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Short Communication

Maternal pre-pregnancy BMI and offspring body composition in young adulthood: the modifying role of offspring sex and birth order

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Abstract

Objective: To investigate if the association between maternal pre-pregnancy BMI and offspring's body composition in late adolescence and young adulthood varies by offspring birth order and sex.

Design: Family cohort study, with data from registers, questionnaires and physical examinations. The main outcome under study was offspring body composition (percentage fat mass (%FM), percentage lean mass (%LM)) measured by dual-energy X-ray absorptiometry.

Setting: Uppsala, Sweden.

Subjects: Two hundred and twenty-six siblings (first-born *v.* second-born; average age 19 and 21 years) and their mothers.

Results: In multivariable linear regression models, maternal pre-pregnancy BMI was positively associated with daughter's %FM, with stronger estimates for first-born ($\beta = 0{\cdot}97$, 95 % CI 0·14, 1·80) *v.* second-born daughters ($\beta = 0{\cdot}64$, 95 % CI 0·08, 1·20). Mother's BMI before her first pregnancy was associated with her second-born daughter's body composition ($\beta = 1{\cdot}05$, 95 % CI 0·31, 1·79 (%FM)) Similar results albeit in the opposite direction were observed for %LM. No significant associations were found between pre-pregnancy BMI and %FM ($\beta = 0{\cdot}59$, 95 % CI − 0·27, 1·44 first-born; $\beta = -0{\cdot}13$, 95 % CI − 0·77, 0·52 second-born) or %LM ($\beta = -0{\cdot}54$, 95 % CI − 1·37, 0·28 first-born; $\beta = 0{\cdot}11$, 95 % CI − 0·52, 0·74 second-born) for sons.

Conclusions: A higher pre-pregnancy BMI was associated with higher offspring %FM and lower offspring %LM in late adolescence and young adulthood, with stronger associations for first-born daughters. Preventing obesity at the start of women's reproductive life might reduce the risk of obesity in her offspring, particularly for daughters.

Keywords
Body composition
Maternal obesity
Dual-energy X-ray absorptiometry
Family study

Preconception and pregnancy are considered sensitive periods for obesity development for both mother and offspring[1]. Detrimental effects linked to excessive weight during pregnancy include gestational diabetes, pre-eclampsia, emergency caesarean delivery, preterm delivery and congenital defects[2–4]. Women with obesity before pregnancy have higher risk of excessive gestational weight gain[5,6] and gaining excessive gestational weight is associated with a higher postpartum weight retention[7]. This vicious circle could have negative consequences on subsequent pregnancies as interpregnancy weight gain has been linked to negative pregnancy outcomes[8,9].

Obese women, on average, give birth to larger offspring, who have an increased risk of obesity[10,11] and higher proportion of fat mass[12–16] later in life. The heritability of BMI and fat mass are reported to be 46–75 %[17] (all ages) and ~60 %[18] (adults), respectively, indicating that some of these effects may be genetically mediated.

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However, birth order may also be of importance as lower birth order has been linked to higher BMI[19], fat mass[12], and overweight or obesity[20].

To our knowledge, there are no studies investigating if birth order modifies the association between mother's pre-pregnancy BMI and her offspring's body composition and whether any such association differs between daughters and sons. The purpose of the present study was to investigate if the association between maternal pre-pregnancy BMI and offspring's body composition in late adolescence or young adulthood, defined as percentage fat mass (%FM) and percentage lean mass (%LM), varies by offspring birth order and sex.

Methods

Data used in the present study come from the Uppsala Family Study (UFS)[21], which includes families with two consecutive singleton offspring delivered at term (38–41 weeks of gestation) within 36 months of each other at the Uppsala Academic Hospital (Uppsala, Sweden) between 1987 and 1995. Families were recruited for a clinical examination in 2000–2002, with 602 sibling pairs (mean age 10·1 years) and their parents participating (31 % of eligible families invited to participate). Information regarding maternal and child characteristics related to pregnancy and delivery was obtained from the Swedish Medical Birth Register.

All 602 families were invited to a second clinical examination in 2010–2012. Members from 301 of the 602 families participated, including 168 sibling pairs (mean age 20·2 years, range 15·3–24·6 years). The participants completed health and lifestyle questionnaires and underwent physical examinations including anthropometric measurements and body composition measurement by dual-energy X-ray absorptiometry (DXA; Lunar Prodigy, GE Healthcare Lunar, Madison, WI, USA). Of the 168 sibling pairs with body composition measurements in the second clinical examination, 113 first- and second-born siblings also had data on their mothers' pre-pregnancy BMI, as well as complete information on other child and maternal relevant covariates. These 113 sibling pairs (n 226) comprised the analytical sample for the study.

Our exposure variables were maternal pre-pregnancy BMI and pre-pregnancy overweight/obesity (BMI $\geq$ 25·0 kg/m^2) for each offspring, which were estimated from mothers' height and self-reported pre-pregnancy weight recorded during their first antenatal care visit and obtained from the Swedish Medical Birth Register. Our outcome variables were offspring %FM and %LM based on DXA readings relative to the total body mass; LM is a composite of non-fat and non-bone tissue. Covariates included offspring's age (years), height (cm) and puberty stage at the time of DXA measurements; and mothers' age at offspring birth (years) and education level at the time of DXA measurements (some university education *v.* less). Puberty stage was estimated based on menarche (assessed by questionnaire) for girls and self-assessed testicular volume by orchidometer for boys[22]. Girls post-menarche were considered post-puberty, while boys were considered post-puberty if their orchidometer values were ≥12 or if they were older than 18 years. All first-born offspring and all but six boys and two girls in the second-born group were post-puberty at the time of DXA measurement.

Statistical analysis

We present characteristics of the study sample as means and standard deviations, or as frequencies and percentages, stratified by birth order and sex. We ran multivariable linear regression models with maternal pre-pregnancy BMI or pre-pregnancy overweight/obesity as exposure and offspring %FM or %LM as outcome. We further assessed the association between mothers' pre-pregnancy BMI and overweight/obesity from her first pregnancy and the body composition of her second-born offspring. All models were stratified by birth order and offspring sex. Model 1 was adjusted for offspring's age at DXA measurement. Model 2 was further adjusted for height at DXA measurement and, among later-born sons, puberty stage. Model 3 further included maternal age and educational level. The statistical software package SAS version 9.4 was used for all statistical analysis and a P value of <0·05 was used to denote statistical significance.

Results

Participants' characteristics are shown in Table 1. First-born offspring were on average 21·2 years old and second-born offspring 19·2 years old at the time of DXA measurements. Girls had higher %FM and lower %LM than boys, with %FM differing by approximately 2 percentage points by birth order for boys (no difference for girls). The mean maternal pre-pregnancy BMI did not differ much by birth order or offspring sex. However, maternal pre-pregnancy overweight/obesity was more common among second-born daughters (23·6 %) compared with the rest (11–12 %).

Mothers' pre-pregnancy BMI was positively and negatively associated with %FM and %LM, respectively, among daughters (Table 2). The association was present for both first- and second-born, but appeared to be stronger among first-born daughters. In the fully adjusted model, a one-unit increase in maternal pre-pregnancy BMI was associated with an increase of 0·9 and 0·6 percentage points of FM among first-born and second-born daughters, respectively. Associations with %LM mirrored those with %FM albeit in the opposite direction. In fully adjusted models, having a mother who was overweight/obese pre-pregnancy was not associated with offspring %FM and was

Table 1 Characteristics of the offspring (born 1987–1995 and examined in 2010–2012) and their mothers from the Uppsala Family Study (113 sibling pairs; *n* 226)

	First-born sons (*n* 60)		Second-born sons (*n* 58)		First-born daughters (*n* 53)		Second-born daughters (*n* 55)	
	Mean or *n*	SD or %	Mean or *n*	SD or %	Mean or *n*	SD or %	Mean or *n*	SD or %
Offspring birth characteristics								
Gestational age (weeks)	39·4	1·1	39·3	1·0	39·4	1·0	39·5	1·1
Birth weight (kg)	3·4	0·6	3·9	0·6	3·5	0·5	3·5	0·6
Birth length (cm)	51·0	2·2	52·0	2·2	50·4	2·1	50·7	2·3
Offspring's characteristics at the time of DXA measurement								
Age at DXA measurement (years)	21·4	1·9	19·0	2·2	21·0	1·9	19·3	1·9
Weight at DXA measurement (kg)	78·4	12·9	74·3	10·8	65·6	10·5	63·7	10·6
Height at DXA measurement (cm)	182·4	6·4	181·8	6·3	167·8	6·6	165·9	7·3
BMI at DXA measurement (kg/m^2)	23·6	3·5	22·5	2·8	23·3	3·6	23·1	3·1
Fat mass at DXA measurement (%)	18·5	8·3	16·5	7·2	31·9	7·7	31·9	8·0
Lean mass at DXA measurement (%)	77·2	8·0	79·2	7·0	64·0	7·5	64·0	7·9
Post-puberty, *n* and %	60	100·0	52	89·7	53	100·0	52	96·3
Maternal characteristics								
Mother's age at birth of child (years)	27·7	3·7	29·5	3·9	27·1	4·1	29·5	4·0
Mother's pre-pregnancy BMI (kg/m^2)	22·2	2·7	22·3	2·9	22·4	2·6	23·1	4·1
Mother's pre-pregnancy overweight/obesity (BMI ≥ 25·0 kg/m^2), *n* and %	7	11·7	7	12·1	6	11·3	13	23·6
Mother's university education at DXA measurement, *n* and %	40	66·7	36	62·1	26	49·1	30	54·6

DXA, dual-energy X-ray absorptiometry.
Data are presented as mean and SD unless indicated otherwise.

Table 2 Associations of mother's pre-pregnancy BMI and overweight/obesity (BMI ≥ 25·0 kg/m^2) with offspring's body composition determined by DXA among a sample of 113 first- and second-born sibling pairs, stratified by birth order and sex, from the Uppsala Family Study

	First-born sons (*n* 60)		Second-born sons (*n* 58)		First-born daughters (*n* 53)		Second-born daughters (*n* 55)	
	β	95 % CI	*β*	95 % CI	*β*	95 % CI	*β*	95 % CI
Percentage fat mass								
Mother's pre-pregnancy BMI, per 1 kg/m^2								
Model 1*	0·57	−0·25, 1·40	−0·11	−0·73, 0·52	**1·04**	**0·26, 1·83**	**0·60**	**0·08, 1·13**
Model 2†	0·62	−0·22, 1·45	−0·15	−0·79, 0·48	**0·98**	**0·18, 1·79**	**0·61**	**0·08, 1·15**
Model 3‡	0·59	−0·27, 1·44	−0·13	−0·77, 0·52	**0·97**	**0·14, 1·80**	**0·64**	**0·08, 1·20**
Mother's pre-pregnancy overweight/obesity *v.* not overweight/obese								
Model 1*	4·56	−2·28, 11·38	1·44	−4·12, 6·99	**6·72**	**0·04, 13·41**	3·90	−1·24, 9·05
Model 2†	4·80	−2·10, 11·71	1·10	−4·58, 6·77	6·64	−0·02, 13·30	3·90	−1·30, 9·10
Model 3‡	4·41	−2·76, 12·57	1·83	−3·93, 7·60	**6·99**	**0·04, 13·94**	4·06	−1·36, 9·48
Percentage lean mass								
Mother's pre-pregnancy BMI, per 1 kg/m^2								
Model 1*	−0·54	−1·33, 0·26	0·09	−0·52, 0·70	**−1·03**	**−1·79, −0·27**	**−0·59**	**−1·10, −0·07**
Model 2†	−0·57	−1·38, 0·23	0·14	−0·48, 0·76	**−0·98**	**−1·75, −0·20**	**−0·60**	**−1·12, −0·07**
Model 3‡	−0·54	−1·37, 0·28	0·11	−0·52, 0·74	**−0·96**	**−1·76, −0·16**	**−0·62**	**−1·17, −0·07**
Mother's pre-pregnancy overweight/obesity *v.* not overweight/obese								
Model 1*	−4·36	−10·94, 2·22	−1·47	−6·90, 3·96	**−6·72**	**−13·17, −0·28**	−3·77	−8·80, 1·26
Model 2†	−4·57	−11·23, 2·09	−1·12	−6·66, 4·42	**−6·65**	**−13·07, −0·23**	−3·77	−8·85, 1·31
Model 3‡	−4·15	−11·06, 2·75	−1·80	−7·45, 3·85	**−6·92**	**−13·63, −0·22**	−3·89	−9·19, 1·41

DXA, dual-energy X-ray absorptiometry.
Significant results are shown in bold.
*Model 1: adjusted for offspring's age at DXA measurement.
†Model 2: Model 1 + offspring's height at DXA measurement and for later-born sons also puberty stage.
‡Model 3: Model 2 + mothers' age at birth of offspring and mothers' education at DXA measurement.

associated with %LM among first-born daughters only (Table 2, Model 3). Mothers' pre-pregnancy BMI and overweight/obesity were not significantly associated with their sons' %FM or %LM.

We further examined the association between mother's pre-pregnancy BMI before her first child was born with the body composition of her second-born offspring. Mothers' BMI before the first pregnancy was associated with %FM and %LM of their second-born daughters but not of their second-born sons (Table 3). These estimates for the daughters were stronger than those for the pregnancy-specific pre-pregnancy BMI. Interpregnancy weight

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Table 3 Associations of mother's pre-pregnancy BMI and overweight/obesity (BMI ≥ 25·0 kg/m²) before her first pregnancy with her second-born offspring's body composition determined by DXA (*n* 113), stratified by sex, Uppsala Family Study

	Second-born sons (*n* 58)		Second-born daughters (*n* 55)	
	β	95 % CI	*β*	95 % CI
Percentage fat mass				
Mother's BMI before first pregnancy, per 1 kg/m²				
Model 1*	−0·15	−0·97, 0·66	**1·01**	**0·31, 1·71**
Model 2†	−0·22	−1·06, 0·62	**1·01**	**0·30, 1·72**
Model 3‡	−0·17	−1·01, 0·68	**1·05**	**0·31, 1·79**
Mother's overweight/obesity before first pregnancy *v.* not overweight/obese				
Model 1*	1·08	−4·91, 7·07	5·72	−8·25, 12·27
Model 2†	0·74	−5·37, 6·84	5·97	−0·77, 12·72
Model 3‡	1·72	−4·52, 7·96	6·55	−0·60, 13·71
Percentage lean mass				
Mother's BMI before first pregnancy, per 1 kg/m²				
Model 1*	0·12	−0·68, 0·91	**−0·98**	**−1·66, −0·29**
Model 2†	0·18	−0·64, 1·01	**−0·98**	**−1·68, −0·29**
Model 3‡	0·14	−0·69, 0·97	**−1·02**	**−1·74, −0·30**
Mother's overweight/obesity before first pregnancy *v.* not overweight/obese				
Model 1*	−1·11	−6·97, 4·75	−5·60	−11·99, 0·79
Model 2†	−0·76	−6·72, 5·21	−5·81	−12·40, 0·78
Model 3‡	−1·67	−7·79, 4·44	−6·31	−13·30, 0·69

DXA, dual-energy X-ray absorptiometry.
Significant results are shown in bold.
*Model 1: adjusted for offspring's age at DXA measurement.
†Model 2: Model 1 + offspring's height at DXA measurement and for later-born sons also puberty stage.
‡Model 3: Model 2 + mothers' age at birth of offspring and mothers' education at DXA measurement.

change was not associated with the second-born offspring's body composition (results not shown). We also tested interactions between maternal pre-pregnancy BMI and birth weight on offspring's body composition, with no interaction effects found (results not shown).

Discussion

Among a sample of Swedish adolescents and young adults, there was a differential association between mothers' pre-pregnancy BMI and her offspring's body composition by birth order and sex. The association between maternal pre-pregnancy BMI (and overweight/obesity) and offspring body composition was stronger for first-born compared with second-born daughters, with weaker and non-significant estimates for sons.

Other studies have observed positive associations between maternal pre-pregnancy BMI and %FM in offspring at ages 6[13], 9[14] and 30 years[12] although few have carried out sex-specific analysis[14]. Maternal FM or BMI was associated with offspring's FM also at infancy (≤1 week) but results regarding sex differences were inconsistent[15,16]. The body composition of 9-year-old girls and boys in the UK was dependent on their mothers' pre-pregnancy BMI, with a stronger association in girls[14], similar to our results in offspring aged 15–25 years. Sex differences in the genetics of BMI have been observed, especially after adolescence[23,24]. Such differences could potentially manifest as stronger mother–daughter compared with mother–son BMI or FM correlations[25,26] and might contribute to the sex differences observed in our results. In addition, cultural factors may also play a role: mothers may have a stronger influence on their daughters than on their sons in terms of dietary and lifestyle patterns, as well as attitudes and norms towards body image.

Animal studies have also found a differential sex effect of maternal nutrition during pregnancy on offspring's body composition, with the female offspring being more affected[27,28]. Female animals seem to be more sensitive to the intra-uterine environment than males as they seem more responsive to placental changes[28]. The sex of the offspring appears to influence both the size of the placenta and its ability to respond to adverse stimuli[29].

Previous research has already suggested that first-borns have a higher BMI compared with later-borns[12,19,20]. However, most of these studies were based on population samples, with only one study based on siblings[20], like ours. It is possible that the differences we observed between first- and second-born siblings were due to age or sexual maturation stage as opposed to birth order. A study of 10–17-year-old children in Lebanon found correlations in FM parameters for mother–children pairs but only among late pubertal sons and post-menarcheal daughters[30]. All first-born and most second-born offspring (90 % of boys and 96 % of girls) in our study were post-puberty. We were therefore unable to adjust for puberty stage in the analysis among second-born daughters but did account for pubertal status of second-born sons. Interestingly, studies also indicate that the heritability of BMI increases during childhood, reaching a peak at age 18–19 years[17,24] – close to the mean age of the second-born offspring in our study – before decreasing again during adulthood[17].

Our finding that pre-pregnancy BMI before the first pregnancy had a stronger association with the body composition of second-born daughters (but no association for second-born sons) than the pregnancy-specific BMI deserves further attention. This result implies that the weight status of the mother at the start of her reproductive life is of importance not only for the first-born but also for the second-born, particularly among daughters.

Strengths of our study include its family design, which allowed us to investigate the effects of maternal pre-pregnancy BMI on first- *v.* second-born full siblings. In addition, we assessed the offspring's actual body composition measured by DXA instead of using BMI as a proxy. As for limitations, pre-pregnancy BMI was recorded 8–12 weeks into pregnancy and may be different from the true pre-pregnancy BMI. Moreover, our sample is relatively small and homogeneous in terms of ethnicity, including only full siblings delivered at term with a maximum interpregnancy interval of 36 months. This is a strength for internal validity, but may limit the generalizability of the results to mothers and siblings with larger interpregnancy intervals, children not born at term, or children of mothers who remained primiparous. Only half of the original UFS families participated in the follow-up examination, and parents who did not come for the second wave were on average younger, less educated and had a higher BMI. Moreover, most mothers in our sample had a normal BMI; this limits our ability to test the hypothesis that overweight/obesity pre-pregnancy influences offspring's body composition. On the other hand, if we observed effects of pre-pregnancy BMI on offspring's body composition even in this small sample with a normal BMI range, we speculate that the effects could be higher and stronger among populations with higher-than-normal BMI. Finally, puberty stage was self-reported albeit with valid methods, with some of the second-born children in the sample not having gone through puberty at the time of DXA measurement. We controlled for puberty stage in our analysis of second-born sons, but it is possible that our results reflect pubertal age rather than birth order.

Conclusion

In conclusion, mothers' pre-pregnancy BMI was associated with daughters' body composition in late adolescence and young adulthood, with stronger effects among the first-born. The mechanisms behind the reported associations and the apparently absent effects among sons remain to be clarified. Moreover, mothers' BMI before their first pregnancy was associated with their second-born daughter's body composition, with stronger associations than those observed for pregnancy-specific BMI. This result implies that preventing overweight and obesity at the start of women's reproductive life may prevent obesity in the first and subsequent offspring. Larger studies employing family designs with multiple offspring are needed to further disentangle the effects of pre-pregnancy BMI on offspring body composition from the possible effects of gestational weight gain and interpregnancy weight change.

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