Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study

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Summary

Background **Maternal obesity has been positively associated with risk of adverse pregnancy outcomes, but evidence of a causal relation is scarce. Causality would be lent support if temporal changes in weight affected risk of adverse pregnancy outcomes.**

Methods **We examined the associations between change in prepregnancy body-mass index (BMI) from the first to the second pregnancies, and the risk of adverse outcomes during the second pregnancy in a nationwide Swedish study of 151 025 women who had their first two consecutive singleton births between 1992 and 2001.**

Findings **Compared with women whose BMI changed between –1·0 and 0·9 units, the adjusted odds ratios for adverse pregnancy outcomes for those who gained 3 or more units during an average 2 years were: pre-eclampsia, 1·78 (95% CI 1·52–2·08); gestational hypertension 1·76 (1·39–2·23); gestational diabetes 2·09 (1·68–2·61); caesarean delivery 1·32 (1·22–1·44); stillbirth 1·63 (1·20–2·21); and large-for-gestational-age birth 1·87 (1·72–2·04). The associations were linearly related to the amount of weight change and were also noted in women who had a healthy prepregnancy BMI for both pregnancies.**

Interpretation **These findings lend support to a causal relation between being overweight or obese and risks of adverse pregnancy outcomes. Additionally they suggest that modest increases in BMI before pregnancy could result in perinatal complications, even if a woman does not become overweight. Our results provide robust epidemiological evidence for advocating weight loss in overweight and obese women who are planning to become pregnant and, to prevent weight gain before pregnancy in women with healthy BMIs.**

Introduction

The increasing prevalence of obesity worldwide has prompted WHO to designate obesity as one of the most important global health threats.[1] The epidemic is especially pronounced in young people; in the USA, for example, 28% of women aged 20–39 years are obese.[2]

The adverse effect of maternal overweight and obesity on the outcome of pregnancy has been suspected for more than 50 years.[3] Large population-based epidemiological studies indicate that high prepregnancy weight or body-mass index (BMI) confers an increased risk of maternal and perinatal complications, including pre-eclampsia, gestational diabetes, caesarean delivery, macrosomia, and stillbirth.[4–11] Although these associations are biologically plausible and the risks seem to increase with the degree of overweight, suggesting that there is a dose-response effect,[4,7,11] the possibility that overweight and obesity share common causes with the outcomes cannot be ruled out. Therefore, causal inference for these associations is still regarded as being speculative.[11]

The argument for a causal association between maternal overweight and adverse pregnancy outcomes would be strengthened if the frequency of these endpoints proved related to changes in exposure over time—ie, that risks were determined by the gain or loss of weight before pregnancy. In a nationwide Swedish cohort study, we examined whether changes in BMI between the beginning of the first and start of the second pregnancies were associated with risks of pre-eclampsia, gestational diabetes, caesarean delivery, stillbirth, and large-for-gestational-age births during the second pregnancy.

Methods

Participants

The population-based Swedish Birth Register contains information about demographic characteristics, reproductive history, anthropometry (weight and height from 1992 onwards), and smoking habits, recorded at the first antenatal visit. Between 1990 and 1998, 93–95% of pregnant women in Sweden attended antenatal care before their 15th week of gestation.[12–14] Complications during pregnancy and delivery are registered when the woman is discharged from hospital and classified according to Swedish versions of the International Classification of Diseases (ICD) ninth and tenth revisions. Information for maternal country of birth and education level can be obtained from the immigration registry and education registry, respectively, through linkage with the unique national registration number which is assigned to all Swedish residents.

The study population consisted of 207 534 women who had first and second consecutive singleton births between 1992 and 2001. Weight and height at the first antenatal visit for the two consecutive pregnancies were available in 151 080 women (73%). There were no substantial differences in the demographic characteristics for women with and those without data for weight. Women for whom data for weight were available had a slightly lower

rate of gestational diabetes (849, 0·6% *vs* 389, 0·7%, p=0·0009), gestational hypertension (831, 0·6% *vs* 389, 0·7%, p=0·0002), and caesarean delivery (15 020, 10% *vs* 6264, 11%, p<0·0001) during the second pregnancy than those for whom such data were not available. There were no differences in the frequency of pre-eclampsia, stillbirth, or large-for-gestational-age births. 55 women with implausible values for weight were excluded, providing a final sample size of 151 025.

The study protocol was presented in writing to the research ethics committee at Karolinska Institutet, who approved the study (number 4863/2005). The data set did not include personal identifiers, such as national registration numbers, names, or addresses. Informed consent was therefore neither possible to obtain, nor required by the research ethics committee.

Study design

We calculated BMI at the first antenatal visit of each pregnancy. Height changed by more than 2 cm between pregnancies in only 3% (5066) of women. We calculated interpregnancy change in BMI as the difference between BMI at the beginning of the first and second pregnancies. We categorised the differences as less than –1 (BMI loss greater than 1 unit), –1 to less than 1, 1 to less than 2, 2 to less than 3, or 3 or more units. Using the education register, we obtained information for the number of years of formal education completed by all women as of Dec 31, 2002, and categorised them as 9 years or less, 10–11 years, 12 years, 13–14 years, or 15 or more years. We calculated the interpregnancy interval as the number of complete months between the birth of the first child and the estimated date of conception of the second child, and classed it as intervals of 11 months or less, 12–23 months, 24–35 months, or 36 months or more. Prepregnancy BMI at the beginning of the first pregnancy was grouped according to conventional cut-off points for underweight (≤18·4), healthy weight (18·5–24·9), overweight (25·0–29·9), and obesity (≥30).[15] Other covariates were grouped according to table 1.

The outcomes considered were maternal and perinatal complications of the second pregnancy according to information recorded at birth (mode of delivery, stillbirth or livebirth, birth weight, gestational age, and infant sex) or at the time of hospital discharge (maternal diseases). Maternal complications were pre-eclampsia (ICD-9 codes 642E-642H and ICD-10 codes O11 and O14), gestational hypertension (ICD-9 codes 642D and 642X, and ICD-10 code O13), gestational diabetes (ICD-9 code 648W and ICD-10 code O244), and caesarean delivery. Perinatal complications included stillbirth and large-for-gestational-age birth. Stillbirth was defined as a fetal death at 28 weeks of gestation or later, and was further classified as term (≥37 completed weeks of gestation) or preterm (≤36 weeks). Large-for-gestational-age births were newborn babies who weighed more than 2 SD above the mean weight for gestational age according to the Swedish reference of fetal growth.[16] In Sweden, early second-trimester ultrasonography to estimate gestational age is routinely offered, and 95% of women accept this offer.[17]

Statistical analysis

We compared the distribution of interpregnancy weight gain as a continuous variable with sociodemographic characteristics and outcome of the first pregnancy as categorical predictors using the Kruskal-Wallis test. We estimated incidence of each outcome during the second pregnancy by categories of change in BMI from the first pregnancy, and tested the linearity of the associations using the Cochran-Armitage test. Women who had had the outcome during the first pregnancy were excluded from that analysis. We estimated odds ratios (OR) and

	Number*	Mean change in BMI (SD)	p value†
Maternal characteristics at first pregnancy			
Age (years)			
≤19	3586	1·36 (2·75)	
20–24	39 488	0·95 (2·17)	
25–29	66 452	0·78 (1·80)	<0·001
30–34	34 215	0·66 (1·70)	
≥35	7284	0·61 (1·66)	
Smoking			
Non-smoker	127 240	0·77 (1·86)	<0·001
Smoker	20 728	0·99 (2·16)	
Prepregnancy BMI (kg/m²)			
≤18·4	5216	1·17 (1·66)	
18·5–24·9	109 009	0·76 (1·64)	<0·001
25·0–29·9	28 713	0·90 (2·35)	
≥30	8087	0·82 (3·20)	
Height (cm)			
≤159	17 362	1·06 (2·13)	
160–164	38 397	0·87 (1·96)	<0·001
165–169	45 708	0·76 (1·87)	
≥170	49 558	0·70 (1·81)	
Country of origin			
Non-Nordic	15 785	1·15 (2·22)	<0·001
Nordic	134 865	0·76 (1·87)	
Years of education			
≤9	12 244	1·15 (2·39)	
10–11	45 365	0·91 (2·01)	
12	36 413	0·81 (1·90)	<0·001
13–14	28 886	0·67 (1·73)	
≥15	27 119	0·57 (1·60)	
Interpregnancy interval (months)			
≤11	29 866	0·66 (1·90)	
12–23	62 288	0·57 (1·73)	<0·001
24–35	32 146	0·88 (1·84)	
≥36	26 590	1·40 (2·24)	

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Complications during first pregnancy			
Pre-eclampsia			
No	144 600	0·79 (1·90)	<0·0001
Yes	6425	1·03 (2·16)	
Gestational hypertension			
No	149 303	0·80 (1·91)	<0·0001
Yes	1722	0·94 (2·14)	
Gestational diabetes			
No	150 005	0·80 (1·91)	0·07
Yes	1020	0·84 (2·22)	
Caesarean delivery			
No	133 406	0·79 (1·89)	<0·0001
Yes	17 619	0·91 (2·02)	
Stillbirth			
No	150 359	0·80 (1·91)	0·004
Yes	666	0·97 (2·14)	
Intrauterine growth			
Large for gestational age	2847	1·04 (2·19)	
Adequate for gestational age	142 827	0·80 (1·90)	<0·0001
Small for gestational age	4769	0·83 (1·96)	
Overall	n =151 025	0·80 (1·91)	

*Totals might be less than 151 025 because of missing values. †Kruskal-Wallis tests.

Table 1: **Change in BMI between first and second pregnancies according to sociodemographic characteristics and outcome of first pregnancy in Swedish women, 1992–2001**

95% CIs for all outcomes by categories of interpregnancy change in BMI using multivariate logistic regression models in which known predictors of maternal BMI and adverse pregnancy outcomes were introduced as adjustment variables. Specifically, the risk of an adverse pregnancy outcome related to interpregnancy BMI change was adjusted for BMI at first pregnancy, height, length of the interpregnancy interval, and maternal characteristics at the second pregnancy, including age, country of origin, years of education, year of delivery, and smoking. Statistical power was poor for subgroup analyses of women who had had the complication during the first pregnancy.

In supplemental analyses, we examined whether BMI at the beginning of the first pregnancy modified the associations between change in BMI during the interpregnancy interval and the incidence of adverse pregnancy outcomes. We stratified these analyses by whether the mother's BMI at the beginning of her first pregnancy was above or below 25, and tested the statistical significance of a cross-product interaction term between BMI at baseline and BMI change between pregnancies. All analyses were done with Statistical Analysis Software version 9.

Role of the funding source

The sponsor played no part in the study design; data collection, data analysis, data interpretation, or in the writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

On average, women gained just over half a BMI unit (median 0·7, IQR –0·3 to 1·7) during a mean interpregnancy interval of 24 months (median 20, IQR 13–31). Weight gain between pregnancies decreased with age, education, height, and BMI at the first pregnancy, and was lower in women of Nordic origin; and increased with smoking at the first pregnancy, the interpregnancy interval, and adverse outcomes during the first pregnancy, including pre-eclampsia, gestational hypertension, caesarean delivery, stillbirth, and a large-for-gestational-age birth (table 1).

The risk of adverse outcomes increased linearly with weight gain between pregnancies, after adjustment for potential confounders (table 2). The risks of pre-eclampsia, gestational hypertension, gestational diabetes, and large-for-gestational-age birth started to rise at weight gains of 1 BMI unit to less than 2 units, and continued to increase progressively thereafter. Furthermore, the risks of pre-eclampsia and large-for-gestational-age birth fell significantly in women who lost more than one BMI unit between pregnancies, compared with the reference group.

The adjusted odds of stillbirth were 63% greater in women who gained 3 or more BMI units between pregnancies than in those whose weight changed by less than 1 BMI unit (p=0·002). Risk of stillbirth increased significantly as category of weight gain increased (p=0·03). This association remained virtually unchanged after we made additional adjustment for maternal diabetes or hypertension during the second pregnancy (OR for BMI change ≥3 *vs* –1 to <1=1·63; 95% CI 1·20–2·20; p value test for trend=0·029). When we examined term and preterm stillbirths separately, we noted a significant linear association with interpregnancy weight change for term stillbirths (adjusted OR for ≥3 BMI units change *vs* –1 to <1=1·87, 95% CI 1·23–2·86; p for trend=0·002), but not for preterm stillbirths (p for trend=0·96).

We assessed whether the results of the analyses changed after realising that some women might have had more than one adverse outcome during their second pregnancy. Of 1523 women with pre-eclampsia only in second pregnancy, 16 also had gestational diabetes, hypertension, or a stillbirth; exclusion of these 16 women did not change the associations between interpregnancy change in BMI and pre-eclampsia. Gestational hypertension and gestational diabetes were correlated: of 701 cases of gestational hypertension and 730 cases of gestational diabetes, 381 mothers had both. The positive associations between interpregnancy change in BMI and each of these outcomes were still linear, strong, and significant after excluding women who had both outcomes.

	Maternal complications								Neonatal complications			
	Pre-eclampsia (n=1523)		Gestational hypertension (n=701)		Gestational diabetes (n=730)		Caesarean delivery (n=6451)		Stillbirth (n=394)		LGA (n=5943)	
	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)
BMI change—all women†												
< –1‡	0·8	0·82 (0·67–0·99)	0·5	1·14 (0·88–1·48)	0·4	0·98 (0·75–1·28)	4·3	0·96 (0·88–1·05)	0·3	1·17 (0·83–1·64)	3·2	0·84 (0·76–0·93)
–1 to <1	0·8	1·00	0·4	1·00	0·4	1·00	4·4	1·00	0·2	1·00	3·3	1·00
1 to <2	1·1	1·23 (1·07–1·41)	0·5	1·39 (1·13–1·70)	0·5	1·32 (1·08–1·62)	4·8	1·05 (0·98–1·13)	0·2	0·99 (0·74–1·32)	4·4	1·32 (1·23–1·41)
2 to <3	1·5	1·63 (1·39–1·91)	0·6	1·49 (1·17–1·91)	0·7	1·67 (1·32–2·11)	5·6	1·19 (1·09–1·29)	0·3	1·11 (0·78–1·56)	5·2	1·55 (1·42–1·68)
≥3	1·9	1·78 (1·52–2·08)	0·7	1·76 (1·39–2·23)	0·9	2·09 (1·68–2·61)	6·6	1·32 (1·22–1·44)	0·5	1·63 (1·20–2·21)	6·6	1·87 (1·72–2·04)
p, trend§	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	0·0002	0·03	<0·0001	<0·0001
BMI change—women less than 25 units¶												
< –1‡	0·6	0·85 (0·64–1·13)	0·3	1·11 (0·74–1·69)	0·3	0·90 (0·59–1·37)	4·1	1·05 (0·94–1·18)	0·3	1·30 (0·85–1·99)	2·2	0·83 (0·72–0·96)
–1 to <1	0·7	1·00	0·3	1·00	0·3	1·00	4·1	1·00	0·2	1·00	2·7	1·00
1 to <2	0·8	1·12 (0·93–1·35)	0·4	1·72 (1·31–2·27)	0·3	1·18 (0·88–1·59)	4·7	1·07 (0·98–1·16)	0·2	1·12 (0·79–1·58)	3·3	1·25 (1·14–1·38)
2 to <3	1·0	1·40 (1·08–1·83)	0·4	1·84 (1·22–2·77)	0·5	1·83 (1·25–2·69)	4·9	1·12 (0·99–1·27)	0·3	1·03 (0·61–1·76)	3·5	1·40 (1·21–1·62)
≥3	0·9	1·36 (0·90–2·06)	0·5	2·48 (1·41–4·35)	0·6	2·28 (1·34–3·88)	6·2	1·33 (1·12–1·59)	0·3	1·32 (0·66–2·66)	3·6	1·64 (1·32–2·03)
p, trend§	0·0003	0·002	0·0003	<0·0001	0·0003	<0·0001	<0·0001	0·005	0·36	0·94	<0·0001	<0·0001

OR=odds ratio. LGA=large for gestational age for livebirths. *Odds ratios and 95% CIs from logistic regression models adjusted for baseline BMI (at first pregnancy), height, interpregnancy interval, and maternal characteristics at second pregnancy, including age, country of origin, years of education, year of delivery, and smoking. For analysis of each endpoint, women with the outcome during first pregnancy were excluded. Only women with complete data were included in multivariate analyses. †Population distribution according to interpregnancy change in BMI categories was: < -1, 11%; -1 to <1, 46%; 1 to <2, 21%; 2 to <3, 11%; ≥3, 11%. ‡Refers to BMI loss greater than 1 unit. §For cumulative incidence rates, from the Cochran-Armitage test. For odds ratios, test for trend corresponds to Wald test for change in BMI when ordinal variable was introduced into logistic regression model as a continuous predictor. ¶Population distribution according to interpregnancy change in BMI was: < -1, 11%; -1 to <1, 58%; 1 to <2, 21%; 2 to <3, 7%; ≥3, 3%.

Table 2: **Adjusted odds ratios for adverse perinatal outcomes during second pregnancy in relation to change in BMI from the first pregnancy for all women and for women with a BMI of less than 25 at the time of both pregnancies***

For gestational hypertension only—ie, after exclusion of women who also had gestational diabetes—the adjusted OR (95% CI) were 0·93 (0·61–1·43) for the less than –1 category, 1·00 (reference) for the –1 to less than 1 category, 1·39 (1·02–1·88) for the 1 to less than 2 category, 1·39 (0·93–2·06) for the 2 to less than 3 category, and 1·79 (1·21–2·63) for the 3 or more category, with an adjusted p for linear trend of 0·0007. For gestational diabetes only—ie, after exclusion of women who also had hypertension—the OR for the same exposure categories were, respectively, 0·40 (95% CI 0·21–0·77), 1·00 (reference), 1·36 (0·97–1·91), 1·91 (1·31–2·79), and 2·90 (2·04–4·12) with an adjusted p value for linear trend of less than 0·0001.

To examine whether the effects of weight gain were independent from those of overweight or obesity, we analysed the risks of adverse pregnancy outcomes in relation to prepregnant weight change in the subset of 97 558 women who had a prepregnant BMI of less than 25 for both pregnancies. The size, direction, and significance of the associations were more-or-less the same as those reported for the whole population, with the exception of risk of stillbirth, which did not increase significantly with prepregnancy weight gain (table 2).

Finally, we tested for interactions between BMI at first pregnancy (classed as <25 or ≥25) and weight change between pregnancies (in five groups as detailed previously in tables). We showed significant interactions with respect to risks of gestational hypertension (p=0·0005), gestational diabetes (p=0·005) and large-for-gestational-age birth (p<0·0001) (table 3). Although weight gain increased the risk of all outcomes in both groups, the linear associations with gestational hypertension, diabetes, and large-for-gestational-age birth were significantly stronger in women whose BMI was less than 25 at the outset, compared with overweight mothers. The effect of interpregnancy BMI change on pre-eclampsia, caesarean delivery, and stillbirth was not significantly affected by BMI status at the first pregnancy.

Discussion

The findings from this large, prospective population-based study show that weight gain during the interpregnancy interval, as estimated from the difference between first-trimester weights, is strongly associated

	Gestational hypertension				Gestational diabetes				LGA‡			
	First pregnancy BMI <25 (n=401)		First pregnancy BMI ≥25 (n=300)		First pregnancy BMI <25 (n=417)		First pregnancy BMI ≥25 (n=313)		First pregnancy BMI <25 (n=3593)		First pregnancy BMI ≥25 (n=2350)	
	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)	Rate (%)	OR (95% CI)
Change in BMI†												
< –1	0·3	1·09 (0·72–1·65)	0·8	0·98 (0·70–1·37)	0·3	0·89 (0·58–1·36)	0·7	0·96 (0·66–1·37)	2·2	0·81 (0·70–0·93)	4·9	0·82 (0·72–0·95)
–1 to <1	0·3	1·00	0·8	1·00	0·3	1·00	0·7	1·00	2·7	1·00	5·9	1·00
1 to <2	0·5	1·86 (1·45–2·38)	0·7	0·81 (0·56–1·16)	0·4	1·35 (1·04–1·74)	0·9	1·29 (0·93–1·81)	3·6	1·35 (1·24–1·47)	7·2	1·25 (1·10–1·41)
2 to <3	0·5	1·94 (1·41–2·67)	0·9	1·02 (0·70–1·49)	0·5	1·95 (1·44–2·64)	1·0	1·36 (0·94–1·96)	4·2	1·64 (1·47–1·83)	7·9	1·38 (1·20–1·59)
≥3	0·5	2·49 (1·79–3·47)	1·0	1·20 (0·87–1·67)	0·7	2·88 (2·15–3·88)	1·2	1·54 (1·11–2·13)	5·1	2·22 (1·99–2·48)	8·8	1·56 (1·38–1·76)
p, trend§	<0·0001	<0·0001	0·22	0·32	<0·0001	<0·0001	0·0002	0·002	<0·0001	<0·0001	<0·0001	<0·0001
p, interaction¶	<0·0001				0·0005				<0·0001			

OR=odds ratio. *Odds ratios are from logistic-regression models adjusted for height, interpregnancy interval, and maternal characteristics at second pregnancy including age, country of origin, years of education, year of delivery, and smoking. For analysis of each endpoint, women who had had the outcome during first pregnancy were excluded. †For women with a first pregnancy BMI of less than 25, the distribution of the population according to the interpregnancy change in BMI categories was: less than –1, 9%; –1 to less than 1, 50%; 1 to less than 2, 22%; 2 to less than 3, 10%; 3 or more, 8%. For women with a first pregnancy BMI of 25 or more, the distribution of change in BMI was: less than –1, 19%; –1 to less than 1, 33%; 1 to less than 2, 18%; 2 to less than 3, 13%; 3 or more, 17%. ‡Large for gestational age, for livebirths. §For cumulative incidence rates, from the Cochran-Armitage test. For the odds ratio, the test for trend corresponds to the Wald test for change in BMI when the ordinal variable was introduced into the logistic regression model as a continuous predictor. ¶Multivariate-adjusted likelihood ratio test for a cross-product term between the change in BMI between pregnancies representing ordinal categories and an indicator variable for baseline BMI of less than 25.

Table 3: **Adjusted odds ratios for obstetric complications in second pregnancy associated with changes in BMI since first pregnancy, by categories of BMI at first pregnancy***

with the risk of major maternal and perinatal complications, independent of whether women are overweight or not. The gain of 1–2 BMI units only during an average 2 years would increase the risk of gestational hypertension, gestational diabetes, or large-for-gestational-age birth by an average of 20–40% and further linear increases in risk would follow weight gain. In view of the large sample size and the general consistency of the associations recorded, the findings are unlikely to be due to chance. The use of standardised records, the relative homogeneity of the population, and the adjustment of the associations by maternal characteristics including age, smoking, and education, are likely to have reduced potential confounding.

Our results indicate that an unmeasured obesity-related factor is unlikely to be an important underlying cause of the increased risks of major maternal and perinatal complications, and strengthen the argument for a causal relation between maternal overweight or obesity and adverse pregnancy outcomes. This finding is of particular relevance, since the rates of overweight and obesity in women of childbearing age continue to increase worldwide. During the study, (1992–2001) the prevalence of overweight and obesity in pregnant women in Sweden increased from 25% to 36%.[18] Similarly, between 1990 and 2002–04, the BMI of pregnant women at first prenatal visit in England increased by an average of 1·4 units, and the prevalence of obesity doubled.[19] In the USA, the prevalence of obesity in women aged 20–39 years tripled from 9% in 1960–62 to 28% in 1999–2000,[2] and in many developing countries, the prevalence of overweight women now surpasses that of underweight women.[20] Since the prevalence of other strong risk factors for maternal and perinatal complications, such as smoking, are decreasing in several developed countries,[21] weight gain between pregnancies is likely to contribute substantially to the causes of adverse pregnancy outcomes.

We showed that a gain of 3 or more BMI units was significantly associated with the risk of stillbirth and that this association was independent of obesity-related diseases in pregnancy, such as pre-eclampsia, gestational hypertension, or diabetes. Consistent with previous analyses of prepregnancy or early pregnancy BMI, the association was stronger for term than for preterm stillbirths.[11,22] The biological mechanisms underlying this association, independent of pregnancy-induced hypertension and gestational diabetes, are speculative. Several of the metabolic and inflammatory disorders that characterise obesity have been documented in pregnant women even in the absence of glucose dysregulation or hypertension. Compared with women of healthy weight, overweight pregnant women present with: dyslipidaemia; higher concentrations of leptin, interleukin-6, and C-reactive protein; and impaired microvascular endothelial function.[23,24] Placental dysfunction during the first trimester of pregnancy has been associated with stillbirth;[25] whether obesity mediated inflammation leads to early endothelial dysfunction of the placenta and subsequent stillbirth warrants further investigation.

Prepregnant weight gain increased the risk of adverse pregnancy outcomes even in women who were not overweight. Additionally, the risks of gestational hypertension, diabetes, and large-for-gestational-age birth in relation to interpregnancy weight gain were higher for

women deemed to have healthy prepregnancy BMI at first pregnancy, than for women who were overweight at that time. These results suggest women do not necessarily need to become overweight or obese to increase their risk of gestational complications. Instead, a modest increase in weight between pregnancies within the healthy BMI category, or enough to shift from the healthy to the overweight category, would be sufficient to increase a woman's average risk of serious adverse outcomes during the next pregnancy.

The public-health implications of this finding are substantial. For example, if a woman 1·65 m tall who weighs 63 kg before the first pregnancy (giving her a BMI of 23) gained about 3 kg (1 BMI unit) between first and second pregnancies, her average risk of gestational diabetes would increase by more than 30%, even if she did not become overweight by the second pregnancy. If she did become overweight, by gaining 6 kg (2 BMI units), her average risk would increase by 100%; and if she became obese, the risk would rise by nearly 200%. The same woman would also substantially increase her average risk of gestational hypertension and large-for-gestational-age birth. By contrast, the loss of at least 1 BMI unit seems to result in reduced risk of large-for-gestational-age birth, and would maintain the risks of gestational diabetes or hypertension at general population level. Our study underscores the importance of avoiding weight gain between pregnancies and accords with the view that even a moderately increased BMI could be deleterious for maternal and neonatal health.

The participants in this study were women whose interpregnancy interval between first and second pregnancies ranged from less than 1 year to 10 years. The results are generalisable to primiparous women. Whether large weight gains before the first pregnancy—eg, during adolescence—or after the second pregnancy would result in similar increases in the incidence of obstetric complications is uncertain. Since we estimated interpregnancy weight gain as the difference between women's weights at first prenatal visits, increases in BMI from the first to the second pregnancy could represent postpartum weight retention.[26] Studies to characterise the burden and predictors of postpartum weight retention should provide clues to the design of interventions to prevent interpregnancy weight gain.

One limitation of our study is the possibility of residual confounding by unmeasured concomitant risk factors or illnesses that could be associated with both interpregnancy weight gain and gestational outcomes. Additionally, we did not have information for week of gestation at the first prenatal visit. Thus the estimate of interpregnancy weight change does not account for pregnancy-related weight gain that might have taken place before booking into prenatal care. However, since 93–95% of women in Sweden attend their first prenatal visit before gestation week 15,[12–14] bias of the interpregnancy weight gain estimate is unlikely. Adjustment for maternal sociodemographic and lifestyle characteristics that might be related to time of first prenatal visit could have partly reduced potential bias. Potential misclassification of change in BMI, due to interpregnancy change in height (seen in 3% of the women) is unlikely to affect our findings, since the proportion of such women was the same whether or not they had the outcomes, but might have introduced some bias in the associations recorded towards the null value. Finally, we could not differentiate the effect of postpartum weight retention from that of other causes of weight gain.

Despite these limitations, our results provide robust epidemiological evidence for advocating weight loss in overweight and obese women who are planning to become pregnant and, more importantly, to prevent weight gain before pregnancy in the larger population of women of healthy weight. High levels of physical activity[27] and dietary modifications[28] are likely to improve weight control in women of childbearing age. Combinations of dietary modification and exercise also seem to be effective in avoidance of postpartum weight retention.[29] Assessment of whether these interventions can be successfully implemented at the population level is a crucial pending task.

Contributors

E Villamor and S Cnattingius had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. E Villamor did statistical analyses and drafted the manuscript. Both authors interpreted the results and revised and approved the final version of the manuscript.

Conflict of interest statement

We declare that we have no conflict of interest.

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