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Effect of Modifiable Risk Factors on Preterm Birth: A Population Based-Cohort

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Abstract *Objectives* The purpose of this study is to evaluate the prevalence, impact, and interaction of short interpregnancy interval (IPI), pre-pregnancy body mass index (BMI) category, and pregnancy weight gain (PWG) on the rate of preterm birth. *Methods* This is a population-based retrospective cohort study using vital statistics birth records from 2006 to 2011 in OH, US, analyzing singleton live births to multiparous mothers with recorded IPI (n = 393,441). Preterm birth rate at <37 weeks gestational age was compared between the referent pregnancy (defined as normal pre-pregnancy maternal BMI, IPI of 12–24 months, and Institute of Medicine (IOM) recommended PWG) and those with short or long IPI, abnormal BMI (underweight, overweight, and obese), and high or low PWG (under or exceeding IOM recommendations). *Results* Only 6 % of the women in this study had a referent pregnancy, with a preterm birth rate of 7.6 % for this group. Short IPIs of <6 and 6–12 months were associated with increased rates of preterm birth rate to 12.9 and 10.4 %, respectively. Low PWG compared to IOM recommendations for pre-pregnancy BMI class was also associated with increased preterm birth rate of 13.2 % for all BMI classes combined. However, the highest rate of preterm birth of 25.2 % occurred in underweight women with short IPI and inadequate weight gain with $_{adj}$OR 3.44 (95 % CI 2.80, 4.23). The fraction of preterm births observed in this cohort that can be attributed to short IPIs is 5.9 %, long IPIs is 8.3 %, inadequate PWG is 7.5 %, and low pre-pregnancy BMI is 2.2 %. *Conclusions* Our analysis indicates that a significant proportion of preterm births in Ohio are associated with potentially modifiable risk factors. These data suggest public health initiatives focused on preterm birth prevention could include counseling and interventions to optimize preconception health and prenatal nutrition.

Keywords Interpregnancy interval · Body mass index · Pregnancy weight gain · Preterm birth

Disclaimer This study includes data provided by the Ohio Department of Health which should not be considered an endorsement of this study or its conclusions.

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Significance

Abnormalities in pregnancy weight gain, pre-pregnancy BMI, and interpregnancy interval impact 25 % of the preterm births in this cohort could identify targets for intervention strategies.

Introduction

The overall rate of preterm birth, defined as birth at <37 weeks gestational age, in the US is 11.4 % (9.9 % for singleton pregnancies), more than twice as high as several

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other high resource countries (Hamilton et al. 2013). Medical advances in treating the consequences of prematurity have led to improved neonatal outcomes, but the driving factors for the high preterm birth rate in the US remain unclear. To better understand public health targets for prevention of prematurity, in this study we examine the composite impact of selected modifiable risk factors for preterm birth including interpregnancy interval (IPI), gestational weight gain, and pre-pregnancy BMI. These factors were selected as they are related to maternal nutritional status and nutrient depletion, factors that have been postulated as triggers of preterm parturition.

Previous studies have demonstrated an association between low pregnancy weight gain (PWG) (below IOM recommendations) and preterm birth (Li et al. 2013; Masho et al. 2013; Xinxo et al. 2013). The direction of the association between PWG and preterm birth varies based on pre-pregnancy BMI, with a linear association seen in underweight women and a U-shaped association noted in average and overweight women (Carnero et al. 2012). Studies of PWG in general have shown increased risk of preterm birth with inadequate weight gain, but decreased risk of preterm birth with excessive compared to the recommended weight gain (Li et al. 2013). However, there are numerous maternal and obstetrical risks associated with excessive weight in pregnancy such as gestational diabetes, macrosomia, increased cesarean risk and birth trauma (McDonald et al. 2011; Landon et al. 2009).

Less well understood is the influence of pre-pregnancy BMI on preterm birth rate. Several studies demonstrate an increase in spontaneous preterm births in underweight women (Wang et al. 2011); however, this may be explained by coexistent risk factors with null effect following adjustment for confounders (Bhattacharya et al. 2007). A US retrospective cohort study revealed an increased risk of all phenotypes of preterm birth (spontaneous and medically indicated) in underweight women (Lynch et al. 2013). A British retrospective cohort study showed increased risk of preterm birth in both underweight and obese mothers (Scott-Pillai et al. 2013).

Short IPI, time from birth to conception of the subsequent pregnancy) have been associated with preterm birth and other adverse neonatal and obstetrical complications in multiple studies (Conde-Agudelo et al. 2006; de Weger et al. 2011; Rodrigues and Barros 2008). Despite the well described risks associated with short IPI s, approximately one in three pregnancies in the US occur at a <18 month interval (Gemmill and Lindberg 2013).

We sought to measure the combined influence of variations in gestational weight gain, IPI, and pre-pregnancy BMI on the rate of preterm birth at <37 weeks. Based on prior studies, we hypothesize that in any BMI category, short IPI and inadequate PWG will be associated with an increased rate of preterm birth. Additionally, we hypothesize that underweight women will have a greater increase in preterm birth rate with a short IPI and inadequate weight gain than women with normal or elevated pre-pregnancy BMI. The value of examining these specific risk factors is twofold. The majority of women possess at least one of these risk factors making the potential impact of modification of these factors quite broad. Additionally, the magnitude of the effect of sharing multiple risk factors on a pregnancy, and their interactions, has not been clearly defined.

Methods

We performed a population-based retrospective cohort study of all live births in Ohio during a 6 year period (2006–2011) using vital statistics birth records from the Ohio Department of Health. The primary exposure variables for this study were IPI (time from one birth to conception of the subsequent pregnancy), pre-pregnancy body mass index (BMI), and amount of PWG as categorized by the Institute of Medicine (IOM) (Rasmussen 2009). The exposure of interest, IPI, is defined as time from the most recent prior birth to the subsequent conception of the index birth. The date of prior birth is recorded in the US birth certificate, which was used for data analyzed in this study. We calculated the IPI by converting the gestational age of the current (index) birth into months and subtracting it from the number of months between prior birth and current birth. Therefore, IPI in this study is defined as time from one birth to conception of the subsequent pregnancy.

We categorized IPI into the following periods: <6, 6–12, 12–24, 24–60, and ≥60 months. The 12–24 month period was chosen as the referent category because it was identified to be the interval of time associated with the lowest rate of preterm birth in this study cohort. Pre-pregnancy BMI was calculated from maternal height and pre-pregnancy weight as recorded on the birth certificate. BMI was categorized according to World Health Organization standards as underweight <18.5 kg/m^2, normal 18.5–24.9 kg/m^2, overweight 25–29.9 kg/m^2, and obese ≥30 kg/m^2. PWG was calculated as the difference between maternal weight at delivery and pre-pregnancy weight, both obtained from the mother's medical record by the birth certificate abstractor. PWG was adjusted to a 40 week gestational length by dividing gestational weight gain by gestational length in weeks and multiplying by 40 to account for lower weight gain in shorter gestational length. Calculations of weight gain in pregnancies of shorter gestational length may be prone to error, but there is no current standardized approach to adjust PWG for gestational length (Chmitorz et al. 2012; Hutcheon et al. 2012, 2013). The standardized PWG was then categorized per IOM recommendations based on pre-pregnancy BMI and classified as having met, exceeded, or been under goal weight gain 2009.

The primary outcome was the frequency of preterm birth (PTB) at <37 weeks gestational age (GA) for each group. For this study, the "combined estimate" of gestational age, defined as the best obstetric estimate of gestational age based on perinatal factors including last menstrual period data and earliest prenatal ultrasound when available, was used for gestational age comparisons. This is the most commonly used gestational age estimation from vital statistic records, and is the birth attendant's final estimate of the gestational age as recorded in the medical record and has been shown to have excellent specificity, negative predictive value, and positive predictive value (Dietz et al. 2014).

The study cohort was derived from all non-anomalous singleton live births in Ohio during the study period (n=892,733). Study exclusions were multiple gestations (n=32,282) and births <20 weeks (n=565) or >44 weeks gestational age (n=39). Analyses were then limited to multiparous mothers with available data on IPI. Primiparous mothers (n=342,243) and those missing IPI or parity status (n=64,593) were excluded. Finally, analyses were limited to women with data on pre-pregnancy BMI and maternal weight at delivery, resulting in final n=393,441. There was minimal missing data, 2% or less, for pregnancy characteristics and outcomes of interest including gestation age at delivery, maternal race, age, parity, gestational hypertension, gestational diabetes, and mode of delivery. BMI and number of prenatal care visits had 10% missing data.

Maternal demographic, behavioral, socioeconomic, prenatal and delivery characteristics, and frequency of preterm birth was compared between IPI and PWG groups, stratified by pre-pregnancy maternal BMI. Comparisons of dichotomous variables were performed with Chi square tests and continuous variables were compared using ANOVA. Multivariate logistic regression estimated the adjusted odds for preterm birth <37 weeks associated with IPI, PWG, and pre-pregnancy BMI including adjustments for confounders. Covariates chosen for the adjusted models were based on biologic plausibility and significant influences noted in bivariate analyses. Stepwise backward selection and removal of non-significant selected covariates (marital status, low education, limited prenatal care, year of delivery, and in vitro fertilization), yielded a final parsimonious model including cigarette smoking, maternal age, and race. Analyses were performed using Stata version 12.1, StataCorp LP, College Station, TX, US. Differences between groups were considered statistically significant if probability value <0.05 or 95% confidence interval was not inclusive of the null value 1.0.

A protocol for this study was approved and a de-identified data set provided by the state of OH, USA, Department of Health. This study was exempt from review by the Institutional Review Board at the University of Cincinnati, Cincinnati, OH, US.

Results

A cohort of 393,441 women with singleton live births was used for this analysis. Less than half of the women had a normal pre-pregnancy BMI (n=184,801, 47.0%). Births to overweight and obese women (n=97,823, 24.9% and n=94,260, 24.0%, respectively) were more common than to underweight women (n=16,557, 4.2%), $p<0.001$. Across all BMI classes, more women exceeded the recommended PWG (n=193,174, 49.1%) than met the goal (n=126,134, 32.1%) or had inadequate weight gain (n=74,133, 18.8%), $p<0.001$. Births following an IPI of 12–24 months occurred in less than a third of women (n=108,624, 27.6%) compared to shorter IPIs of 6–12 months (n=53,558, 13.6%) and <6 months (n=29,050, 7.4%) and longer IPIs of 24–60 months (n=137,719, 35.0%) and ≥60 months (n=64,490, 16.4%).

Maternal characteristics associated with inadequate PWG were black race, low education level, limited prenatal care, tobacco use, and prior preterm birth, as shown in Table 1. These characteristics were also associated with short IPI (not shown). Women with a normal BMI were more likely to have characteristics of non-black race, higher education level, less Women, Infants, and Children (WIC) use, and more private insurance compared to underweight, overweight, or obese women, Table 1.

Preterm birth <37 weeks GA complicated 10.1% of all singleton non-anomalous live births in the study cohort, with 1.5% of births occurring at <32 weeks and 0.7% at 20–28 weeks. Analyzing the exposures independently, low pre-pregnancy BMI, short IPI, and inadequate PWG were all associated with increased frequency of preterm birth. Looking specifically at pre-pregnancy BMI, the preterm birth rate in the normal BMI group was 9.8% and in overweight women was 9.6%, $p=0.032$. Preterm birth occurred more frequently in underweight women (15.1%) and obese women (10.2%) compared to women with a normal BMI ($p<0.001$ for both comparisons), Fig. 1a.

The lowest preterm birth rate (8.8%) was observed following IPI of 12–24 months compared to births following inadequate IPI of 6–12 months (10.4%) and <6 months (13.0%) and longer IPIs of 24–60 months (9.4%) and ≥60 months (12.1%), $p<0.001$ for each comparison, Fig. 1b.

Overall, inadequate PWG was associated with the highest preterm birth rate of 13.2% ($p<0.001$ compared to recommended weight gain) with recommended and excessive PWG associated with similar rates of preterm birth (9.2 and

Table 1 Maternal characteristics by IOM recommended pregnancy weight gain categories and pre-pregnancy body mass index

	Pregnancy weight gain compared to IOM recommendations			Pre-pregnancy body mass index			
	Under	Met	Over	Underweight	Normal	Overweight	Obese
	N=74,133	N=126,134	N=193,174	N=16,557	N=184,801	N=97,823	N=94,260
Demographic factors							
Age (years)	28.1 (5.7)	28.7 (5.5)	28.8 (5.4)	26.7 (5.4)	28.7 (5.5)	28.7 (5.5)	28.7 (5.4)
Race							
Caucasian	74.4 % (55,417)	81.8 % (103,178)	79.6 % (152,416)	81.8 % (13,601)	82.2 % (152,550)	77.2 % (75,851)	75.6 % (71,261)
Black	18.7 % (13,919)	13.6 % (17,523)	16.0 % (30,599)	12.5 % (2072)	12.3 % (22,788)	17.6 % (17,281)	21.0 % (19,795)
Hispanic	5.6 % (3387)	3.9 % (4359)	4.1 % (7792)	2.8 % (473)	3.8 % (7122)	4.3 % (4174)	3.0 % (2828)
Socioeconomic factors							
Married	59.3 % (44,187)	65.5 % (84,607)	65.2 % (124,815)	53.6 % (8909)	66.9 % (124,129)	64.0 % (62,908)	60.9 % (57,663)
≤HS education	50.3 % (37,438)	40.6 % (52,435)	40.6 % (77,846)	54.7 % (9101)	39.0 % (72,442)	42.9 % (42,100)	46.6 % (44,076)
Insurance							
Medicaid	42.0 % (31,263)	35.6 % (45,972)	36.1 % (69,199)	49.2 % (8177)	33.1 % (61,371)	36.6 % (35,918)	43.3 % (40,968)
Private	42.0 % (31,265)	51.3 % (66,264)	50.9 % (97,404)	36.7 % (6106)	53.0 % (98,412)	49.3 % (48,462)	44.3 % (41,953)
WIC use	44.9 % (33,404)	37.8 % (48,771)	39.3 % (75,255)	47.7 % (7937)	34.0 % (63,105)	40.2 % (39,478)	49.6 % (46,910)
Tobacco use	28.2 % (21,032)	25.7 % (33,148)	23.8 % (45,653)	41.0 % (6823)	24.5 % (45,470)	24.3 % (23,811)	25.1 % (23,729)
Prenatal care							
Limited (≤5 visits)	12.3 % (9178)	7.6 % (9758)	7.5 % (14,457)	12.0 % (1997)	8.6 % (16,006)	8.3 % (8169)	7.6 % (7221)
Pregnancy characteristics							
Parity	3.0 (1.5)	3.0 (1.5)	2.8 (1.3)	2.8 (1.2)	2.8 (1.2)	2.9 (1.4)	2.9 (1.4)
Prior preterm birth	6.3 % (4653)	5.4 % (6971)	5.2 % (10,007)	7.9 % (1311)	5.3 % (9862)	5.3 % (5176)	5.6 % (5282)
Gestational HTN	2.2 % (1667)	2.7 % (3418)	3.8 % (7255)	1.1 % (190)	1.7 % (3159)	3.4 % (3345)	6.0 % (5646)
Gestational DM	6.6 % (4920)	4.5 % (5831)	5.7 % (10,836)	2.2 % (357)	3.0 % (5609)	5.8 % (5668)	10.5 % (9953)
Route of delivery							
Vaginal	74.9 % (55,821)	72.9 % (94,177)	69.1 % (132,430)	79.9 % (13,298)	76.8 % (142,703)	70.5 % (69,347)	60.2 % (57,080)
Cesarean	25.0 % (18,643)	27.1 % (34,960)	30.9 % (59,115)	20.1 % (3330)	23.2 % (42,915)	29.5 % (28,891)	39.8 % (37,582)
Interpregnancy interval							
<6 months	9.2 % (6811)	6.3 % (7896)	7.4 % (14,343)	7.2 % (1187)	6.6 % (12,115)	7.9 % (7702)	8.5 % (8046)
6–12 months	14.9 % (11,066)	12.9 % (16,216)	13.6 % (26,276)	15.0 % (2477)	13.9 % (25,659)	13.5 % (13,207)	13.0 % (12,215)
12–24 months	27.2 % (20,150)	27.9 % (35,239)	27.6 % (53,235)	31.0 % (5128)	29.5 % (54,582)	26.6 % (25,969)	24.3 % (22,945)
24–60 months	33.4 % (24,751)	36.1 % (45,585)	34.5 % (67,383)	34.4 % (5695)	35.4 % (65,381)	34.7 % (33,982)	34.7 % (32,661)
≥60 months	15.3 % (11,355)	16.8 % (21,198)	16.5 % (31,937)	12.5 % (2070)	14.6 % (27,064)	17.3 % (16,963)	19.5 % (18,393)

Comparisons between each maternal characteristic listed in the first column and the weight gain and body mass index groups were statistically significant at p value <0.006. Dichotomous variables are presented as percent (n) for corresponding group. Continuous variables are presented as mean (standard deviation)

IOM Institute of Medicine, *HS* high school, *WIC* Special Supplement Program for Women Infants and Children, *HTN* hypertension, *DM* diabetes mellitus

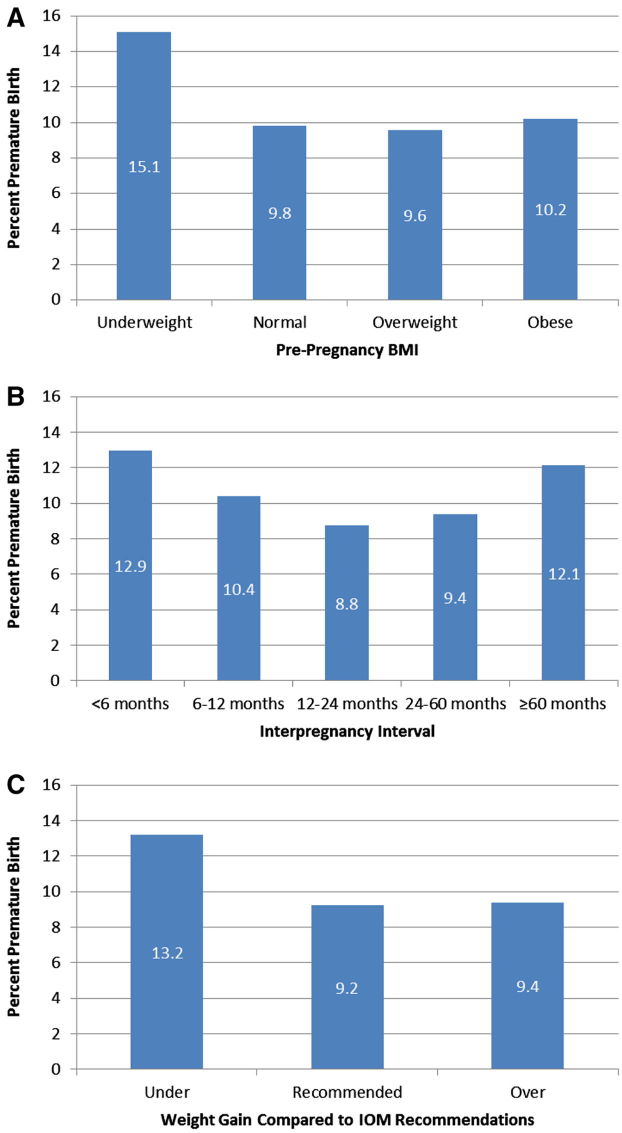

Fig. 1 Frequency of premature birth with individual risk factors. Frequency of premature birth (%) based on individual characteristics of pre-pregnancy BMI (**a**), interpregnancy interval (**b**), and pregnancy weight gain (**c**)

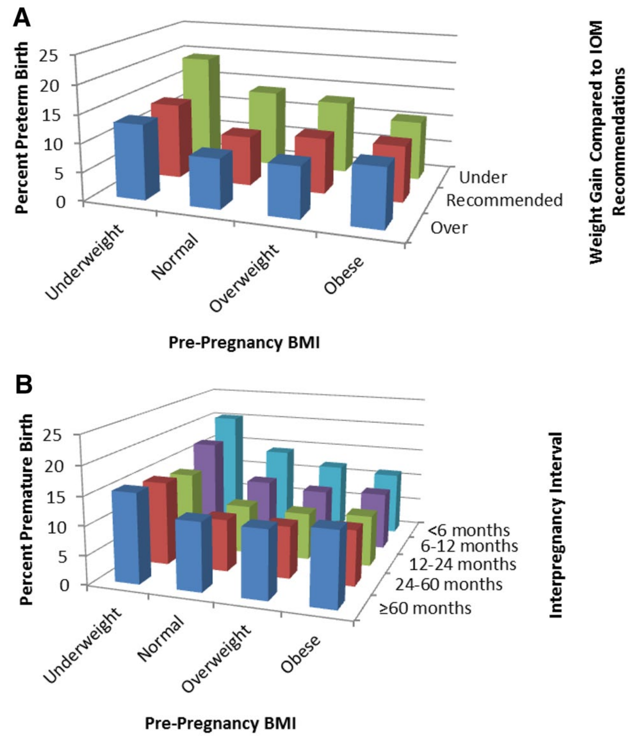

Fig. 2 Frequency of premature birth stratified by pre-pregnancy BMI. Frequency of preterm birth (%) stratified by pre-pregnancy BMI with pregnancy weight gain (**a**) or interpregnancy interval (**b**)

9.3 %, respectively), Fig. 1b. Inadequate PWG was associated with an increased rate of preterm birth in all BMI categories, with the largest relationship seen in women with lowest pre-pregnancy BMI, Fig. 2a ($p<0.001$ for underweight, normal, and overweight women with $p=0.024$ for obese women).

For underweight women, with the highest baseline risk of preterm birth (15.1 %), both short IPI and inadequate weight gain were associated with an increased rate of preterm birth. The highest rate of preterm birth of 25.2 % occurred when underweight women conceived following a short IPI <6 months and had inadequate PWG ($p<0.001$ for comparison between inadequate PWG and recommended PWG in each IPI category for this BMI class), Fig. 3a. Inadequate PWG was associated with a PTB rate of 16.7 % even in women with normal IPI ($p<0.001$) for underweight women. Short IPI of <6 months even with recommended PWG was associated with a PTB rate of 17.2 % for underweight women.

Similarly, for normal weight women, the rate of preterm birth was greater in women with inadequate PWG and short and long IPIs, Fig. 3b. The trends are similar to underweight women, though the risk of PTB is not as significantly increased. In overweight women, trends continued to be similar to normal weight and underweight women, Fig. 3c. The results for obese women show no statistical difference in preterm birth rate by PWG within any of the IPI categories, Fig. 3d. However, even in obese women, the rate of preterm birth is higher in women with the shortest IPI <6 months and longest IPI ≥60 months, $p<0.001$, compared to reference IPI.

Overall, only 6.1 % of women (n = 24,006) had a "referent" pregnancy defined as normal pre-pregnancy BMI, IPI 12–24 months, and recommended IOM PWG. In these women, the rate of preterm birth was 7.6 %, the lowest of any group. Table 2 shows the odds ratios (95 % confidence intervals) for preterm birth associated with IPI and PWG with adjustment for maternal age, race, and smoking status. The odds of preterm birth were increased for all underweight and overweight/obese women, compared to women

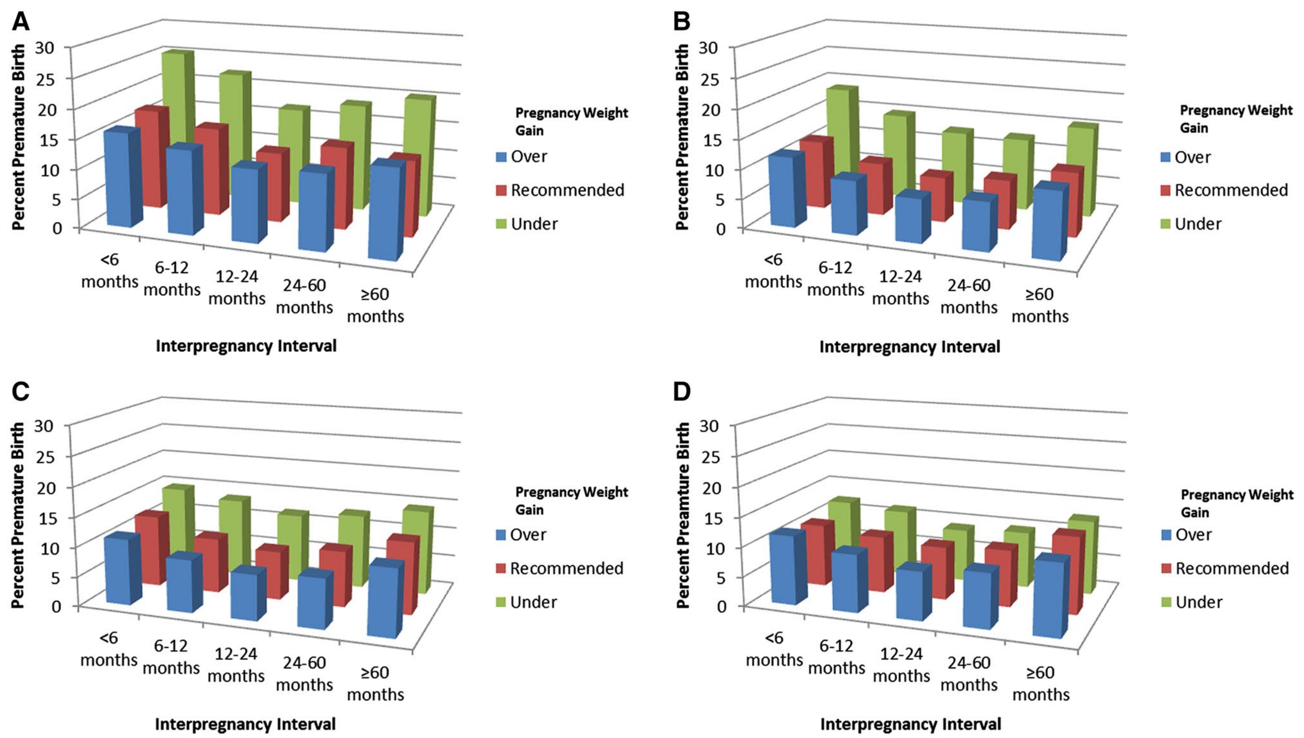

Fig. 3 Frequency of premature birth in individual BMI categories. Frequency of preterm birth (%) in each pre-pregnancy BMI category [underweight (**a**), normal (**b**), overweight (**c**), and obese (**d**)] based on the combined influence of pregnancy weight gain and interpregnancy interval

with normal BMI. The most robust risk increase attributed to BMI alone was 47 % and occurred in underweight women (95 % CI 1.24, 1.75), even after adjustment for important coexistent risk factors for preterm birth. Inadequate PWG showed an increased risk for PTB within each BMI category. Even with ideal IPI there was 1.08 fold increased odds of preterm birth (95 % CI 1.13, 1.27) for obese women and up to a 2.22 fold increased odds (95 % CI 1.92, 2.56) for underweight women. Short IPI <6 months similarly increased the odds of PTB within each BMI category even with ideal PWG with risk increase ranging from 1.37 fold (95 % CI 1.17, 1.61) for obese women to 2.16 fold (95 % CI 1.53, 3.06) for underweight women. With the combined influence of both inadequate PWG and short IPI <6 months, the odds of PTB was robustly increased for normal weight women at 2.30 fold (95 % CI 2.09, 2.53) and underweight women 3.44 fold (95 % CI 2.80, 4.23). Analysis of interaction terms found a significant interaction between excess PWG and short IPI in women with obese BMI ($p=0.045$). All other tests for interaction between each of the PWG categories and IPI categories were not statistically significant in any BMI category (p values >0.05).

Table 3 demonstrates the population attributable fraction of each pregnancy risk factor on preterm birth for the study cohort. The fraction of preterm births observed in this cohort attributed to short IPI is 5.90 % and long IPI is 8.32 % while the fraction of preterm births attributed to inadequate PWG is 7.45 %. A further 2.2 % of the preterm births are explained by underweight BMI (Table 3). Combined, almost one quarter of the preterm births in this cohort exhibit these potentially modifiable risk factors.

Discussion

Potentially modifiable risk factors for preterm birth are pervasive, with >90 % of women in this study demonstrating at least one such factor. Fewer than half of women in Ohio (47 %) begin pregnancy with a normal weight, and even fewer women (32 %) achieve the IOM targeted PWG for their BMI category. Low pre-pregnancy BMI, short IPI, and inadequate PWG were all robustly related to the frequency of preterm birth. These risk factors combined contribute to nearly 25 % of the preterm births in this cohort (though the coexistent risk factors may cause this to be an overestimate). Additionally, smoking and race do not significantly alter the adjusted odds for preterm birth in women with low BMI or inadequate PWG.

Strengths of the study arise from a large population based data set that is generalizable to a wide population. The three risk factors addressed in this study are potentially modifiable and offer health care providers important opportunities to reduce the rate of preterm birth. Because pre-pregnancy BMI and IPI are factors determined prior to pregnancy,

Table 2 Odds ratio with 95% confidence interval by risk factor

PWG[a] and IPI category	Body mass index			
	Obese	Overweight	Normal	Underweight
Normal weight gain				
No. (%)	4575 (3.8)	5296 (4.5)	24,006 (20.2)	1362 (1.1)
Preterm birth, No. (%)	374 (8.2)	435 (8.2)	1832 (7.6)	161 (11.8)
OR (95% CI)	1.08 (0.96–1.21)	1.08 (0.97–1.21)	1	1.62 (1.37–1.93)
Adjusted[b] OR (95% CI)	1.01 (0.90–1.14)	1.04 (0.93–1.16)	–	1.47 (1.24–1.75)
Short IPI (<6 months), No. (%)	1608 (1.4)	1854 (1.6)	4201 (3.5)	233 (0.2)
Preterm birth, No. (%)	189 (11.7)	226 (12.2)	493 (11.7)	40 (17.2)
OR (95% CI)	1.61 (1.37–1.89)	1.68 (1.45–1.95)	1.61 (1.45–1.79)	2.51 (1.79–3.54)
Adjusted[b] OR (95% CI)	1.37 (1.17–1.61))	1.44 (1.25–1.67)	1.42 (1.27–1.58)	2.16 (1.53–3.06)
Inadequate weight gain				
No. (%)	4512 (3.8)	3015 (2.5)	11,082 (9.3)	1541 (1.3)
Preterm birth, No. (%)	407 (9.0)	351 (11.6)	1389 (12.5)	257 (16.7)
OR (95% CI)	1.20 (1.07–1.34)	1.59 (1.41–1.80)	1.73 (1.61–1.87)	2.42 (2.10–2.79)
Adjusted[b] OR (95% CI)	1.08 (0.97–1.21)	1.43 (1.27–1.61)	1.65 (1.53–1.77)	2.22 (1.92–2.56)
Short IPI (<6 months), No. (%)	1463 (1.2)	1105 (0.9)	3719 (3.0)	523 (0.4)
Preterm birth, No. (%)	178 (12.2)	161 (14.6)	694 (18.7)	132 (25.2)
OR (95% CI)	1.68 (1.42–1.98)	2.06 (1.73–2.46)	2.78 (2.52–3.05)	4.09 (3.34–5.01)
Adjusted[b] OR (95% CI)	1.38 (1.17–1.63)	1.69 (1.41–2.01)	2.30 (2.09–2.53)	3.44 (2.80–4.23)
Excess weight gain				
No. (%)	56,911 (14.4)	65,963 (16.8)	63,275 (16.1)	7025 (1.8)
Preterm birth, No. (%)	5811 (10.2)	5871 (8.9)	5507 (8.7)	925 (13.2)
OR (95% CI)	1.38 (1.30–1.45)	1.18 (1.12–1.25)	1.15 (1.09–1.22)	1.84 (1.69-2.00)
Adjusted[b] OR (95% CI)	1.24 (1.10–1.38)	1.06 (0.94–1.18)	1.10 (1.05–1.15)	1.69 (1.39–1.99)
Short IPI (<6 months), No. (%)	4975 (1.3)	4743 (1.2)	4194 (1.1)	431 (0.1)
Preterm birth, No. (%)	530 (10.7)	529 (11.2)	502 (12.0)	69 (16.0)
OR (95% CI)	1.44 (1.30–1.60)	1.52 (1.37–1.68)	1.65 (1.48–1.82)	2.31 (1.78-3.00)
Adjusted[b] OR (95% CI)	1.18 (0.96–1.40)	1.37 (1.22–1.52)	1.48 (1.27–1.69)	2.12 (1.89–2.35)

No number, *IPI* interpregnancy interval, *PWG* pregnancy weight gain

[a]Pregnancy weight gain is per IOM recommendations based on BMI category

[b]Adjusted for maternal age, smoking, and race

efforts to educate primary care providers on the importance of preconception health become particularly important. This study is unique in the combined analysis of these three risk factors—low pre-pregnancy BMI, inadequate PWG, and short IPI—on preterm birth risk. In this large population-based cohort study, we found the highest rate of preterm birth recorded in women with low pre-pregnancy BMI, inadequate weight gain, and with short IPI, perhaps implicating nutritional depletion in these cases of preterm birth.

Any study based on vital statistics data, such as birth certificates, has limitations that must be considered. Birth certificates are not designed for research and their use in such context must take that into consideration. Data accuracy is known to vary (Reichman and Hade 2001; Reichman and Schwartz-Soicher 2007); measures such as birth weight, demographic characteristics, and method of delivery are more accurately reported, while others, such as prenatal care and alcohol/tobacco use may be less reliable (Reichman and Hade 2001; Reichman and Schwartz-Soicher 2007). Missing data is a possible concern, but our study cohort demonstrates very little missing data, particularly regarding the outcomes and covariates studied. Also, information provided in the birth certificates does not allow determination of the cause(s) of preterm birth. Thus, our generation of hypotheses to explain these effects is limited. However, approximately two-thirds or more preterm births are spontaneous, and the risk factors discussed are typically associated with spontaneous preterm birth. PWG was categorized using IOM recommendations established midway through the study period, therefore differences in counseling over the study could have influenced the weight gain trends, although this would not likely affect the association between weight gain and preterm birth observed in our analysis. Demographic and pregnancy differences between

Table 3 Population attributable fraction

	Exposed	Prevalence	Exposed case[a]	Risk exposed	Non-exposed	Non-exposed case[a]	Risk non-exposed	Relative risk	PAF (%)
<6 months IPI	29,050	0.0738	3761	0.1295	364,391	35,820	0.0983	1.478	**3.41**
6–12 months IPI	53,588	0.1362	5575	0.1040	339,853	34,006	0.1001	1.188	**2.49**
12–24 months IPI	108,624	0.2761	9515	0.0876	284,817	30,066	0.1056	1.000	0.00
24–60 months IPI	137,719	0.3500	12,904	0.0937	255,722	26,677	0.1043	1.070	**2.38**
≥60 months IPI	64,490	0.1639	7826	0.1214	328,951	31,755	0.0965	1.385	**5.94**
Underweight BMI	16,557	0.0421	2496	0.1508	376,884	37,085	0.0984	1.536	**2.20**
Normal BMI	184,801	0.4697	18,140	0.0982	208,640	21,441	0.1028	1.000	0.00
Overweight BMI	97,823	0.2486	9351	0.0956	295,618	30,230	0.1023	0.974	−0.65
Obese BMI	94,260	0.2396	9595	0.1018	299,181	29,986	0.1002	1.037	0.88
Inadequate PWG	74,133	0.1884	9785	0.1320	319,308	29,796	0.0933	1.427	**7.45**
Normal PWG	126,134	0.3206	11,664	0.0925	267,307	27,917	0.1044	1.000	0.00
Excess PWG	193,174	0.4910	18,114	0.0938	200,267	21,467	0.1072	1.014	0.68
Smoking	98,482	0.2503	12,567	0.1276	294,959	27,014	0.0916	1.393	**8.96**
Black	62,780	0.1596	9890	0.1575	330,654	29,691	0.0898	1.754	**10.74**

Bold font indicates significant PAF

IPI interpregnancy interval, *BMI* body mass index, *PWG* pregnancy weight gain, *PAF* population attributable fraction

[a]Case: defined as preterm birth at <37 weeks gestational age

births in Ohio compared to elsewhere in the US could also limit generalizability of this study's findings.

Poor maternal nutritional status may influence gestational length and can be influenced by all three of the variables discussed. An adequate supply of maternal nutrients is necessary for continuation of pregnancy otherwise the balance between maternal and fetal needs is disturbed which may lead to preterm birth. This has been proposed as an etiology of preterm birth in women with short IPIs (King 2003). It follows that with underweight BMI or inadequate weight gain during pregnancy also reflect poor maternal nutritional status. Relative deficiencies of micronutrients such as folic acid and iron may exacerbate this effect in the case of short IPI as these micronutrients are depleted during pregnancy and breastfeeding. The protective interaction we see of obese BMI with short IPI further supports a nutritional/metabolic stress contribution arising from inadequate time between pregnancies (Winkvist et al. 1992; King 2003).

Conclusions

The majority of pregnant women in this population-based statewide cohort had one or more modifiable risk factors for adverse pregnancy outcomes. Inadequate PWG, short IPI, and low pre-pregnancy BMI all are associated with an increased risk of preterm birth. And importantly, all three factors assessed in this study-pre-pregnancy BMI, PWG, and IPI-are all risk factors that can be modified either prior to or during pregnancy. Targeting short IPI with appropriate contraception counseling is a common practice of obstetric care providers in attempt to modify this important risk factor. However, on a population basis, inadequate PWG is seen much more commonly than short IPI and is the only risk factor that remains modifiable once a women presents for obstetrical care while pregnant. Attention should be paid to educational interventions to ensure adequate nutrition and weight gain during pregnancy. Improvements in these modifiable risk factors could have significant influence of birth timing and infant mortality worldwide.

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Compliance with Ethical Standards

Conflict of Interest The authors report no conflict of interest.

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