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Estimating the impact of change in pre-pregnancy body mass index on development of Gestational Diabetes Mellitus: An Australian population-based cohort

Kirsten I. Black [a,b,*], Francisco Schneuer [c], Adrienne Gordon [a,b], Glynis P. Ross [a,d], Adam Mackie [b], Natasha Nassar [c]

[a] Central Clinical School, Faculty of Medicine and Health, and Charles Perkins Centre, University of Sydney, Australia
[b] Department of Women's Health, Neonatology and Paediatrics, Royal Prince Alfred Hospital, Sydney Local Health District, Australia
[c] Child Population and Translational Health Research, The Children's Hospital at Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Australia
[d] Department of Endocrinology, Royal Prince Alfred Hospital, Sydney Local Health District, Australia

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ABSTRACT

Background: International studies examining maternal overweight and obesity have found GDM risk increases with increasing weight gain between pregnancies.
Aim: The study aimed to estimate the association between pre-pregnancy maternal body mass index (BMI), change in BMI between pregnancies and Gestational Diabetes Mellitus (GDM) amongst women with consecutive births in an Australian cohort.
Methods: We used a population cohort of women who had at least two consecutive singleton births between 2010 and 2017 in one NSW health district to investigate the risk of GDM in the pregnancy after the index pregnancy, BMI change between pregnancies and the impact of BMI change on risk of GDM.
Findings: Of 10,074 women 1987 (16.7%) had no GDM in the index pregnancy but GDM in the subsequent one while 823 (8.2%) had GDM in both pregnancies. No change in BMI between pregnancies occurred in 47% of women, while 12% had a decrease and 41% an increase. After adjusting for socio-demographic characteristics and selected maternal and perinatal confounders, a reduction in BMI between births in women without GDM in the index pregnancy was associated with a 36% lower risk in GDM (aRR: 0.64; 95% CI: 0.49–0.85), while an increase in BMI was associated with increased risk of GDM with the greatest risk amongst those who gained 4+ kg/m^2 (aRR 2.27; 95%CI: 1.88–2.75).
Conclusion: Interpregnancy weight change is an important modifiable risk factor for the risk of GDM in a subsequent pregnancy. Clinical guidelines and health messages about interpregnancy weight change are important for all women.

Statement of significance

Problem

Rising rates of maternal overweight and obesity place women and their babies at risk of pregnancy complications, including Gestational Diabetes Mellitus (GDM) as well as long term adverse outcomes.

What is already known

International studies examining maternal overweight and obesity have found GDM risk increases with increasing weight gain between pregnancies.

What this paper adds

This study points to the need for effective interventions in Australia to minimise weight gain between pregnancies for all women and interventions to support weight loss before or between pregnancies in women with a high BMI.

* Corresponding author at: Speciality of Obstetrics, Gynaecology and Neonatology, Central Clinical School, Faculty of Medicine and Health, The University of Sydney, Rm 94, The Tavern, Medical Foundation Building, NSW, Australia.
E-mail address: kirsten.black@sydney.edu.au (K.I. Black).

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1. Introduction

The reproductive consequences of rising maternal overweight and obesity include an increased risk of Gestational Diabetes Mellitus (GDM) which now complicates 13% pregnancies worldwide [1]. GDM, defined as glucose intolerance first evident in pregnancy, is associated with a range of adverse perinatal outcomes including pre-eclampsia, birth by caesarean section (C/S), fetal macrosomia and neonatal intensive care admission [2]. There are also intergenerational effects of GDM which may manifest in childhood with greater risk of obesity [3] and in adulthood with an increased risk of metabolic disease [4]. Mothers who develop GDM have an increased likelihood of later developing type 2 diabetes and cardiovascular disease [5].

In Australia there has been a rising trend in the incidence of GDM from an aged standardised female population rate of 6.1 in 2006−7 to 16.1 in 2017–2018 for women 15–49 years [6]. The main factors contributing to this have been rising community prevalence of overweight and obesity, increasing maternal age and changes to the ethnic profile of Australian women through migration of women from Asia and Africa [7]. New recommendations for the testing and diagnosis of GDM [7], the endorsement of these recommendations by The Royal Australian and New Zealand College of Obstetricians and Gynaecologists and the Australasian Diabetes in Pregnancy Society (ADIPS) [8] and implementation in the years following have increased the number of women diagnosed with GDM [9].

The risk factors for GDM include previous GDM, advanced maternal age, non-white ethnicity, a family history of diabetes and overweight and obesity [10]. Many of these are not modifiable, with the exception of maternal overweight and obesity. Studies from Europe and the United States examining maternal overweight and obesity have consistently found the risk of GDM to increase with increasing weight gain between pregnancies [11–13]. This effect depends on a women's pre-pregnancy body mass index (BMI) in her first pregnancy, with normal weight women being at higher risk for development of GDM if they gain weight subsequent to the next pregnancy [11]. Additionally the impact of the loss of BMI units appears to be variable, with a lower risk of GDM only accruing to women who were overweight or obese in the first pregnancy [13]. In this longitudinal cohort study we sought to estimate the association between prepregnancy BMI, interpregnancy BMI changes and GDM amongst a multiethnic Australian maternity cohort of women having consecutive births.

2. Methods

The study included women giving birth to at least two consecutive singleton infants of at least 20 weeks gestation at Royal Prince Alfred Hospital or Canterbury Hospital in the Sydney Local Health District (SLHD), New South Wales, Australia between October 2010 and December 2017. About 8% of births in the state occur in this health district [14].

Maternal demographic, pregnancy and birth information was obtained from the SLHD electronic Cerner Maternity system database where routine pregnancy, birth and postpartum data are entered by all healthcare providers. Clinical diagnoses related to hospital admissions were coded using the 10th edition of the International Classification of Diseases–Australian modification (ICD-10-AM) including the study outcome of interest (GDM) in the birth admission (ICD-10-AM O24.4). Diagnosis of GDM previously involved a two-step process. Since January 2015, the ADIPS criteria for GDM diagnosis involve an oral glucose tolerance test at 24–28 weeks, undertaken earlier if higher risk [8]. GDM diagnosis is made if one or more are present: fasting blood glucose $\geq$ 5.1 mmol/L; 1 h $\geq$ 10.0 mmol/l or a 2 h $\geq$ 8.5 mmol/l after a 75 g glucose load.

The main study exposure was change in BMI between two consecutive births. BMI was defined as weight in kilograms divided by height in square metres (kg/m^2) and calculated using self-reported pre-pregnancy weight and height recorded at the first antenatal visit. BMI was categorised according to World Health Organization guidelines: underweight (<18.5 kg/m^2), normal weight (18.5−24.9 kg/m^2), overweight (25−29.9 kg/m^2) and obese (30+ kg/m^2) [15]. Change in BMI was calculated as the pre-pregnancy BMI for the second birth minus the pre-pregnancy BMI in the index birth and grouped into five categories: <−1 kg/m^2, −1 to <1 kg/m^2 (reference), 1 to <2 kg/m^2, 2 to <4 kg/m^2, and 4+ kg/m^2 [16].

2.1. Statistical analysis

We compared socio-demographic and characteristics of the index birth by categories of BMI change using contingency tables (Table 1). We then stratified the study sample and subsequent analyses by women diagnosed with and without GDM for the index birth. Crude (univariable) and multivariable association between BMI change and GDM diagnosed at the subsequent birth were assessed and corresponding relative risks (RR) with 95% confidence intervals (CI) were estimated using generalised estimating equations fitting robust Poisson models with a log-link and exchangeable correlation to account for the effect of women having multiple consecutive births and adjusting for potential confounders. Only significant confounders were kept in multivariable models ($p < 0.05$). From the final models, we determined individual predicted probability of GDM for a subsequent birth and calculated standardised GDM rates with 95% CI for index BMI (categorised as underweight/ normal or overweight/obese) and category of BMI change. We also conducted sensitivity analyses restricting to primipara women with a first and second birth only. For those with GDM in the index birth, we estimated crude and adjusted recurrence risk including additional adjustment for the type of treatment received during the index pregnancy. Robustness of findings was assessed by imputing missing height and weight data (n = 1826/11,900) using a Markov Chain Monte Carlo method and repeating analysis to compare with complete case analysis [17]. Missing values of other explanatory variables were minimal (<1.5%). All analyses were conducted using SAS, 9.4 (SAS Institute, Cary, NC, USA). We also conducted an extra sensitivity analysis, restricting analysis of data to the years 2010–2014) before the change in GDM criteria was introduced.

2.2. Ethics approval

The Sydney Local Health District Research Ethics Committee granted approval for analysis of archived electronic health data (Protocol: X16-0100).

3. Results

There were 10,392 women and 11,900 consecutive births, with 1340 women having two or more consecutive births. A total of 1826 (15.3%) women were excluded from the main analysis because of missing height and weight data. For complete case analysis (n = 8667), nearly half (n = 4705, 47%) of women had no change in BMI between consecutive births, while 12% had a decrease and 41% an increase in their BMI (Table 1). Compared with women who had no change in their BMI between consecutive births, those who had an increase in BMI were more likely to be younger, overweight or obese, not married, smokers during pregnancy and from more disadvantaged socio-economic backgrounds. They were also more likely to give birth by caesarean section, have large for gestational age (LGA) babies and longer interpregnancy intervals (IPI) (Table 1).

A total of 1574 (13.2%) women had GDM in the initial pregnancy, of which 657 (41.7%) were treated with insulin, 42 (2.7%) with oral hypogylacaemic therapy and 875 (55.6%) with diet only. One in six women (n = 1987, 16.7%) had no GDM in their index pregnancy and GDM diagnosed in the subsequent pregnancy and 823 (8.2%) had GDM diagnosed in both their index and subsequent pregnancy.

Table 1
Maternal and birth characteristics by pre-pregnancy BMI change of women having consecutive singleton births in Sydney, New South Wales, Australia, 2010–2017.

Maternal characteristics	<−1 kg/m^2 (N = 1244) n (%)	−1 to <1 kg/m^2 (N = 4705) n (%)	1 to <2 kg/m^2 (N = 1731) n (%)	2 to <4 kg/m^2 (N = 1615) n(%)	4+ kg/m^2 (N = 779) n (%)	Total (N = 10,074) n (%)
Maternal Age						
<25 years	210 (16.9)	502 (10.7)	190 (11.0)	269 (16.7)	189 (24.3)	1360 (13.5)
25–29 years	369 (29.7)	1333 (28.3)	570 (32.9)	574 (35.5)	271 (34.8)	3117 (30.9)
30–34 years	474 (38.1)	2011 (42.7)	670 (38.7)	525 (32.5)	241 (30.9)	3921 (38.9)
35+ years	191 (15.4)	859 (18.3)	301 (17.4)	247 (15.3)	78 (10.0)	1676 (16.6)
Pre-pregnancy BMI						
<18.5 kg/m^2	23 (1.8)	339 (7.2)	145 (8.4)	106 (6.6)	41 (5.3)	654 (6.5)
18.5–24 kg/m^2	588 (47.3)	3329 (70.8)	1109 (64.1)	930 (57.6)	395 (50.7)	6351 (63.0)
25–29 kg/m^2	376 (30.2)	727 (15.5)	341 (19.7)	404 (25.0)	205 (26.3)	2053 (20.4)
30+ kg/m^2	257 (20.7)	310 (6.6)	136 (7.9)	175 (10.8)	138 (17.7)	1016 (10.1)
Marital status						
Married/defacto	1126 (90.5)	4446 (94.5)	1639 (94.7)	1502 (93.0)	699 (89.7)	9412 (93.4)
Divorced/never married	113 (9.1)	255 (5.4)	90 (5.2)	112 (6.9)	80 (10.3)	650 (6.5)
Nationality						
Australia or NZ	705 (56.7)	2241 (47.6)	791 (45.7)	707 (43.8)	348 (44.7)	4792 (47.6)
Other	539 (43.4)	2463 (52.3)	939 (54.2)	908 (56.3)	431 (55.4)	5280 (52.4)
Smoking during pregnancy						
No	1166 (93.7)	4558 (96.9)	1662 (96.0)	1544 (95.6)	715 (91.8)	9645 (95.7)
Yes	70 (5.6)	142 (3.0)	62 (3.6)	64 (4.0)	59 (7.6)	397 (3.9)
Parity						
Nulliparous	777 (62.5)	3239 (68.8)	1196 (69.1)	1115 (69.0)	533 (68.4)	6860 (68.1)
Parous	458 (36.8)	1460 (31.0)	529 (30.6)	495 (30.7)	240 (30.8)	3182 (31.6)
Socio-economic disadvantage (quintiles)						
1 (Most disadvantaged)	393 (31.6)	1205 (25.6)	545 (31.5)	610 (37.8)	347 (44.5)	3100 (30.8)
2, 3 and 4	496 (39.9)	2020 (42.9)	714 (41.2)	658 (40.7)	298 (38.3)	4186 (41.6)
5 (Least disadvantaged)	341 (27.4)	1405 (29.9)	444 (25.6)	312 (19.3)	120 (15.4)	2622 (26.0)
GDM						
Total	217 (17.4)	585 (12.4)	224 (12.9)	240 (14.9)	141 (18.1)	1407 (14)
Treated with insulin	95 (7.6)	243 (5.2)	88 (5.1)	106 (6.6)	63 (8.1)	595 (5.9)
Diet only	115 (9.2)	325 (6.9)	130 (7.5)	129 (8)	74 (9.5)	773 (7.7)
Year of birth						
2010–2011	286 (23.0)	979 (20.8)	362 (20.9)	340 (21.1)	158 (20.3)	2125 (21.1)
2012–2013	427 (34.3)	1615 (34.3)	637 (36.8)	578 (35.8)	286 (36.7)	3543 (35.2)
2014–2015	358 (28.8)	1431 (30.4)	473 (27.3)	477 (29.5)	239 (30.7)	2978 (29.6)
2016–2017	173 (13.9)	680 (14.5)	259 (15.0)	220 (13.6)	96 (12.3)	1428 (14.2)
Gestational age						
<37 weeks	76 (6.1)	250 (5.3)	95 (5.5)	111 (6.9)	52 (6.7)	584 (5.8)
37+ weeks	1168 (93.9)	4455 (94.7)	1636 (94.5)	1504 (93.2)	727 (93.3)	9490 (94.2)
Labour onset						
Spontaneous	723 (58.1)	2881 (61.2)	1048 (60.5)	880 (54.5)	406 (52.1)	5938 (58.9)
Induced	395 (31.8)	1428 (30.4)	516 (29.8)	559 (34.6)	281 (36.1)	3179 (31.6)
No labour	124 (10.0)	394 (8.4)	167 (9.6)	176 (10.9)	92 (11.8)	953 (9.5)
Type of birth						
Vaginal birth	771 (62.0)	2971 (63.1)	1046 (60.4)	897 (55.5)	403 (51.7)	6088 (60.4)
Instrumental delivery	190 (15.3)	821 (17.4)	285 (16.5)	286 (17.7)	138 (17.7)	1720 (17.1)
Caesarean section-emergency	184 (14.8)	617 (13.1)	281 (16.2)	296 (18.3)	171 (22.0)	1549 (15.4)
Caesarean section-elective	98 (7.9)	296 (6.3)	119 (6.9)	136 (8.4)	67 (8.6)	716 (7.1)
Outcome of birth						
Alive at discharge	1236 (99.4)	4654 (98.9)	1706 (98.6)	1597 (98.9)	766 (98.3)	9959 (98.9)
Stillbirth/ neonatal death	8 (0.7)	51 (1.0)	25 (1.4)	18 (1.2)	12 (1.5)	114 (1.2)
Baby sex						
Male	655 (52.7)	2418 (51.4)	885 (51.1)	799 (49.5)	387 (49.7)	5144 (51.1)
Female	588 (47.3)	2287 (48.6)	846 (48.9)	816 (50.5)	392 (50.3)	4929 (48.9)
Birthweight by gestational age						
Not SGA or LGA	994 (79.9)	3875 (82.4)	1412 (81.6)	1264 (78.3)	611 (78.4)	8156 (81.0)
SGA < 10th centile	140 (11.3)	559 (11.9)	208 (12)	204 (12.6)	88 (11.3)	1199 (11.9)
LGA > 10th centile	107 (8.6)	268 (5.7)	110 (6.4)	145 (9.0)	80 (10.3)	710 (7.0)
Interpregnancy interval						
<6 months	71 (5.7)	262 (5.6)	113 (6.5)	112 (6.9)	72 (9.2)	630 (6.3)
6–11 months	234 (18.8)	854 (18.2)	306 (17.7)	284 (17.6)	135 (17.3)	1813 (18.0)
12–17 months	324 (26)	1202 (25.5)	384 (22.2)	310 (19.2)	131 (16.8)	2351 (23.3)
18–23 months	231 (18.6)	902 (19.2)	275 (15.9)	246 (15.2)	96 (12.3)	1750 (17.4)
24–59 months	357 (28.7)	1418 (30.1)	609 (35.2)	605 (37.5)	296 (38.0)	3285 (32.6)
60+ months	27 (2.2)	67 (1.4)	44 (2.5)	58 (3.6)	49 (6.3)	245 (2.4)
Mean weight change in kg (SD)	−6.5 (7.4)	0.2 (1.3)	3.8 (0.8)	7.4 (1.7)	15.5 (7.7)	

Percentages may not add to 100 due to missing values.

3.1. Interpregnancy BMI change and GDM in subsequent pregnancy according to GDM in index pregnancy

Among women without GDM in the index pregnancy, a reduction or no change in BMI between births resulted in GDM in the subsequent pregnancy in 6% and 8% respectively. In contrast, a rise in BMI resulted in increasing rates of GDM to 11%, 15% and 23% for women who gained 1–<2 kg/m^2, 2–<4 kg/m^2 and for 4+ kg/m^2, respectively (Table 2). After adjusting for confounders, a reduction in BMI between births was associated with a 36% lower risk in GDM (aRR: 0.64; 95% CI: 0.49−0.85), while an increase in BMI was associated with greater GDM risk (1–<2 kg/m^2 adjusted RR (aRR) 1.35; 95% CI: 1.14–1.61; 2–<4 kg/m^2: aRR 1.61; 95% CI: 1.36–1.90 and 4+ kg/m^2: aRR 2.27; 95% CI: 1.88–2.75) (Table 2). Women who were overweight or obese had an increased risk of GDM which was greater for obese women (overweight aRR: 1.54; 95% CI: 1.33–1.78; obese aRR: 1.96; 95% CI: 1.62–2.36) (Table 2). When restricting the analysis for the years 2010–2014 prior to the change in GDM criteria, similar results were found (Supplementary Table 1).

For women with GDM in the index pregnancy, over half (n = 823, 57.8%) had a recurrence of GDM; this was more likely amongst women who were overweight or obese compared with women with normal pre-pregnancy BMI (overweight aRR: 1.16; 95% CI: 1.04–1.28; obese aRR: 1.14; 95% CI: 1.01–1.28) (Table 2). Increasing BMI between births resulted in an increased risk of recurrence (2–<4 kg/m^2: aRR 1.17; 95% CI: 1.03–1.32; 4+ kg/m^2: aRR 1.32; 95% CI: 1.16–1.51). Compared with women treated with diet only, women treated with insulin had a 24% increased risk of GDM recurrence (aRR 1.24; 95% CI: 1.08–1.31). Results using multiple imputation of missing data were similar (Table 2) and restricting analysis to primipara women resulted in similar, but slightly increased GDM risk estimates by BMI change categories (Supplementary Table 2).

Standardised GDM rates were lowest for women who had a reduction in BMI between births and were increasingly higher for those who had no change or an increase in BMI between births (Fig. 1). Taking into account initial BMI in the index pregnancy, increasing BMI between births up to an increase of 4+ kg/m^2 resulted in a "dose-dependent" increase in GDM rates in a subsequent birth from 4% to 17%, 5% to 18%, 8% to 26% and 9% to 33% for women who were underweight, normal weight, overweight or obese, respectively (Fig. 1).

3.2. Interpregnancy BMI change and GDM in subsequent pregnancy according to BMI in index pregnancy

For women without previous GDM, when results were stratified by BMI-status in the index pregnancy, *regardless* of whether women were underweight/ normal weight or overweight/obese in the index pregnancy, an increase in BMI between consecutive births resulted in a 30% increased risk of GDM for women who gained 1–<2 kg/m^2 to a 2.2-fold increase in risk for those that gained 4+ kg/m^2 (Table 3). For women who were overweight or obese, a reduction in BMI between consecutive births resulted in an almost 50% lower risk of GDM (aRR 0.56; 95% CI: 0.39−0.81) (Table 3).

For women with previous GDM, those under-or normal weight in the index pregnancy had a 31%–41% increased risk of GDM recurrence regardless of whether they had a reduction or increase in BMI between consecutive births (Table 3). They also had a 38% increased risk of GDM in the subsequent birth if they were previously treated with insulin (aRR 1.38; 95% CI: 1.21–1.57) (Table 3). For women who were overweight or obese, a reduction in BMI between births reduced the risk of GDM recurrence (aRR 0.74; 95% CI: 0.61−0.91) whereas an increase in BMI by 4+ kg/m^2 resulted in a 21% increased risk of recurrence (aRR 1.21; 95% CI: 1.03–1.43) (Table 3).

Table 2
Association between change in BMI and initial BMI with GDM in subsequent pregnancy by GDM status in the index pregnancy, New South Wales, Australia, 2010-2017.

	GDM n (%)	Complete data analysis: Crude RR (95% CI)	Complete data analysis: Adjusted RR (95% CI)	Imputed analysis: Adjusted RR (95% CI)[c]
Women without GDM[a]				
BMI change				
<−1 kg/m^2	61 (5.9)	0.75 (0.57, 0.97)	0.64 (0.49, 0.85)	0.69 (0.55, 0.86)
−1 to <1 kg/m^2	326 (7.9)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to <2 kg/m^2	170 (11.3)	1.41 (1.19, 1.69)	1.35 (1.14, 1.61)	1.31 (1.11, 1.53)
2 to <4 kg/m^2	207 (15.1)	1.88 (1.60, 2.22)	1.61 (1.36, 1.90)	1.59 (1.36, 1.85)
4+ kg/m^2	144 (22.6)	2.83 (2.37, 3.38)	2.27 (1.88, 2.75)	2.21 (1.87, 2.62)
Initial BMI				
<18.5 kg/m^2	52 (8.7)	1.02 (0.77, 1.34)	0.84 (0.63, 1.12)	0.84 (0.66, 1.08)
18.5–24 kg/m^2	486 (8.6)	1.00 (reference)	1.00 (reference)	1.00 (reference)
25–29 kg/m^2	239 (14.3)	1.70 (1.47, 1.97)	1.54 (1.33, 1.78)	1.58 (1.38, 1.80)
30+ kg/m^2	131 (17.0)	1.98 (1.65, 2.37)	1.96 (1.62, 2.36)	2.02 (1.71, 2.39)
Women with previous GDM[b]				
BMI change				
<−1 kg/m^2	111 (51.2)	0.94 (0.81, 1.1)	0.93 (0.80, 1.08)	0.9 (0.78, 1.04)
−1 to <1 kg/m^2	319 (54.5)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to <2 kg/m^2	134 (59.8)	1.1 (0.97, 1.26)	1.10 (0.96, 1.26)	1.09 (0.96, 1.24)
2 to <4 kg/m^2	154 (64.2)	1.18 (1.05, 1.33)	1.17 (1.03, 1.32)	1.18 (1.05, 1.32)
4+ kg/m^2	98 (69.5)	1.28 (1.12, 1.46)	1.32 (1.16, 1.51)	1.29 (1.14, 1.47)
Initial BMI				
<18.5 kg/m^2	25 (47.2)	0.88 (0.66, 1.19)	0.86 (0.62, 1.21)	0.92 (0.70, 1.22)
18.5–24 kg/m^2	388 (53.7)	1.00 (reference)	1.00 (reference)	1.00 (reference)
25–29 kg/m^2	248 (64.1)	1.20 (1.09, 1.33)	1.16 (1.04, 1.28)	1.14 (1.04, 1.26)
30+ kg/m^2	155 (63.5)	1.18 (1.05, 1.33)	1.14 (1.01, 1.28)	1.12 (1.00, 1.25)
Initial GDM				
Diet only	402 (52.0)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Insulin treated	397 (66.7)	1.29 (1.19, 1.41)	1.24 (1.13, 1.36)	1.25 (1.15, 1.36)

RR: relative risk; CI: confidence interval.
[a] Models adjusted for maternal age, nationality, parity, socio-economic disadvantage, gestational age, labour onset, SGA, baby discharge status and interpregnancy interval.
[b] Models adjusted for maternal age, IPI and baby discharge status.
[c] Estimates applying multiple imputation to include women with missing BMI; There was no evidence of interaction between intial BMI with BMI change or IPI ($p > 0.2$).

4. Discussion

This population-based cohort of over 10,000 pregnancies has confirmed the importance of interpregnancy weight change as a modifiable risk factor associated with the risk of GDM in a subsequent pregnancy. Compared to women who maintained their weight between

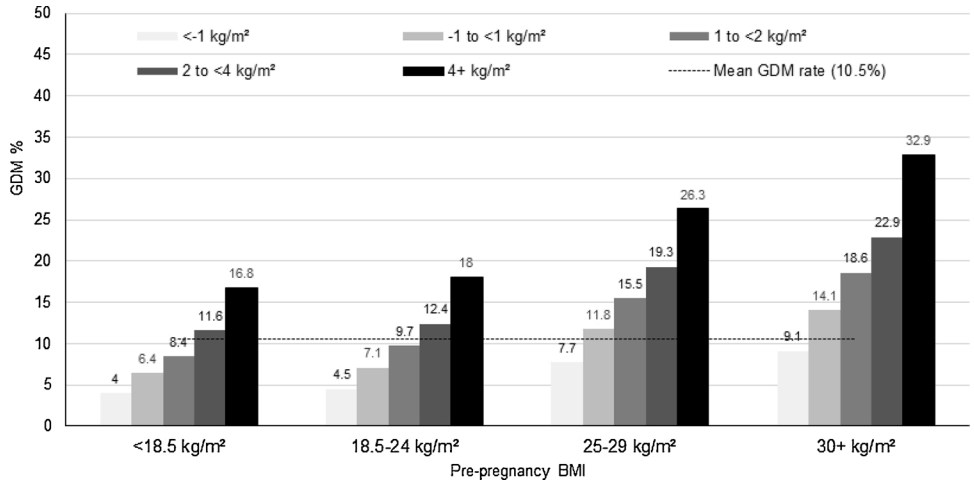

Fig. 1. Standardised rates of GDM in a subsequent pregnancy by prepregnancy BMI in the index pregnancy and change in BMI among women without previous GDM. Rates represent average GDM rates (predicted) resulting from models adjusted for maternal age, nationality, parity, socioeconomic disadvantage, gestational age. labour onset, small for gestational age, baby discharge status and interpregnancy interval.

Table 3
Association between change in BMI between initial and subsequent birth and GDM among women who are underweight/normal weight or overweight/obese by GDM status in the index pregnancy.

	Underweight/normal weight				Overweight/obese			
	GDM n (%)	Complete data analysis Crude RR (95% CI)	Complete data analysis Adjusted RR (95% CI)	Imputed data analysis Adjusted RR (95% CI)c	GDM n (%)	Complete data analysis Crude RR (95% CI)	Complete data analysis Adjusted RR (95% CI)	Imputed data analysis Adjusted RR (95% CI)[c]
Women without previous GDM[a]								
BMI change								
<−1 kg/m^2	17 (4.3)	0.76 (0.51, 1.11)	0.82 (0.55, 1.22)	0.8 (0.55, 1.18)	12 (4.8)	0.54 (0.38, 0.78)	0.56 (0.39, 0.81)	0.57 (0.40, 0.82)
−1 to <1 kg/m^2	150 (6.3)	1.00 (reference)	1.00 (reference)	1.00 (reference)	52 (11.6)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to <2 kg/m^2	78 (9.6)	1.35 (1.08, 1.69)	1.30 (1.04, 1.64)	1.28 (1.02, 1.60)	38 (16.6)	1.40 (1.06, 1.85)	1.37 (1.04, 1.81)	1.37 (1.05, 1.80)
2 to <4 kg/m^2	90 (13.6)	2.02 (1.64, 2.49)	1.82 (1.46, 2.28)	1.81 (1.46, 2.25)	39 (13.8)	1.40 (1.08, 1.81)	1.32 (1.02, 1.71)	1.36 (1.06, 1.76)
4+ kg/m^2	47 (18.6)	2.64 (2.04, 3.41)	2.27 (1.72, 2.99)	2.25 (1.72, 2.95)	55 (30.6)	2.25 (1.74, 2.91)	2.18 (1.68, 2.82)	2.21 (1.72, 2.86)
Women with previous GDM[b]								
BMI change								
<−1 kg/m^2	45 (57.0)	1.31 (1.04, 1.64)	1.33 (1.07, 1.65)	1.31 (1.05, 1.63)	66 (47.8)	0.74 (0.61, 0.91)	0.74 (0.61, 0.91)	0.74 (0.60, 0.90)
−1 to <1 kg/m^2	176 (48.4)	1.00 (reference)	1.00 (reference)	1.00 (reference)	143 (64.7)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to <2 kg/m^2	73 (56.6)	1.19 (0.97, 1.46)	1.21 (0.99, 1.47)	1.21 (1.00, 1.47)	61 (64.2)	0.99 (0.83, 1.19)	1.00 (0.83, 1.19)	0.99 (0.83, 1.19)
2 to <4 kg/m^2	72 (55.8)	1.24 (1.02, 1.50)	1.25 (1.03, 1.52)	1.25 (1.03, 1.51)	82 (73.9)	1.14 (0.98, 1.32)	1.14 (0.98, 1.32)	1.13 (0.98, 1.31)
4+ kg/m^2	47 (62.7)	1.39 (1.13, 1.70)	1.42 (1.16, 1.75)	1.41 (1.15, 1.74)	51 (77.3)	1.21 (1.03, 1.42)	1.21 (1.03, 1.43)	1.21 (1.03, 1.43)
Initial GDM								
Diet only	228 (47.0)	1.00 (reference)	1.00 (reference)	1.00 (reference)	174 (60.4)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Insulin treated	174 (66.2)	1.43 (1.25, 1.62)	1.38 (1.21, 1.57)	1.40 (1.23, 1.60)	223 (67.2)	1.12 (0.99, 1.26)	1.11 (0.99, 1.25)	1.11 (0.99, 1.25)

RR: relative risk; CI: confidence interval.
[a] Models adjusted for maternal age, nationality, parity, socio-economic disadvantage, gestational age, labour onset, SGA, baby discharge status and interpregnancy interval.
[b] Models were adjusted for maternal age, IPI and baby discharge status.
[c] Estimates applying multiple imputation to include women with missing BMI.

consecutive births (−1 to <1 BMI change), we found a higher risk of GDM amongst women who increased their weight by ≥1 BMI unit from the index to the subsequent pregnancy. This risk was dose-dependent and increased with increasing BMI gain between pregnancies regardless of the index pregnancy BMI. The impact of BMI gain on GDM risk was greatest amongst women of normal weight in the index pregnancy. Conversely, losing weight (≥1 BMI unit) between pregnancies lowered the risk of GDM only amongst women who were overweight or

obese in the index pregnancy. However, under or normal weight women with a history of GDM in the index pregnancy had an increased risk of GDM recurrence regardless of whether they had a reduction or increase in BMI between consecutive births, suggesting the importance of a range of non-modifiable risk factors.

4.1. Interpretation

Our findings are consistent with previous research exploring the relationship between BMI change between pregnancies and GDM. A Norwegian birth cohort study of 24,198 mothers in their first two pregnancies similarly reported a greater impact of weight gain in women with a BMI < 25 at first pregnancy on GDM risk, as did a Swedish population study [11]. The Norwegian study also noted a preventative effect of GDM in overweight women who reduced their weight by over two BMI units between pregnancies [12]. Likewise a retrospective Californian study documented an increase in GDM risk with a rise in BMI between pregnancies and a decrease in GDM risk only amongst those who were overweight or obese and lost weight [13]. In a previous Australian study, an interpregnancy increase of $\geq$3 BMI units amongst multiparous women had an adjusted odds ratio of 3.2 for GDM [18]. Our own research previously estimated that a reduction in BMI category from obesity to overweight, could have prevented 14.2% of GDM diagnoses between 2010–2014 [19].

Predictors of GDM recurrence have been examined in several studies. A meta-analysis of risk factors identified the stronger factors to be insulin use, multiparity, macrosomia, BMI and weight gain between pregnancies [20]. In our study 57.8% of women had GDM recurrence and 41% had an increase in BMI between pregnancy. This highlights the need to improve care for women in the interpregnancy interval and specifically the potential of clinical and public health messages to target the modifiable factors of BMI and interconception weight gain. However, while dietary and/or physical activity interventions have been shown to be effective in achieving postpartum weight loss [21], an understanding of the impact of such weight loss on perinatal outcomes in subsequent pregnancies is lacking [22] as are data from interventional studies to prevent GDM between pregnancies [23]. Robust data from trials on lifestyle interventions aimed at reducing GDM recurrence are likely to emerge in the next few years to better inform clinical guidelines [24].

5. Strengths and limitations

Using a single population-based sample ensured internal consistency, due to the exposure and outcomes variables having been similarly defined over time. Collection of data over many years and with a large sample size meant we could present precise proportions for key outcome variables, with adjustment for many relevant confounders. In the area health service where the study took place, only the self-reported pre-pregnancy BMI is consistently documented at the booking visit. Although this method may lead to underreporting of pre-pregnancy BMI, a systematic review concluded that such error did not largely bias associations between pregnancy-related weight and birth outcomes [25]. Further, while measured weight is preferable, self-report is a cost-effective and practical measurement approach. The change in diagnosis of GDM occurred during the study period, significantly increasing the misclassification of diabetes diagnosis is possible, but unlikely to be differential and therefore likely to have minimal or no impact on the results. Further, the findings when only examining data before the change in criteria showed very little change in adjusted risk estimates and associations compared to the overall cohort. In our study up to one in seven women did not have a BMI recorded with an international study reporting similar rates of missing data [26]. However, we found consistent findings following imputation of missing data.

6. Conclusion

These findings have potential implications for healthcare and public health strategies such that promoting healthy weight in the interpregnancy period may be important for all women. Further, encouraging overweight and obese women to lose weight prior to the next pregnancy may be an effective strategy to reduce the risk of subsequent GDM. However, future trials in this area need to not only address the question of whether interventions pre/interpregnancy are effective for weight loss but whether such weight loss impacts upon important clinical outcomes in a subsequent pregnancy such as GDM. Such knowledge has the potential to significantly reduce both the health costs related to the pregnancy but also the subsequent costs from the delayed and intergenerational impacts of GDM.

Conflict of interest

There are no conflicts of interest to declare.

Ethical statement

The Sydney Local Health District Research Ethics Committee granted approval for analysis of archived electronic health data (Protocol: X16-0100).

Author contribution

KB, AG, GP, AM and NN were involved in designing the study. FS and NN were involved in statistical analysis and write up. All authors contributed to the writing of the final manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.wombi.2021.12.007.

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