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# Interpregnancy weight change and recurrence of gestational diabetes mellitus: a population-based cohort study

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**Objective** To estimate recurrence risk of gestational diabetes mellitus (GDM) by interpregnancy weight change.

**Design** Population-based cohort study.

**Setting and population** Data from the Swedish (1992–2010) and the Norwegian (2006–2014) Medical Birth Registries on 2763 women with GDM in first pregnancy, registered with their first two singleton births and available information on height and weight.

**Methods** Interpregnancy weight change (BMI in second pregnancy minus BMI in first pregnancy) was categorised in six groups by BMI units. Relative risks (RRs) of GDM recurrence were obtained by general linear models for the binary family and adjusted for confounders. Analyses were stratified by BMI in first pregnancy (<25 and ≥25 kg/m<sup>2</sup>).

**Main outcome measure** GDM in second pregnancy.

**Results** Among overweight/obese women (BMI ≥25), recurrence risk of GDM decreased in women who reduced their BMI by 1–2

units (relative risk [RR] 0.80, 95% CI 0.65–0.99) and >2 units (RR 0.72, 95% CI 0.59–0.89) and increased if BMI increased by ≥4 units (RR 1.26, 95% CI 1.05–1.51) compared with women with stable BMI (–1 to 1 units). In normal weight women (BMI <25), risk of GDM recurrence increased if BMI increased by 2–4 units (RR 1.32, 95% CI 1.08–1.60) and ≥4 units (RR 1.61, 95% CI 1.28–2.02) compared with women with stable BMI.

**Conclusion** Interpregnancy weight loss reduced risk of GDM recurrence in overweight/obese women. Weight gain between pregnancies increased recurrence risk for GDM in both normal and overweight/obese women. Our findings highlight the importance of weight management in the interconception window in women with a history of GDM.

**Keywords** Body mass index, gestational diabetes, interpregnancy, recurrence, weight change.

**Linked article** This article is commented on by C Scifres, p. 1617 in this issue. To view this mini commentary visit <https://doi.org/10.1111/1471-0528.16397>

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## Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of various degrees that is detected during pregnancy.<sup>1</sup> Women with GDM have increased risks of metabolic syndrome,<sup>2</sup> type 2 diabetes mellitus<sup>3</sup> and cardiovascular disease later in life.<sup>4</sup> Children born to women with GDM have an increased risk of high birthweight and long-term metabolic disease, indicating transmission of

risk through generations due to genetic, epigenetic and environmental influence.<sup>5</sup> The incidence of GDM in Europe varies by country and population but has increased over the last decades,<sup>6</sup> contributing to a considerable increase in national medical costs.<sup>7</sup> The recurrence risk of GDM is high,<sup>8</sup> and an American population-based study found that close to 50% of women with GDM in their first pregnancy also developed GDM in their second pregnancy.<sup>9</sup>

Numerous risk factors for GDM have been identified, including maternal age, prepregnancy body mass index (BMI), nonwhite ethnicity, family history of diabetes mellitus, weight gain in early adulthood and cigarette smoking; however, findings are inconsistent and vary across studies.<sup>8,10</sup> Weight change between pregnancies may be an independent risk factor for GDM in women without GDM in first pregnancy,<sup>11,12</sup> and weight loss in women who were overweight at start of first pregnancy has been associated with reduced risk of GDM in second pregnancy,<sup>12,13</sup> although not consistently in all studies.<sup>11,14</sup> The high prevalence of overweight<sup>15</sup> and the increasing trend of GDM in reproductive women across the world emphasise the necessity to focus on weight change as a modifiable risk factor for GDM.

Understanding of underlying mechanisms of GDM is scarce and limits the ability for targeted interventions. As maternal weight is amenable to intervention, evidence of a preventive effect of weight loss on GDM recurrence will be crucial in public health strategies promoting healthy weight in the entire reproductive window. We pursued this by using population-based family data from two Scandinavian countries.

The specific aims were to estimate the association between weight change from first to second pregnancy and recurrence risk for GDM, and to explore the modifying role of BMI in first pregnancy.

## Methods

### Study design

This population-based cohort study has analysed harmonised and pooled data from the Swedish (1992–2010) and Norwegian (2006–2014) Medical Birth Registries. The study periods were based on available information on maternal height and weight in the two registries and an established research collaboration between Sweden and Norway. The unique national identification numbers assigned to each citizen residing in these countries, enabled linkage of all births to each woman. Mothers with their first two successive singleton births during the study periods constituted the study unit in the analyses. Both national birth registries have collected data prospectively<sup>16,17</sup> and are based on compulsory notification of all live- and stillbirths. Antenatal, obstetric and early neonatal care data are by law collected by standardised notification forms, and include demographic characteristics, reproductive history, maternal health before and during pregnancy, pregnancy and delivery complications, and outcomes.<sup>18,19</sup>

In the Swedish data, maternal height and weight measured in light clothing at the first antenatal visit were registered from 1992. Roughly 90% of Swedish women had their first antenatal visit before 12 completed weeks.<sup>16</sup> In

Norway, self-reported height and prepregnancy weight from the antenatal charts were included when electronic notification of births was implemented in the birth registry. The implementation was gradual and initiated at different years for the more than 50 delivery units in the country (from 2006 to 2014) and was not linked to a specific type of delivery unit or specific group of delivering women.<sup>17</sup> Smoking habits at the beginning of pregnancy have been registered in Sweden since 1983 and in Norway since 1999. Educational level represents the highest achieved level of education obtained from the Education Registry in Sweden and from the National Education Database at Statistics Norway. Information on mother's country of birth was obtained from the Swedish Immigration Registry and Statistics Norway.

### Population

We included women with singleton births in first and second pregnancy, without diabetes mellitus prior to first pregnancy. Women who had developed diabetes mellitus type 1 or 2 by the time of their second pregnancy were excluded. To evaluate the association between weight change and recurrence of GDM, we focused on women with GDM in first pregnancy whose BMI was reported in both pregnancies. There was no patient or public involvement in the development of this research.

### Exposure and outcome

Maternal weight was registered in kilograms (kg) and maternal height in meters (m) with three digits in both birth registries. In cases with missing height in one pregnancy, height in the other pregnancy was used. If height differed by less than  $-2$  or  $+2$  cm we used the registered height in first pregnancy. If height differed by more than  $-2$  or  $+2$  cm,  $z$ -scores for height (observed height – population mean height/population standard deviation) was calculated based on the population of women with GDM in first pregnancy who had no difference in registered height in first and second pregnancy. Women with  $z$ -scores for height  $>4$  or  $<-4$  in first or second pregnancy were excluded, as data were considered implausible. BMI in first and second pregnancy was calculated from weight in kg divided by height in  $m^2$  and categorised as underweight ( $<18.5$ ), normal weight (18.5–24.9), overweight (25.0–29.9), obese class I (30–34.9) and obese class II/III ( $\geq 35$ ).<sup>20</sup> In stratified analyses, BMI in first pregnancy was dichotomised into  $<25$  and  $\geq 25$ .<sup>20</sup> Interpregnancy interval was calculated as date of second birth minus date of first birth minus gestational age of second pregnancy and was categorised into  $<12$ , 12–23, 24–35 and  $\geq 36$  months. To have an equal distribution of women within strata, year of second birth was categorised according to 30 percentiles (1992–2001, 2002–2006, 2007–2014).

The main exposure was interpregnancy weight change, defined as BMI in second pregnancy minus BMI in first pregnancy, expressed as units BMI ( $\text{kg}/\text{m}^2$ ) (one BMI unit is equivalent to approximately a 2.7-kg reduction or increase in weight in a woman who is 1.68 m tall and weighs 65 kg). Interpregnancy weight change was categorised as:  $<-2$ ,  $-2$  to  $<-1$ ,  $-1$  to  $<1$  (stable BMI, used as reference),  $1$  to  $<2$ ,  $2$  to  $<4$  and  $\geq 4$   $\text{kg}/\text{m}^2$ .<sup>12,21</sup>

The main outcome was GDM (yes/no), notified via a check box on the birth notification form or as diagnostic codes according to the International Classification of Diseases (ICD) Swedish version 9 (648W) and ICD-10 (O244). The diagnostic criteria of GDM during the entire study period in Norway were: fasting plasma glucose levels  $<7.0$  mmol/l and serum blood glucose following an oral glucose tolerance test (2 hours after intake of 75 g oral glucose) of  $\geq 7.8$  mmol/l but  $<11.1$  mmol/l, defined according to the National Guidelines by the Norwegian Society of Gynaecology and Obstetrics.<sup>22</sup> For Sweden, the main diagnostic criterion for the disease was based on a 75-g oral glucose tolerance test with a fasting capillary blood glucose level  $\geq 6.1$  mmol/l and/or a 2-hour capillary blood glucose  $\geq 9.0$  mmol/l.<sup>23,24</sup> In Norway and most parts of Sweden, selective glucose tolerance tests are performed based on known risk factors.<sup>22–24</sup> However, practices concerning screening and diagnostic criteria of GDM in Sweden vary in the different healthcare settings.<sup>23,24</sup>

### Statistical analysis

Chi-square tests were used to indicate associations and linear trends. Generalised linear models with log link, binomial distribution and exponentiated regression coefficients were used to calculate relative risks (RR) with 95% confidence intervals (CI) for the association between recurrent GDM and interpregnancy weight change categories. The reference category was stable weight ( $-1$  to  $<1$  BMI units). We used the theoretical framework directed acyclic graphs (DAG) with 'dagitty' version 2.3 (www.dagitty.net) to visualise possible causal pathways<sup>25</sup> (Figure S1). Maternal age at second delivery ( $<25$ ,  $25$ – $29$ ,  $\geq 30$  years), year of second birth (1992–2001, 2002–2006, 2007–2014), education in years ( $<10$ ,  $\geq 10$ ), maternal country of birth (Nordic [Norway, Sweden, Denmark, Finland and Iceland], non-Nordic, missing), smoking at the start of second pregnancy (yes, no, missing) and interpregnancy interval ( $<24$ ,  $\geq 24$  months), were considered possible confounders and adjusted for in the multivariable model.<sup>8,10,26</sup> We handled missing data on covariates (3.9%, 108/2763) by including simple imputation methods and assigning a separate value for missing data in the adjusted model. We also performed missing imputation using chained equations (MICE)<sup>27</sup> with logistic regression for smoking, maternal country of birth and maternal education; however, adjusted models were

almost unchanged. A potential effect modification by BMI in first pregnancy (BMI  $<25$  and BMI  $\geq 25$ ) was evaluated by including an interaction term (BMI in first pregnancy  $\times$  BMI change between pregnancies) in the multiplicative model (assessed by likelihood-ratio test). Analyses were stratified by BMI in first pregnancy, interpregnancy interval, maternal education, smoking at the start of second pregnancy, year of second birth and maternal country of birth.

Finally, as a sensitivity analysis, we evaluated whether interpregnancy weight change trajectories influenced GDM recurrence risk additionally to that of the absolute BMI in second pregnancy (Table S1). By combining BMI categories (BMI  $<25$ ,  $25.0$ – $29.9$  and  $\geq 30$   $\text{kg}/\text{m}^2$ )<sup>20</sup> in first and second pregnancy, we were able to calculate absolute risks of GDM recurrence with 95% CI for each of the nine interpregnancy weight change trajectories.

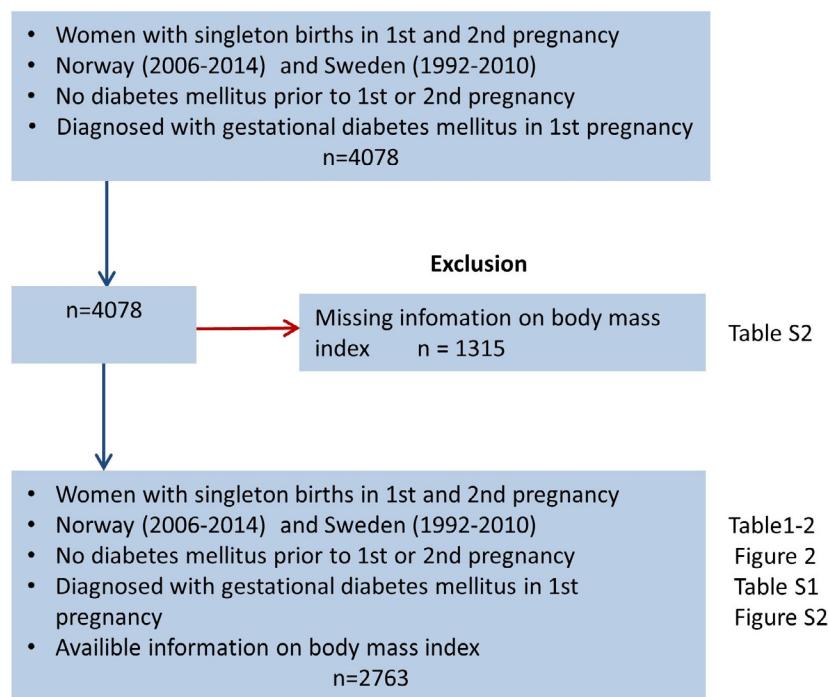
Associations were considered statistically significant at the 5% level. The statistical analyses were performed using STATA IC Statistical software version 15 and IBM SPSS statistical software version 25 (www.spss.com).

## Results

Inclusions and exclusions are shown in Figure 1. In the two registries, 614 432 women had singleton first and second births without established diabetes mellitus. Among these, 4078 women were registered with GDM in their first pregnancy (2957 in Sweden and 1121 in Norway). After excluding 1315 (32.2%) women with missing information on BMI, a total of 2763 women (2414 Swedish and 349 Norwegian women) were left for analyses of GDM recurrence risk. The population with available information on BMI in both pregnancies ( $n = 2763$ ) was compared with the population with missing information on BMI ( $n = 1315$ ) with respect to maternal characteristics and risk of GDM recurrence (Table S2). There was a higher proportion of missing data and a higher absolute risk of GDM recurrence (571/1315, 43.4%) in the population with missing information on BMI.

The overall recurrence risk for GDM in second pregnancy was 39% (Table 2). BMI in first pregnancy and maternal age in second pregnancy were associated with GDM recurrence (Table 1). For women with BMI  $<25$  and  $\geq 25$  in first pregnancy, the recurrence rates were 33.6% (425/1264) and 43.6% (653/1499), respectively (Tables S3 and S4).

In women with GDM in first pregnancy, 19.7% had a weight loss  $>1$  BMI unit, 39.8% were stable in weight and 40.5% increased their weight by  $\geq 1$  BMI unit (Table 2). Among women with weight loss of  $>2$  BMI units between first and second pregnancy, 85% ( $n = 225$ ) were overweight (BMI  $\geq 25$ ) and 15% ( $n = 39$ ) were normal weight at the



**Figure 1.** Flow chart showing inclusion and exclusion in our study.

start of first pregnancy. Compared with women who were stable in weight between pregnancies, women with weight loss  $>2$  BMI units had a 20% lower risk of GDM recurrence (adjusted RR [aRR] 0.80, 95% CI 0.66–0.97) (Table 2, Figure S2). GDM recurrence increased linearly across categories of BMI change between first and second pregnancy ( $P$ -value for trend;  $<0.0001$ ) (Figure S2). Women gaining  $\geq 4$  BMI units had a 42% increased risk of GDM recurrence (aRR 1.42, 95% CI 1.22–1.65) compared with women with a stable weight. Stratified analyses revealed similar trends between BMI change and risk of GDM recurrence in women with BMI  $<25$  and  $\geq 25$  in first pregnancy (Figure 2, Tables S3 and S4). There was no interaction between BMI in first pregnancy ( $<25$  and  $\geq 25$  kg/m<sup>2</sup>) and interpregnancy weight change categories ( $\chi^2 = 3.78$ ,  $P = 0.582$ , likelihood-ratio test). Crude and adjusted regression models were almost identical.

Overweight women (BMI  $\geq 25$ ) who reduced their weight between pregnancies by  $>2$  or 1–2 BMI units, had a 28% (aRR 0.72, 95% CI 0.59–0.89) and 20% (aRR 0.80, 95% CI 0.65–0.99) lower risk of GDM recurrence respectively, compared with overweight women with stable weight (Figure 2, Table S4). In women with BMI  $<25$  in first pregnancy, reduced weight was not associated with a significantly reduced risk of GDM recurrence (Figure 2, Table S3). Women who gained  $\geq 4$  BMI units from first to second pregnancy had an increased risk of GDM recurrence,

independent of BMI in first pregnancy ( $<25$  and  $\geq 25$ ). The crude and adjusted models differed only slightly. The association between interpregnancy weight change and GDM recurrence in second pregnancy remained in stratified analyses of maternal age, country of birth, year of second birth, interpregnancy interval, smoking at the start of second pregnancy and education (data not shown).

In sensitivity analyses, investigating absolute GDM recurrence risk by categories of BMI in first and second pregnancy (Table S1) we found that for women whose BMI at second pregnancy was 25.0–29.9 (overweight), the lowest risk of GDM recurrence in second pregnancy (26.8%, 95% CI 16.7–39.1) was found for women who reached this BMI category by losing weight (from BMI  $\geq 30$  in first pregnancy), whereas the highest risk (44.7%, 95% CI 38.4–51.1) was found for women who gained weight (from BMI  $<25$  in first pregnancy). Similar trends were found both for women who had BMI  $\geq 30$  and BMI  $<25$  in second pregnancy.

## Discussion

### Main findings

Overweight/obese women (BMI  $\geq 25$ ) with weight loss  $>2$  or 1–2 BMI units between pregnancies, had a 28% (aRR 0.72, 95% CI 0.59–0.89) and 20% (aRR 0.80, 95% CI 0.65–0.99) lower risk of GDM recurrence, respectively, compared

**Table 1.** Maternal characteristics of women with gestational diabetes mellitus (GDM) in first pregnancy\* according to recurrence of GDM ( $n = 2763$ ); Pooled data from the Swedish (1992–2010) and the Norwegian (2006–2014) Medical Birth Registries

	GDM recurrence				Total	Absolute risk (%)	Chi-square P-value
	No	%	Yes	%			
<b>BMI 1st pregnancy (kg/m<sup>2</sup>)</b>							
<18.5	39	2.3	19	1.8	58	32.8	<0.0005**
18.5–24.9	800	47.5	406	37.7	1206	33.7	
25–29.9	458	27.2	323	30.0	781	41.4	
≥30	388	23.0	330	30.6	718	46.0	
<b>Maternal age 2nd pregnancy (years)</b>							
<25	173	10.3	60	5.6	233	25.8	<0.0005**
25–29	487	28.9	294	27.3	781	37.6	
≥30	1025	60.8	724	67.2	1749	41.4	
<b>Smoking at the start of 2nd pregnancy</b>							
No	1497	88.8	969	89.9	2466	39.3	0.18
Yes (daily/sometimes)	155	9.2	81	7.5	236	34.3	
Missing	33	2.0	28	2.6	61	45.9	
<b>Maternal country of birth</b>							
Nordic	1227	72.8	743	68.9	1970	37.7	0.08
Non-Nordic	451	26.8	331	30.7	782	42.3	
Missing	7	0.4	4	0.4	11	36.4	
<b>Maternal education (years)</b>							
<10	193	11.5	121	11.2	314	38.5	0.95
10–14	964	57.2	623	57.8	1587	39.3	
>14	505	29.9	319	29.6	824	38.7	
Missing	23	1.4	15	1.4	38	39.5	
<b>Marital status</b>							
Married/cohabiting	1614	96.9	1045	97.5	2659	39.3	0.36
Other	52	3.1	27	2.5	79	34.2	
Missing	19		6		25		
<b>Interpregnancy interval (months)</b>							
<12	373	22.1	215	19.9	588	36.6	0.54
12–23	641	38.0	416	38.6	1057	39.4	
24–35	321	19.1	220	20.4	541	40.7	
≥36	350	20.8	227	21.1	577	39.3	
<b>Mother's height (cm)</b>							
<160	354	21.0	237	22.0	591	40.1	0.47
160–164	506	30.0	297	27.6	803	37.0	
165–169	458	27.2	291	27.0	749	38.9	
≥170	367	21.8	253	23.5	620	40.8	
<b>Total</b>	<b>1685</b>	<b>100</b>	<b>1078</b>	<b>100</b>	<b>2763</b>	<b>39.0</b>	

\*Women with singleton pregnancies without diabetes mellitus prior to first pregnancy.

\*\*P-value for chi-square trend.

with overweight women with stable weight. Gaining weight between pregnancies was associated with increased risk of GDM recurrence in women with a BMI <25 as well as ≥25 in first pregnancy.

### Strengths and limitations

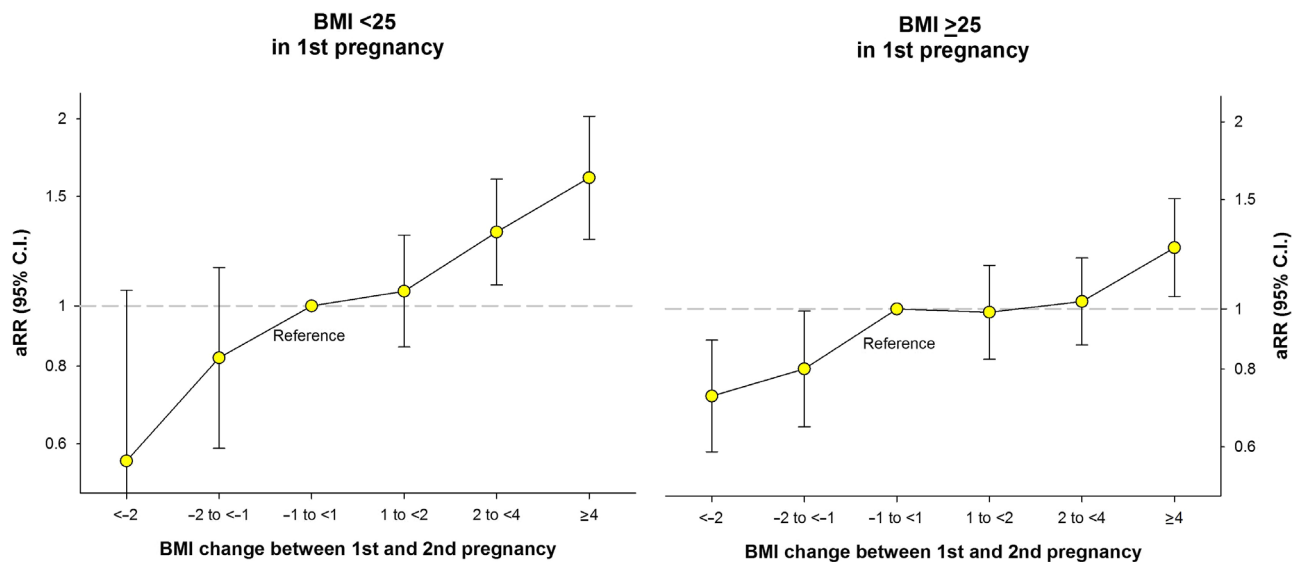
The family design enabled us to study how weight change from first to second pregnancy revealed a heterogeneity in risk of GDM recurrence, which underlines that GDM

recurrence is not only determined by genetic factors but seems amenable to intervention. A large sample size enabled us to show a dose–response association between weight change from first to second pregnancy and risk of recurrent GDM. The relation remained consistent across strata, suggesting weight to be part of a metabolic mechanism behind GDM. Despite strengths, there are some limitations of our study. Self-reported height and weight may have introduced misclassification bias; however, in women

**Table 2.** Overall relative risk (RR) for recurrence of gestational diabetes mellitus (GDM) in second pregnancy; Pooled data from the Swedish Medical Birth Registry (1992–2010) and the Norwegian Medical Birth Registry (2006–2014) ( $n = 2763$ )

BMI change from 1st to 2nd pregnancy		1st pregnancy	2nd pregnancy	Risk for GDM recurrence in 2nd pregnancy					
Units, kg/m <sup>2</sup>	N (%)	Mean BMI	Mean BMI	n/N	GDM (%)	Crude RR	95% CI	Adj RR*	95% CI
<-2	264 (9.6)	31.6	27.6	82/264	31.1	0.81	0.67–0.99	0.80	0.66–0.97
-2 to <-1	279 (10.1)	27.4	26.0	93/279	33.3	0.87	0.73–1.04	0.86	0.71–1.03
-1 to <1	1100 (39.8)	25.9	25.9	421/1100	38.3	1.00	Reference	1.00	Reference
1 to <2	463 (16.8)	25.9	27.3	180/463	38.9	1.02	0.89–1.16	1.02	0.89–1.17
2 til <4	471 (17.0)	26.5	29.3	202/471	42.9	1.12	0.99–1.27	1.15	1.02–1.31
≥4	186 (6.7)	28.5	34.4	100/186	53.8	1.40	1.21–1.64	1.42	1.22–1.65
Total	2763 (100)	26.9	27.5	1078/2763	39.0				

\*Analyses adjusted for maternal age (<25 [reference], 25–29, ≥30), year of second birth (1992–2001 [reference], 2002–2006, 2007–2014), maternal education (<10 years, ≥10 years [reference]), interpregnancy interval (<24 months, ≥24 months [reference]), maternal country of birth (Nordic [reference], non-Nordic, missing) and maternal smoking at the start of second pregnancy (no [reference], yes, missing).



**Figure 2.** Adjusted relative risk (aRR) for recurrence of gestational diabetes mellitus (GDM) in women with body mass index (BMI) <25 ( $n = 1264$ ) and ≥25 ( $n = 1499$ ) in first pregnancy; Pooled data from the Swedish (1992–2010) and the Norwegian Medical Birth Registry (2006–2014). Analyses are adjusted for maternal age (<25 [reference], 25–29, ≥30), year of second birth (1992–2001 [reference], 2002–2006, 2007–2014), maternal education (<10 years, ≥10 years [reference]), interpregnancy interval (<24 months, ≥24 months [reference]), maternal country of birth (Nordic [reference], non-Nordic, missing), maternal smoking at the start of second pregnancy (no [reference], yes, missing).

of reproductive age, self-reported height and weight differs only slightly from direct measures and has been found to give valid estimates in research and for clinical use.<sup>28</sup> Data on height and weight were collected before the outcome GDM, and possible misclassification of BMI would therefore be independent of the outcome and non-differential.<sup>29</sup> Selection bias due to missing data on BMI is a possibility, however, as the absolute risk of GDM recurrence in our study population was lower than in the population with missing BMI information (39.0 versus 43.6%); this will likely bias risk estimates towards the null

and underestimate the true association between weight change and GDM recurrence. The high proportion of missing data in the Norwegian data is suggested to be randomly missing across the population,<sup>17</sup> and if lack of information is randomly assigned, impact on risk estimates would be minor.<sup>16,29</sup> In both Norway and Sweden, a risk-based screening strategy for GDM is used. This may result in under-reporting of GDM. Thus, our results may not be generalisable to potentially more heterogeneous populations where universal screening for GDM is established.

We could not distinguish between weight change in the interpregnancy interval and gestational weight gain during first pregnancy, and reported weight change could be a product of both. Unmeasured confounding by diet, exercise and lifestyle changes cannot be excluded.

No core outcome set was used in this study.

## Interpretation

Our results demonstrate that interpregnancy weight change may alter GDM recurrence trajectory in a population of women characterised by high GDM recurrence. The dose–response association between interpregnancy weight change and GDM recurrence indicates that maternal weight is a likely causal factor behind GDM. These findings complement studies which have found that interpregnancy weight change modified risk of GDM in a second pregnancy in a population of women who did not have GDM in their first pregnancy.<sup>11,12</sup> Studies have investigated interpregnancy weight change and risk of GDM in a second pregnancy; however, authors have typically included women both with and without GDM in first pregnancy<sup>13,30</sup> or excluded women with GDM in first pregnancy.<sup>11,12</sup> Difference in design and methodology make interpretation of these results difficult.

The gestational diabetes mellitus recurrence rate in our study is consistent with American cohort studies of similar design, revealing a 41%<sup>31</sup> and 38%<sup>13</sup> GDM recurrence rate. The high GDM recurrence rate may be due to underlying impairment following GDM from first pregnancy, suggesting that the impaired  $\beta$ -cell function continues even after the stresses of pregnancy have ended.<sup>32</sup> Defects in maternal insulin sensitivity and secretion, may be unmasked in response to metabolic stressors of a subsequent pregnancy.<sup>33</sup> However, results from our study suggest the possibility of altering the natural GDM recurrence trajectory by changing women's weight from first to second pregnancy. Weight loss in overweight/obese individuals improves adiposity-induced systemic inflammation,<sup>34</sup> and interpregnancy weight loss in overweight women may improve insulin sensitivity and  $\beta$ -cell function, resulting in a better ability to cope with the physiological demands<sup>1,35,36</sup> of decreased insulin sensitivity in the subsequent pregnancy. In contrast, weight gain is likely to increase the pressure on the glucose metabolism, causing a sub-clinically decreased insulin sensitivity, which may limit the metabolic capacity in both normal weight and overweight women. This may explain the increased risk of GDM recurrence associated with interpregnancy weight gain found in women with BMI <25 and women with BMI  $\geq$ 25 in our study. Generally, GDM is likely to represent detection of a chronic condition of low and falling  $\beta$ -cell compensation for chronic insulin resistance, rather than development of an acute condition of pregnancy.<sup>37</sup> This hypothesis is further

strengthened by the strong association between GDM and later type 2 diabetes mellitus.<sup>3</sup>

Results from our sensitivity analysis indicate that the interpregnancy weight change trajectories (weight loss or weight gain) add to the risk associated with the absolute BMI at second pregnancy, which is most evident for women overweight at second pregnancy. Although confidence intervals were wide and overlapping, our results are likely to have clinical importance.

Despite the well-known high risk of GDM recurrence, care for women in the interconception period is lacking.<sup>38</sup> The majority of women in our study (40.5%) had an interpregnancy weight gain, underlining the tendency for women to gain rather than reduce weight between pregnancies.<sup>39</sup> Only 19.7% of women had an interpregnancy weight loss >1 BMI unit. These results are comparable to the 41.1% weight gain and 13.1% weight loss in a Swedish study of similar design.<sup>21</sup> Among women with an interpregnancy weight loss of >2 BMI units, 85% ( $n = 225$ ) had a BMI  $\geq$ 25 at the start of first pregnancy. This is evidence that overweight/obese women who experience GDM in their first pregnancy, may make an effort to reduce their weight by the second pregnancy. A potential benefit of interpregnancy weight loss on GDM recurrence should not, however, come at the expense of increased risk of adverse outcomes in a subsequent pregnancy. A similar study from the UK found that women with a weight loss >1 BMI unit had an increased risk of small for gestational age (SGA) in second pregnancy, independent of BMI in first pregnancy.<sup>40</sup> However, in a cohort study from Australia, they revealed an increased risk of SGA only among normal weight women with an interpregnancy weight loss.<sup>30</sup> Among women with a BMI  $\geq$ 25 in first pregnancy, an interpregnancy weight loss  $\geq$ 2 BMI units was even associated with a reduced risk of SGA.<sup>30</sup>

## Conclusion

Overweight/obese women with a weight loss >1 BMI unit from first to second pregnancy had a 20–28% lower risk of GDM recurrence, compared with overweight/obese women who were stable in weight. Gaining weight between pregnancies was associated with increased risk of GDM recurrence in women who had BMI < 25 and women with BMI  $\geq$  25 in first pregnancy. Our results may have implications for both healthcare and public health strategies, aiming at promoting healthy weight in the interconception window in women with a history of GDM. If interpregnancy weight change is able to alter GDM recurrence trajectory, future research should explore whether interpregnancy weight change may modify the strong association between GDM and later type 2 diabetes mellitus.



### Disclosure of interests

None declared. Completed disclosure of interests forms are available to view online as supporting information.

### Contribution to authorship

LMS, RS and N-HM contributed to the conceptualisation of this study. LMS analysed the data, wrote the original draft of the manuscript and is responsible for the reviewing and editing of the manuscript. N-HM, RS and KK reviewed the analyses and contributed with skills in methodology. N-HM, RS, KK SC, A-KW and LGK contributed with critical comments to the analyses and in the reviewing and writing of this manuscript. RS is guarantor for data quality. LMS is the corresponding author and the guarantor of this study.

### Details of ethics approval

The project was approved in Sweden by the regional ethics committee at Karolinska Institutet, Stockholm (No. 2012/1813-31/4, 31 April 2012) and in Norway by the Regional Ethics Committee REK VEST (2015/1728, 5 November 2015). All data handled by the researchers were anonymous, and as we did not have additional patient contact, individual consent was not required for the use of these compulsorily collected national data.

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### Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1.** Proposed directed acyclic graph for the pathways between interpregnancy weight change (Diff BMI 1st – 2nd) and gestational diabetes mellitus recurrence (GDM 2nd) in our study.

**Figure S2.** Overall adjusted relative risk (aRR) for recurrence of gestational diabetes mellitus (GDM) in second pregnancy in pooled data from the Swedish (1992–2010) and the Norwegian Medical Birth Registry (2006–2014) ( $n = 2763$ ).

**Table S1.** Absolute risks (%) and proportions ( $n/N$ ) of gestational diabetes mellitus (GDM) recurrence in second pregnancy by categories of body mass index (BMI) in first and second pregnancy; Pooled data from the Swedish Medical Birth Registry (1992–2010) and the Norwegian Medical Birth Registry (2006–2014) ( $n = 2763$ ).

**Table S2.** Maternal characteristics of women with gestational diabetes mellitus (GDM) in first pregnancy according to available information on body mass index (BMI). Pooled data from the Swedish (1992–2010) and the Norwegian (2006–2014) Medical Birth Registry ( $n = 4078$ ).

**Table S3.** Relative risk (RR) for recurrence of gestational diabetes mellitus (GDM) in second pregnancy in women with body mass index (BMI)  $<25$  at first pregnancy. Pooled data from the Swedish Medical Birth Registry (1992–2010) and the Norwegian Medical Birth Registry (2006–2014) ( $n = 1264$ ).

**Table S4.** Relative risk (RR) for recurrence of gestational diabetes mellitus (GDM) in second pregnancy in women with body mass index (BMI)  $\geq 25$  in first pregnancy; Pooled data from the Swedish Medical Birth Registry (1992–2010) and the Norwegian Medical Birth Registry (2006–2014) ( $n = 1499$ ). ■

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