33	(2.1)	12	(1.6)	0.74(0.38-1.45)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	2	(0.1)	0		
p-value		*0.5056*			
Mechanism of Injury					
Fall from height	12	(0.8)	9	(1.2)	1.53(0.64-3.65)
Fall same level	25	(1.6)	10	(1.3)	0.82(0.39-1.71)
Transportation-related	23	(1.5)	12	(1.6)	1.07(0.53-2.15)
Other	17	(1.1)	7	(0.9)	0.84(0.35-2.04)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	2	(0.1)			
p-value		*0.8401*			

Table 3.2 continued…

Number of body parts injured					
None	9	(0.5)	2	(0.3)	Unable to Calc
1	54	(3.5)	21	(2.7)	0.79(0.48-1.33)
2+	15	(1.0)	15	(2.0)	2.04(0.99-4.20)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	1	(0.1)			
p-value		*0.1180*			
Injury location					
Abdomen alone	10	(0.6)	6	(0.8)	1.23(0.44-3.39)
Abdomen and other location(s)	7	(0.5)	6	(0.8)	1.75(0.59-5.23)
Non-abdominal injury	59	(3.8)	26	(3.4)	0.90(0.56-1.44)
No injury	1477	(94.9)	723	(95.0)	1.0(ref)
Missing	3	(0.2)	0		
p-value		*0.7067*			

CHAPTER V

CONTRIBUTION OF FINDINGS AND POTENTIAL FOR FUTURE RESEARCH

Current Research

Preterm delivery (PTD) accounts for over one-third of all infant deaths in the United States (2, 3). In 2008, 12.3 percent of all live births were preterm; this equates to a preterm infant being born every minute (4, 5). The rate of preterm delivery in the United States continues to grow despite efforts to identify risk factors and preventive interventions. A potential risk factor of preterm delivery that has been under studied is injury, particularly less severe injuries that do not lead to maternal or fetal death. Severe injuries requiring emergency room visits or hospitalizations have been associated with prematurity but the effect of less severe injuries is largely unknown (74, 76, 77, 124). Although highly studied, few definitive occupational risk factors for preterm delivery have been established. Given that two-thirds of pregnant women continue to work during their pregnancy these exposures must be further explored.

Before one can study risk factors for preterm delivery, prematurity must be properly classified through rigorous definition of an infant's gestational age at delivery. Several measures exist for estimating gestational age at delivery: self-reported date of last menstrual period (LMP), ultrasound examination before 21 weeks gestation and clinical estimate on the birth certificate. This analysis and previous research have found that using ultrasound gestational age dating in infants with growth restriction may violate the fundamental assumption of ultrasound dating: that fetal growth is fairly uniform early in pregnancy. Our analysis demonstrated that ultrasound dating of women with suspected intrauterine growth restriction under-estimated gestational age by 1.5 weeks, on average, relative to dating based on a first trimester LMP. This led to an increased likelihood that such deliveries would be erroneously classified as preterm and not small for gestational age.

The analysis in Chapter II provides a statistical approach to ascertain and adjust for the inherent underestimate of gestational age based on ultrasound examination of fetuses with suspected growth restriction. The ultrasound adjustment varied by the week the ultrasound examination was completed, maternal age at delivery, smoking in the first or second trimester, and vaginal bleeding in the first trimester. This thorough examination of gestational age at delivery among infants that are suspected to be born small for gestational age reduces the likelihood of misclassifying the infant as a premature increasing the validity of our analyses of examining prenatal occupational and injury exposures as risk factors for preterm delivery.

The majority of women continue to work during pregnancy and association of occupational lifting, standing and psychological stress on prematurity reported by other studies is mixed. This analysis is the first to control for state anxiety, perceived stress, and off the job physical activity while simultaneously studying the effects of lifting, standing, repetitive tasks and inadequate breaks at work on preterm delivery. Among women who worked continuously during the first 20 weeks of pregnancy, those reporting high perceived stress (score ≥ 7) (105), a measure of chronic stress, were 63% (aOR 1.63; 95% CI 1.11-2.38) more likely to delivery preterm than those with a low stress score (≤ 2). In addition, lifting greater than 20 pounds away from work for greater than 120 minutes per day was associated with a 2-fold increased risk of preterm delivery, but an association with lifting at work was not found. Further studies are needed to determine the component(s) of lifting that may increase risk of preterm delivery, such as what is being lifted (e.g., children versus boxes), where it is being lifted from (e.g., the floor versus a shelf at waist height), and the use of proper lifting technique. It is of interest that although we controlled for covariates that have previously been ignored, such as off the job physical activity and non-work related stress, our risk estimates of lifting, standing in one position, repetitive tasks and inadequate breaks are similar to those from earlier findings.

In our analysis of occupational exposures as a risk factor for spontaneous preterm delivery (Chapter III), we compared report of labor induction on the birth certificate and report of induction on the medical chart review to determine if birth certificate induction could be reported for subjects without a medical chart review. Using the medical chart review as the gold standard, the sensitivity of the birth certificate was 87.2% and the specificity was 26.9%. Given the low specificity, we limited the analysis to only those subjects with a medical chart review for fear that the induced preterm deliveries would be contaminated with a high proportion of spontaneous preterm deliveries.

The analysis in Chapter IV (prenatal injury) provides a first look at the prevalence and risk factors associated with injury during pregnancy among controls in a case-control study of preterm delivery. Pre-eclampsia is estimated to occur in approximately 5% of all pregnancies and screening for this disease occurs at each prenatal care visit through measurement of a woman's blood pressure and checking her urine for protein. Over 5% of control women reported an injury during pregnancy, yet little or no inquiry about injury is done at prenatal visits. Women at high-risk for pregnancy-related complications that are regularly screened for during prenatal care are also at increased risk of injury therefore should be targeted for education about this important public health issue.

Selection bias is present in IHIPS. As reported in Chapter II through IV less than 60% of women selected from the birth certificate were able to be contacted by phone. Women who were contacted by phone and completed the telephone interview were more likely to be white, 25 years of age or older at delivery, have a least one year of college education, and less likely to smoke during pregnancy than women who were not interviewed (Table 4.1). This bias of a largely homogenous sample may explain our inability to find a relationship between maternal race, education, and income and risk of preterm delivery (Table 2.1). Previous research has established that younger age, lower education and household income as risk factors for preterm delivery but we were not able to recruit these women into our sample and therefore no risk relationship was found. In a sub-analysis of maternal education and smoking during pregnancy, we examined the risk of preterm delivery among whites and non-whites that were interviewed (data not shown). Non-white interviewed women were twice as likely to deliver preterm if they had less than a college education or if they smoked at any time during pregnancy: the results among whites were similar to those seen in Table 2.1. This supports the hypothesis that because we recruited a homogenous population the risk of preterm delivery among those that we under-recruited (non-whites) are not seen in our overall analysis of risk for preterm delivery. The selection bias in IHIPS may have affected the results in Chapter III (occupation and PTD) by under reporting occupational physical and psychological stress of all subjects selected for IHIPS as we recruited women with non-physically demanding jobs (represented by large amount of subjects not lifting or standing at work). The women we failed to interview were younger and less educated: precisely the type of women that may be in more physically or psychologically demanding jobs. Therefore, the results we found are likely an under-estimate of risk of preterm delivery association with occupational characteristics. In our analysis of prenatal injury and risk of preterm delivery (Chapter IV), we found that the control subjects at increased risk of injury were younger, and less educated. Those at greatest risk of injury in our analysis are those subjects that we under-recruited therefore the estimate of injury in our sample is likely an under-estimate of injury during pregnancy among all women selected for IHIPS.

Future Studies

To determine the extent of error in ultrasound gestational age dating among fetus' with fetal growth restriction, prospective studies of serial ultrasounds are needed to establish when ultrasounds may first detect growth restriction, and if an individual growth curve, instead of comparison to national curves, is more predictive of infant morbidity and mortality. Also, with the increasing use of ultrasound gestational age dating in infants, a national growth curve for identifying small for gestational age based on this dating need to be created. In order for this to be developed, ultrasound estimates of gestational age at delivery must be added to the standard birth certificate, or at the very least, the source of the clinical or obstetric estimates of gestational age at delivery should be recorded. If a growth curve based on LMP dating and a curve based on ultrasound dating is available, researchers could apply the appropriate curve to their population and therefore compare “apples to apples” instead of comparing two, often discordant, estimates of gestational age.

Due to the high cost and prohibitive nature of direct observations of work, standardized questionnaires need to be developed to measure more accurately the characteristics and frequency of occupational exposures such as awkward postures, lifting, and standing. A standardized questionnaire would increase researcher’s ability to compare results across populations instead of the current mixed results seen due to differences in measurement. The Karasek Job Content Questionnaire (65) is widely used to estimate work psychological stress during pregnancy and although highly validated in non-pregnant populations little is known about its validity among a pregnant population of working women. Validation studies of this questionnaire in pregnant populations are needed to support its continued use in estimating psychological work risks for preterm delivery.

In addition, exploration into the effect of work modification on risk of preterm delivery should be studied. Since the 1970’s the French have allowed women with identified risk factors for preterm delivery to reduce their physical effort both in the home and at work. All French women are provided early access to free prenatal care involving education on lifestyle risk factors for adverse pregnancy outcomes, recognition of early warning signs for preterm delivery, and use of maternity work leave and reduction of physical activity (128). Unlike in the United States, French women on maternity leave, regardless if it is before or after delivery, receive governmental financial compensation and do not have to use employment-related benefits (sick leave or vacation) to support their families. These modifications have led to almost a halving of the French preterm delivery rate from 8.2% to 4.9% in just 16 years. A case-control study of Canadian women (53) found that demanding postures, and high job strain were associated with preterm delivery but these associations were weaker when the exposure was eliminate following preventive measures for preterm delivery.

To estimate the extent that injuries occur during pregnancy and the effect they may have on pregnancy outcome, population based studies must be pursued. Current studies measure more severe injuries requiring an emergency room visit or hospitalization representing only a small proportion of the injuries actually sustained during pregnancy. In the only population-based study to date, Dunning (80) found that one in four women fell during pregnancy but the extent of other types of injuries is largely unknown. The prevalence of injuries during pregnancy is likely greater than the 25% Dunning (80) reported; therefore the costs and public health impact of these injuries must be estimated.

Currently, little is known about the amount of counseling a woman receives on injuries, particularly the risk of falling, during routine prenatal care. It has been noted that women receive little education on proper restraint in a motor vehicle during pregnancy. To increase counseling on injury during pregnancy, education of those administering care to pregnant women must take place. In order to develop an educational program, a measurement of current injury knowledge among those in practice, as well as medical students, will determine targeted areas of instruction.

It is of interest that although we examined risk factors for injury in what we believed to be a low-risk pregnancy population (subjects delivering an infant at $\geq$ 37 weeks), the characteristics associated with injury still described a traditionally high risk pregnancy population (younger age, less education, and lower household income). This supports the importance of counseling all women on the risk of injury during pregnancy not just those considered to be at high risk for adverse pregnancy outcomes.

Finally, the living conditions of women at high risk for injury during pregnancy have not been examined. For example, are these women more likely to fall because they live on the second floor of an apartment building with dimly light narrow stairs? Many of the environmental circumstances related to falls could be reduced by evaluating the effectiveness of evidence based fall prevention programs for the elderly among pregnant populations. For other injuries, population based studies of the environment in which injuries occur are needed to determine prevention strategies.

In conclusion, accurate classification of preterm delivery and small for gestational age is vital to examining risk factors for these pregnancy outcomes. This analysis provides a statistical method to correct for the inherent bias of ultrasound measuring restricted fetal growth as a ‘younger’ infant. In addition, the analysis in Chapter IV identified characteristics of injuries, such as number of body parts injured, injury mechanism, and location of the injury, which may increase the risk factor for preterm delivery. Preterm delivery risks associated with occupational characteristics, although highly studied, have not involved standardized measurements of these exposures making comparison across studies difficult. Our analysis (Chapter III) found increased risk of preterm delivery associated with repetitive tasks and inadequate breaks but only suggestive results related to standing and lifting at work. Further research, as summarized above, is need to supplement our understanding of how these factors may impact the risk of preterm delivery.

Table 4.1 Birth certificate characteristics of all subjects selected to participate in IHIPS compared to those that completed an interview for IHIPS, 2002-2005.

	Controls		Preterm Delivery		Small for gestational age	
	Selected	Interviewed	Selected	Interviewed	Selected	Interviewed
Age at delivery						
18-19	111(5.8)	36(4.0)	159(7.4)	37(5.7)	247(9.5)	59(6.4)
20-24	459(23.9)	164(18.0)	572(26.7)	129(19.7)	757(29.1)	195(21.0)
25-29	637 (33.1)	308(33.8)	611(28.5)	179(27.3)	826(31.7)	358(38.6)
30-34	475(24.7)	267(29.3)	526(24.6)	206(31.5)	514(19.8)	223(24.0)
35+	241(12.5)	137(15.0)	275(12.8)	104(15.9)	258(9.9)	93(10.0)
Race						
White	1692(87.9)	836(91.7)	1768(82.5)	608(92.8)	2177(83.7)	822(88.6)
Black	155(8.1)	51(5.6)	251(11.7)	31(4.7)	213(8.2)	47(5.1)
Asian	47(2.4)	14(1.5)	86(4.0)	12(1.8)	153(5.9)	38(4.1)
Other /Mixed	30(1.6)	11(1.2)	38(1.8)	4(0.6)	59(2.3)	21(2.3)
Education						
<= High School	674(35.1)	190(20.8)	973(45.5)	163(24.9)	1227(47.2)	262(28.3)
College (1-4 yrs)	993(51.6)	554(60.8)	957(44.7)	383(58.5)	1092(42.0)	506(54.6)
College (5+ yrs)	256(13.3)	168(18.4)	211(9.9)	109(16.6)	279(10.7)	159(17.2)
Prenatal care						
1^{st} tri	1738(90.6)	865(94.9)	1854(87.7)	615(94.2)	2269(87.7)	869(93.6)
2^{nd} tri	152(7.9)	40(4.4)	219(10.4)	35(5.4)	271(10.5)	53(5.7)
3^{rd} tri	28(1.5)	7(0.8)	42(2.0)	3(0.5)	47(1.8)	6(0.7)

Table 4.1 continued…

County of Residence						
Black Hawk	314(16.3)	170(18.6)	354(16.5)	130(19.9)	417(16.0)	152(16.4)
Johnson	243(12.6)	124(13.6)	230(10.7)	95(14.5)	328(12.6)	152(16.4)
Polk	1007(52.4)	460(50.4)	1150(54.7)	293(44.7)	1321(50.8)	451(48.6)
Scott	359(18.7)	158(17.3)	408(19.0)	136(20.8)	536(20.6)	173(18.6)
Tobacco Use						
Yes	237(12.3)	71(7.8)	373(17.4)	73(11.2)	629(24.2)	162(17.5)
No	1684(87.6)	839(92.0)	1766(82.4)	582(88.9)	1971(75.8)	765(82.4)

REFERENCES

1. Callaghan WM, MacDorman MF, Rasmussen SA, et al. The contribution of preterm birth to infant mortality rates in the United States. Pediatrics. 2006;118(4):1566-73.

2. Pennell CE, Jacobsson B, Williams SM, et al. Genetic epidemiologic studies of preterm birth: guidelines for research. Am J Obstet Gynecol. 2007;196(2):107-18. (doi: 10.1016/j.ajog.2006.03.109).

3. Trends in Preterm-Related Infant Mortality by Race and Ethnicity: United States, 1999-2004, 2010.

4. Hamilton BE, Martin JA, Ventura SJ. Births: Preliminary Data for 2008. National Center for Health Statistics: Division of Vital Statistics, editor. , 2009.

5. Ananth CV, Vintzileos AM. Epidemiology of preterm birth and its clinical subtypes. J Matern Fetal Neonatal Med. 2006;19(12):773-82.

6. Martin JA, Hamilton BE, Sutton PD, et al. Births: Final Data for 2007. National Center for Health Statistics: Division of Vital Statistics, editor. , 2008.

7. Mattison DR, Damus K, Fiore E, et al. Preterm delivery: a public health perspective. Paediatr Perinat Epidemiol. 2001;15 Suppl 2:7-16.

8. Stanton AL, Lobel M, Sears S, et al. Psychosocial aspects of selected issues in women's reproductive health: current status and future directions. J Consult Clin Psychol. 2002;70(3):751-70.

9. Davidoff MJ, Dias T, Damus K, et al. Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. Semin Perinatol. 2006;30(1):8-15.

10. Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics. 2007;120(1):e1-9.

11. Hickey CA, Cliver SP, Mulvihill FX, et al. Employment-related stress and preterm delivery: a contextual examination. Public Health Rep. 1995;110(4):410-8.

12. Pompeii LA, Savitz DA, Evenson KR, et al. Physical exertion at work and the risk of preterm delivery and small-for-gestational-age birth. Obstet Gynecol. 2005;106(6):1279-88.

13. Savitz DA, Murnane P. Behavioral influences on preterm birth: a review. Epidemiology. 2010;21(3):291-9. (doi: 10.1097/EDE.0b013e3181d3ca63).

14. Boyd HA, Poulsen G, Wohlfahrt J, et al. Maternal contributions to preterm delivery. Am J Epidemiol. 2009;170(11):1358-64. (doi: 10.1093/aje/kwp324).

15. Wilcox AJ, Skjaerven R, Lie RT. Familial patterns of preterm delivery: maternal and fetal contributions. Am J Epidemiol. 2008;167(4):474-9. (doi: 10.1093/aje/kwm319).

16. Berkowitz GS, Blackmore-Prince C, Lapinski RH, et al. Risk factors for preterm birth subtypes. Epidemiology. 1998;9(3):279-85.

17. Goffinet F. Primary predictors of preterm labour. Bjog. 2005;112 Suppl 1:38-47.

18. Goldenberg RL, Iams JD, Mercer BM, et al. The preterm prediction study: the value of new vs standard risk factors in predicting early and all spontaneous preterm births. NICHD MFMU Network. Am J Public Health. 1998;88(2):233-8.

19. Moutquin JM. Classification and heterogeneity of preterm birth. Bjog. 2003;110 Suppl 20:30-3.

20. Muglia LJ, Katz M. The enigma of spontaneous preterm birth. N Engl J Med. 2010;362(6):529-35. (doi: 10.1056/NEJMra0904308).

21. Wier ML, Pearl M, Kharrazi M. Gestational age estimation on United States livebirth certificates: a historical overview. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:4-12.

22. Savitz DA, W. TJ,Jr, Dole N, et al. Comparison of pregnancy dating by last menstrual period, ultrasound scanning, and their combination. Am J Obstet Gynecol. 2002;187(6):1660-6.

23. Waller DK, Spears WD, Gu Y, et al. Assessing number-specific error in the recall of onset of last menstrual period. Paediatr Perinat Epidemiol. 2000;14(3):263-7.

24. Pearl M, Wier ML, Kharrazi M. Assessing the quality of last menstrual period date on California birth records. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:50-61.

25. Haglund B. Birthweight distributions by gestational age: comparison of LMP-based and ultrasound-based estimates of gestational age using data from the Swedish Birth Registry. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:72-8.

26. Wingate MS, Alexander GR, Buekens P, et al. Comparison of gestational age classifications: date of last menstrual period vs. clinical estimate. Ann Epidemiol. 2007;17(6):425-30.

27. Mustafa G, David RJ. Comparative accuracy of clinical estimate versus menstrual gestational age in computerized birth certificates. Public Health Rep. 2001;116(1):15-21.

28. Qin C, Hsia J, Berg CJ. Variation between last-menstrual-period and clinical estimates of gestational age in vital records. Am J Epidemiol. 2008;167(6):646-52.

29. Alexander GR, Tompkins ME, Petersen DJ, et al. Discordance between LMP-based and clinically estimated gestational age: implications for research, programs, and policy. Public Health Rep. 1995;110(4):395-402.

30. Blaas HG, Eik-Nes SH, Bremnes JB. The growth of the human embryo. A longitudinal biometric assessment from 7 to 12 weeks of gestation. Ultrasound Obstet Gynecol. 1998;12(5):346-54. (doi: 10.1046/j.1469-0705.1998.12050346.x).

31. Hoffman CS, Messer LC, Mendola P, et al. Comparison of gestational age at birth based on last menstrual period and ultrasound during the first trimester. Paediatr Perinat Epidemiol. 2008;22(6):587-96.

32. Olesen AW, Thomsen SG. Prediction of delivery date by sonography in the first and second trimesters. Ultrasound Obstet Gynecol. 2006;28(3):292-7. (doi: 10.1002/uog.2793).

33. Morin I, Morin L, Zhang X, et al. Determinants and consequences of discrepancies in menstrual and ultrasonographic gestational age estimates. Bjog. 2005;112(2):145-52.

34. Kallen K. Mid-trimester ultrasound prediction of gestational age: advantages and systematic errors. Ultrasound Obstet Gynecol. 2002;20(6):558-63.

35. Blondel B, Morin I, Platt RW, et al. Algorithms for combining menstrual and ultrasound estimates of gestational age: consequences for rates of preterm and postterm birth. Bjog. 2002;109(6):718-20.

36. Thorsell M, Kaijser M, Almstrom H, et al. Expected day of delivery from ultrasound dating versus last menstrual period--obstetric outcome when dates mismatch. Bjog. 2008;115(5):585-9.

37. Waldenstrom U, Axelsson O, Nilsson S. Ultrasonic dating of pregnancies: effect on incidence of SGA diagnoses. A randomised controlled trial. Early Hum Dev. 1992;30(1):75-9.

38. Goldenberg RL, Davis RO, Cutter GR, et al. Prematurity, postdates, and growth retardation: the influence of use of ultrasonography on reported gestational age. American Journal of Obstetrics & Gynecology. 1989;160(2):462-70.

39. Das UG, Sysyn GD. Abnormal fetal growth: intrauterine growth retardation, small for gestational age, large for gestational age. Pediatr Clin North Am. 2004;51(3):639,54, viii. (doi: 10.1016/j.pcl.2004.01.004).

40. Alexander GR, Himes JH, Kaufman RB, et al. A United States national reference for fetal growth. Obstet Gynecol. 1996;87(2):163-8.

41. Boulet SL, Alexander GR, Salihu HM, et al. Fetal growth risk curves: defining levels of fetal growth restriction by neonatal death risk. Am J Obstet Gynecol. 2006;195(6):1571-7. (doi: 10.1016/j.ajog.2006.03.069).

42. Reuss ML, Hatch MC, Susser M. Early ultrasound dating of pregnancy: selection and measurement biases. J Clin Epidemiol. 1995;48(5):667-74.

43. Gardosi J, Geirsson RT. Routine ultrasound is the method of choice for dating pregnancy. Br J Obstet Gynaecol. 1998;105(9):933-6.

44. Gardosi J, Francis A. Early pregnancy predictors of preterm birth: the role of a prolonged menstruation-conception interval. BJOG. 2000;107(2):228-37.

45. Hogue CJ, Hoffman S, Hatch MC. Stress and preterm delivery: a conceptual framework. Paediatr Perinat Epidemiol. 2001;15 Suppl 2:30-40.

46. Widmaier E, Raff H, Strang KT. Vander's Human Physiology: The Mechanisms of Body Function. 10th ed. New York, NY: McGraw-Hill, 2006.

47. Obel C, Hedegaard M, Henriksen TB, et al. Stress and salivary cortisol during pregnancy. Psychoneuroendocrinology. 2005;30(7):647-56.

48. Wadhwa PD, Dunkel-Schetter C, Chicz-DeMet A, et al. Prenatal psychosocial factors and the neuroendocrine axis in human pregnancy. Psychosom Med. 1996;58(5):432-46.

49. de Weerth C, Buitelaar JK. Physiological stress reactivity in human pregnancy--a review. Neurosci Biobehav Rev. 2005;29(2):295-312.

50. Pike IL. Maternal stress and fetal responses: evolutionary perspectives on preterm delivery. Am J Hum Biol. 2005;17(1):55-65.

51. Wadhwa PD, Culhane JF, Rauh V, et al. Stress, infection and preterm birth: a biobehavioural perspective. Paediatr Perinat Epidemiol. 2001;15 Suppl 2:17-29.

52. Launer LJ, Villar J, Kestler E, et al. The effect of maternal work on fetal growth and duration of pregnancy: a prospective study. Br J Obstet Gynaecol. 1990;97(1):62-70.

53. Croteau A, Marcoux S, Brisson C. Work Activity in Pregnancy, Preventive Measures, and the Risk of Preterm Delivery. Am J Epidemiol. 2007.

54. Klebanoff MA, Shiono PH, Carey JC. The effect of physical activity during pregnancy on preterm delivery and birth weight. Am J Obstet Gynecol. 1990;163(5 Pt 1):1450-6.

55. Luke B, Mamelle N, Keith L, et al. The association between occupational factors and preterm birth: a United States nurses' study. Research Committee of the Association of Women's Health, Obstetric, and Neonatal Nurses. Am J Obstet Gynecol. 1995;173(3 Pt 1):849-62.

56. Saurel-Cubizolles MJ, Zeitlin J, Lelong N, et al. Employment, working conditions, and preterm birth: results from the Europop case-control survey. J Epidemiol Community Health. 2004;58(5):395-401.

57. Teitelman AM, Welch LS, Hellenbrand KG, et al. Effect of maternal work activity on preterm birth and low birth weight. Am J Epidemiol. 1990;131(1):104-13.

58. Ahlborg GA,Jr. Physical work load and pregnancy outcome. J Occup Environ Med. 1995;37(8):941-4.

59. Ceron-Mireles P, Harlow SD, Sanchez-Carrillo CI. The risk of prematurity and small-for-gestational-age birth in Mexico City: the effects of working conditions and antenatal leave. Am J Public Health. 1996;86(6):825-31.

60. Magann EF, Evans SF, Newnham JP. Employment, exertion, and pregnancy outcome: assessment by kilocalories expended each day. Am J Obstet Gynecol. 1996;175(1):182-7.

61. Misra DP, Strobino DM, Stashinko EE, et al. Effects of physical activity on preterm birth. Am J Epidemiol. 1998;147(7):628-35.

62. McDonald AD. Prematurity and work in pregnancy. London: British Medical Association, 1988.

63. Saurel-Cubizolles MJ, Subtil D, Kaminski M. Is preterm delivery still related to physical working conditions in pregnancy? J Epidemiol Community Health. 1991;45(1):29-34.

64. Berkowitz GS, Kelsey JL, Holford TR, et al. Physical activity and the risk of spontaneous preterm delivery. J Reprod Med. 1983;28(9):581-8.

65. Karasek R, Brisson C, Kawakami N, et al. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychol. 1998;3(4):322-55.

66. Mamelle N, Laumon B, Lazar P. Prematurity and occupational activity during pregnancy. Am J Epidemiol. 1984;119(3):309-22.

67. Occupational Information Network (O*Net). : US Department of Labor/Employment and Training Administration & North Carolina Employment Security Commission, 2009.

68. Meyer JD, Warren N, Reisine S. Job control, substantive complexity, and risk for low birth weight and preterm delivery: An analysis from a state birth registry. Am J Ind Med. 2007;50(9):664-75.

69. Brett KM, Strogatz DS, Savitz DA. Employment, job strain, and preterm delivery among women in North Carolina. Am J Public Health. 1997;87(2):199-204.

70. Figa-Talamanca I. Occupational risk factors and reproductive health of women. Occup Med (Lond). 2006;56(8):521-31.

71. Escriba-Aguir V, Perez-Hoyos S, Saurel-Cubizolles MJ. Physical load and psychological demand at work during pregnancy and preterm birth. Int Arch Occup Environ Health. 2001;74(8):583-8.

72. Hobel CJ, Goldstein A, Barrett ES. Psychosocial stress and pregnancy outcome. Clin Obstet Gynecol. 2008;51(2):333-48. (doi: 10.1097/GRF.0b013e31816f2709).

73. Web-based Injury Statistics Query and Reporting System (WISQARS) , 2009.

74. El-Kady D, Gilbert WM, Anderson J, et al. Trauma during pregnancy: an analysis of maternal and fetal outcomes in a large population. Am J Obstet Gynecol. 2004;190(6):1661-8.

75. Schiff MA, Holt VL, Daling JR. Maternal and infant outcomes after injury during pregnancy in Washington State from 1989 to 1997. J Trauma. 2002;53(5):939-45.

76. Sperry JL, Casey BM, McIntire DD, et al. Long-term fetal outcomes in pregnant trauma patients. Am J Surg. 2006;192(6):715-21.

77. El Kady D. Perinatal outcomes of traumatic injuries during pregnancy. Clin Obstet Gynecol. 2007;50(3):582-91.

78. Brown HL. Trauma in pregnancy. Obstet Gynecol. 2009;114(1):147-60. (doi: 10.1097/AOG.0b013e3181ab6014).

79. Klinich KD, Flannagan CA, Rupp JD, et al. Fetal outcome in motor-vehicle crashes: effects of crash characteristics and maternal restraint. Am J Obstet Gynecol. 2008;198(4):450.e1,450.e9. (doi: 10.1016/j.ajog.2008.02.009).

80. Dunning K, Lemasters G, Bhattacharya A. A major public health issue: the high incidence of falls during pregnancy. Matern Child Health J. 2010;14(5):720-5. (doi: 10.1007/s10995-009-0511-0).

81. Slattery ML, Edwards SL, Caan BJ, et al. Response rates among control subjects in case-control studies. Ann Epidemiol. 1995;5(3):245-9.

82. Zhang J, A. BW,Jr. Birth-weight-for-gestational-age patterns by race, sex, and parity in the United States population. Obstet Gynecol. 1995;86(2):200-8.

83. Martin JA. United States vital statistics and the measurement of gestational age. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:13-21.

84. Lynch CD, Zhang J. The research implications of the selection of a gestational age estimation method. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:86-96. (doi: 10.1111/j.1365-3016.2007.00865.x).

85. Campbell S, Warsof SL, Little D, et al. Routine ultrasound screening for the prediction of gestational age. Obstet Gynecol. 1985;65(5):613-20.

86. Mongelli M, Wilcox M, Gardosi J. Estimating the date of confinement: ultrasonographic biometry versus certain menstrual dates. Am J Obstet Gynecol. 1996;174(1 Pt 1):278-81.

87. Bottomley C, Bourne T. Dating and growth in the first trimester. Best Pract Res Clin Obstet Gynaecol. 2009;23(4):439-52. (doi: 10.1016/j.bpobgyn.2009.01.011).

88. Larsen T, Nguyen TH, Greisen G, et al. Does a discrepancy between gestational age determined by biparietal diameter and last menstrual period sometimes signify early intrauterine growth retardation? BJOG. 2000;107(2):238-44.

89. Alexander GR, Kogan MD, Himes JH. 1994-1996 U.S. singleton birth weight percentiles for gestational age by race, Hispanic origin, and gender. Matern Child Health J. 1999;3(4):225-31.

90. American Congress of Obstetrics and Gynecology. Ultrasonography in Pregnancy. , 2009.

91. Yang H, Kramer MS, Platt RW, et al. How does early ultrasound scan estimation of gestational age lead to higher rates of preterm birth? Am J Obstet Gynecol. 2002;186(3):433-7.

92. Mook-Kanamori DO, Steegers EA, Eilers PH, et al. Risk factors and outcomes associated with first-trimester fetal growth restriction. JAMA. 2010;303(6):527-34. (doi: 10.1001/jama.2010.78).

93. Dietz PM, England LJ, Callaghan WM, et al. A comparison of LMP-based and ultrasound-based estimates of gestational age using linked California livebirth and prenatal screening records. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:62-71.

94. Mercer BM, Merlino AA, Milluzzi CJ, et al. Small fetal size before 20 weeks' gestation: associations with maternal tobacco use, early preterm birth, and low birthweight. Am J Obstet Gynecol. 2008;198(6):673.e1,7; discussion 673.e7-8. (doi: 10.1016/j.ajog.2008.01.036).

95. Kramer MS, Lydon J, Seguin L, et al. Stress pathways to spontaneous preterm birth: the role of stressors, psychological distress, and stress hormones. Am J Epidemiol. 2009;169(11):1319-26.

96. Hamilton BE, Martin JA, Ventura SJ. Births: Preliminary Data for 2006. Department of Health and Human Services, editor. , 2007.

97. Goldenberg RL, Culhane JF, Iams JD, et al. Epidemiology and causes of preterm birth. Lancet. 2008;371(9606):75-84. (doi: 10.1016/S0140-6736(08)60074-4).

98. Mozurkewich EL, Luke B, Avni M, et al. Working conditions and adverse pregnancy outcome: a meta-analysis. Obstet Gynecol. 2000;95(4):623-35.

99. Bonzini M, Coggon D, Palmer KT. Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. Occup Environ Med. 2007;64(4):228-43.

100. Newman RB. Occupational fatigue and preterm premature rupture of membranes. National Institute of Child Health and Human Development Maternal-Fetal Medicine, Units Network. St. Louis, MO: Mosby, 2001.

101. Fortier I, Marcoux S, Brisson J. Maternal work during pregnancy and the risks of delivering a small-for-gestational-age or preterm infant. Scand J Work Environ Health. 1995;21(6):412-8.

102. Tuntiseranee P, Geater A, Chongsuvivatwong V, et al. The effect of heavy maternal workload on fetal growth retardation and preterm delivery. A study among southern Thai women. J Occup Environ Med. 1998;40(11):1013-21.

103. Wadhwa PD, Garite TJ, Porto M, et al. Placental corticotropin-releasing hormone (CRH), spontaneous preterm birth, and fetal growth restriction: a prospective investigation. Am J Obstet Gynecol. 2004;191(4):1063-9. (doi: 10.1016/j.ajog.2004.06.070).

104. Spielberger CD, Gorsuch RL, Lushene R, et al. State – Trait Anxiety Inventory. 855 Oak Grove Ave., Suite 215, Menlo Park, CA 94025: Mind Garden Inc., 1970.

105. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24(4):385-96.

106. Lobel M. Conceptualizations, measurement, and effects of prenatal maternal stress on birth outcomes. J Behav Med. 1994;17(3):225-72.

107. Johnson TD. Maternity Leave and Employment: Patterns of First-time Mothers: 1961-2003. 2008.

108. Labor force participation rates among mothers , 2010.

109. Bodin L, Axelsson G, Ahlborg GA,Jr. The association of shift work and nitrous oxide exposure in pregnancy with birth weight and gestational age. Epidemiology. 1999;10(4):429-36.

110. Peoples-Sheps MD, Siegel E, Suchindran CM, et al. Characteristics of maternal employment during pregnancy: effects on low birthweight. Am J Public Health. 1991;81(8):1007-12.

111. Ahlborg GA,Jr. Validity of exposure data obtained by questionnaire. Two examples from occupational reproductive studies. Scand J Work Environ Health. 1990;16(4):284-8.

112. Juhl M, Andersen PK, Olsen J, et al. Physical exercise during pregnancy and the risk of preterm birth: a study within the Danish National Birth Cohort. Am J Epidemiol. 2008;167(7):859-66. (doi: 10.1093/aje/kwm364).

113. Lobel M, DeVincent CJ, Kaminer A, et al. The impact of prenatal maternal stress and optimistic disposition on birth outcomes in medically high-risk women. Health Psychol. 2000;19(6):544-53.

114. Both MI, Overvest MA, Wildhagen MF, et al. The association of daily physical activity and birth outcome: a population-based cohort study. Eur J Epidemiol. 2010;25(6):421-9. (doi: 10.1007/s10654-010-9458-0).

115. Lindbohm ML. Women's reproductive health: some recent developments in occupational epidemiology. New York, N.Y.: Alan R. Liss, 1999.

116. Hedegaard M, Henriksen TB, Secher NJ, et al. Do stressful life events affect duration of gestation and risk of preterm delivery? Epidemiology. 1996;7(4):339-45.

117. Petrone P, Talving P, Browder T, et al. Abdominal injuries in pregnancy: a 155-month study at two level 1 trauma centers. Injury. 2010. (doi: 10.1016/j.injury.2010.06.026).

118. Aufforth R, Edhayan E, Dempah D. Should pregnancy be a sole criterion for trauma code activation: a review of the trauma registry. Am J Surg. 2010;199(3):387,9; discussion 389-90. (doi: 10.1016/j.amjsurg.2009.09.008).

119. Weiss HB, Songer TJ, Fabio A. Fetal deaths related to maternal injury. JAMA. 2001;286(15):1863-8.

120. Kuo C, Jamieson DJ, McPheeters ML, et al. Injury hospitalizations of pregnant women in the United States, 2002. Am J Obstet Gynecol. 2007;196(2):161.e1,161.e6. (doi: 10.1016/j.ajog.2006.09.015).

121. Sirin H, Weiss HB, Sauber-Schatz EK, et al. Seat belt use, counseling and motor-vehicle injury during pregnancy: results from a multi-state population-based survey. Matern Child Health J. 2007;11(5):505-10. (doi: 10.1007/s10995-007-0190-7).

122. McFarlane J, Parker B, Soeken K, et al. Assessing for abuse during pregnancy. Severity and frequency of injuries and associated entry into prenatal care. JAMA. 1992;267(23):3176-8.

123. Smith PH, Earp JA, DeVellis R. Measuring battering: development of the Women's Experience with Battering (WEB) Scale. Womens Health. 1995;1(4):273-88.

124. Schiff MA, Daling JR. Pregnancy-associated injury hospitalizations: maternal and fetal outcomes. Paediatric and Perinatal Epidemiology. 2001;15(4):A29.

125. Weiss HB, Sauber-Schatz EK, Cook LJ. The epidemiology of pregnancy-associated emergency department injury visits and their impact on birth outcomes. Accid Anal Prev. 2008;40(3):1088-95. (doi: 10.1016/j.aap.2007.11.011).

126. McCrory JL, Chambers AJ, Daftary A, et al. Dynamic postural stability in pregnant fallers and non-fallers. BJOG. 2010;117(8):954-62. (doi: 10.1111/j.1471-0528.2010.02589.x).

127. Butler EE, Colon I, Druzin ML, et al. Postural equilibrium during pregnancy: decreased stability with an increased reliance on visual cues. Am J Obstet Gynecol. 2006;195(4):1104-8. (doi: 10.1016/j.ajog.2006.06.015).

128. Papiernik E, Goffinet F. Prevention of preterm births, the French experience. Clin Obstet Gynecol. 2004;47(4):755,67; discussion 881-2.