2015

Trends in medically-indicated versus spontaneous preterm birth, 2004-2013

BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

TRENDS IN MEDICALLY-INDICATED VERSUS SPONTANEOUS

PRETERM BIRTH, 2004-2013

by

MELISSA ROSE LEYNES ADA

B.A., Stanford University, 2013

Submitted in partial fulfillment of the

requirements for the degree of

Master of Science

2015

Approved by

First Reader
           _____

           Karen Symes, Ph.D.
           Assistant Dean of Student Affairs
           Associate Professor of Biochemistry

Second Reader
           _____

           Heather H. Burris, M.D., M.P.H.
           Attending Neonatologist
           Assistant Professor of Pediatrics
           Harvard University, School of Public Health

DEDICATION

I would like to dedicate this work to my parents for their unconditional support and love.

ACKNOWLEDGMENTS

TRENDS IN MEDICALLY-INDICATED VERSUS SPONTANEOUS

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ABSTRACT

Background: Despite decades of research aimed at prevention, preterm birth remains an enormous leading cause of infant mortality in the United States and worldwide. Of concern, racial disparities in preterm birth remain an intractable public health issue. In an effort to reduce preterm birth, organizations such as the American Congress of Obstetricians and Gynecologists (ACOG) released policy statements in 2009 aimed at reducing early elective deliveries. Subsequently, the incidence of preterm birth in the United States has decreased, but whether this decrease is due to a reduction in iatrogenic or "medically-indicated" preterm birth is unknown. Further, the effect of the reduction in early elective deliveries on racial disparities is unknown. Our hypotheses were that 1) after 2009, preterm births would be less likely to be medically-indicated than due to spontaneous causes and 2) black-white differences in preterm births would be unchanged.

Objectives: 1) Determine the proportion of preterm deliveries at Beth Israel Deaconess Medical Center (BIDMC) from 2004-2013 that were medically-indicated versus spontaneous. 2) Due to persistent disparities, determine if shifts in type of preterm delivery varied by race/ethnicity.

Methods: We reviewed the first 87 deliveries in 2013 and randomly selected 15% of the records for each year from 2004-2013. Additionally, we reviewed 69 charts to oversample black women's deliveries. We manually abstracted data from BIDMC's online medical record and designated each delivery as either *medically-indicated* (preeclampsia, poor fetal growth, hypertension, or other fetal/maternal condition) or *spontaneous* (preterm labor, preterm premature rupture of membranes or cervical incompetence). Two reviewers independently reviewed 18 records for concordance of medically-indicated versus spontaneous preterm birth typing. If the first reviewer could not phenotype the delivery, then a neonatologist and obstetrician were consulted. We reviewed 971 out of the 5,566 preterm deliveries and included 930 that were confirmed preterm and had a clear medically-indicated or spontaneous phenotype. We dichotomized the time period into *early* (2004-2009) and *late* (2010-2013). Statistical methods included comparisons of early versus late using Chi-Square tests, logistic regression models to adjust for potential confounding variables, and stratified analyses (singletons and black versus white).

Results: There were 46,981 deliveries at our institution during the study period, 5,566 of which were preterm. Among the 930 preterm deliveries sampled from the 10-year period, 45.6% were medically-indicated with a non-significant, subtle difference between the early (48.3%) and late (41.9%) ($P=0.05$) time periods. The odds ratios of medically-indicated versus spontaneous preterm birth in late versus early were 0.77 ($P=0.05$) and 0.73 ($P=0.03$) for all participants, unadjusted and adjusted, respectively. While not

statistically significant, a higher proportion of preterm deliveries among black women were medically-indicated in the early (50.4%) versus late (40.6%) periods (*P*=0.19). There was a similar trend among white women between the early (50.0%) and late (46.9%) periods (*P*=0.48). The odds ratios of medically-indicated versus spontaneous preterm birth from late versus early were 0.67 (*P*=0.19) and 0.63 (*P*=0.14) for black participants, unadjusted and adjusted, respectively. For white participants, the odds ratios were 0.88 (*P*=0.48) for unadjusted and 0.80 for adjusted (*P*=0.20). Overall at BIDMC, the preterm delivery rate was significantly higher in the early period (12.3%) compared to the later period (11.2%) (*P*=0.0003). While we observed a reduction of preterm birth among all women, black women experienced a 20.8% decrease (from 16.2% in the early period to 12.8% in the late) in preterm birth, while white women experienced just a 4.9% decrease (from 12.4% to 11.7%), resulting in a narrowing of the racial disparity of preterm birth in our institution.

Conclusion: At a Massachusetts birth hospital we found a reduction in the incidence of preterm deliveries over a 10-year period that coincided with policy efforts to reduce early elective deliveries. There was a reduction in the proportion of preterm births that were medically-indicated from 48.3% to 41.9%. The reduction in medically-indicated preterm birth was most evident among black women at BIDMC with concurrent decrease in the overall preterm birth rate among black women resulting in a near elimination of the racial disparity in preterm birth at BIDMC. Future work includes statistical analysis to account for the oversampling of deliveries in 2013 as well as oversampling of black women's

deliveries using inverse probability weighting. We also plan to analyze which underlying

conditions (preeclampsia, intrauterine growth restriction, fetal distress, etc.) were

responsible for the reduction of the medically-indicated deliveries.

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LIST OF ABBREVIATIONS

17 P…………………………………………………17 alpha-hydroxyprogesterone caproate

ACOG…………………………...American Congress of Obstetricians and Gynecologists

BIDMC………………………………………………….Beth Israel Deaconess Medical Center

CCI……………………………………………………….Committee on Clinical Investigations

DALY……………………………………………………….Disability Adjusted Life Year

HMO…………………………………………………Health Maintenance Organization

HIPAA………………………….Health Insurance Portability and Accountability Act

HIV………………………………………………………Human Immunodeficiency Virus

IRB………………………………………………………..Institutional Review Board

IUGR………………………………………………...Intrauterine Growth Restriction

IVF……………………………………………………………In Vitro Fertilization

MR…………………………………………………………………Medical Record

OR………………………………………………………………………Odds Ratio

PTL………………………………………………………………….Preterm Labor

PPROM…………………………………………..Preterm Premature Rupture of Membranes

PHI………………………………………………………..Protected Health Information

REDCap…………………………………………………...Research Electronic Data Capture

SMFM………………………………………………….Society for Maternal-Fetal Medicine

INTRODUCTION

Preterm birth is the leading cause of infant mortality worldwide. Approximately 11% of infants in the United States are born preterm (Martin, Hamilton, Osterman, Curtin, & Mathews, 2013), and those who survive not only face significant morbidity, but also burdensome financial and emotional costs to their families and the greater society. Despite medical and technological advances in the past 30 years, preterm birth is still a significant public health problem today (Kistka *et al.*, 2007). The World Health Organization defines preterm birth as any live birth between 20 and 37 completed weeks of gestation since the first day of a woman's last menstrual period. Preterm birth is currently the second leading cause of mortality in children under 5 years of age and the single most important direct cause of mortality in a child's first month of life (Howson, Kinney, McDougall, & Lawn, 2013). Of the 130 million infants born annually worldwide, about 15 million are born preterm and 1 million of them die as a direct result of their prematurity. Researchers are able to trace only half of these deaths to identifiable causes (Howson *et al.*, 2013; Muglia & Katz, 2010).

In addition to mortality, preterm birth also generates significant long-term morbidities including medical fragility and developmental abnormalities. In the Global Burden of Disease, preterm birth constitutes about 3% of all Disability Adjusted Life Years (DALYs), more than for HIV and malaria (Howson *et al.*, 2013). In other words, preterm birth has a greater number of healthy years lost due to disability. Furthermore, according to Howson *et al.* (2013), "the annual societal economic cost in 2005 (medical,

educational and lost productivity combined) associated with preterm birth in the United

States was at least $26.2 billion. During that same year, the average first-year medical

costs, including both inpatient and outpatient care, were about 10 times greater for

preterm ($32,325) than for term infants ($3,325). The average length of stay was nine

times as long for a preterm newborn (13 days), compared with a baby born at term (1.5

days)." Furthermore, even once discharged from the neonatal intensive care unit, preterm

infants are at higher risk for readmission (Escobar *et al*., 2006) than their counterparts.

Perhaps most importantly, preterm infants who survive are at higher risk than their full

term counterparts for developmental delays, behavioral disorders (Huddy, Johnson, &

Hope, 2001; Saigal & Doyle, 2008) and for requiring special education (Simms, Cragg,

Gilmore, Marlow, & Johnson, 2013).

Epidemiology and pathophysiology of preterm birth

Preterm birth affects both developed and developing countries. In the United

States, preterm birth rates increased by more than one-third between 1981 and 2006, but

the rate has decreased ever since from 12.8% at the peak in 2006 to 11.4% in 2013 (an

11% decrease) (Child Trends Databank; Martin *et al*., 2013) (**Figure 1**). This downward

trend in preterm birth was also seen locally in Massachusetts, from 9.2% in 2004 to 8.8%

in 2013 (Massachusetts Department of Health, 2004-2013) (**Figure 2**). On a global level,

there is a disparity between high and low-income countries' survival rates for extremely

preterm babies. Blencowe *et al*. (2012) assessed preterm birth data in 2010 from 184
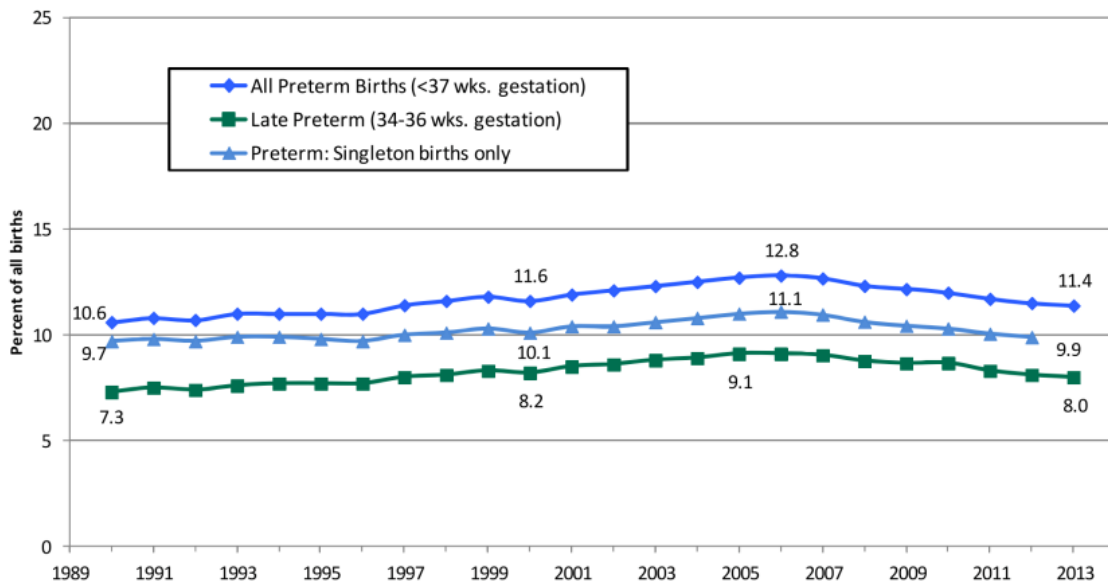
Figure 1. National preterm birth rates, 1990-2013. The overall preterm birth rate in the United States increased from 1990 with a peak at 12.8% in 2006. There has been a steady decline ever since for overall preterm birth, as well as for late preterm and singleton births only. (Figure downloaded from Child Trends Databank at http://www.childtrends.org/?indicators=preterm-births).
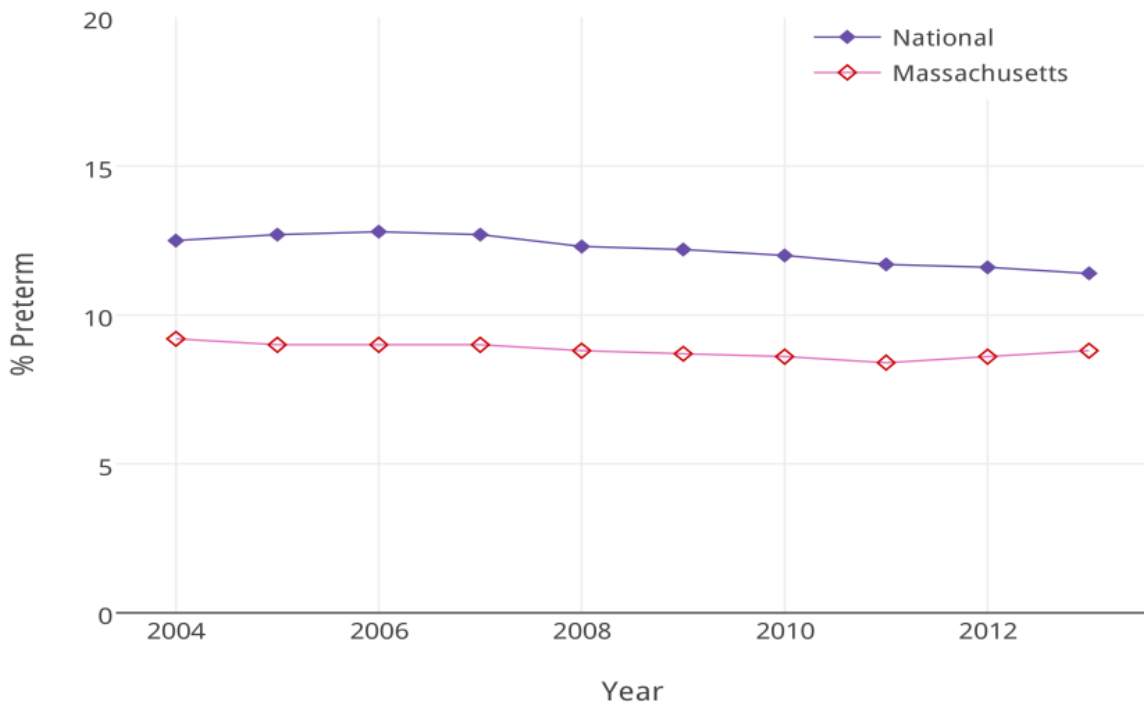
Figure 2. National and Massachusetts preterm birth, 2004-2013. There has been a downward trend in preterm birth from 2004 to 2013, from 12.5% to 11.4% at the national level and 9.2% to 8.8% at the state level. (Figure adapted from Massachusetts Department of Health, 2004-2013).

countries and observed that in high-income countries, more than 90% of babies born extremely preterm survived, while in low-income countries, only 10% of these babies survived.

Preterm birth can be separated into four categories based on gestational age: extremely preterm (less than 28 completed weeks), very preterm (28 to less than 32 weeks), moderately preterm (32 to less than 34 weeks), or late preterm (34 to less than 37 weeks) (Blencowe *et al.*, 2012). Extremely premature births compose about 5% of preterm births, very premature about 10%, moderately premature about 15%, and late preterm about 70% (Shapiro-Mendoza & Lackritz, 2012).

Preterm birth arises from several pathophysiologic states that for the purposes of epidemiologic studies can be dichotomized into spontaneous causes or other diseases that lead to a decision to deliver an infant early (medically-indicated preterm birth). Spontaneous preterm births include deliveries resulting from spontaneous preterm labor (PTL) and preterm premature rupture of membranes (PPROM), and they account for about 50-80% of all preterm births (Savitz *et al.*, 2005). "Preterm labor is usually defined as regular contractions accompanied by cervical change at less than 37 weeks' gestation…PPROM is defined as spontaneous rupture of the membranes at less than 37 weeks' gestation at least one hour before the onset of contractions" (Goldenberg, Culhane, Iams, & Romero, 2008). Medically-indicated births constitute about 20-50% (Savitz *et al.*, 2005) of all preterm births and result in interventions for maternal or fetal disorders such as preeclampsia, intrauterine growth restriction (IUGR) or fetal distress (Goldenberg *et al.*, 2008).

Racial disparities and risk factors for preterm birth

Preterm birth does not equally occur among all pregnant women. Black women have the highest rates, "in the range of 16-18%...compared with 5-9% for white women. Black women are also three to four times more likely to have a very early preterm birth than women from other racial or ethnic groups" (Goldenberg *et al*., 2008). Although preterm birth rates in 2013 decreased from 2012 for non-Hispanic whites and non-Hispanic blacks, there is still a disparity between the races. The preterm birth rate for non-Hispanic whites decreased from 11.7% in 2006 to 10.2% in 2013, and the rate for non-Hispanic blacks declined from 18.5% in 2006 to 16.3% in 2013 (**Figure 3**) (Martin *et al*., 2013). In terms of spontaneous preterm births, white women are more prone to preterm labor, while black women are more likely to have PPROM (Goldenberg *et al*., 2008). More specifically, black women have a double to triple increased risk for PPROM than white women (Menon, 2008). Even after controlling for maternal medical and socioeconomic factors, the disparity in preterm birth rates between black and white women remains largely unchanged and unexplained (Goldenberg *et al*., 2008; Kistka *et al*., 2007).

The literature on preterm birth has increased exponentially in the past two decades, but the main causes of preterm birth are still largely unknown. According to Menon (2008), preterm birth is a "complex phenotype and is not initiated by a single etiologic agent." However, there are maternal psychosocial and physiological risk factors that have been shown to be associated with preterm birth.
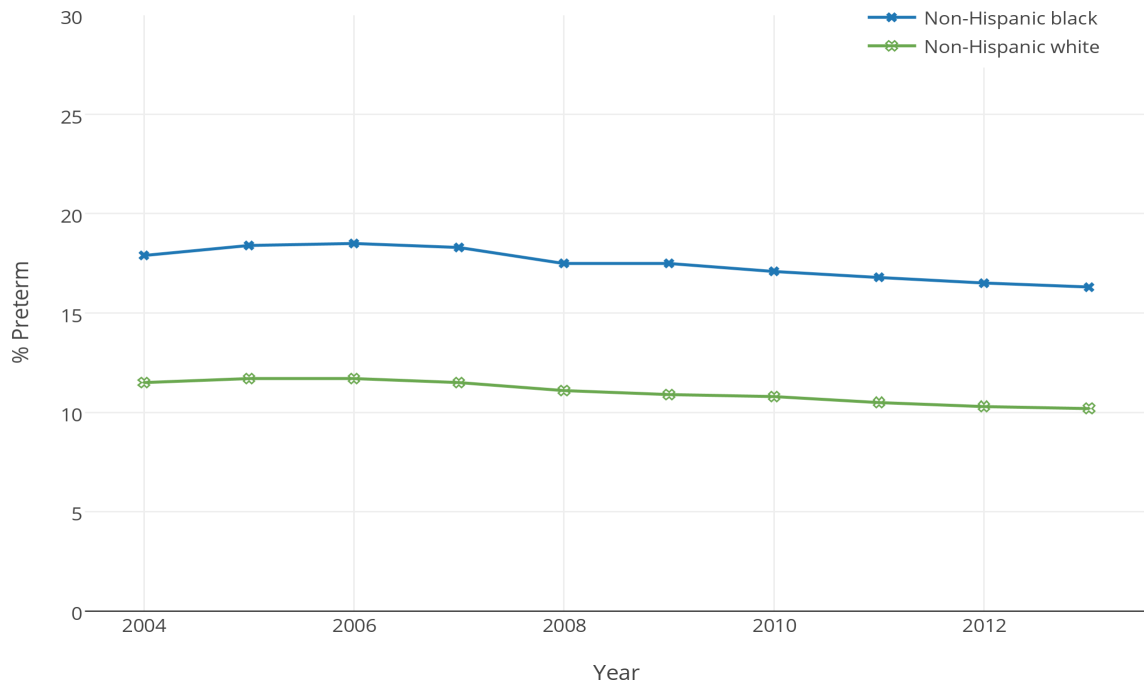
Figure 3. Preterm birth by race/ethnicity, 2004-2013. Although preterm birth rates have steadily decreased since 2006, there is still a wide and consistent disparity between Non-Hispanic black and Non-Hispanic white women. (Figure adapted from Martin *et al*., 2013).

Psychosocial stress before and during pregnancy contributes to the risk for preterm birth. For instance, living in neighborhoods with high poverty and segregation has been shown to be associated with preterm birth, even after adjusting for individual socioeconomic status and health behaviors (Kramer, Hogue, Dunlop, & Menon, 2011). Furthermore, experience with discrimination increases the risk for preterm birth, with odds ratios of 2.0 or greater for black women without a high school education reporting discrimination (Kramer *et al.*, 2011).

Among immigrant groups, the greater the amount of time spent living in the United States, the higher the preterm birth rate (Goldenberg *et al.*, 2008; Kramer *et al.*, 2011). Howard, Marshall, Kaufman, & Savitz (2006) found that in New York City, there was substantial heterogeneity in the black population in terms of preterm birth and low birth weight, with United States-born black women at higher risk than foreign-born mothers. Furthermore, the landmark study by David and Collins in 1997 demonstrated that the risk of low birth weight (which incompletely overlaps with preterm birth) among African-born black women was closer to the risk among white women, but was much higher among United States-born black women. Since African-born black women were more likely to be genetically distinct from white women than from United States-born black women, this study provided evidence that the risk of preterm birth was less likely to be due to genetic differences and more likely to be social and environmental (David & Collins, 1997).

Physiological risk factors for preterm birth include short interpregnancy intervals, multiple gestations, infections, short cervical length, and maternal history of preterm birth

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(Blencowe *et al*., 2012; Goldenberg *et al*., 2008). After adjusting for confounding

variables, an interpregnancy interval of less than 6 months yields more than a two-fold

increased risk of preterm birth. Multiple gestations constitute only about 2-3% of infants,

but account for 15-20% of all preterm births (Goldenberg *et al*., 2008). Infections such as

"urinary tract infections, malaria, bacterial vaginosis, HIV and syphilis are all associated

with increased risk of preterm birth" (Blencowe *et al*., 2013). Intrauterine infection and

inflammation can lead to cervical insufficiency, triggering early labor and delivery

(Blencowe *et al*., 2013). Cervical shortening can be preceded by infection, but this is not

always the case. Short cervical length (defined as less than 25 mm) and maternal history

of preterm birth are the strongest indicators for a woman's risk of delivering early

(Goldenberg *et al*., 2008; Kramer *et al*., 2011). According to Kramer *et al*. (2011),

"women whose first birth was preterm had 3.8 times the odds of a preterm birth as those

whose first birth was term" and "women who were themselves born preterm have higher

risk of delivering a preterm infant." Other physiological risk factors include young or

advanced maternal age, low maternal body-mass index, pre-existing non-communicable

disease, and hypertensive disease of pregnancy (Blencowe *et al*., 2012).

Interventions for spontaneous preterm birth

The obstetric community developed practices to prevent spontaneous preterm

birth in women affected by short cervical length and prior preterm birth. The effective

interventions in the current literature for women with short cervical length *and* prior

spontaneous preterm births include 1) 17 alpha-hydroxyprogesterone caproate (17P) and

2) cervical cerclage (Orzechowski, Boelig, Baxter, & Berghella, 2014; Schoen, Tabbah, Iams, Caughey, & Berghella, 2014). 17P is a natural progesterone conjugate given intramuscularly once a week or as a vaginal suppository, and cervical cerclage is the "surgical placement of a suture or tape around the cervix in an attempt to prevent dilatation and subsequent preterm birth (Newnham *et al*., 2014). It is estimated that between 10,000 and 23,000 preterm births would be prevented annually in the United States with these interventions, respectively (Schoen *et al*., 2014).

However, for women with *no prior preterm birth*, "vaginal progesterone has been shown to reduce the incidence of spontaneous preterm birth at less than 33-34 weeks of gestation by approximately 45% in women with short cervix observed on transvaginal ultrasound with singleton pregnancies before 24 weeks of gestation" (Orzechowski *et al*., 2014). The Society for Maternal-Fetal Medicine (SMFM) and the American Congress of Obstetricians and Gynecologists (ACOG) do not require universal transvaginal ultrasonogram cervical length screening, but they state it can be considered as a preterm birth prevention strategy (Orzechowski *et al*., 2014).

Other obstetric interventions to reduce the morbidity and mortality of spontaneous preterm birth include regionalized perinatal care to ensure well-coordinated tertiary care referrals, treatment with tocolytic agents to slow down labor, antenatal corticosteroids to speed up the baby's lung development, antibiotics to prevent infection, and optimum timing of indicated preterm birth (Iams, Romero, Culhane, & Goldenberg, 2008). However, results of studies of the effectiveness of tocolytics for spontaneous preterm birth are inconclusive and primarily used with the purpose of prolonging pregnancy by 48

hours prior in order to allow corticosteroids to take effect. Antibiotics are often reserved

PPROM and any concern for chorioamnionitis or group-B streptococcal prophylaxis

(Muglia & Katz, 2010; Smith, Devane, Begley, Clarke, & Higgins, 2009).

Public policies and campaigns to reduce medically-indicated preterm birth

The increase in preterm birth rates can be partially explained by the increase in

medically-indicated preterm birth, leading researchers to figure out why. Goldenberg and

colleagues (2008) found that medically-indicated rates increased almost 50% within a

decade (**Figure 4**). In a study on the trends of preterm birth rates among black and white

women from 1989 to 1997 in the United States, Demissie *et al*. (2001) observed that the

greatest factors associated with increased preterm birth in both races were preterm

induction of labor and preterm cesarean delivery. In another study looking at 2003 to

2007 data, more than half of all medically-indicated late preterm births were carried out

in absence of a strong medical indication (Gyamfi-Bannerman, Fuchs, Young, &

Hoffman, 2011).

Concerned about these practices, the March of Dimes Foundation, a non-profit

organization, launched a national campaign in 2007 called "Healthy Babies are Worth the

Wait" to educate the public on the importance of preventing non-indicated inductions and

cesareans (Shapiro-Mendoza & Lackritz, 2012). Similarly, ACOG released

recommendations in 1999 and again in 2009 stating that induced or cesarean deliveries

less than 39 weeks' gestation should only be performed with valid medical and obstetric

indications. More recently in 2013, ACOG and SMFM recommended the cessation of
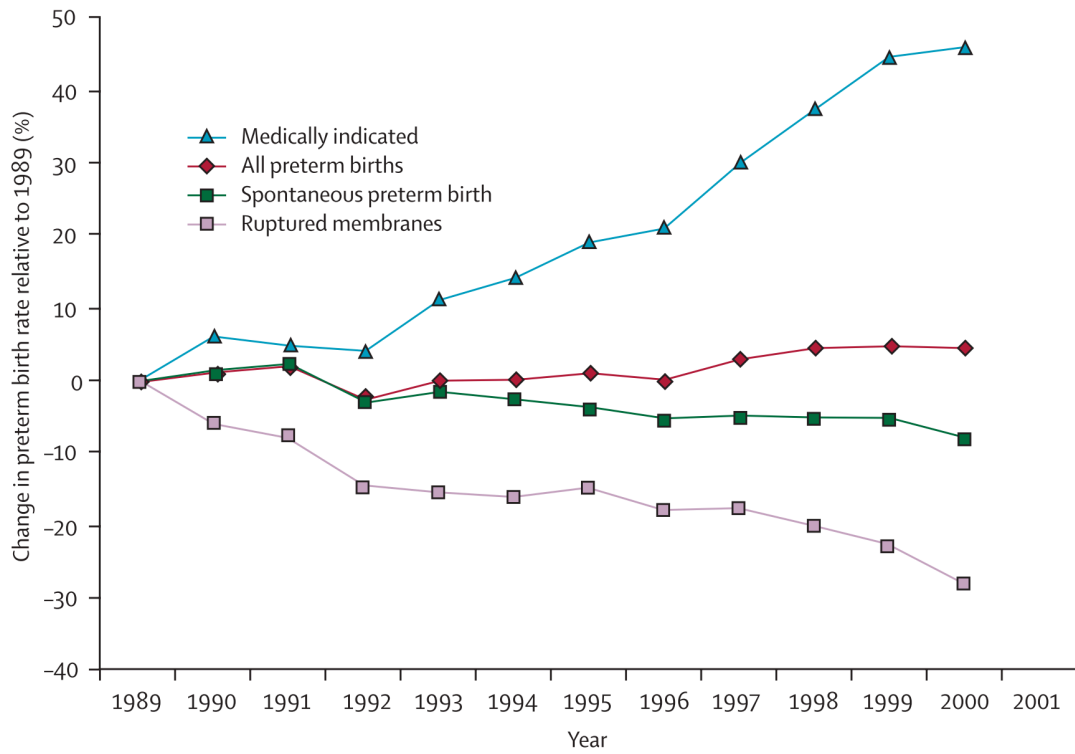
Figure 4. Change in spontaneous and medically-indicated preterm birth rates relative to 1989. While spontaneous preterm birth rates decreased from 1989, medically-indicated rates increased almost 50% within a decade. (Figure adapted from Goldenberg *et al.*, 2008).

non-indicated deliveries at less than 39 weeks' gestation (Schoen *et al.*, 2014). These public policies and national campaigns may have had some modest success as "the cesarean delivery rate declined to 32.7% of U.S. births in 2013, down from 32.8% for 2010-2012. The rate peaked in 2009 at 32.9% after increasing every year since 1996 (20.7%)" (Martin *et al.*, 2013).

Objectives

In an effort to reduce preterm birth, organizations such as the March of Dimes, ACOG and SMFM launched national campaigns and released policy statements aimed at reducing elective early term (37-38 weeks) deliveries. Whether these policies have influenced the proportion of preterm deliveries that are spontaneous versus medically-indicated is unknown. Further, the effect of the reduction in elective early deliveries on racial disparities is unknown.

We hypothesized that these policies, as well as an increased awareness of complications among late preterm infants would lead to fewer medically-indicated preterm births and an unchanged racial disparity in preterm birth rates between black white women.

As a result, the objectives of this paper are the following:

1) To determine the proportion of preterm deliveries at BIDMC from 2004-2013 that were medically-indicated versus spontaneous

2) Due to persistent racial disparities, to determine if shifts in type of preterm delivery varied by race or ethnicity

METHODS

Institutional Review Board (IRB) process

We submitted our New Research Application (Title: Preterm birth data repository) to the Beth Israel Deaconess Medical Center (BIDMC) Committee on Clinical Investigations (CCI)/Institutional Review Board on August 18, 2014. We aimed to create a repository and use the data collected for a retrospective cohort study. Given that both the repository and the study required no contact with participants, we submitted the application for Expedited Review (as opposed to review by the Full Board). We also sought a Health Insurance Portability and Accountability Act (HIPAA) Waiver of Authorization to use Protected Health Information (PHI) and to waive the informed consent process. The required documents were approved, and our protocol (#2014P-000244) was activated on September 2, 2014.

Definitions

We defined *medically-indicated* preterm birth as delivery due to preeclampsia, poor fetal growth, hypertension, or other fetal/maternal condition. We defined a delivery as *spontaneous* preterm birth if it followed preterm labor, preterm premature rupture of membranes or cervical incompetence.

Data collection

Eligible deliveries were accessed from BIDMC's Birth Log, an electronic delivery database. We included women who delivered infants preterm (< 37 weeks' completed gestation) from January 1, 2004 through December 31, 2013. We abstracted the medical record number, date of birth, birth weight, and gestational age of all eligible babies from BIDMC's Birth Log. We reviewed the first 87 deliveries in 2013, and then calculated the time required to review at least 100 records per year for the 10-year period. We then randomly sampled 15% of the rest of 2013 and 15% of the records from 2004-2012. We additionally reviewed 69 charts to oversample black women due to small numbers of black women in the original sample.

In 2011 and 2012, our institution transitioned to a fully electronic medical record by eliminating paper outpatient medical records, using electronic documentation, and scanning paper medical records (starting from 2008) into the online medical record's "Scanned Inpatient Records" (Feinbloom, 2012). We manually abstracted the following data from the medical records:

- Infant data
    - Number of gestation (singleton versus multiples)
    - Medical record number
    - Birth weight
    - Mode of delivery
    - Date of birth
    - Estimated due date

- o   Best obstetric gestational age at delivery

- o   Birth log gestational age at delivery

- o   Address (for later geocoding for another project)

- Maternal demographic and medical information

  - o   Medical record number

  - o   Race/ethnicity

  - o   Age at delivery

  - o   Insurance status

  - o   Gravidity

  - o   Parity

  - o   Short cervix (defined as less than 25 mm)

  - o   Use of assisted fertility/reproduction in this pregnancy

  - o   Progesterone administration

  - o   Receipt of a cerclage

  - o   Use of other preterm prevention devices (i.e. pessary)

  - o   Induction medications

  - o   Other induction devices

Data were collected and managed using Research Electronic Data Capture

(REDCap) electronic data capture tools hosted at BIDMC (Harris *et al.*, 2009). We

created our preterm data repository on September 5, 2014. After finalizing the list of data

to include, we moved the project into production on September 16, 2014. There were a

total of 11 revisions during production, and the final data collection tool was titled "MR

Data Collection" (**Figure 5**). We created a total of 971 records in REDCap. Records were

created for each delivery (as opposed to for each birth in the case of multiple gestations).

Two reviewers independently reviewed a random sample of 18 records for

concordance for medically-indicated versus spontaneous preterm birth typing. After

realizing 100% concordance, the first reviewer (MA) consulted the neonatologist (HB)

when more than one reason for preterm delivery was stated (44 records). The

neonatologist independently reviewed the chart, and if her opinion differed from the

primary reviewer's, the neonatologist's determination was selected as the final reason.

The obstetrician (SS) was consulted about 2 records for a more definite determination

when the neonatologist was unsure.

We reviewed 971 preterm deliveries, excluded 30 that were not actually preterm

(greater than 37 weeks' gestation) or had no gestational age listed (**Figure 6**). We

excluded another 11 because we were unable to determine whether the preterm birth was

medically-indicated or spontaneous. Our final dataset included 930 confirmed preterm

deliveries that were either medically-indicated or spontaneous.

Figure 5. Sample of blank record from REDCap. Data collected included infant data, maternal demographic and medical data, and outcome of delivery. Only infant information is shown here.
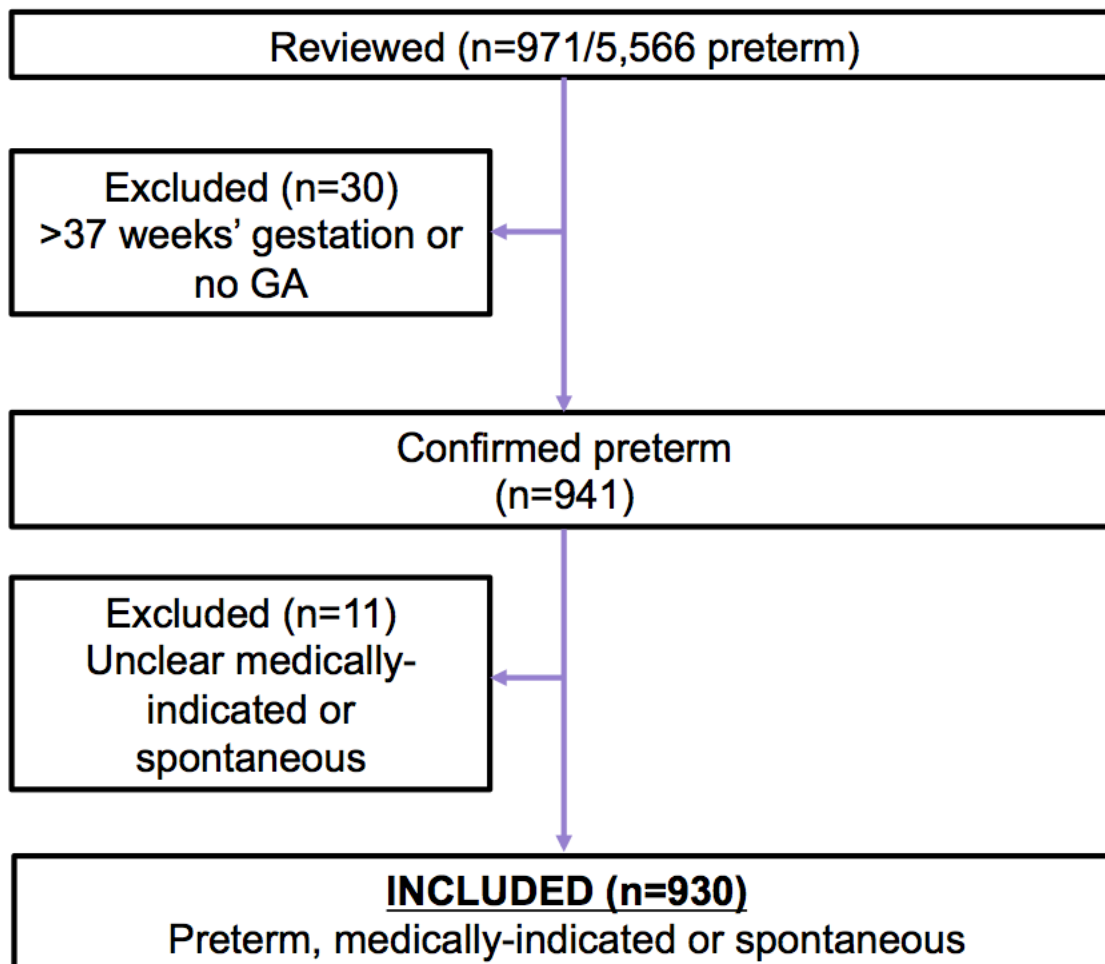
Figure 6. Exclusion and inclusion criteria. We reviewed 971 preterm deliveries, excluded 30 that were not actually preterm (> 37 weeks' gestation) or had no gestational age, and excluded 11 with an unclear medically-indicated or spontaneous phenotype. Our final dataset included 930 confirmed preterm deliveries that were either medically-indicated or spontaneous.

Statistical analyses

We dichotomized the time period into *early* (2004-2009) and *late* (2010-2013) since 2009 was the year ACOG released their recommendations to reduce non-elective early term deliveries. We compared the early versus late periods using Chi-Square tests. Logistic regression models were used to adjust for potential confounding variables, such as maternal age, gestational age at delivery, singleton versus multiple gestations, race/ethnicity, parity, insurance status, and year of delivery. We also completed stratified analyses for singleton and black versus white preterm deliveries.

RESULTS

Overall and singletons preterm at BIDMC, 2004-2013

During the 10-year study period, 5,566/46,981 deliveries at BIDMC were preterm (11.8%). There was a significant reduction in overall preterm birth at our institution from 12.3% in the early period to 11.2% in the late period (P=0.0003). Among singletons, there was also a significant reduction in overall preterm birth from 10.0% in the early period to 9.0% in the late period (P=0.0004) (**Figure 7**). We analyzed for singletons because of known reductions in the incidence of multiple gestations during the past decade due to in vitro fertilization (IVF) practice changes. Since 2003, there has been an exponential increase of women electing to have a single embryo transfer, rather than multiple (Centers for Disease Control and Prevention, 2014) (**Figure 8**). Multiple gestations are more likely to deliver early, so these changes in IVF practices might have contributed to the decrease in preterm deliveries.

Characteristics of BIDMC preterm deliveries

Out of the 930 preterm deliveries we sampled at BIDMC from 2004 to 2013, there were 424 medically-indicated and 506 spontaneous. The following are characteristics of these deliveries (**Table 1**):
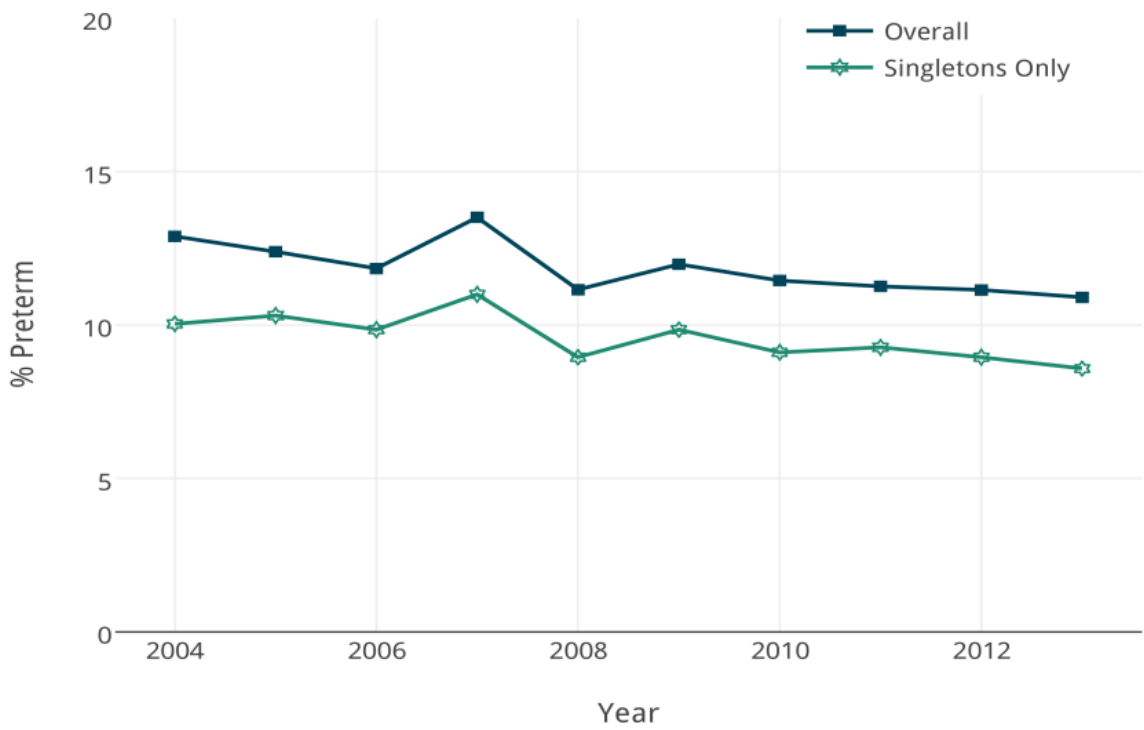
Figure 7. Overall and singletons preterm at BIDMC, 2004-2013. There was a

significant reduction in overall preterm birth at our institution from 12.3% in the early

period to 11.2% in the late period. Among singletons, there was also a significant

reduction in overall preterm birth from 10.0% in the early period to 9.0% in the late

period.
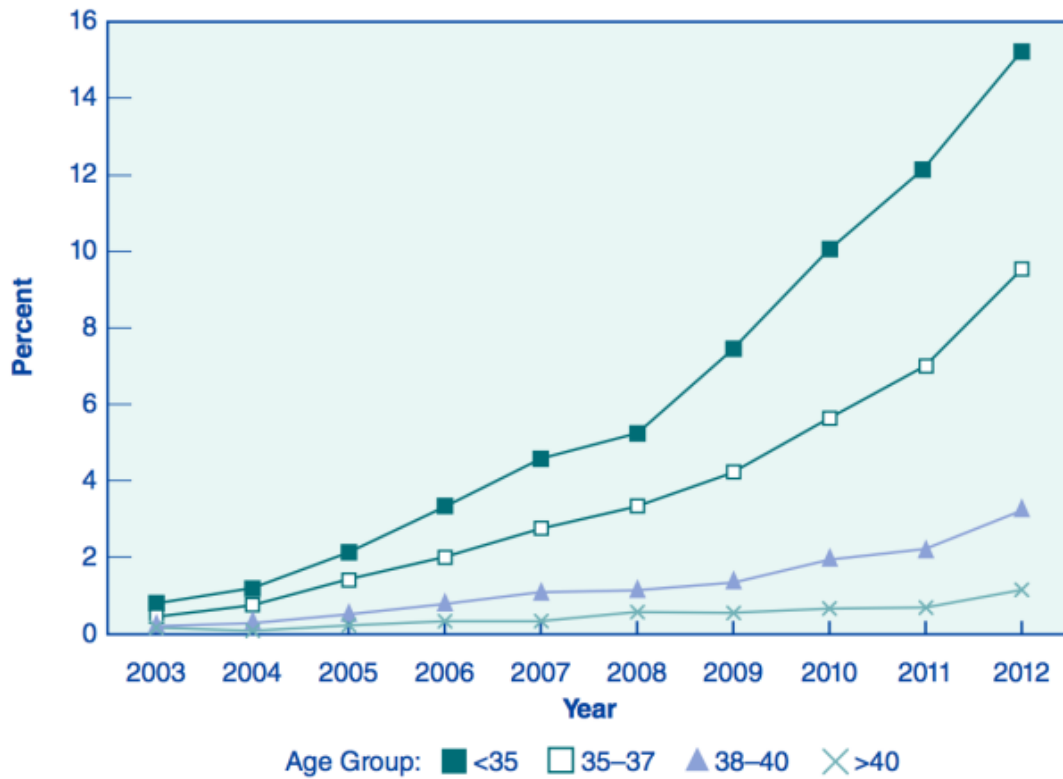
Figure 8. In vitro fertilization practice changes, 2003-2012. Since 2003, there has been

an exponential increase of women electing to have a single embryo transfer, rather than

multiple (Centers for Disease Control and Prevention, 2014)

	Medically-indicated (n=424)		Spontaneous (n=506)	
	n	**Row %**	**n**	**Row %**
Gestational age				
<30 weeks	44	31.9	94	68.1
30-31 weeks	36	43.4	47	56.6
32-34 weeks	82	47.1	92	52.9
34-36 weeks	262	49.0	273	51.0
Maternal age at delivery				
<25 years	34	38.2	55	61.8
25- 34 years	207	41.3	294	58.7
> 34 years	183	53.8	157	46.2
Year of delivery				
2004-2009	258	48.3	276	51.7
2010-2013	166	41.9	230	58.1
Race/ethnicity				
Asian	23	29.9	54	70.1
Black	88	46.8	100	53.2
Hispanic	22	38.6	35	61.4
White	265	48.7	279	51.3
Other/unknown	25	41.7	35	58.3
Insurance status				
Private	147	45.4	177	54.6
HMO	164	46.7	187	53.3
Medicaid	107	44.8	132	55.2
Self-pay/other/uninsured	6	37.5	10	62.5
Parity				
Multiparous	182	45.0	222	55.0
Primiparous	242	46.1	283	53.9
Number of gestations				
Singleton	248	46.4	286	53.6
Multiple	176	44.4	220	55.6

*28 preterm deliveries could not be categorized based on data in medical record, two missing race/ethnicity, one missing parity.

Table 1. Characteristics of 930 preterm deliveries at BIDMC, 2004-2013

Gestational age. As gestational age increases, the proportion of preterm births that were medically-indicated deliveries increased as well. For deliveries less than 30 weeks' gestation, there were 31.9% medically-indicated and 68.1% spontaneous. For deliveries between 30 weeks, 0 days and 31 weeks, 6 days gestation, there were 43.4% medically-indicated and 56.6% spontaneous. For deliveries between 32 0/7 and 33 6/7 weeks' gestation, there were 49.0% medically-indicated and 51.0% spontaneous.

Maternal age at delivery. Older mothers were more likely to have medically-indicated deliveries, while younger mothers were more likely to have spontaneous deliveries. Mothers who gave birth younger than 25 years of age were 38.2% medically-indicated and 61.8% spontaneous. Between 25 and 34 years of age, 41.3% were medically-indicated and 58.7% were spontaneous. For mothers older than 34 years, 53.8% were medically-indicated and 46.2% were spontaneous.

Year of delivery. We characterized 2004 to 2009 as "early" and 2010 to 2013 as "late". In the early period, there were 48.3% medically-indicated deliveries and 51.7% spontaneous. In the late period, there were 41.9% medically-indicated and 58.1% spontaneous. Therefore, we saw a reduction in medically-indicated deliveries and an increase in spontaneous deliveries over the past 10 years.

Race/ethnicity. Black and white women did not differ in the proportion of preterm births that were medically-indicated versus spontaneous preterm deliveries. For preterm

deliveries among black women, 46.8% were medically-indicated and 53.2% were spontaneous, while for white women, 48.7% were medically-indicated and 51.3% were spontaneous. Preterm deliveries among Asian women were less likely to be medically-indicated (29.9%) than spontaneous (70.1%). Preterm deliveries among Hispanic women were also less likely to be medically-indicated (38.6%) than spontaneous (61.4%).

Insurance status. The type of insurance was not associated with proportion of preterm births that were medically-indicated versus spontaneous. For preterm deliveries among women with private insurance, 45.4% were medically-indicated and 54.6% were spontaneous. For preterm births among women with health maintenance organization (HMO) insurance, 46.7% were medically-indicated and 53.3% were spontaneous. For preterm births among women with Medicaid or public insurance, 44.8% were medically-indicated and 55.2% were spontaneous. For preterm births among women who were self-pay, uninsured or had other insurance, 37.5% were medically-indicated and 62.5% were spontaneous.

Parity. Parity is defined as the number of deliveries greater than 20 weeks' gestation. Our data included multiparous (delivered more than 1 child) and primiparous (delivered only the current delivery from our dataset) women. Parity was not associated with medically-indicated versus spontaneous preterm birth. For preterm births among multiparous women, 45.0% were medically-indicated and 55.0% were spontaneous. For

preterm births among primiparous women, 46.1% were medically-indicated and 53.9% were spontaneous.

Number of gestations. Singletons (one birth only) and multiples (more than one birth) had similar percentages of medically-indicated and spontaneous preterm births. For preterm births among singletons, 46.4% were medically-indicated and 53.6% were spontaneous. For preterm births among multiples, 44.4% were medically-indicated and 55.6% were spontaneous.

Medically-indicated versus spontaneous preterm deliveries

Visual inspection of the percentage of medically-indicated preterm deliveries versus spontaneous preterm deliveries (n=930) (**Figure 9**) reveals a non-significant difference between early (48.3%) and late (41.9%) for medically-indicated births (*P*=0.05). Multivariable logistic models revealed little evidence of confounding. When we adjusted for maternal age, gestational age at delivery, singleton versus multiple gestations, and maternal race/ethnicity, the adjusted odds of a medically-indicated versus a spontaneous preterm delivery were lower in the late versus early period (adjusted OR 0.73, 95% CI: 0.56, 0.96) (**Table 2**). Furthermore, adjustment for parity or insurance status did not change these estimates.
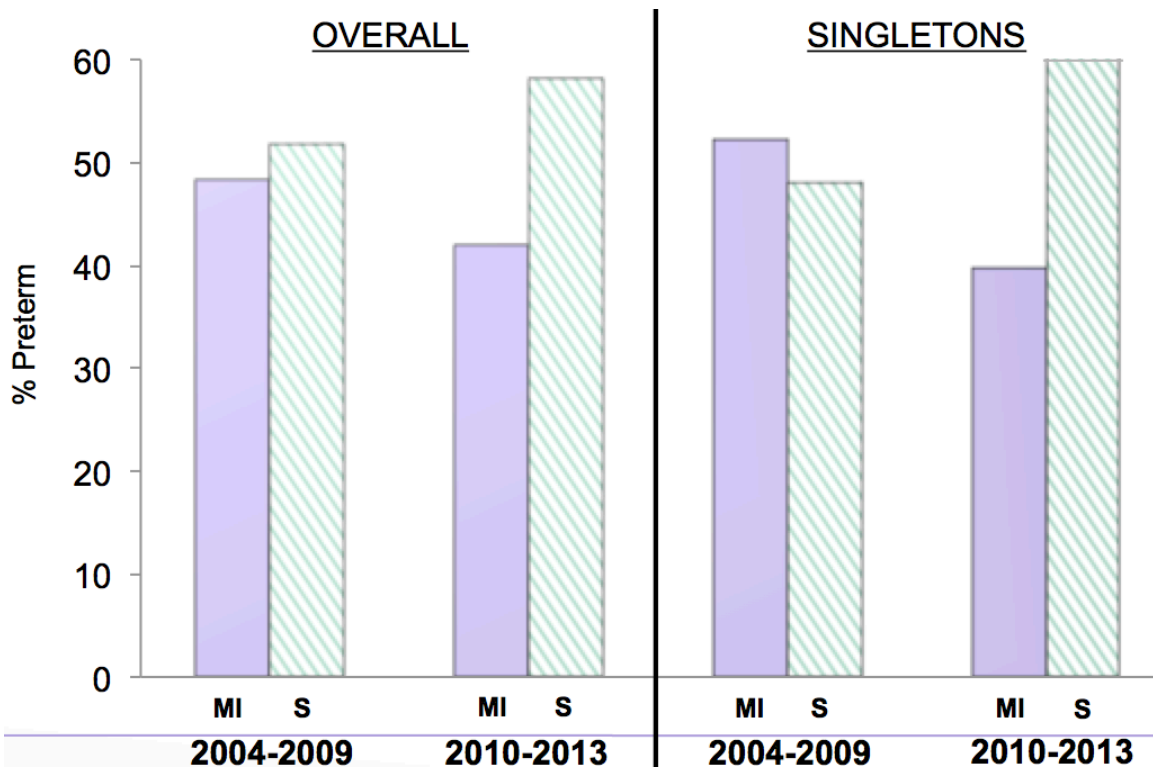
Figure 9. Medically-indicated versus spontaneous preterm birth for overall and singletons, comparing early versus late. In the early period for both overall and singletons, the percentages of medically-indicated and spontaneous preterm birth were roughly the same. In the late period, there was a difference, which was non-significant for overall, but significant for singletons.

	Odds Ratio (95% CI)	P
All Participants (n=930)		
Unadjusted	0.77 (0.59, 1.00)	0.05
Adjusted[1]	0.73 (0.56, 0.96)	0.03
Singleton Gestations (n=534)		
Unadjusted	0.61 (0.43, 0.86)	0.005
Adjusted[2]	0.61 (0.43, 0.87)	0.007

[1]Adjusted for maternal age, gestational age at delivery, singleton vs. multiple gestations, and race/ethnicity
[2]Adjusted for maternal age, gestational age at delivery, and race/ethnicity

Table 2. Odds of medically-indicated versus spontaneous from late period compared to early at BIDMC. Preterm birth was less likely to be medically-indicated in the late period compared to the early period. This was seen among all and singleton gestations.

Medically-indicated versus spontaneous preterm singleton deliveries

Among the 534 singletons in our study, there was a significant reduction in the proportion of preterm births that were medically-indicated between the early (52.1%) and late (39.8%) periods (*P*=0.005) (**Figure 9**). Multivariable logistic models in this subset of singletons also revealed little evidence of confounding. When we adjusted for maternal age, gestational age at delivery, and maternal race/ethnicity, the adjusted odds of a medically-indicated versus a spontaneous preterm delivery were lower in the late versus early period (adjusted OR 0.61, 95% CI: 0.43, 0.87) (**Table 2**).

Black and white preterm deliveries at BIDMC, 2004 – 2013

During the 10-year study period at BIDMC among black women, 754/5,065 (14.9%) of deliveries were preterm versus just 3,136/25,827 (12.1%) among white women. In 2004, the preterm delivery rate was 15.6% for black women and 13.1% for white women (**Figure 10**). The highest rates of preterm birth at BIDMC were in 2007 with 18.1% for black women and 13.6% for white women. The rates steadily decreased to 12.1% for black women and 11.4% for white women in 2013.

Medically-indicated and spontaneous preterm birth among black and white

In our study there were 188 preterm deliveries among black women. We observed a non-significant reduction in the proportion of preterm deliveries among black women that were medically-indicated in the late (40.6%) versus early (50.4%) period (*P*=0.19). Among preterm deliveries for white women, we observed an even more subtle, non-

Figure 10. Reduction in preterm birth in both black and white women, 2004-2013.

In 2004, the preterm delivery rate was 15.6% for black women and 13.1% for white

women (**Figure 10**). The rates steadily decreased to 12.1% for black women and 11.4%

for white women in 2013.

significant reduction in medically-indicated preterm deliveries from 50.0% in the early

period to 46.9% in the late period (*P*=0.48) (**Figure 11**). In models adjusting for maternal

age, gestational age at delivery, and singleton versus multiple gestations, the odds of

medically-indicated versus spontaneous preterm delivery were non-significantly lower in

the late versus early periods for black (adjusted OR 0.63, 95% CI: 0.34, 1.16) and white

(adjusted OR 0.80, 95% CI: 0.56, 1.16) women (**Table 3**). When comparing preterm

deliveries among black versus white women, these results suggest that black women had

more of a reduction in the risk of medically-indicated preterm birth in the late versus

early periods, but a test for interaction was not significant (*P*=0.49).
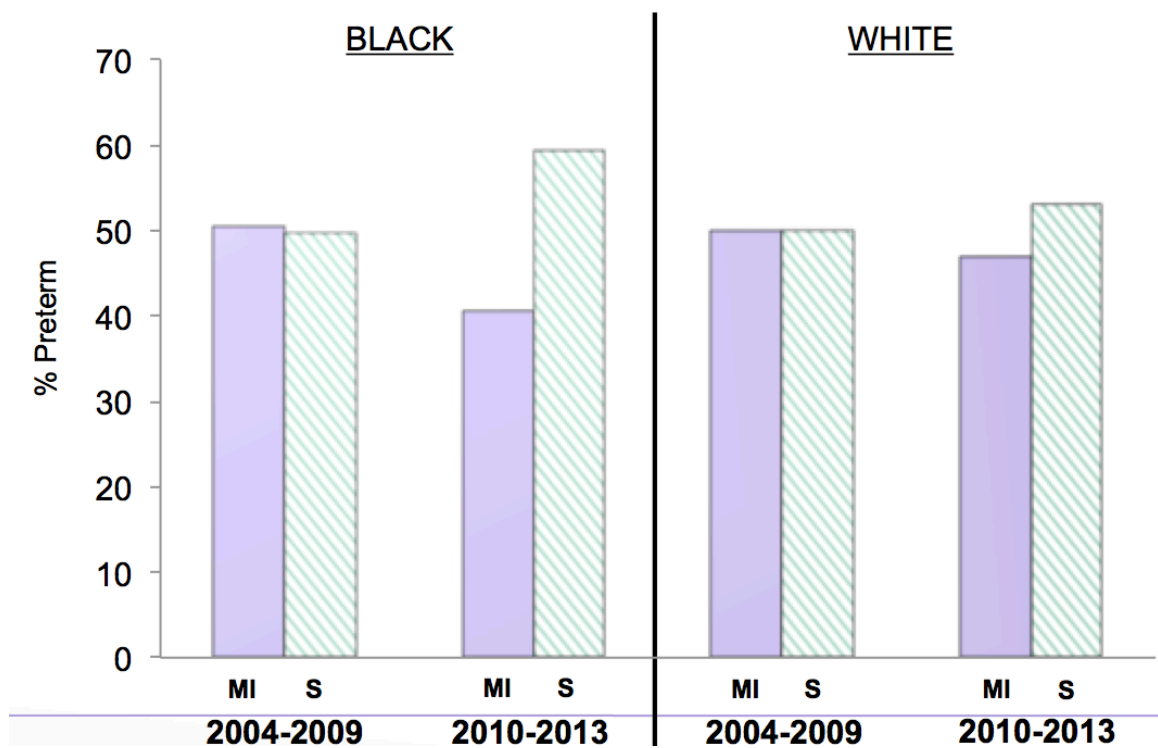
Figure 11. Medically-indicated versus spontaneous preterm birth among black and white women, comparing early versus late. In the early period for both black and white women, the percentages of medically-indicated and spontaneous preterm birth were about the same. In the late period, there was a decrease in medically-indicated for both black and white women, but this was more noticeable in black women. Both reductions were non-significant.

	Odds Ratio (95% CI)	P
Black Participants (n=188)		
Unadjusted	0.67 (0.37, 1.22)	0.19
Adjusted[3]	0.63 (0.34, 1.16)	0.14
White Participants (n=544)		
Unadjusted	0.88 (0.63, 1.24)	0.48
Adjusted[3]	0.80 (0.56, 1.13)	0.20

[3]Adjusted for maternal age, gestational age at delivery, and singleton vs. multiple gestations

Table 3. Odds of medically-indicated versus spontaneous among black and white participants from late period compared to early at BIDMC. Black women had more of a reduction in the risk of medically-indicated preterm birth in the late versus early periods, but these results were not significant.

DISCUSSION

## *Summary*

The reduction in preterm birth at Beth Israel Deaconess Medical Center over the last 10 years is consistent with state and national data. The reduction in medically-indicated birth at BIDMC over the past 10 years was from 48.3% in the early period to 41.9% in the later period. This was most evident among black women with a concurrent decrease in overall preterm birth among black women.

Strengths and limitations

We performed a thorough retrospective chart review of the medical records. Data that we collected are usually unavailable at the state level and is difficult to obtain using automated techniques. Another strength is that two separate reviewers analyzed a subset of records and showed complete concordance.

A limitation of this study is that it was retrospective. Unmeasured factors may be responsible for the changes in preterm birth rate, resulting in residual confounding. Furthermore, preterm clinical subtypes (spontaneous and medically-indicated) remain heterogeneous categories, since they include several diagnoses.

Speculations

The reduction in medically-indicated preterm births could be contributing to the overall reduction in preterm birth. Black women may be benefitting from public health

interventions, thereby narrowing the racial disparity. We observed a narrowing of our

racial disparity in preterm birth when we compare our results at BIDMC to those of

Massachusetts (**Figure 12**). At BIDMC from 2004-2013, black women experienced a

20.8% decrease in preterm birth, while white women experienced a 4.9% decrease. In

Massachusetts during the same 10 years, black women experienced a 10.6% decrease,

while white women experienced a 5.8% decrease. Our data at BIDMC illustrates a

greater narrowing of the racial gap, while the state level data still shows a consistent

disparity between black and white women.

Next steps/future work

We plan to apply inverse probability weights as a statistical technique to account

for the oversampling of deliveries in 2013 and of black women. We also plan to analyze

the underlying conditions responsible for the reduction of the medically-indicated

deliveries. We will ascertain which diagnosis (preeclampsia, intrauterine growth

restriction, hypertension, or other fetal/maternal condition) contributed most to the

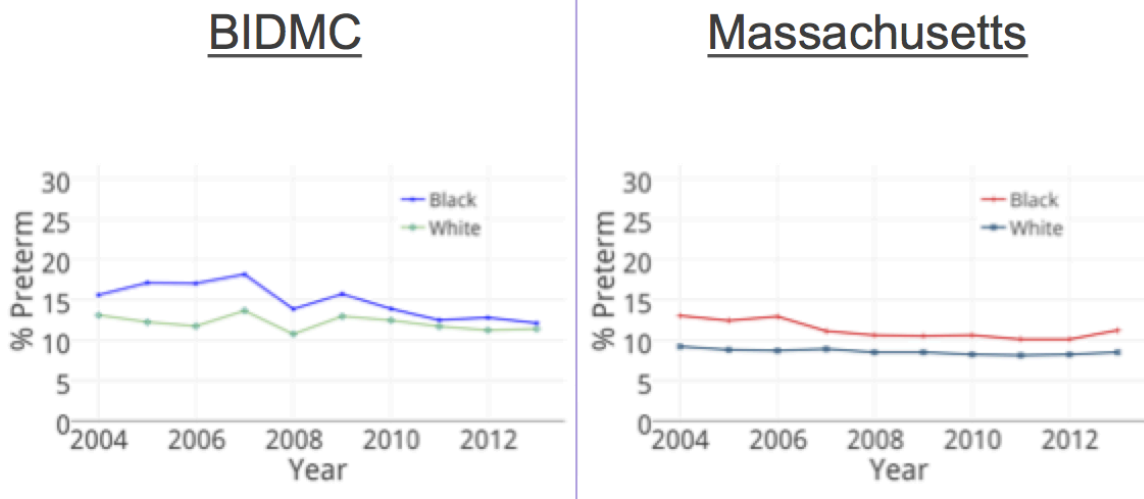medically-indicated delivery phenotype.

Figure 12. Comparison of BIDMC and Massachusetts racial disparity. The gap

between black and white preterm deliveries has narrowed more so at BIDMC than

Massachusetts overall.

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CURRICULUM VITAE

MELISSA ROSE LEYNES ADA

mlada@bu.edu • 714.606.6898 • Birth Year: 1990
Permanent Address: 3307 E Ridgeway Road • Orange, CA • 92867
Current Address: 58 Queensberry Street, Apt #6 • Boston, MA • 02215

Education:

Sept '13 – present   **Boston University School of Medicine**, Boston, MA
M.S. Degree in Medical Sciences (expected May 2015)

Sept '09 – June '13   **Stanford University**, Stanford, CA
B.A. Degree in Human Biology
(Area of Concentration: Socio-Cultural Determinants of International Health)

Sept '05 – May '09   **Fairmont Preparatory Academy**, Anaheim, CA
Medical Magnet Student, President's Award

Research:

Aug '14 – present   Graduate Student Researcher at Beth Israel Deaconess Medical Center in Boston, MA
- Principal Investigator: Heather H. Burris, MD MPH
- Thesis: "Trends in Spontaneous versus Medically-Indicated Preterm Birth, 2004-2013"
  - Created a preterm birth data repository in REDCap (Research Electronic Data Capture), a data management and survey tool
  - Went through more than 2000 online medical records in Beth Israel's online database
- SPEC (Spontaneous Prematurity and Epigenetics of the Cervix) Study
  - Approached new patients in the OB/GYN and Maternal and Fetal Medicine waiting rooms to ask if they were interested in participating in this study
  - Consented subjects and interviewed them with two questionnaires
  - Collected bloods and cervical swabs; stored samples in clinical laboratories

Mar '11 – June '13   Research Assistant at Veterans Affairs of Palo Alto
- Principal Investigator: Jamie Zeitzer, PhD

- Poster Presentation at the annual HB-REX Poster Symposium on August 4, 2011
  - Title: "Post-illuminance pupillary response following millisecond light exposure: a window onto ipRGC function"
- Worked with ELISA for cortisol assays and helped out with a sleep study by taking saliva samples and administering PVT (Psychomotor Vigilance Tests)

June '08 – Aug '08 Research Assistant and Volunteer at the University of Southern California
- Principal Investigator: Jeanine Yip, DPT
- Researched the effect of physical therapy on stroke and Parkinson's patients
  - Aided in patient evaluations for LEAPS (Locomotor Experience Applied Post-Stroke)
  - Transcribed and recorded data into Microsoft Excel
  - Transported patients to and from research locations

Work Experience:

Sept '14 – Dec '14 Graduate-level Biochemistry (BI751) Tutor at Boston University School of Medicine

Aug '14 – present Graduate Student Researcher at Beth Israel Deaconess Medical Center in Boston, MA
- Principal Investigator: Heather H. Burris, MD MPH
- SPEC (Spontaneous Prematurity and Epigenetics of the Cervix) Study

Jan '10 – Mar '10 Tutor of elementary and middle school students for EPATT (East Palo Alto Tennis & Tutoring)

Jul '09 – Sept '09 Sales Trainee and Representative for CUTCO
- Gave presentations of cutlery knives and sold to customers

Feb '06 – May '06 Cheerleader role, Hannah Montana TV show on Disney Channel
Photographed as daughter of General Kuribayashi in the movie, *Letters from Iwo Jima*

Awards:

Mar '15 New England Perinatal Society (NEPS) Conference
- Abstract ("Trends in Spontaneous versus Medically-Indicated Preterm Birth, 2004-2013") accepted as 10-minute oral platform presentation
- Awarded "Best Presentation in Maternal-Fetal Medicine"
- Awarded Educational Grant of $160

June '11 – Aug '11 Stanford Human Biology Research Exploration Program (HB-REX) Grant of $5,600 to conduct research at the VA Palo Alto for

10 weeks

July '10 – Sept '10   Claude Buss Fellow/Stanford Coordinator for VIA ALC1 (Volunteers in Asia, American Language & Culture Session 1), a program that enables students from Taiwan, Japan, and Korea to take English classes at Stanford and be exposed to American culture for 6 weeks ($1,000 award)
- Planned recreational activities, such as rock-climbing at the gym and a kayaking trip
- Gave a 30-minute presentation on the perspectives of beauty in America and Asia
- Acted as a Resident Assistant to the students

Leadership Experience:

Sept '12 – May '13   Co-President for Stanford H.E.L.P. (Health Education for Life)
Mar '12 – June '13   Vive Perú Campus Coordinator at Stanford University
June '11 – June '12   PASU Secretary/Historian Co-Chair
June '10 – June '11   PASU Community Service Co-Chair
Jul '10 – Sept '10   Claude Buss Fellow/Stanford Coordinator for VIA (Volunteers in Asia)
Sept '09 – June '10   PASU (Pilipino American Student Union) Frosh Intern for Secretary/Historian Committee

Community Service:

Jan '14 – May '14   Volunteer at Boston Medical Center Pediatric Department's bWell Center in Boston, MA (45 hours)
- Approached parents and asked if they were interested in any of our free resources
- Promoted partnerships with Boston Public Library and Boston Public Schools
- Conducted sessions at the Jump Rope Clinic by describing the program and timing the patient's number of jumps in 30 seconds
- Lead hourly activities in the waiting room, including play-dough making, paper bag puppets, and obstacle courses

Dec '11 – Jan '12   Clinical Medicine Volunteer with the non-profit, Vive Perú, in Trujillo, Peru (120 hours)
- Lived with a host family, shadowed doctors and nurses at a maternal and child health clinic named Santa Lucia de Moche, took a medical Spanish class, and took down patient history in Spanish during the free medical campaign

Sept '11 – Dec '11   Adult Volunteer at CONIN (Corporación para la Nutrición Infantil) Malnutrition Clinic in Santiago, Chile while studying abroad (70 hours)

- Entertained and fed malnourished children while developing close personal relationships

Apr '11 – June '13   PFC (Pacific Free Clinic) Referrals Committee Member (150 hours)
- Attended free clinic for uninsured individuals in San Jose, CA, and referred them to other hospitals, community centers, and clinics in the county
- Contacted various centers by phone to update current information on tuberculosis testing
- Worked on a project to get patient navigators for PFC patients

Sept '10 – Jan '13   Health Educator for Stanford H.E.L.P. (Health Education for Life) (500 hours)
- Taught health education to 6th and 8th graders in Kennedy Middle School and Selby Lane Middle School in Menlo Park and Atherton, CA

Nov '09 – May '13   SPOON (Stanford Project On Hunger) Volunteer (35 hours)
- Cooked and served food for the homeless at the Palo Alto Opportunity Center in Palo Alto, CA

Sept '07 – present   Pianist at elderly homes and church in Orange County, CA (60 hours total)

Sept '07 – June '09   Junior Volunteer at St. Joseph Hospital, Orange, CA (150 hours)
- Messenger service: delivered supplies and medical records to nurses' stations
- Telephone dispatcher: received calls from nurses and assigned volunteers to take the call

Shadowing Experience:

Aug '14 – present   Neonatology at Beth Israel Deaconess Medical Center in Boston, MA (12 hours)

June '12 – Aug '12   Summer with Tri County Medical Group in Orange County and Los Angeles, CA (85 hours)

Dec '11 – Jan '12   Vive Perú in Trujillo, Peru (80 hours)

Oct '10 – Dec '10   Stanford Immersion in Medicine Series (SIMS) Program (16 hours)