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Maternal weight change before pregnancy in relation with birthweight and risks of adverse pregnancy outcomes

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Short title: Maternal weight change related to birthweight

Abstract

Maternal weight change before pregnancy can be considered an indicator of maternal energy balance and nutritional status before conception, and may be involved in early life programming. We aimed to investigate the association of maternal Weight Change Before Pregnancy (WCBP) with fetal growth and adverse pregnancy outcomes. Data are from the French EDEN mother-child cohort of 1756 mother-child pairs; information on mother's weight at 20 years, weight just before pregnancy, fetal anthropometry at second and third trimesters, infant's birthweight and pregnancy complications were recorded. The average annual WCBP between 20 years and start of pregnancy (in kg/year) was categorized as: "Weight Loss" (n=320), "Moderate weight gain" (n=721) and "High weight gain" (n=715). The associations of WCBP with fetal and newborn characteristics and with adverse pregnancy outcomes were analyzed, adjusting for maternal and pregnancy characteristics, including the mother's prepregnancy BMI. Interactions between WCBP and prepregnancy BMI were tested. Birthweight and estimated fetal weight in the third trimester increased significantly with increasing WCBP in mothers with BMI <25kg/m². In these mothers, weight loss before pregnancy was associated with a higher risk of newborns small for gestational age (SGA). Whatever the prepregnancy BMI, WCBP was positively associated with a maternal risk of gestational diabetes and hypertension. The ponderal history of mothers before pregnancy can impact on fetal growth and on pregnancy outcomes such as gestational diabetes or hypertension. Our analysis is the first to report that in non-overweight women, those who lost weight before pregnancy are at higher risk of having SGA newborns.

Keywords: Weight change, birthweight, adverse pregnancy outcomes

Introduction

Many studies have examined maternal prepregnancy BMI in relation with birthweight [1-5] and other pregnancy outcomes such as anaemia, gestational diabetes, pre-eclampsia, caesarean section [6, 7]. In animals and humans, some studies suggest that maternal ponderal history before pregnancy could also be associated with birthweight and pregnancy outcomes, independently of attained BMI [8, 9]. Indeed, maternal weight change before pregnancy can be considered as an indicator of maternal energy balance and nutritional status before conception. Women may start pregnancy at a similar BMI, but be on a weight gain or a weight loss dynamic, or in a phase of weight stability. Studying whether weight change before pregnancy influences pregnancy outcomes independently of prepregnancy BMI will help in understanding the close relationship between maternal nutritional status and fetal growth. Hedderson et al. [10] and Rudra et al. [11] reported that US women who gained more weight in the 5 years before pregnancy or after the age of 18 years, had an increased risk of gestational diabetes mellitus, independently of their BMI before pregnancy. Villamor and Cnattingius documented that Swedish women who gained more weight between two consecutive pregnancies had increased risks for gestational hypertension, gestational diabetes and a stillbirth in the second pregnancy, after adjustment for BMI before the first pregnancy, even in non overweight women in both pregnancies [9]. None of these studies investigated the association between weight change before pregnancy and fetal growth or birthweight. There is evidence of an association between birthweight and the risk of chronic diseases in adulthood, such as diabetes and cardiovascular disease [12]. A relation between a mother's weight change before pregnancy and fetal growth would suggest that maternal weight dynamics before pregnancy could be involved in the mechanisms of adult health programming through fetal growth.

The aim of this study was to investigate the association of maternal weight change between age 20 years and pregnancy, with fetal growth and adverse pregnancy outcomes, while taking into account maternal BMI just before pregnancy.

Subjects and methods

Participants

Data were collected for mother-child pairs enrolled in the ongoing EDEN cohort (study of pre- and early postnatal determinants of child development and health), from University Hospitals in Nancy and Poitiers, France [13]. The primary aim of the EDEN cohort is the study of prenatal and early postnatal nutritional, environmental, and social determinants of the child's development and health [14]. Women attending their first prenatal visit before 24 weeks of gestation at the two maternity departments were invited to participate in this study. Enrolment in the study started in February and September 2003 respectively, in Poitiers and Nancy, and lasted 27 months in each centre. Exclusion criteria were: twin or multiple pregnancies, known diabetes before pregnancy, plans to move outside the region in the next three years, French illiteracy. Among eligible women 55% (2002 women) accepted to participate (1 034 women in Nancy and 968 in Poitiers). They are being followed, along with their offspring, for five years.

Written consent was obtained for the mother at the study entry and for her offspring after delivery. The EDEN study has been approved by the ethics committee (Comité Consultatif pour la Protection des personnes dans la Recherche Biomédicale) of Kremlin Bicêtre Hospital, and the Commission Nationale de l'Informatique et des Libertés (CNIL).

Study design

The mothers' weight at age 20 years, weight before pregnancy and educational level were obtained by interview at inclusion. At 24-28 weeks of amenorrhea, women answered a self-administered questionnaire and had a first clinical examination performed by midwife research assistants. Maternal height was measured with a wall Seca 2006 stadiometer (Hamburg, Germany) to the nearest 0.2 cm. After a 5-minutes rest, three measures of systolic

blood pressure (SBP) were performed at two minute intervals with an Omron M4I device (Omron Healthcare Europe, Hoofddorp, The Netherlands). Women came to the examination fasting and received a 50g glucose load. Glucose was measured before and one hour after the glucose challenge. Measures of fetal anthropometry (head circumference (HC), abdominal circumference (AC), biparietal diameter (BD), femoral length (FL)) were obtained by ultrasound at about 22 weeks, and at about 32 weeks of amenorrhea.

At delivery, neonates were weighed using electronic Seca scales (Hamburg, Germany: Seca 737 in Nancy and Seca 335 in Poitiers). On average two days after delivery, a second clinical examination was performed by the same research assistants; the mother's weight was measured using an electronic Terraillon SL 351 (Hanson Ltd,UK) to the nearest 0.1kg.

Additional data were extracted from the maternity clinical records: clinical diagnosis of gestational diabetes, gestational hypertension, parity, and also for gestational diabetes and gestational hypertension in previous pregnancies for multiparous women. Data on the mother's health prior to the current pregnancy were also collected by questionnaire at 24-28 weeks of amenorrhea. Data on cigarette smoking during the third trimester of gestation were obtained by questionnaire in the post partum period.

The average annual weight change before pregnancy (WCBP in kg/year) was defined as the difference between the weight reported just before pregnancy and the weight at 20 years, divided by the time difference (number of years). WCBP was then categorized into three groups as "Weight Loss" (<0.0 kg/year, n=320), and two categories of Weight Gain Before Pregnancy (WGBP), separated by the median ("Moderate WGBP"=0.0-0.55 kg/year, n=721 and "High WGBP" > 0.55 kg/year, n=715). Pregnancy weight gain was calculated as measured weight after delivery minus reported weight at inclusion. Prepregnancy Body Mass Index (BMI) was reported as weight (kg) divided by measured height (m) squared. Systolic blood pressure was calculated as the mean of three measures of SBP at 24-28 weeks of

gestation. Women were considered as having a history of severe health disorder directly or indirectly associated with weight change when they had either cancer or diagnosed anaemia before pregnancy. Smoking status in pregnancy was defined as a binary variable (whether or not women smoked in the third trimester) and smoking habit was defined as the average daily number of cigarettes smoked during pregnancy.

Large for gestational age (LGA) and small for gestational age (SGA) were defined respectively as birthweight over the 90^{th} percentile and below the 10^{th} percentile of French gestational age and gender specific reference curves [15]. Preterm delivery was defined as gestational age by < 37 completed weeks. We estimated fetal weight (EFW) during the second and third trimester of gestation, for women who had ultrasound scans at 20-25 and 30-35 weeks (n=1645), using the Hadlock formula:

$\log_{10}EFW=1.3596\ (0.00386*AC*LF)+(0.0064*HC)+(0.00061*BD*AC)+(0.0424*AC)+(0.174*LF)$ [16].

Where AC represents abdominal circumference, FL is femoral length, HC is head circumference and BD represents biparietal diameter.

Statistical analyses

For this analysis, we excluded women under 21 years of age at the beginning of pregnancy (n=80) and also those with a prepregnancy BMI > 40kg/m² (n=13), as there was little variability in WCBP in these women. In the remaining women, weight at 20 years, birthweight and prepregnancy BMI were missing for respectively 101 (5.3%), 28 (1.5 %) and 24 (1.3%) women, thus the analysis is based on 1756 women. Maternal characteristics, pregnancy characteristics, newborn characteristics and pregnancy outcomes are described according to WCBP categories. Associations were tested by analysis of variance for quantitative traits or by a χ^2 test for proportions, with trend tests across the three WCBP categories. Trend tests by linear or polytomic logistic regression analysis, compared maternal,

pregnancy, fetal and newborn and pregnancy outcome characteristics across the three WCBP categories.

We hypothesized that associations with WCBP could differ in normal vs overweight women before pregnancy. As there was an interaction between BMI before pregnancy and WCBP on birthweight, analyses were stratified on prepregnancy BMI < or ≥ 25kg/m^2. For risks of SGA and LGA there were not enough obese women (≥ 30kg/m^2) to constitute a separate category. The risks of SGA and LGA and the mean of birthweight and EFW were estimated after adjustment for recruitment centre, gestational age and newborn gender for birthweight only, smoking habits, maternal age, parity, educational level, pregnancy weight gain, prepregnancy BMI and height. Trend tests were used again. We also tested interactions between current age, parity, maternal smoking and WCBP, on fetal and newborn characteristics. We were not able to investigate potential interactions on gestational hypertension (one and three cases respectively in "Weight Loss" and "Moderate WGBP" categories in women with BMI ≥ 25kg/m²) nor on gestational diabetes (respectively two and five cases). However we tested the interactions between WCBP and prepregnancy BMI on quantitative 1h-blood glucose and SBP.

We also examined whether exclusion of (or adjustment for) gestational diabetes and/or gestational hypertension changed the relation between WCBP and mean birthweight.
We performed further investigations on the observed the link between WCBP and fetal growth or the risk of SGA and LGA. First, we excluded women with cancer before pregnancy (there was only a small number of cases) and additionally we adjusted for the mother's history of anaemia before pregnancy. In further sensivity analyses, we assessed risks of SGA in women with BMI <25kg/m² with "Weight Loss" category divided in two classes separated by the median and risks of LGA in women with BMI ≥25kg/m² with "High WGBP" in two categories. We also display the results after restricting the analysis to women with BMI

between 18.5 and 25kg/m². Finally, in multiparous women only, the relations between WCBP and both newborn characteristics and pregnancy complications, were investigated after adjusting for history of gestational diabetes and gestational hypertension.

All analyses used Statistical Analysis Software (SAS) version 9.

Results

Mothers with a moderate WGBP were older at pregnancy, had a lower weight at age 20 and a higher educational level (**Table 1**). BMI just before pregnancy was the same in the two lower categories of WCBP (21.3kg/m²). There was no apparent relation between WCBP and cancer prior to pregnancy. The proportion of women with anaemia before pregnancy was higher in those who had lost weight before pregnancy, but not significantly. In multiparous women, the proportion of women with a history of gestational hypertension tended to be higher in women with high WGBP but the relation was not significant, whereas a significant positive relation between WCBP and history of gestational diabetes was found. Smoking during pregnancy was more frequent in women who lost weight than in those who gained weight before pregnancy. There were 43% (n=758) primiparous mothers who accepted to participate in the EDEN study, 38% (n=660) with one previous delivery and 19% (n=334) with two or more deliveries. Multiparous women were slightly under-represented in the weight loss category (but there was no significant difference in parity between categories of WCBP, P=0.12).

Gestational age did not differ significantly according to categories of WCBP. Crude mean birthweight, and mean EFW at second and third trimesters increased significantly with WCBP categories. The percentage of SGA decreased (13.4% to 5.0%) and the percentage of LGA increased (4.4% to 10.9%) with WCBP.

The association between WCBP and mean birthweight changed according to prepregnancy BMI *(*P for interaction = 0.03, BMI as a continuous trait). As illustrated in Figure 1, in women with prepregnancy BMI below 25kg/m², mean birth weight increased with increasing WCBP, even after further adjustment for prepregnancy BMI within strata, whereas no association was observed in women with BMI over 25kg/m². As shown in Table 2, the same interaction was observed for the third trimester EFW (*P* = 0.06), and accordingly, the

adjusted odds ratios for SGA decreased across categories of WCBP in non-overweight women.

There was no significant interaction between current age, parity or maternal smoking and WCBP on fetal and newborn characteristics (P values for interactions for birthweight respectively= 0.72; 0.87; 0.34). Associations were not modified by the time-gap between age 20 years and pregnancy, parity and smoking status.

The observed relation between WCBP and birthweight remained consistent in the following sensitivity analyses: exclusion of mothers with cancer before pregnancy and adjusting for anaemia prior to pregnancy, exclusion of gestational diabetes and/or gestational hypertension (data not shown). When we excluded women with gestational diabetes and gestational hypertension from analyses and performed additional adjustment for 1hr-blood glucose and SBP at 6 months of pregnancy, adjusted mean birthweight increased from 3245±22g in "Weight Loss" category to 3337±20g in "High WGBP" category (P trend=0.006) in women with prepregnancy BMI < 25kg/m².

When we subdivided "Weight Loss" category in two classes by the median in women with BMI < 25kg/m² with "Moderate WGBP" as reference, higher risks of SGA were found in both "Weight Loss" classes (OR 1.72 CI 95% 0.93-3.19 in the lower category and OR 1.80 CI 95% 1.01-3.21 in the other category). When "High WGBP" category was divided in two classes in women with BMI ≥ 25kg/m² there was again no increase risk of LGA in the higher category of WCBP compared to the others. The results observed in women with normal BMI (18.5-25kg/m², exclusion of underweight women) were similar to those observed in all women with BMI<25kg/m² (data not shown).

The percentage of women with gestational diabetes increased from 2.5% in the lowest category of WCBP to 11% in the highest one and gestational hypertension from 2.2% to 7.3%. After adjustment for recruitment centre, maternal age, prepregnancy BMI, height,

educational level, parity, smoking habit at 3rd trimester of pregnancy and pregnancy weight gain, the positive association with gestational diabetes remained statistically significant with an OR of 1.9 (95%CI 1.1-3.3) in high compared to moderate WGBP women as well as gestational hypertension (*P* trend 0.006, **Figure 2**). No interaction was found between WCBP and BMI before pregnancy for blood glucose or SBP indicating that the relation between WCBP and gestational diabetes or hypertension was similar whether the mother is overweight or not at the beginning of pregnancy (results not shown).

Finally, in multiparous women only, adjusting for history of gestational diabetes and gestational hypertension did not change the results (results not shown).

Discussion

Our main finding is that in women who were not overweight, weight loss before pregnancy was associated with poor fetal growth and SGA. To investigate whether the increased risk of SGA in women who lost weight before pregnancy was due to extreme weight loss, we divided the "Weight Loss" group into two categories separated by the median and the risk of SGA was similar in the two categories and was lower in women who gained weight before pregnancy.

Weight loss before pregnancy in women with normal weight may have been due to diseases that could also have affected fetal growth. Indeed women in the "Weight Loss" category tended to have more anaemia prior to pregnancy, but the association was not significant. When women with cancer prior to pregnancy were removed from analysis while taking into account anaemia before pregnancy the results were unchanged. Non-overweight women who lost weight were heavier at 20 years than the others; most of them may have lost weight voluntarily or experienced a change in their lifestyle favoring weight loss.

Our results are consistent with animal models that suggest that weight loss due to nutritional restriction before pregnancy is associated with fetal growth retardation and low birthweight [17]. Rumball et al. found that ewes exposed to undernutrition before pregnancy had smaller fetuses [8]. Weight loss is multifactorial, and whatever its causes (nutritional and/or metabolic factors, psychological state) weight loss may impact on fetal growth.

BMI before pregnancy is positively associated with fetal growth and birthweight, heavier women giving birth to heavier babies [1]. The absence of an association between WCBP and birthweight in overweight women, suggests that whatever their weight dynamic before pregnancy, these women have sufficient nutrients availability for fetal development.

Our results confirm the previous findings on the influence of maternal weight change before pregnancy or between pregnancies, on risks for gestational diabetes and gestational

hypertension [9-11, 18-21]. Indeed, Hedderson et al. and Villamor et al. concluded that independently of prepregnancy BMI or BMI in the first pregnancy, women who gained more weight before pregnancy or between two consecutive pregnancies, had significantly higher risks of pre-eclampsia, gestational hypertension, gestational diabetes, stillbirths and large for gestational age infants [10, 18]. Weight change before pregnancy and weight change between successive pregnancies may not be comparable. Weight change before pregnancy may be the result of nutrition, physical activity, diseases and general standards of living while interpregnancy weight change includes, among other factors, post-partum weight retention. However, in our study, the results did not differ significantly according to parity, indicating that post-partum weight retention included in the WCBP of the multiparous women did not have a major impact on the relations we found. Besides, studies on interpregnancy weight change reported changes in a short span of time (1 to 2 years) whereas in our study WCBP could refer to changes over a far longer period, 9 to 10 years on average.

It has been previously shown that overweight women who lost weight before pregnancy had a reduced risk of gestational diabetes and gestational hypertension [9]. In our study, the risk of gestational diabetes and hypertension tended to be reduced in women who lost weight before pregnancy. The association was not statistically significant probably due to the power of the study which was only sufficient to detect the trends. Taking into account the history of gestational diabetes and gestational hypertension did not modify our findings. Our results indicate that weight loss before pregnancy could be recommended to overweight women, in order to reduce the risks of gestational diabetes and gestational hypertension, without increasing the risk of small for gestational age babies.

Our study is the first to report maternal ponderal history before pregnancy, in relation with birthweight and the risk of adverse pregnancy outcomes in France. Characteristics of women (including parity) who accepted to participate in the EDEN study could be compared

to those for women who were included in the French nationally representative perinatal survey in 2003 (year of the start of the EDEN study) [22]. Our study may lack power for stratified analyses and interaction tests, but the observed trends did not indicate that factors such as parity modified the results. However, a possible source of bias for the present analysis is that data on maternal prepregnancy weight and weight at 20 years are based on self-reports. It has been recognized that body weight is particularly underestimated among overweight women [23, 24]. However a recent validation study in women of reproductive age found that 84% of women were classified into appropriate BMI categories on the basis of self-reported weights and heights [25]. It is difficult to tell whether a misreporting bias could account for the lack of association in overweight women. Weight at 20 years may be difficult to recall but the age at start of pregnancy (time since age 20 years) did not influence the results. Recall bias is also possible if women who had experienced large weight changes recalled better or worse their weight at 20 years.

Conclusion

Our results suggest that the ponderal history of the mothers before pregnancy can impact on fetal growth and on pregnancy outcomes such as gestational diabetes or hypertension. Our analysis is the first to report that in non-overweight women, those who lost weight before pregnancy are at higher risk of SGA. This confirms that in humans, maternal weight dynamic before conception could play a role in the process of early-life programming.

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Figure legends

Figure 1: Mean birthweight according to categories of weight change before pregnancy by strata of prepregnancy body mass index (BMI), adjusted for centre, gestational age, newborn gender, smoking habit at 3rd trimester of pregnancy, age, parity, educational level, pregnancy weight gain, prepregnancy body mass index and height.

Categories of weight change before pregnancy were defined as: Weight Loss (< 0.0kg/year); Moderate WGBP (0.0-0.55 kg/year); High WGBP: (≥ 0.55kg/year).

Figure 2: Odds ratios for gestational diabetes and gestational hypertension according to weight change before pregnancy adjusted for centre, maternal age, prepregnancy body mass index, height, educational level, parity, smoking habit at 3rd trimester of pregnancy and pregnancy weight gain.

Categories of weight change before pregnancy were defined as: Weight Loss (< 0.0kg/year); Moderate WGBP (0.0-0.55 kg/year); High WGBP: (≥ 0.55kg/year).

Table 1: Maternal and newborn characteristics and pregnancy complications according to average weight change before pregnancy since the age of 20 years

		Weight Loss (< 0.0 kg/year) mean= -1.08	**Moderate WGBP** (0.0-0.55 kg/year) mean= 0.20	**High WGBP** (≥ 0.55kg/year) mean= 1.68	***P* trend**
N		320	721	715	
Maternal characteristics	n				
Age at inclusion (years)	1756	29.0 ± 4.5	30.3 ± 4.7	28.6 ± 4.4	<0.0001
Total weight change before pregnancy (kg)	1756	-5.4 ± 4.9	2.3 ± 2.2	11.7 ± 7.2	<0.0001
Weight before pregnancy (kg)	1756	56.8 ± 9.3	56.8 ± 7.8	69.1 ± 12.3	<0.0001
Weight at 20 years (kg)	1756	62.2 ± 12.0	54.5 ± 7.7	57.4 ± 9.0	<0.0001
Maternal height (cm)	1756	162.9 ± 5.9	163.3 ± 6.2	163.8 ± 6.3	0.03
Body mass index before pregnancy (kg/m²)	1756	21.3 ± 3.4	21.3 ± 2.7	25.7 ± 4.4	<0.0001
Overweight before pregnancy (body mass index ≥25 kg/m² % (n))	1756	11.6 (37)	8.5 (61)	48.9 (350)	<0.0001
Maternal educational level (% (n)) ‡	1734				0.01
1 (Before admission at university)		29 (94)	22 (159)	22 (225)	
2 (Admission at university)		20 (63)	14 (102)	22 (155)	
3 (at least 2 years after admission at university)		51 (163)	64 (460)	47 (335)	
Parity (% (n)) ‡	1754				0.12
0		48 (155)	42 (302)	43 (303)	
1		34 (110)	39 (283)	37 (267)	
≥ 2		17 (55)	19 (136)	20 (143)	

Cancer before pregnancy (% (n))	1755	0 (0)	1.0 (7)	0.7 (5)	0.38
Anaemia before pregnancy (% (n))	1756	17.5 (56)	15.4 (109)	14.6 (106)	0.26
Gestational diabetes for the previous pregnancy (% (n)) *	1198	2.4 (5)	3.0 (15)	7.5 (37)	0.0007
Gestational hypertension for the previous pregnancy (% (n)) *	1198	6.3 (13)	6.1 (30)	8.9 (44)	0.13
Pregnancy characteristics					
Pregnancy weight gain (kg)	1729	9.6 ± 4.8	9.3 ± 4.4	8.4 ± 5.8	0.002
Smoking during 3rd trimester (% (n))	1726	21.2 (67)	14.2 (100)	14.3 (101)	0.02
Number of cigarettes smoked, for smokers (mean ± sd))	268	7.9 ± 4.8	7.1 ± 4.4	7.5 ± 5.3	0.02
1hr-plasma glucose at 24-28 week gestation (mmol/l)	1699	6.2 ± 1.4	6.3 ± 1.4	6.6 ± 1.5	<0.0001
Systolic blood pressure at 24-28 weeks (mmHg)	1736	117 ± 12	118 ± 12	120 ± 13	<0.0001
Pregnancy complications					
Gestational diabetes (% (n))	1755	2.5 (8)	4.2 (30)	11 (76)	<0.0001
Gestational hypertension (% (n))	1755	2.2 (7)	3.3 (24)	7.3 (52)	<0.0001

m ± sd if not otherwise stated

‡ **Trends are tested with polytomic logistic regression**

* **multiparous women only**

Table 2: Fetal and newborn characteristics by categories of weight change before pregnancy, separately in non overweight and overweight women

	Weight Loss (< 0.0kg/year)		**Moderate WGBP** (0.0-0.55kg/year)		**High WGBP** (≥ 0.55kg/year)		***P* for interaction***	***P* trend**
Adjusted risk of small for gestational age‡								
	cases/n	OR (95% CI)	cases/n	OR (95% CI)	cases/n	OR (95% CI)		
Body mass index <25kg/m²	42/283	1.76 (1.10-2.81)	50/659	1	21/365	0.87 (0.47-1.59)	0.05	0.01
Body mass index ≥ 25kg/m²	1/37	NA	9/61	NA	15/350	NA		
Adjusted risk of large for gestational age‡								
Body mass index < 25kg/m²	13/283	0.77 (0.40-1.49)	44/659	1	32/365	1.13 (0.64-2.00)	0.66	0.32
Body mass index ≥25kg/m²	1/37	NA	7/61	NA	46/350	NA		
Adjusted Estimated fetal weight at Third-trimester (g)†								
	n	mean ± sem	n	mean ± sem	n	mean ± sem		
Body mass index < 25kg/m²	264	1955 ± 14.3	611	1989 ± 9.8	346	1992± 13.7	0.06	0.06
Body mass index ≥ 25kg/m²	37	2034 ± 44	54	2011 ± 37	333	2046 ± 15		0.63

Adjusted Estimated fetal weight at Second-trimester (g)†

Body mass index < 25kg/m²	268	522 ± 3.7	619	524 ± 2.4	343	525 ± 3.5	0.48	0.44
Body mass index ≥ 25kg/m²	35	535 ± 11.2	56	535 ± 8.7	325	535 ±3.6		0.79

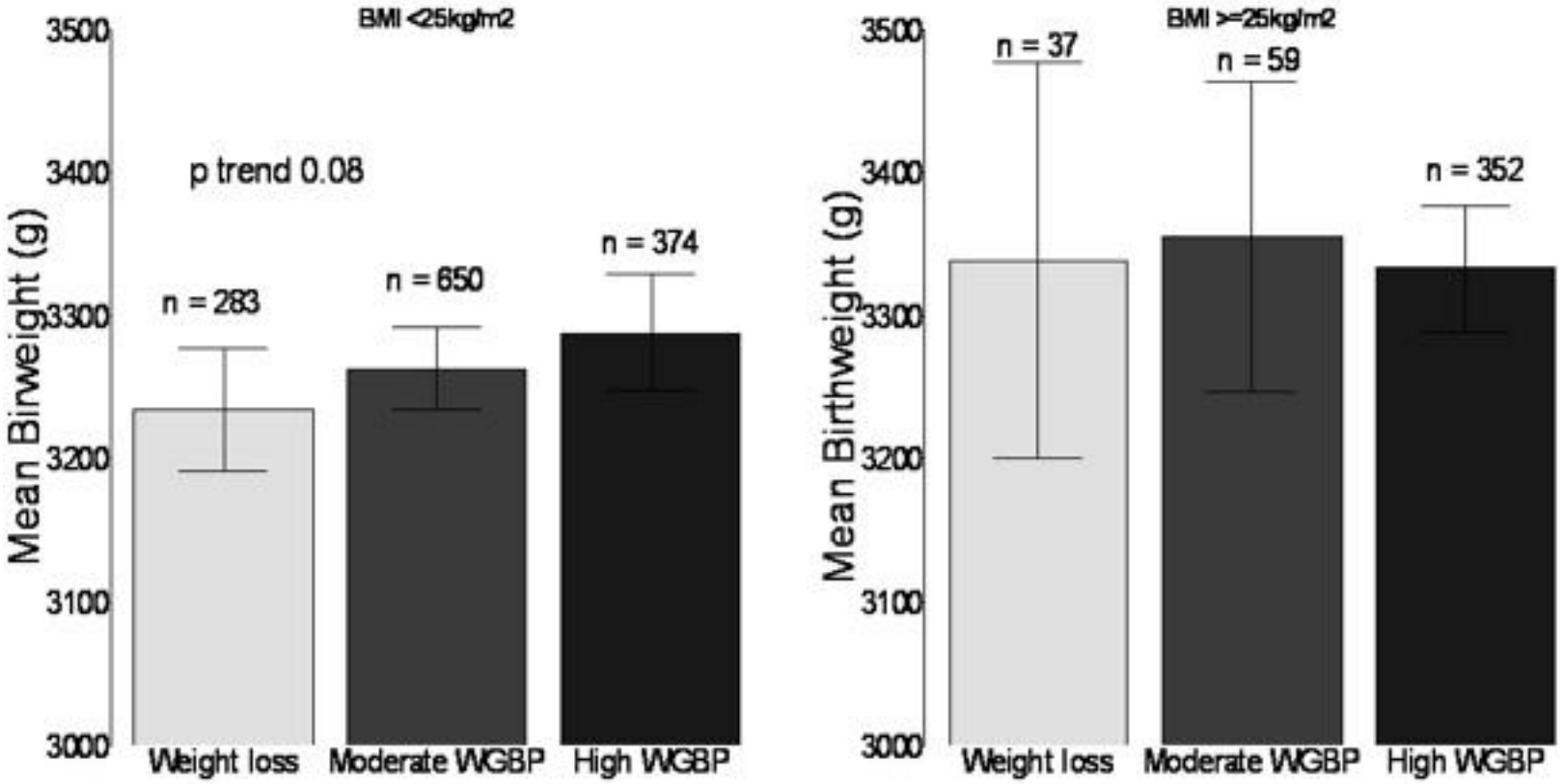
‡adjusted for centre, maternal age, prepregnancy body mass index, height, educational level, parity, smoking habit at 3rd trimester of pregnancy and pregnancy weight gain.

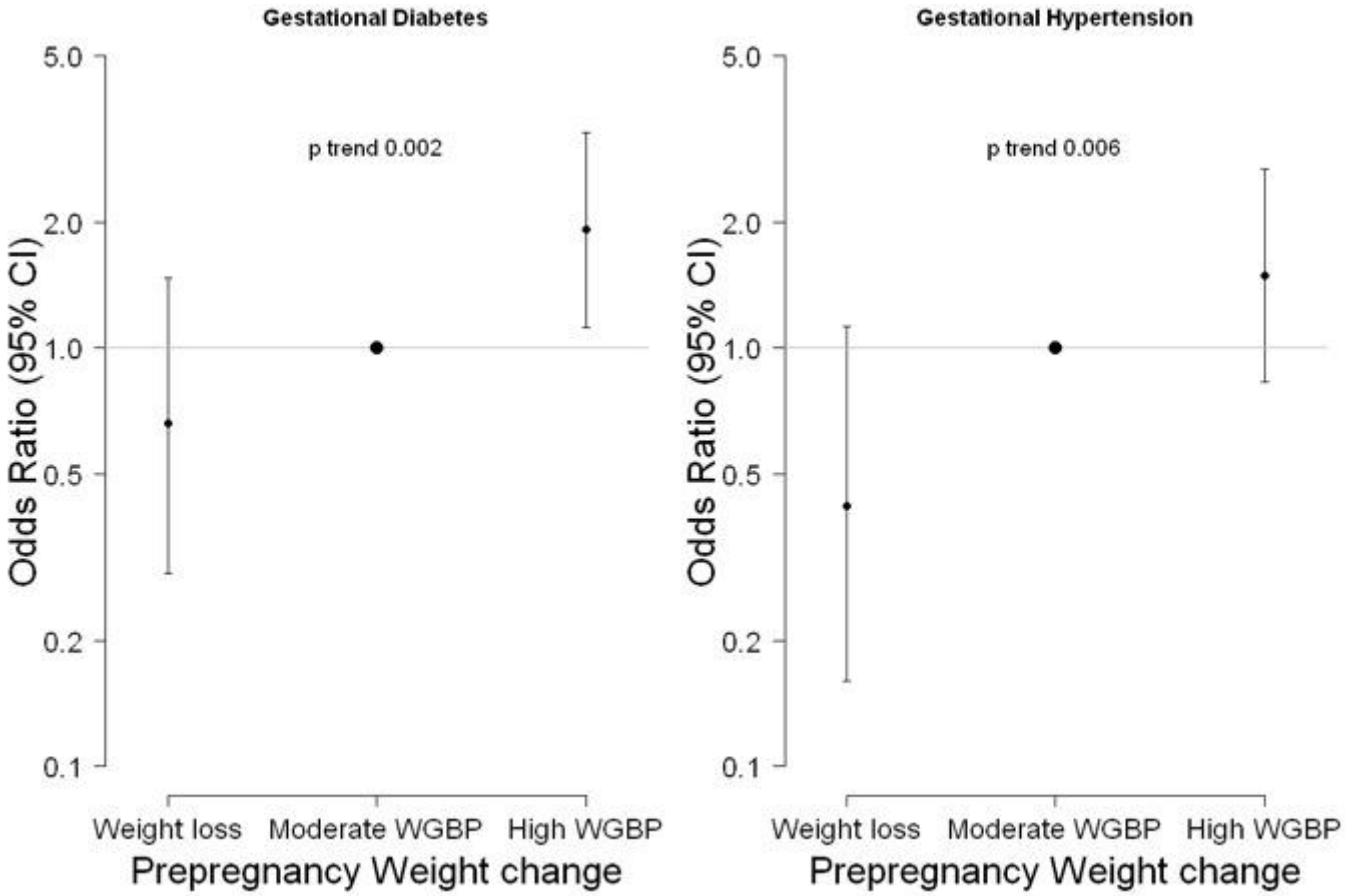
†Estimated fetal weight adjusted for centre, gestational age at ultrasound, newborn gender, women smoking habits, maternal age, parity, educational level, pregnancy weight gain, prepregnancy body mass index and height

sem= Standard Error of the Mean

NA= Not able to be calculated because of low event rate

***interaction between weight change before pregnancy and body mass index (as a continuous variable)**


BMI <25kg/m2
p trend 0.08
n = 283
n = 650
n = 374
Mean Birweight (g)
3500
3400
3300
3200
3100
3000
Weight loss
Moderate WGBP
High WGBP
BMI >=25kg/m2
n = 37
n = 59
n = 352
Mean Birthweight (g)
3500
3400
3300
3200
3100
3000
Weight loss
Moderate WGBP
High WGBP


Gestational Diabetes
p trend 0.002
Odds Ratio (95% CI)
5.0
2.0
1.0
0.5
0.2
0.1
Weight loss
Moderate WGBP
High WGBP
Prepregnancy Weight change
Gestational Hypertension
p trend 0.006
Odds Ratio (95% CI)
5.0
2.0
1.0
0.5
0.2
0.1
Weight loss
Moderate WGBP
High WGBP
Prepregnancy Weight change