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EXERCISE IN PREGNANCY: AN ASSOCIATION WITH PLACENTAL WEIGHT?

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Condensation

In a cohort of 80,515 pregnancies, placental weight decreased with increasing frequency of leisure time exercise.

Short version of title

Exercise and placental weight

Abstract

Background: Women with high levels of physical exercise have increased demand for oxygen and nutrients. Thus, in pregnancies of women with high levels of exercise it is conceivable that the supply of oxygen and nutrients to the placenta is sub-optimal, and growth could be impaired.

Objective: To study the association of frequency of exercise during pregnancy with placental weight and placental to birthweight ratio.

Study design: A prospective study of 80,515 singleton pregnancies in the Norwegian Mother and Child Cohort Study. Frequency of exercise was self-reported by a questionnaire at pregnancy weeks 17 and 30. Information on placental weight and birthweight was obtained by linkage to the Medical Birth Registry of Norway.

Results: Placental weight decreased with increasing frequency of exercise (tests for trend, $P<0.001$). For non-exercisers in pregnancy week 17, crude mean placental weight was 686.1 g compared to 667.3 g in women exercising ≥ 6 times weekly (difference 18.8 g; 95% CI: 12.0 to 25.5). Likewise, in non-exercisers in pregnancy week 30, crude mean placental weight was 684.9 g compared to 661.6 g in women exercising ≥ 6 times weekly (difference 23.3 g; 95% CI: 14.9 to 31.6). The largest difference in crude mean placental weight were seen between non-exercisers at both time points and women exercising ≥ 6 times weekly at both time points (difference 31.7 g; 95% CI: 19.2 to 44.2). Frequency of exercise was not associated with placental to birthweight ratio.

Conclusion: We found decreasing placental weight with increasing frequency of exercise in pregnancy. The difference in placental weight between non-exercisers and women with exercising ≥ 6 times weekly was small, and may have no clinical implications.

Key words: Birthweight, exercise, placental weight, pregnancy, the Norwegian Mother and Child Cohort Study

INTRODUCTION

Exercise increases the demand for oxygen and nutrients in working skeletal muscles.[1, 2] Thus, in pregnant women with high exercise levels, it is conceivable that the supply of oxygen and nutrients to the growing fetal-placental unit may be sub-optimal. The growth of the fetal-placental unit could thereby be affected. Results from clinical[3] and observational studies[4, 5] suggest that women with high levels of exercise during pregnancy give birth to offspring with slightly lower mean birthweight than women with low levels of exercise without increasing the risk of having offspring with birthweight below 2500 g or below the 10th percentile.[4, 6]

The placenta plays a key role in fetal growth and development.[7, 8] Except for one epidemiological study in Denmark,[4] studies on the association of exercise during pregnancy with placental weight are based on small study samples, and the results are inconsistent.[9-11] The findings in the Danish study[4] suggest that placental weight may decrease with increasing frequency of exercise in early pregnancy (test for trend, P=0.060). A disproportional size of the placenta relative to birthweight may indicate an unfavorable intrauterine environment for the fetus.[12] Two small studies have addressed a possible association of exercise during pregnancy with placental weight relative to birthweight, but the results in these studies were conflicting.[10, 11]

Therefore, we studied whether frequency of exercise in pregnancy is associated with placental weight or with placental weight relative to birthweight. We used information about exercise in pregnancy weeks 17 and 30 in a cohort of 80,815 women with singleton pregnancy.

MATERIALS AND METHODS

Study design, study population and follow-up

During the years1999–2008, all pregnant women scheduled to give birth at 50 hospitals in Norway were targeted for recruitment to the Norwegian Mother and Child Cohort Study (www.fhi.no/morogbarn).[13] The women were recruited at routine fetal ultrasonographic examination in pregnancy weeks 17–19. This examination is part of the public antenatal health care program, offered free of charge to all pregnant women living in Norway. The Norwegian Mother and Child Cohort Study had no exclusion criteria, and 40.6% of all eligible women agreed to participate. The present study is based on version 8 of the quality-assured data files, released for research in 2014.

Data were obtained through two self-administered questionnaires, distributed and returned by postal mail. The first questionnaire was completed during the second trimester (mean 17.4 weeks, standard deviation (SD) 2.2 weeks) and included questions about socio-demographic factors, general health, reproductive history, and leisure time exercise. The second questionnaire was completed during the third trimester (mean 30.6 weeks, SD 1.5 weeks) and included questions about maternal health and leisure time exercise. Information about placental weight, birthweight and other pregnancy outcomes was obtained by linkage to the Medical Birth Registry of Norway. This registry contains information about all births in Norway after pregnancy week 16 as obtained by compulsory notification by the midwife or the doctor attending the delivery.[14]

Of the women who agreed to participate in the Norwegian Mother and Child Cohort Study, 94.9% returned the first questionnaire and 91.0% returned the second questionnaire. Women

with a singleton pregnancy, and who had answered both questionnaires, were eligible for our data analyses, a total of 87,076 women. We excluded 6561 women with missing information on one or more of the following study factors: exercise in pregnancy week 17 (559 missing), exercise in pregnancy week 30 (573 missing), placental weight (2317 missing), birthweight (52 missing), pre-pregnancy body mass index (BMI) (2242 missing), and smoking during pregnancy (1465 missing), leaving 80,515 singleton pregnancies to our study sample (Figure 1).

Study factors

Placental weight in grams (g) was our main outcome measure. The newborn and the placenta were routinely weighed shortly after birth. According to Norwegian standardized routines, the placentas were placed in a bowl immediately after birth, and weighed fresh with membranes and umbilical cord attached, independent of delivery mode.[15] The weight of the bowl was subtracted from the sum weight. The placental to birthweight ratio was calculated as placental weight (g) divided by birthweight (g).

The main exposure variables were frequency of leisure time exercise in pregnancy weeks 17 and 30. In the questionnaires, the participants reported how often they performed the following exercises: strolling, brisk walking, running (jogging or orienteering), bicycling, training in fitness center, swimming, aerobics (low or high impact), prenatal aerobic, dancing, cross-country skiing, ball games, horseback riding and other exercises.[16, 17] Based on the definition of exercise by Caspersen et al[18] strolling was categorized as non-exercise. We combined all exercise frequencies (excluding strolling) into one variable categorized as: never, 1–3 times monthly, 1–2 times weekly, 3–5 times weekly and ≥ 6 times weekly. Non-exercisers were those who responded "never" to all exercises listed or who reported strolling

only.[16] We also combined frequency of exercise at pregnancy weeks 17 and 30 into one variable, and we categorized the frequency at both time points as follows: never, < 3 times weekly, ≥ 3 times weekly, and ≥ 6 times weekly. Switch in frequency of exercise from week 17 to week 30 was defined as: change in frequency.

The associations of type of exercise with placental weight were investigated in supplementary analyses. We grouped type of exercise as: no exercise (strolling or none), brisk walking, non-weight bearing exercise (cycling or swimming), low impact exercise (prenatal aerobics, low impact aerobics, dancing, cross-country skiing, or fitness training), high impact exercise (running, jogging, orienteering, or ballgames), and other exercise (horseback riding or other). A mixed exercise group included women without a single dominant type of exercise (for example one session of jogging and one session of swimming weekly).

We identified potentially confounding factors by using directed acyclic graphs (DAGs)[19] and assessed factors that may be associated with leisure time exercise[20] and with placental weight.[21] Values for confounding factors were obtained from the questionnaires: BMI (kg/m^2) before pregnancy based on self-reported weight and height, cigarette smoking during pregnancy (yes/no), nausea with vomiting before pregnancy week 17 (yes/no) and years of education (< 13 years, 13-16 years, ≥ 17 years, and missing). Additionally, we obtained information from the Medical Birth Registry of Norway on maternal age (years), parity (para 0, para 1, and para ≥2), maternal diabetes (including diabetes type 1, type 2 and gestational diabetes) (yes/no), preeclampsia (yes/no), and hemoglobin concentrations < 9 g/dl in pregnancy (yes/no).

Statistical methods

The associations of exercise frequency and type with placental weight and with placental to birthweight ratio were estimated as crude and adjusted unstandardized beta coefficients with 95% confidence intervals (CI) by applying linear regression analyses. The beta coefficients can be interpreted as change in placental weight (g) by change in category of exercise frequency. Non-exercisers were used as the reference group. We performed separate analyses in women with BMI < 25 kg/m^2 and in women with BMI ≥ 25 kg/m^2, and also in primiparous and in multiparous women. We used General Linear Model with polynomial contrast to assess trends in mean placental weight and placental to birthweight ratio according to increasing frequency of exercise. In additional analyses, we also studied the association of exercise frequency with the odds of having placental weight among the 5% smallest using logistic regression analyses, and we used the nonparametric trend test (nptrend) to assess trends according to increasing frequency of exercise. We used the statistical software packages IBM SPSS version 20.0 (IBM Corp., Armonk, NY, USA) and STATA 14 SE (StataCorp, College Station, TX, USA) for the statistical analyses.

Ethical considerations

The Norwegian Mother and Child Cohort Study was approved by the Regional Committee for Medical and Health Research Ethics (S-97045; S-95113) and by the Norwegian Data Protection Authority. All participants signed an informed consent form. This particular study is approved by The Norwegian Mother and Child Cohort Study steering committee at the Norwegian Institute of Public Health (PDB 1595; ref. 14/1185).

RESULTS

Mean maternal age was 30.2 years (SD 4.5 years), 45.8% were first-time mothers, and in 68.6% of the women pre-pregnancy BMI was < 25 kg/m^2. Overall, mean placental weight was 680.1 g (SD 197.0 g), and mean birthweight was 3607.1 g (SD 541.5 g) (Table 1).

In pregnancy week 17, 22.4% of the women never took part in leisure time exercise, and in pregnancy week 30 the proportion of non-exercisers was 32.7%. A total of 13.3% of the women were non-exercisers at both time points (Table 2). The corresponding proportions of women who exercised ≥ 6 times weekly were 5.0%, 2.9% and 1.3%.

Crude mean placental weight decreased by increasing frequency of exercise in pregnancy week 17, and the crude mean decrease in placental weight from non-exercisers to women exercising ≥ 6 times weekly was 18.8 g (95% CI: 12.0 to 25.5) (test for trend, P<0.001) (Table 2). Similar pattern was observed for exercise in pregnancy week 30, and the crude decrease in mean placental weight from non-exercisers to women exercising ≥ 6 times weekly was 23.3 g (95% CI: 14.9 to 31.6) (test for trend, P<0.001). Women who exercised ≥ 6 times weekly in pregnancy week 17 and in pregnancy week 30, had 31.7 g (95% CI: 19.2 to 44.2) lower placental weight than non-exercising women (test for trend, P<0.001).

Overall, the lowest mean placental weight was observed in women who exercised ≥ 6 times weekly in both pregnancy week 17 and 30, followed by women who exercised ≥ 6 times weekly in pregnancy week 30 and women who exercised ≥ 6 times weekly in pregnancy week 17 (Table 2).

After adjustment for the potentially confounding factors listed above, the associations of exercise frequency in pregnancy with placental weight were attenuated, and the decreasing

trend was no longer statistically significant for exercise frequency in pregnancy week 17 (Table 2).

Pre-pregnancy BMI and parity were the main confounding factors. In separate analysis in women with BMI < 25 kg/m^2 and in women with BMI ≥ 25 kg/m^2, as well as in primiparous and in multiparous women, the trend of decreasing placental weight with increasing frequency of exercise was still present (Table 3). Again, adjustment for other study factors attenuated the associations. However, a statistically significant inverse trend was present in women with BMI < 25 kg/m^2 (test for trend, P=0.003) and in primiparous women (test for trend, P=0.037).

Frequency of exercise in pregnancy was also positively associated with the risk (crude odds ratio) of having a placenta among the 5% smallest (tests for trend, P<0.01) (Table 4). The associations were attenuated after adjusting for the other study factors.

The mean placental to birthweight ratio was 0.1893 (SD 0.0496) (Table 1). We found no association of frequency of exercise with placental to birthweight ratio (Table 5). Adjustment for the potentially confounding factors did not alter this finding (data not shown).

In supplementary analyses, we found that high impact exercise in pregnancy week 17 was associated with 21.2 g (95% CI: 15.5 to 26.9) lower placental weight than no exercise (Supplementary Table). Similar association was estimated for high-impact exercise in pregnancy week 30 (difference 22.0 g; 95% CI: 12.3 to 31.6). Among the women who reported exercise > 6 times weekly in pregnancy week 17, a total of 29.3% also reported high impact exercise (data not shown).

COMMENT

In this prospective cohort study of 80,515 singleton pregnancies, we found that placental weight decreased with increasing frequency of exercise during pregnancy. We found no association of exercise frequency with placental weight relative to birthweight.

The participation rate in the Norwegian Mother and Child Cohort Study was rather low (40.6%). Women younger than 25 years and women with low socioeconomic status were underrepresented.[13] However, mean placental weight in our sample did not differ from mean placental weight in all singleton pregnancies in Norway during the study period.[22] We have no reason to believe that the association of exercise frequency with placental weight in our sample is not valid for all pregnancies in Norway.[23]

Self-reported exercise often represents an overestimate.[24] Our estimated associations of exercise with placental weight could therefore represent underestimates. However, the questions used to assess exercise frequency in our study have shown acceptable validity when compared to accelerometer in a sub-sample of pregnant women within the Norwegian Mother and Child Cohort.[17] By using prospective study design frequency of exercise is unlikely to be systematically erroneous reported by placental weight.

The trend of decreasing placental weight with increasing frequency of exercise was attenuated after adjustment for potentially confounding factors. The most important confounding factors were pre-pregnancy BMI and parity. We made separate analyses among women with BMI < 25 and BMI $\geq$ 25, in addition to among para 0 and para $\geq$1 women. We found decreasing placental weight with increasing frequency of exercise also in these sub-groups of women, however, the trend was not statistically significant in all sub-groups. Duration of pregnancy is

closely linked to placental weight. In the Norwegian Mother and Child Cohort Study, exercise was not associated with duration of pregnancy, and thus not a confounding factor.[16] Nevertheless, we made supplementary analyses restricted to pregnancies lasting 37 weeks or longer, and the estimated associations in these pregnancies were non-different from the sample as a whole (data not shown).

Comparison with other studies

A study of 79,692 pregnancies from the Danish National Birth Cohort reported decreasing placental weight with increasing frequency of exercise in the first part of pregnancy (test for trend, P=0.060).[4] Other studies that have addressed the association of exercise in pregnancy with placental weight are small, and the results from these studies are conflicting.[9-11] The association of exercise in pregnancy with placental to birthweight ratio were estimated in two of the above studies, and both high[10] and low[11] ratio were reported. Whether exercise in the third trimester of pregnancy is associated with placental weight, has to our knowledge, not previously been studied.

Interpretation

We found decreasing placental weight with increasing frequency of exercise during pregnancy. Placental to birthweight ratio, however, was not associated with frequency of exercise. This finding suggests that birthweight and placental weight decrease in similar patterns by increased frequency of exercise.

High frequency of exercise in pregnancy has been associated with a slightly lower mean birthweight[3-6] and with reduced risk of having a newborn with high birthweight.[4, 6, 25] Our results suggest that pregnant women who exercise at high levels, have increased odds of

having a placenta among the 5% smallest. Thus, our findings suggest that high exercise frequency may lead to a shift in the placental weight distribution towards smaller placentas.

In previous studies, both high and low placental to birthweight ratio have been linked to adverse pregnancy outcomes.[12] Since we found no association of exercise frequency with placental to birthweight ratio, pregnancies in high frequency exercisers may not be high risk pregnancies. Women with high exercise levels have better cardiovascular fitness than women who do not exercise.[26] Therefore, it is plausible that the blood flow to the uterus is increased. If so, the availability of oxygen and nutrition for the fetal-placental circulation may be normal or even increased although the placenta is small. Unfortunately, we had no information about the blood flow to the uterus or about the fetal-placental circulation. We also lacked specific information about intensity and duration of exercise. We used type of exercise as a proximate measure for such information. Only women who engaged in high impact exercise had significant decrease in placental weight, and a large proportion of the high impact exercisers were also frequent exercisers. Hence, our results give little reason to believe that exercise > 6 times weekly may harm the pregnancy or that the present recommendations of at least 20 to 30 minutes daily exercise at moderate intensity in pregnancy should be changed.[27] However, we cannot completely rule out possible adverse effects of very high exercise volumes on placental growth.

In conclusion, placental weight decreased with increasing frequency of exercise in this study of 80,515 pregnancies. However, the difference in mean placental weight was small between non-exercisers and women with daily exercise.

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TABLE 1. Characteristics of the study sample (n=80,515 singleton pregnancies).

Characteristics	**No. (%)**	**Mean (SD)**
Maternal age, years		30.2 (4.5)
Pre-pregnancy body mass index, kg/m^2		24.1 (4.3)
Parity		
Para 0	36,880 (45.8)	
Para 1	28,461 (35.3)	
Para ≥ 2	15,174 (18.8)	
Maternal diabetes	1158 (1.4)	
Preeclampsia	2873 (3.6)	
Hemoglobin < 9 g/dl	289 (0.4)	
Nausea with vomiting	29,373 (36.5)	
Educational level, years		
≥ 17	18,458 (22.9)	
13-16	31,943 (39.7)	
≤ 12	26,125 (32.4)	
Missing	3989 (5.0)	
Smoking during pregnancy	6618 (8.2)	
Married /Cohabitant	77,493 (96.2)	
Gestational length, weeks[a]		39.5 (1.7)
Birthweight, g		3607.1 (541.5)
Placental weight, g		680.1 (197.0)
Placental to birthweight ratio		0.1893 (0.0496)

SD, standard deviation; *g*,grams; [a] n = 80,200.

TABLE 2. The associations of exercise frequency during pregnancy with placental weight (n=80,515 singleton pregnancies).

Exercise frequency during pregnancy		**Placental weight, g**				
	No. of pregnancies (%)	**Mean (SD)**	**Crude B (95% CI)**	**Test for trend**	**Adjusted B[a] (95% CI)**	**Test for trend**
Pregnancy week 17						
Never (reference)	18,008 (22.4)	686.1 (189.7)	0.0	*P*<0.001	0.0	*P*=0.079
1-3 times monthly	15,975 (19.8)	683.9 (194.1)	-2.2 (-6.4 to 2.0)		-0.7 (-4.9 to 3.5)	
1-2 times weekly	23,683 (29.4)	681.2 (216.0)	-4.9 (-8.7 to -1.1)		-0.3 (-4.1 to 3.6)	
3-5 times weekly	18,852 (23.4)	672.7 (183.7)	-13.3 (-17.4 to -9.3)		-3.9 (-8.0 to 0.2)	
≥ 6 times weekly	3997 (5.0)	667.3 (182.0)	-18.8 (-25.5 to -12.0)		-3.6 (-10.4 to 3.2)	
Pregnancy week 30						
Never (reference)	26,315 (32.7)	684.9 (187.5)	0.0	*P*<0.001	0.0	*P*=0.036
1-3 times monthly	15,486 (19.2)	682.7 (181.4)	-2.2 (-6.1 to 1.7)		0.9 (-3.0 to 4.8)	
1-2 times weekly	21,581 (26.8)	680.4 (224.0)	-4.5 (-8.0 to -1.0)		2.0 (-1.6 to 5.6)	
3-5 times weekly	14,802 (18.4)	671.6 (193.2)	-13.2 (-17.2 to -9.3)		-1.7 (-5.8 to 2.3)	
≥ 6 times weekly	2331 (2.9)	661.6 (152.1)	-23.3 (-31.6 to -14.9)		-5.9 (-14.3 to 2.4)	
Combined week 17&30						
Never (reference)	10,710 (13.3)	685.7 (180.2)	0.0	*P*<0.001	0.0	*P*=0.020
< 3 times weekly	22,213 (27.6)	682.0 (214.8)	-3.7 (-8.2 to 0.9)		2.0 (-2.6 to 6.5)	
Change in frequency[b]	36,843 (45.8)	681.5 (195.3)	-4.1 (-8.4 to 0.1)		1.7 (-2.6 to 5.9)	
≥ 3 times weekly	9698 (12.0)	667.2 (183.2)	-18.4 (-23.9 to -13.0)		-3.8 (-9.3 to 1.8)	

≥ 6 times weekly	1051 (1.3)	654.0 (140.5)	-31.7 (-44.2 to -19.2)	-10.9 (-23.4 to 1.5)

Linear regression analyses with associations presented as unstandardized beta coefficients (B) with 95% confidence intervals and tests for trend using General Linear Model with polynomial contrast. [a]Adjusted for pre-pregnancy BMI (kg/m^2), parity, diabetes, preeclampsia, maternal age, hemoglobin < 9g/dl, nausea with vomiting before pregnancy week 17, education level, smoking during pregnancy.

[b] Switching from exercising < 3 times weekly to ≥ 3 times weekly or vice versa from week 17 to week 30, or switching from never at one time point to exercising at any frequency at the other time point.

SD, standard deviation; *CI*, confidence interval; *g*, grams; *BMI*, body mass index.

TABLE 3. The associations of exercise frequency at pregnancy week 30 with placental weight stratified by maternal pre-pregnancy BMI and parity.

Exercise frequency at pregnancy week 30		**Placental weight, g**				
	No. of pregnancies (%)	**Mean (SD)**	**Crude B (95% CI)**	**Test for trend**	**Adjusted B[a] (95% CI)**	**Test for trend**
Pre pregnancy BMI < 25 kg/m^2 (n=55,194)						
Never (reference)	16,341 (29.6)	670.4 (176.2)	0.0	*P*<0.001	0.0	*P*=0.003
1-3 times monthly	10,172 (18.4)	668.3 (176.3)	-2.1 (-6.8 to 2.5)		-0.9 (-5.5 to 3.8)	
1-2 times weekly	15,201 (27.5)	668.7 (207.2)	-1.7 (-5.9 to 2.4)		0.5 (-3.7 to 4.7)	
3-5 times weekly	11,477 (20.8)	663.9 (192.8)	-6.5 (-11.0 to -2.0)		-3.2 (-7.7 to 1.4)	
≥ 6 times weekly	2003 (3.6)	656.0 (150.0)	-14.4 (-23.1 to -5.7)		-9.7 (-18.5 to -0.9)	
Pre pregnancy BMI ≥ 25 kg/m^2 (n=25,321)						
Never (reference)	9974 (39.4)	708.6 (202.5)	0.0	*P*=0.127	0.0	*P*=0.429
1-3 times monthly	5314 (21.0)	710.2 (187.7)	1.6 (-5.5 to 8.7)		3.0 (-4.1 to 10.0)	
1-2 times weekly	6380 (25.2)	708.2 (257.5)	-0.4 (-7.1 to 6.3)		2.1 (-4.6 to 8.9)	
3-5 times weekly	3325 (13.1)	698.3 (192.1)	-10.3 (-18.7 to -2.0)		-6.0 (-14.4 to 2.4)	
≥ 6 times weekly	328 (1.3)	696.0 (160.6)	-12.6 (-36.1 to 10.8)		-6.1 (-29.5 to 17.3)	
Primiparous women, para 1 (n=36,880)						
Never (reference)	9539 (25.9)	668.0 (193.7)	0.0	*P*<0.001	0.0	*P*=0.037
1-3 times monthly	6579 (17.8)	666.7 (174.0)	-1.3 (-7.4 to 4.7)		0.3 (-5.7 to 6.3)	
1-2 times weekly	10,768 (29.2)	665.4 (210.8)	-2.6 (-7.9 to 2.7)		0.1 (-5.3 to 5.4)	
3-5 times weekly	8428 (22.9)	662.2 (205.6)	-5.9 (-11.5 to -0.2)		-0.4 (-6.1 to 5.3)	

≥ 6 times weekly	1566 (4.2)	650.6 (138.7)	-17.4 (-27.7 to -7.2)		-9.8 (-20.1 to 0.5)	
Multiparous women, ≥ para 2 (n=43,635)						
Never (reference)	16,776 (38.4)	694.5 (193.7)	0.0	*P*=0.042	0.0	*P*=0.606
1-3 times monthly	8907 (20.4)	694.5 (185.8)	0.0 (-5.1 to 5.2)		1.2 (-4.0 to 6.3)	
1-2 times weekly	10,813 (24.8)	695.3 (235.5)	0.8 (-4.0 to 5.6)		3.5 (-1.4 to 8.3)	
3-5 times weekly	6374 (14.6)	684.2 (174.6)	-10.3 (-16.1 to -4.5)		-4.3 (-10.1 to 1.4)	
≥ 6 times weekly	765 (1.8)	684.2 (174.3)	-10.3 (-24.8 to 4.3)		-0.1 (-14.6 to 14.3)	

Linear regression analyses with associations presented as unstandardized beta coefficients (B) with 95% confidence intervals and tests for trend using General Linear Model with polynomial contrast.

[a]Adjustments for diabetes, preeclampsia, maternal age, hemoglobin < 9g/dl, nausea with vomiting before pregnancy week 17, education level, smoking during pregnancy, additional adjustment in pre-pregnancy BMI strata was parity, whereas additional adjustment in parity strata was pre-pregnancy BMI.

BMI, body mass index; *SD*, standard deviation; *CI*, confidence interval; *g*, grams.

TABLE 4. The associations of exercise frequency during pregnancy with 5th percentile placental weight (80,515 singleton pregnancies).

Exercise frequency during pregnancy		**Placental weight 5th percentile**		
	No. of pregnancies	**No of pregnancies (%)**	**Crude OR (95% CI)**	**Adjusted OR[a] (95% CI)**
Pregnancy week 17				
Never (reference)	18,008	795 (4.4)	1.0	1.0
1-3 times monthly	15,975	700 (4.4)	0.99 (0.89 to 1.10)	0.99 (0.89 to 1.09)
1-2 times weekly	23,683	1154 (4.9)	1.11 (1.01 to 1.22)	1.06 (0.96 to 1.16)
3-5 times weekly	18,852	958 (5.1)	1.16 (1.05 to 1.28)	1.04 (0.95 to 1.15)
≥ 6 times weekly	3997	235 (5.9)	1.35 (1.16 to 1.57)	1.14 (0.97 to 1.32)
			Test for trend, *P*<0.001	
Pregnancy week 30				
Never (reference)	26,315	1225 (4.7)	1.0	1.0
1-3 times monthly	15,486	704 (4.5)	0.98 (0.89 to 1.07)	0.95 (0.86 to 1.04)
1-2 times weekly	21,581	985 (4.6)	0.98 (0.90 to 1.07)	0.91 (0.84 to 1.00)
3-5 times weekly	14,802	785 (5.3)	1.15 (1.05 to 1.26)	1.01 (0.91 to 1.11)
≥ 6 times weekly	2331	143 (6.1)	1.34 (1.12 to 1.60)	1.11 (0.92 to 1.33)
			Test for trend, *P*<0.001	
Combined week 17&30				

Never (reference)	10,710	491 (4.6)	1.0	1.0
< 3 times weekly	22,213	1038 (4.7)	1.02 (0.91 to 1.14)	0.97 (0.86 to 1.08)
Change in frequency[b]	36,843	1700 (4.6)	1.01 (0.91 to 1.12)	0.94 (0.85 to 1.05)
≥ 3 times weekly	9698	545 (5.6)	1.24 (1.09 to 1.40)	1.06 (0.93 to 1.20)
≥ 6 times weekly	1051	68 (6.5)	1.44 (1.11 to 1.87)	1.15 (0.88 to 1.50)
			Test for trend, *P*=0.001	

Crude and adjusted odds ratios estimated by using logistic regression analyses for the association between exercise frequency during pregnancy and 5th percentile placental weight. Trends according to increasing frequency of exercise were assessed by using the nonparametric trend test.

[a] Odds ratios adjusted for pre-pregnancy body mass index (kg/m^2), parity, diabetes, preeclampsia, maternal age, hemoglobin < 9g/dl, nausea with vomiting before pregnancy week 17, education level, smoking during pregnancy.

[b] Switching from exercising < 3 times weekly to ≥ 3 times weekly or vice versa from week 17 to week 30, or switching from never at one time point to exercising at any frequency at the other time point.

OR, odds ratio; *CI*, confidence interval.

TABLE 5. The associations of exercise frequency during pregnancy with placental to birthweight ratio (n=80,515 singleton pregnancies).

Exercise frequency	**No. of pregnancies (%)**	**Placental to birthweight ratio**		
		Mean ratio (SD)	**Crude B (95% CI)**	**Test for trend**
Pregnancy week 17				
Never (reference)	18,008 (22.4)	0.1903 (0.0489)	0.0	*P*=0.267
1-3 times monthly	15,975 (19.8)	0.1890 (0.0487)	-0.001 (-0.002 to -0.001)	
1-2 times weekly	23,683 (29.4)	0.1893 (0.0547)	-0.001 (-0.002 to 0.001)	
3-5 times weekly	18,852 (23.4)	0.1887 (0.0467)	-0.002 (-0.003 to -0.001)	
≥ 6 times weekly	3997 (5.0)	0.1894 (0.0453)	-0.001 (-0.003 to 0.001)	
Pregnancy week 30				
Never (reference)	26,315 (32.7)	0.1898 (0.0489)	0.0	*P*=0.448
1-3 times monthly	15,486 (19.2)	0.1889 (0.0450)	-0.001 (-0.002 to 0.001)	
1-2 times weekly	21,581 (26.8)	0.1893 (0.0561)	-0.001 (-0.001 to 0.001)	
3-5 times weekly	14,802 (18.4)	0.1890 (0.0490)	-0.001 (-0.002 to 0.001)	
≥ 6 times weekly	2331 (2.9)	0.1889 (0.0373)	-0.001 (-0.003 to 0.001)	
Combined week 17&30				
Never (reference)	10,710 (13.3)	0.1904 (0.0501)	0.0	*P*=0.232
< 3 times weekly	22,213 (27.6)	0.1890 (0.0545)	-0.001 (-0.003 to -0.001)	
Change in frequency[a]	36,843 (45.8)	0.1895 (0.0483)	-0.001 (-0.002 to 0.001)	

≥ 3 times weekly	9698 (12.0)	0.1884 (0.0465)	-0.002 (-0.003 to -0.001)
≥ 6 times weekly	1051 (1.3)	0.1888 (0.0323)	-0.002 (-0.005 to 0.002)

Linear regression analyses with associations presented as unstandardized beta coefficients (B) with 95% confidence intervals and *P*-value for trend using General Linear Model with polynomial contrast.

[a] Switching from exercising < 3 times weekly to ≥ 3 times weekly or vice versa from week 17 to week 30, or switching from never at one time point to exercising at any frequency at the other time point.

SD, standard deviation; *CI*, confidence interval.

Figure legends

FIGURE 1: Flow chart of the study sample (n=80,515).

SUPPLEMENTARY TABLE. The associations of exercise type during pregnancy with placental weight (n=80,515 singleton pregnancies).

Exercise type during pregnancy		**Placental weight, g**		
	No. of pregnancies (%)	**Mean (SD)**	**Crude B (95% CI)**	**Adjusted B[a] (95% CI)**
Pregnancy week 17				
Non-exerciser (reference)	18,008 (22.4)	686.1 (189.7)	0.0	0.0
Brisk walking	12,774 (15.9)	677.6 (222.4)	-8.4 (-13.2 to 3.7)	-2.0 (-6.7 to 2.7)
Non-weight bearing exercise	8,363 (10.4)	677.5 (186.6)	-8.5 (-13.4 to -3.7)	-4.1 (-8.9 to 0.7)
Low impact exercise	9,642 (12.00)	677.2 (199.0)	-8.8 (-13.7 to -4.0)	1.5 (-3.4 to 6.4)
High impact exercise	4,367 (5.4)	664.9 (168.2)	-21.2 (-26.9 to -15.5)	-8.5 (-14.3 to -2.8)
Other exercise	3,878 (4.8)	674.4 (180.3)	-11.7 (-18.0 to -5.4)	-2.4 (-8.7 to 3.8)
Mixed exercise	23,483 (29.2)	682.8 (198.1)	-3.2 (-7.0 to 0.5)	-0.5 (-4.2 to 3.2)
Pregnancy week 30				
Non-exerciser (reference)	26,315 (32.7)	684.9 (187.5)	0.0	0.0
Brisk walking	10,558 (13.1)	672.1 (191.8)	-12.7 (-17.0 to -8.4)	-2. 7 (-7.0 to 1.6)
Non-weight bearing exercise	6,859 (8.5)	682.8 (244.6)	-2.1 (-8.3 to 4.1)	2.7 (-3.5 to 8.9)
Low impact exercise	8,781 (10.9)	672.9 (214.3)	-12.0 (-17.0 to -7.0)	-0.4 (-5.4 to 4.6)
High impact exercise	899 (1.1)	662.9 (143.7)	-22.0 (-31.6 to -12.3)	-8.6 (-18.0 to 0.9)
Other exercise	5,500 (6.8)	680.4 (168.6)	-4.4 (-9.4 to 0.6)	4.7 (-0.3 to 9.6)
Mixed exercise	21,603 (26.8)	681.0 (195.0)	-3.8 (-7.3 to -0.4)	0.7 (-2.8 to 4,1)

Linear regression analyses with associations presented as unstandardized beta coefficients (B) with 95% confidence intervals. [a]Adjusted for pre-pregnancy BMI (kg/m^2), parity, diabetes, preeclampsia, maternal age, hemoglobin < 9g/dl, nausea with vomiting before pregnancy week 17, education level, smoking during pregnancy.

SD, standard deviation; *CI*, confidence interval; *g*, grams.