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Associations of maternal obesity and excessive weight gain during pregnancy with subcutaneous fat mass in infancy

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ABSTRACT

Background: Not much is known about the associations of maternal obesity and excessive gestational weight gain with body fat in infancy.
Objective: To examine the associations of maternal pre-pregnancy body mass index and gestational weight gain with infant subcutaneous fat.
Methods: In a population-based prospective cohort study among 845 mothers and their infants, we obtained maternal pre-pregnancy body mass index and measured maternal weight during pregnancy. At 1.5, 6 and 24 months, we estimated infant total subcutaneous fat (sum of biceps, triceps, suprailiacal and subscapular skinfold thicknesses) and central-to-total subcutaneous fat ratio (sum of suprailiacal and subscapular skinfold thicknesses/total subcutaneous fat).
Results: Maternal body mass index was positively associated with higher infant body mass index from 6 months onwards. Maternal body mass index was not associated with infant subcutaneous fat measures at 1.5 or 6 months. A 1-standard deviation scores (SDS) higher maternal body mass index was associated with a 0.09 (95% Confidence Interval 0.01, 0.17) SDS higher infant total subcutaneous fat at 24 months, but not with central-to-total subcutaneous fat ratio. No associations were present for maternal total or period-specific gestational weight gain with infant fat.
Conclusion: Maternal body mass index was positively associated with infant body mass index and total subcutaneous fat in late infancy. Maternal total and period-specific gestational weight gain were not associated with infant body fat mass measures.

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1. Introduction

Maternal pre-pregnancy obesity and excessive weight gain during pregnancy are associated with an increased risk of obesity in childhood [1,2]. Body mass index is a suboptimal measure of body fat mass and provides no information about body fat distribution [3]. Several studies have shown that compared to body mass index, central fat distribution is more strongly associated with an adverse cardiovascular risk profile [4]. Previously, we reported that maternal obesity and excessive weight gain especially in early-pregnancy seem to be associated with an adverse body fat distribution, such as higher android-to-gynoid fat mass ratio, at 6 years [5,6]. We have also shown that maternal pre-pregnancy

body mass index tended to be more strongly associated with childhood total and abdominal fat than paternal body mass index, suggesting that intra-uterine mechanisms might be involved [6]. Thus far, previous studies did not assess the associations and explore the underlying mechanisms of maternal obesity and excessive weight gain during pregnancy with detailed offspring fat mass measures already from early infancy onwards, which is a well-known critical period for adiposity development in later life [7]. Skinfold thickness is a valid measurement of total and regional subcutaneous fat mass in infancy [8]. We have previously shown that subcutaneous fat mass measured by skinfolds tends to track throughout infancy and is positively associated with cholesterol levels at school-age children [9,10].

Therefore, we examined in a population-based prospective cohort study among 845 parents and their infants, the associations of maternal pre-pregnancy body mass index and weight gain in different periods of pregnancy with subcutaneous fat mass measures throughout infancy.

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We also compared the strength of the associations of maternal and paternal body mass index with infant fat mass measures to obtain further insight in the underlying mechanisms.

2. Methods

2.1. Study design

This study was embedded in the Generation R Study, a population-based prospective cohort study from early pregnancy onwards among 9778 mothers and their children living in Rotterdam, the Netherlands [11]. The local Medical Ethical Committee approved the study. Written informed consent was obtained from parents. Additional detailed assessments of growth and development were conducted in a subgroup of Dutch mothers and their children from late pregnancy onwards. Of all approached women, 80% agreed to participate. From the total of 1205 mothers and their singleton children participating in the subgroup study, 1033 mothers had information about pre-pregnancy body mass index. Missing information about pre-pregnancy body mass index was mainly because of later enrolment in the study and nonparticipation in the first questionnaire. Body mass index or skinfold thicknesses measured at the age of 1.5, 6 or 24 months were available in 845 children (Flow chart is given in Supplemental Fig. S1). Missing body fat mass measurements during infancy were due to loss to follow-up or crying behavior.

2.2. Parental anthropometrics

As previously described, maternal pre-pregnancy weight was obtained by questionnaire at enrolment [11]. Maternal height (cm) and paternal height (cm) and weight (kg) were measured without shoes and heavy clothing at enrolment. Body mass index (kg/m^2) was calculated. Maternal and paternal body mass index were categorized into 4 categories (underweight (<20 kg/m^2), normal weight (20–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2)). We measured maternal weight without shoes and heavy clothing at median 12.8 (95% range 9.9,17.0), 20.4 (95% range 18.6,22.7) and 30.4 (95% range 28.5,32.5) weeks of gestation. In a subgroup of 509 mothers, information about maximum weight during pregnancy was assessed by questionnaire 2 months after delivery. Based on the timing of maternal weight measurements within our study cohort, we defined early-, mid- and late-pregnancy weight, using self-reported and measured maternal weight data, as: at 13 weeks of gestation (median 12.8, 95% range 9.9,18.9); at 26 weeks of gestation (median 29.9, 95% range 20.4,31.6); and at 40 weeks of gestation (median 39.0, 95% range 32.6,42.0), respectively. Using this method, information about early-, mid- and late-pregnancy weight was available for 762, 824 and 493 mothers, respectively. Among the subgroup of mothers with maximum weight during pregnancy available, we defined excessive gestational weight gain in relation to maternal pre-pregnancy body mass index according to the Institute of Medicine (IOM) guidelines [12].

2.3. Body fat measurements during infancy

We measured weight to the nearest gram in naked infants at the age of 1.5 and 6 months by using an electronic infant scale and at 24 months by using a mechanical personal scale (SECA, Almere, The Netherlands). Body length at the age of 1.5 and 6 months was measured in supine position to the nearest millimeter by using a neonatometer and body height at 24 months was measured in standing position by using a Harpenden stadiometer (Holtain Limited, Dyfed, UK). Body mass index (kg/m^2) was calculated. We measured skinfold thicknesses at the ages of 1.5, 6 and 24 months on the left side of the body at the biceps, triceps, suprailiacal and subscapular area by using a skinfold caliper (Slim Guide, Creative Health Products) [9]. We calculated total subcutaneous fat mass from the sum of all four skinfold thicknesses, and central subcutaneous fat mass from the sum of suprailiacal and subscapular skinfold thicknesses [13]. Measurements of body fat quantity and distribution require appropriate adjustment for body size or total fat mass, respectively, in order to undertake informative comparisons between children and within children over time. To create total subcutaneous fat mass independent of length or height and central subcutaneous fat mass independent of total subcutaneous fat mass, we estimated the optimal adjustment by log-log regression analyses [14]. Based on these analyses, total subcutaneous fat mass was only weakly correlated with length at 1.5 and 6 months or height at 24 months, and was not adjusted for it. A central-to-total subcutaneous fat mass ratio was calculated as central divided by total subcutaneous fat mass.

2.4. Covariates

Information on maternal and paternal age, educational level and parity was obtained at enrolment [11]. Information on maternal smoking was assessed by questionnaires during pregnancy. First trimester maternal nutritional information was obtained by food frequency questionnaire. Information about pregnancy complications, mode of delivery, child's sex, gestational age and weight at birth was obtained from medical records [15]. Information about breast feeding duration and timing of introduction of solid foods was obtained by questionnaires in infancy.

2.5. Statistical analysis

First, we examined differences in subject characteristics between maternal body mass index categories with 1-way ANOVA tests and χ^2 tests. Next, we examined the associations of maternal and paternal body mass index with infant subcutaneous fat mass measures at each time period using linear regression models. We also used repeated measurement regression models to assess the associations of parental pre-pregnancy overweight with the repeatedly measured infant fat mass measures. These models take the correlation between repeated measurements of the same subject into account, and allow for incomplete outcome data. Third, we examined the associations of maternal maximum gestational weight gain and excessive gestational weight gain according to the IOM criteria with infant subcutaneous fat mass measures using linear regression models. Since maternal weight measurements throughout pregnancy are strongly correlated, we performed conditional linear regression analyses to assess the independent associations of maternal pre-pregnancy weight and early-, mid- and late-pregnancy weight gain with infant subcutaneous fat mass measures. We obtained standardized residuals for each weight measurement from the regression of maternal weight at a specific time point on prior maternal weight measurements. These weight variables are statistically independent from each other, and can be simultaneously included in the regression models [16].

Models were adjusted for maternal and childhood socio-demographic and lifestyle-related characteristics. Covariates were included based on associations with the exposures and outcomes of interest in previous studies, or a change in effect estimates > 10%. We constructed SDS ((observed value − mean) / SD) for parental body mass index and gestational weight gain and infant fat mass measures to enable comparison of effect estimates. Since no significant interactions between parental body mass index or maternal gestational weight gain and child's sex in the associations with infant subcutaneous fat mass measures were present, no further stratified analyses were performed. Missing values in covariates were multiple-imputed, by using Markov chain Monte Carlo approach. Five imputed datasets were created and analyzed together. All statistical analyses were performed using the Statistical Package of Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Subject characteristics

Characteristics of included mothers, fathers and their children are given in Table 1. Non-response analyses showed that as compared to mothers who did not participate in the follow-up studies, those who did participate were slightly older, had a higher educational level and their children were breastfed for a longer period (p < 0.05), but no differences were observed regarding maternal and paternal body mass index and maternal weight gain during pregnancy (Supplemental Table S1).

3.2. Parental body mass index and infant body fat

Table 2 shows the associations of maternal and paternal body mass index with infant subcutaneous fat mass measures. We observed no associations of maternal pre-pregnancy body mass index with infant body fat mass measures at 1.5 months. A higher maternal pre-pregnancy body mass index was associated with higher infant body mass index from 6 months onwards (difference at 6 and 24 months: 0.09 (95% Confidence Interval (CI) 0.01,0.17) SDS, 0.17 (95% CI 0.09,0.26) SDS per 1-SDS higher maternal body mass index, respectively). A higher maternal pre-pregnancy body mass index was also associated with higher infant total subcutaneous fat mass at 24 months (difference: 0.09 (95% CI 0.01, 0.17) SDS per 1-SDS higher maternal body mass index), but not with infant central-to-total subcutaneous fat mass ratio. A higher paternal body mass index was only associated with higher infant body mass index at 1.5 and 24 months (p-values < 0.05). Including both maternal and paternal body mass index in the same model did not change the effect estimates for infant fat mass measures at 1.5, 6 and 24 months.

Supplemental Fig. S2 shows that maternal pre-pregnancy overweight was associated with higher infant body mass index growth from 6 months onwards, resulting in higher body mass index at 24 months (all p-values < 0.05). Maternal pre-pregnancy overweight also tended to be associated with higher total subcutaneous fat mass and central-to-total subcutaneous fat mass ratio at 24 months (difference: 0.09 (95% CI 0.01,0.17) SDS, 0.08 (95% CI −0.01,0.17) SDS for maternal pre-pregnancy overweight as compared to maternal pre-pregnancy normal weight, respectively). No associations of paternal overweight with infant body fat mass measures were present.

3.3. Maternal gestational weight gain and infant body fat

Table 3 shows no consistent associations for maternal maximum and excessive gestational weight gain with infant body mass index and subcutaneous fat mass measures at 1.5, 6 and 24 months. Excessive maternal gestational weight gain was only associated with higher infant body

Table 1
Characteristics of mothers, fathers and their children.[a]

Characteristics	Total group (N = 845)	Maternal underweight (N = 113)	Maternal normal weight (N = 518)	Maternal overweight (N = 151)	Maternal obesity (N = 63)	P-value
Maternal characteristics						
Age, mean (SD), years	31.8 (4.1)	31.4 (4.8)	32.0 (4.0)	31.7 (3.8)	31.1 (4.2)	0.206
Education (higher education), n (%)	548 (65.2)	70 (61.9)	368 (71.5)	86 (57.3)	24 (38.1)	<0.001
Parity (nulliparous), n (%)	522 (61.8)	71 (62.8)	322 (62.6)	89 (58.9)	40 (63.5)	0.878
Body mass index, mean (SD), kg/m^2	23.5 (4.1)	19.0 (0.7)	22.2 (1.4)	26.9 (1.4)	34.1 (3.5)	<0.001
Maximum gestational weight gain, mean (SD), kg	15.5 (5.7)	14.7 (4.9)	15.8 (5.2)	16.2 (6.0)	12.7 (8.6)	0.005
Excessive gestational weight gain (IOM criteria), n (%)	242 (47.9)	13 (20.0)	132 (42.9)	76 (78.4)	23 (59.0)	<0.001
Weight in early-pregnancy, mean (SD), kg	70.8 (12.9)	57.6 (5.9)	67.1 (6.5)	80.8 (7.7)	100.0 (12.9)	<0.001
Weight in mid-pregnancy, mean (SD), kg	78.0 (13.3)	64.6 (6.1)	74.4 (7.7)	88.5 (8.5)	105.4 (12.9)	<0.001
Weight in late-pregnancy, mean (SD), kg	84.5 (13.5)	71.2 (6.8)	80.9 (8.3)	94.8 (9.2)	112.7 (13.7)	<0.001
Total energy intake, mean (SD), kcal	2119 (512)	2246 (504)	2131 (510)	2040 (481)	1969 (568)	0.069
Smoking during pregnancy (yes), n (%)	186 (23.3)	27 (26.0)	112 (23.0)	38 (25.9)	9 (15.0)	0.351
Gestational diabetes, n (%)	9 (1.1)	0 (0)	3 (0.6)	4 (2.7)	2 (3.2)	0.034
Gestational hypertensive disorders, n (%)	62 (7.6)	4 (3.5)	27 (5.4)	15 (10.1)	16 (29.6)	<0.001
Paternal characteristics						
Age, mean (SD), years	33.9 (5.1)	33.5 (5.6)	34.1 (5.0)	33.6 (4.2)	33.9 (6.3)	0.517
Education (higher education), n (%)	472 (64.2)	68 (68.7)	312 (68.7)	73 (55.7)	19 (37.3)	<0.001
Body mass index, mean (SD), kg/m^2	25.2 (3.2)	24.5 (2.9)	25.0 (2.9)	26.0 (3.6)	26.6 (4.4)	<0.001
Birth and infant characteristics						
Boys, n (%)	439 (52.0)	60 (53.1)	277 (53.5)	69 (45.7)	33 (52.4)	0.405
Gestational age at birth, median (95% range), weeks	40.3 (35.9–42.4)	40.0 (36.0–42.0)	40.4 (35.9–42.6)	40.4 (35.6–42.4)	39.9 (34.3–42.8)	0.013
Birth weight, mean (SD), g	3515 (537)	3342 (527)	3530 (526)	3582 (545)	3542 (576)	0.002
Cesarean delivery, n (%)	119 (14.9)	13 (11.9)	71 (14.8)	21 (14.4)	14 (22.2)	0.326
Breastfeeding duration, mean (SD), months	4.4 (3.9)	4.7 (4.2)	4.6 (3.8)	4.4 (3.9)	2.7 (3.6)	0.008
Introduction of solids foods (before 6 months), n (%)	600 (80.2)	71 (73.9)	371 (79.6)	116 (86.6)	42 (80.8)	0.004
Infant fat mass measures						
1.5 months						
Age, mean (SD), months	1.6 (0.5)	1.6 (0.4)	1.7 (0.5)	1.5 (0.4)	1.6 (0.5)	0.029
Body mass index, mean (SD), kg/m^2	15.2 (1.4)	14.9 (1.3)	15.2 (1.4)	15.3 (1.5)	15.1 (1.4)	0.273
Total subcutaneous fat mass, mean (SD), mm	24.4 (7.5)	23.6 (7.8)	24.7 (7.8)	23.9 (6.7)	24.4 (7.0)	0.538
Central-to-total subcutaneous fat mass ratio, mean (SD)	0.50 (0.05)	0.50 (0.05)	0.50 (0.05)	0.50 (0.04)	0.50 (0.04)	0.949
6 months						
Age, mean (SD), months	6.5 (0.7)	6.6 (0.7)	6.5 (0.7)	6.6 (0.8)	6.4 (0.6)	0.252
Body mass index, mean (SD), kg/m^2	16.8 (1.3)	16.6 (1.3)	16.7 (1.3)	16.9 (1.4)	17.1 (1.4)	0.068
Total subcutaneous fat mass, mean (SD), mm	27.1 (6.5)	26.3 (6.1)	27.0 (6.3)	27.7 (7.4)	27.5 (5.7)	0.420
Central-to-total subcutaneous fat mass ratio, mean (SD)	0.47 (0.06)	0.47 (0.06)	0.46 (0.06)	0.47 (0.05)	0.48 (0.06)	0.163
24 months						
Age, mean (SD), months	25.3 (1.2)	25.3 (1.1)	25.3 (1.2)	25.2 (1.2)	25.4 (1.0)	0.804
Body mass index, mean (SD), kg/m^2	15.9 (1.3)	15.6 (1.4)	15.8 (1.2)	16.1 (1.3)	16.6 (1.4)	<0.001
Total subcutaneous fat mass, mean (SD), mm	27.6 (7.3)	26.9 (6.2)	27.4 (7.3)	27.6 (7.3)	30.0 (9.2)	0.078
Central-to-total subcutaneous fat mass ratio, mean (SD)	0.43 (0.07)	0.44 (0.07)	0.42 (0.06)	0.43 (0.06)	0.45 (0.08)	0.013

[a] Values are observed data and represent means (SD), medians (95% range) or numbers of subjects (valid %). Total subcutaneous fat mass = biceps + triceps + suprailiacal + subscapular skinfold thicknesses. Central-to-total subcutaneous fat mass ratio = (suprailiacal + subscapular skinfold thicknesses) / total subcutaneous fat mass. SD, standard deviation. IOM criteria, Institute of Medicine criteria.

Table 2
Associations of parental body mass index with infant subcutaneous fat mass measures.[a]

Model	Fat mass measures in standard deviation scores Difference (95% confidence interval)								
	1.5 months			6 months			24 months		
	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio
Maternal model									
n = 845	n = 729	n = 694	n = 694	n = 739	n = 733	n = 733	n = 659	n = 631	n = 631
Unadjusted model	0.05 (−0.03,0.12)	0 (−0.08,0.08)	0.04 (−0.04,0.11)	0.09 (0.02,0.17)*	0.04 (−0.04,0.11)	0.01 (−0.07,0.08)	0.19 (0.11,0.25)**	0.08 (0.01,0.16)*	0.08 (0.01,0.16)*
Adjusted model[b]	0.03 (−0.04,0.10)	−0.02 (−0.10,0.06)	0.04 (−0.04,0.12)	0.09 (0.01,0.17)*	0.02 (−0.06,0.10)	0.02 (−0.06,0.10)	0.17 (0.09,0.26)**	0.09 (0.01,0.17)*	0.08 (−0.01,0.17)
Paternal model									
n = 797	n = 687	n = 656	n = 656	n = 700	n = 693	n = 693	n = 621	n = 597	n = 597
Unadjusted model	0.12 (0.05,0.20)*	−0.02 (−0.10,0.06)	0.06 (−0.01,0.14)	0.05 (−0.02,0.13)	−0.01 (−0.09,0.06)	0.02 (−0.06,0.09)	0.10 (0.02,0.18)*	0.03 (−0.05,0.11)	0.08 (−0.01,0.16)
Adjusted model[c]	0.10 (0.03,0.17)*	−0.02 (−0.10,0.05)	0.06 (−0.02,0.13)	0.04 (−0.04,0.12)	−0.03 (−0.11,0.05)	0.03 (−0.05,0.11)	0.08 (0.01,0.16)*	0.02 (−0.06,0.10)	0.07 (−0.01,0.15)
Combined maternal and paternal model									
n = 797	n = 687	n = 656	n = 656	n = 700	n = 693	n = 693	n = 621	n = 597	n = 597
Unadjusted model									
Maternal body mass index	0.02 (−0.06,0.09)	0 (−0.08,0.08)	0.03 (−0.05,0.11)	0.09 (0.01,0.16)*	0.04 (−0.04,0.11)	0.01 (−0.07,0.08)	0.18 (0.10,0.26)**	0.08 (0.01,0.16)*	0.07 (−0.01,0.15)
Paternal body mass index	0.12 (0.04,0.19)*	−0.02 (−0.10,0.06)	0.06 (−0.02,0.14)	0.03 (−0.05,0.11)	−0.02 (−0.10,0.06)	0.01 (−0.07,0.09)	0.06 (−0.02,0.13)	0.01 (−0.07,0.09)	0.06 (−0.02,0.14)
Adjusted model[d]									
Maternal body mass index	0.01 (−0.06,0.08)	−0.02 (−0.11,0.06)	0.05 (−0.04,0.13)	0.09 (0.01,0.17)*	0.03 (−0.06,0.11)	0.02 (−0.06,0.11)	0.17 (0.09,0.26)**	0.09 (0.01,0.18)*	0.07 (−0.02,0.16)
Paternal body mass index	0.10 (0.03,0.16)*	−0.02 (−0.10,0.06)	0.05 (−0.03,0.13)	0.02 (−0.05,0.10)	−0.04 (−0.12,0.05)	0.02 (−0.06,0.10)	0.05 (−0.03,0.13)	0 (−0.08,0.09)	0.06 (−0.02,0.14)

[a] Values are regression coefficients (95% confidence interval) from linear regression models that reflect differences in subcutaneous fat mass measures in standard-deviation scores at 1.5, 6 and 24 months per standard-deviation scores change in maternal and paternal pre-pregnancy body mass index. Total subcutaneous fat mass = biceps + triceps + suprailiacal + subscapular skinfold thicknesses. Central-to-total subcutaneous fat mass ratio = (suprailiacal + subscapular skinfold thicknesses) / total subcutaneous fat mass.

[b] Maternal model includes maternal age and educational level, parity, maternal total energy intake, smoking habits and weight gain until 30 weeks of gestation, gestational diabetes, gestational hypertensive disorders, child's sex and gestational age-adjusted birthweight standard-deviation scores, cesarean delivery, breast feeding duration and timing of introduction of solid foods (for 6 and 24 months outcomes).

[c] Paternal model includes the same potential confounders as maternal model but paternal age and educational level instead of maternal age and educational level.

[d] Combined maternal and paternal model includes all potential confounders.

* P-value < 0.05.
** P-value < 0.01.

mass index at 6 months (difference: 0.30 (95% CI 0.11,0.48) SDS for excessive maternal weight gain as compared to non-excessive weight gain). No associations were observed for maternal weight gain measured until 30 weeks of gestation with infant body fat mass measures (Supplemental Table S2). In Supplemental Fig. S3, early-pregnancy weight gain was associated with higher total subcutaneous fat mass at 6 months, but not at older ages. No independent associations were observed for maternal mid- and late-pregnancy weight gain with infant fat mass measures.

4. Discussion

This study showed that maternal pre-pregnancy body mass index was positively associated with infant body mass index and total subcutaneous fat mass from 6 months onwards. Maternal total and period-specific gestational weight gain were not associated with infant body fat mass measures.

A higher maternal pre-pregnancy body mass index is associated with higher body mass index from early childhood onwards [1,2]. Also, maternal pre-pregnancy obesity seems to be associated with an adverse offspring body fat pattern, characterized by higher total fat mass and abdominal fat mass levels from the age of 2 years onwards [17–19]. A study among 325 infants showed that maternal pre-pregnancy obesity was positively associated with total fat mass already throughout infancy [20]. In the current study, we observed that maternal pre-pregnancy body mass index was already associated with a higher infant body mass index and total subcutaneous fat mass from

the age of 6 months onwards. No associations were observed for central-to-total subcutaneous fat mass ratio at all ages. Thus, maternal obesity seems to influence total body fat mass development already from early infancy onwards.

By comparing the strength of associations of maternal and paternal body mass index with offspring fat mass outcomes, further insight into the underlying mechanisms can be obtained. Stronger maternal associations would suggest that intra-uterine programming effects might be part of the underlying mechanisms, whereas similar or stronger paternal associations suggests that genetics and lifestyle-related characteristics might explain the observed associations. Previous studies comparing the strength of associations of parental body mass index with infant and childhood body mass index have reported inconsistent associations [21–23]. We have shown, among 4871 parents and their 6-year-old children, that maternal pre-pregnancy body mass index was more strongly associated with childhood total fat mass and android-to-gynoid fat mass ratio, as compared to paternal body mass index [6]. In this current study, we observed more consistent and stronger associations for maternal pre-pregnancy body mass index with infant subcutaneous fat mass measures from the age of 6 months onwards, as compared to the associations of paternal body mass index with infant outcomes. At 1.5 months, we observed stronger associations for paternal body mass index with infant body mass index as compared to maternal body mass index. Thus, these results suggest that intra-uterine programming effects may become more apparent at later ages. The intra-uterine programming effects may involve increased placental transfer of nutrients during fetal development. This may subsequently

Table 3
Associations of maternal maximum gestational weight gain with infant subcutaneous fat mass measures.[a]

| | Fat mass measures in standard deviation scores Difference (95% confidence interval) | | | | | | | | |
| | 1.5 months | | | 6 months | | | 24 months | | |
	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio	Body mass index	Total subcutaneous fat mass	Central-to-total subcutaneous fat mass ratio
Maximum gestational weight gain model									
n = 501	n = 447	n = 430	n = 430	n = 466	n = 460	n = 460	n = 433	n = 414	n = 414
Unadjusted	0.10 (0.01,0.19)*	−0.03 (−0.12,0.07)	−0.02 (−0.11,0.08)	0.11 (0.02,0.20)*	0.06 (−0.04,0.15)	0.04 (−0.05,0.14)	0 (−0.10,0.09)	−0.05 (−0.14,0.05)	−0.10 (−0.20,-0.01)*
Adjusted	0.05 (−0.04,0.14)	−0.04 (−0.14,0.06)	0.01 (−0.09,0.12)	0.09 (−0.01,0.19)	0.09 (−0.01,0.19)	0.07 (−0.03,0.17)	0.01 (−0.09,0.10)	−0.04 (−0.14,0.06)	−0.11 (−0.21,−0.01)*
Excessive gestational weight gain model[b]									
n = 242	n = 219	n = 212	n = 212	n = 225	n = 222	n = 222	n = 213	n = 202	n = 202
Unadjusted	0.19 (0.01,0.37)*	0 (−0.19,0.19)	0.04 (−0.15,0.23)	0.32 (0.14,0.50)**	0.11 (−0.07,0.30)	0.11 (−0.08,0.29)	0.12 (−0.07,0.30)	−0.01 (−0.20,0.19)	−0.11 (−0.31,0.08)
Adjusted	0.12 (−0.06,0.29)	−0.03 (−0.23,0.18)	0.09 (−0.11,0.30)	0.30 (0.11,0.48)**	0.13 (−0.06,0.32)	0.16 (−0.03,0.35)	0.16 (−0.04,0.35)	0.03 (−0.17,0.23)	−0.14 (−0.34,0.07)

[a] Values are regression coefficients (95% confidence interval) from linear regression models that reflect differences in subcutaneous fat mass measures in standard-deviation scores at 1.5, 6 and 24 months per standard-deviation scores change in maternal maximum gestational weight gain or for excessive weight gain as compared to the reference group (insufficient and sufficient weight gain). Total subcutaneous fat mass = biceps + triceps + suprailiacal + subscapular skinfold thicknesses. Central-to-total subcutaneous fat mass ratio = (suprailiacal + subscapular skinfold thicknesses) / total subcutaneous fat mass.

[b] Adjusted for maternal age and educational level, parity, pre-pregnancy body mass index (for models with maximum gestational weight gain as a continuous variable), maternal total energy intake, smoking habits during pregnancy, gestational diabetes, gestational hypertensive disorders, child's sex and gestational age-adjusted birthweight standard-deviation scores, cesarean delivery, breast feeding duration and timing of introduction of solid foods (for 6 and 24 months outcomes).

* P-value < 0.05.
** P-value < 0.01.

cause permanent adaptations in appetite, energy metabolism and neuro-endocrine function in offspring, which predispose individuals to a greater risk of obesity in later life [21]. These findings could also be explained by a stronger influence of maternal lifestyle-related characteristics on child's lifestyles and subsequent body fat mass. However, previous studies have suggested that maternal and paternal diet and physical activity are both associated with child's diet and physical activity, without a stronger maternal influence [24,25]. Also, since we adjusted our analyses for multiple potential confounders the influence of lifestyle-related characteristics on our findings might be limited.

Next to maternal pre-pregnancy obesity, higher maternal total gestational weight gain is also associated with a higher childhood body mass index, total fat mass levels and waist circumference [26,27]. We did not observe consistent associations of maternal total gestational weight gain with early infant fat mass measures. It has been suggested that the associations of maternal weight gain with offspring fat mass outcomes may depend upon the timing of gestational weight gain. A prospective cohort study among 5154 UK mothers and their children showed that maternal weight gain during early-pregnancy was positively associated with childhood body mass index and total fat mass [22]. In line with these findings, we have previously shown that a higher maternal weight gain, especially in early-pregnancy, is associated with a higher childhood body mass index, total body fat mass and abdominal fat mass levels at the age of 6 years [5]. However, these associations were weaker as compared to the associations for maternal pre-pregnancy body mass index with these offspring fat mass measures. A study among 977 Greek mothers and their children aged 4 years showed that maternal weight gain during early-pregnancy was positively associated with childhood body mass index, waist circumference and sum of skinfold thickness [28]. In the current study, no associations were present for maternal early-, mid- and late-pregnancy weight gain during pregnancy with early infant fat mass measures. Thus, maternal weight gain during pregnancy seems not to influence fat mass development in early infancy, but the effects may become more apparent at older offspring ages.

Strengths of this study were the prospective design with extensive maternal data collection from early pregnancy onwards and detailed infant body fat measurements available. Of the 1033 mothers and their singleton children with pre-pregnancy body mass index available, 82% (845) had information on infant body fat measures. The non-response could lead to biased effect estimates if the associations of maternal obesity during pregnancy with infant body fat were different between participants included and excluded in the analyses. This seems unlikely since no differences were observed between participants and non-participants regarding parental pre-pregnancy body mass index and maternal gestational weight gain. A limitation of our study might be the generalizability of our findings to other ethnic groups, due to our homogenous ethnic study population. Maternal pre-pregnancy body mass index and maximum gestational weight gain were self-reported, which may have led to misclassification and underestimation of the reported associations. However, we observed similar results when we used maternal weight measured at enrolment (results not shown) and weight gain measured until 30 weeks of gestation. Skinfold thickness is a valid measure to estimate infants subcutaneous fat mass but provides no information about intra-abdominal fat mass [8]. However, infant's body fat is mainly located subcutaneously in the first two years of life [29]. Also, inter- and intra-observer measurement error might be larger compared to other anthropometric measurements [30,31].

5. Conclusions

A higher maternal pre-pregnancy body mass index is associated with higher infant body mass index and total subcutaneous fat mass from the age of 6 months onwards. Maternal gestational weight gain was not associated with infant body fat. Further studies are needed to obtain insight into the causality of the observed associations, and the underlying biological mechanisms.

Conflicts of interest

None of the authors had a financial or personal conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.earlhumdev.2017.03.006.

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