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Improving outcomes in gestational diabetes: does gestational weight gain matter?

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What's new?

- Gestational diabetes is associated with pre-pregnancy obesity and excessive gestational weight gain.
- However, there is no clear evidence to guide weight management after diagnosis of gestational diabetes (at 28 weeks).
- In this study, excessive gestational weight gain was strongly associated with fetal growth and difficult deliveries in women with gestational diabetes.
- Women who gained weight after diagnosis needed higher insulin doses and had higher postnatal glucose concentrations.
- Keeping weight stable after diagnosis of gestational diabetes should be a priority to improve outcomes for both mother and child; 28 weeks is not too late to offer advice or intervention.
- A clinical trial to guide weight management in women with gestational diabetes would be extremely useful to confirm these findings and provide clear targets for weight gain after diagnosis.

Abstract

Aim Excessive gestational weight gain increases risk of gestational diabetes mellitus (GDM) but it remains unclear whether weight control after GDM diagnosis improves outcomes. We assessed whether: (1) total gestational weight gain during pregnancy (0–36 weeks); (2) early

gestational weight gain (0–28 weeks, before GDM diagnosis); or (3) late gestational weight gain (28–36 weeks, after diagnosis) are associated with maternal–fetal outcomes.

Methods Some 546 women with GDM who delivered viable singleton infants at a single UK obstetric centre (October 2014 to March 2017) were included in this retrospective observational study.

Results Higher total gestational weight gain was associated with Caesarean section [n = 376; odds ratio (OR) 1.05; confidence intervals (CI) 1.02–1.08, $P < 0.001$] and large for gestational age (OR 1.08; CI 1.03–1.12, $P < 0.001$). Higher late gestational weight gain (28–36 weeks; n = 144) was associated with large for gestational age (OR 1.17; CI 1.01–1.37, $P < 0.05$), instrumental deliveries (OR 1.26; CI 1.03–1.55, $P < 0.01$), higher total daily insulin doses (36 weeks; beta coefficient 4.37; CI 1.92–6.82, $P < 0.001$), and higher post-partum 2-h oral glucose tolerance test concentrations (beta coefficient 0.12; CI 0.01–0.22, $P < 0.05$). Women who avoided substantial weight gain after GDM diagnosis had 0.7 mmol/l lower postnatal 2-h glucose and needed half the amount of insulin/day at 36 weeks compared with women with substantial weight gain after diagnosis. There were no significant associations between early gestational weight gain (0–28 weeks) and pregnancy outcomes.

Conclusions These findings suggest that controlling gestational weight gain should be a priority following GDM diagnosis to optimize pregnancy outcomes and improve maternal postnatal glucose homeostasis. The period after diagnosis of GDM (often 28 weeks gestation) is not too late to offer lifestyle advice or intervention to improve weight management and pregnancy outcomes.

<H1>Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycaemia with first onset or recognition in pregnancy and is associated with a range of maternal–fetal complications including Caesarean delivery and an increased risk of large for gestational age (LGA; > 90th percentile) infants [1,2]. GDM occurs more commonly in women who are overweight or obese prior to pregnancy, and in those with excessive gestational weight gain [3,4]. Despite the importance of weight in the aetiology of GDM, it remains unclear if women with GDM can benefit from limiting gestational weight gain.

Excessive gestational weight gain in normoglycaemic pregnancies can contribute to poor outcomes for both mother and child. Women with excessive gestational weight gain are at higher risk of hypertensive disorders [5], LGA [6], macrosomia [7] depression [8], and developing Type 2 diabetes and cardiometabolic disease in later life [9]. Infants exposed to excess gestational weight gain *in utero* have increased body weight, increased fat mass and increased blood pressure in childhood [10–12]. However, weight control in pregnancy is controversial, and concerns have been raised about safety [13].

Despite these concerns, for women with GDM (a weight-related comorbidity), weight control might feasibly improve metabolic health and reduce pregnancy complications [13–15]. Recent work demonstrates that strategies to limit gestational weight gain within the context of GDM can be safe, feasible and acceptable to women [16].

The aim of this study was to assess whether total gestational weight gain (0–36 weeks) is associated with pregnancy outcomes in women with GDM. Because many women are not diagnosed with GDM until 28 weeks, we also assessed whether early (0–28 weeks) or late (28–36 weeks) weight gain is associated with pregnancy outcomes.

<H1>Methods

<H2>Population and standard care

Women with a diagnosis of GDM who delivered a singleton infant at a viable gestation (≥ 24 weeks) at the Cambridge Universities NHS Foundation Trust between October 2014 and March 2017 were included in this retrospective observational study. The study was approved as a service evaluation, and our Institutional Review Board granted approval for further analysis of the data for research purposes. Because our hospital uses a paperless system (Epic E-hospital system), women were identified using searches of the electronic hospital records. The accuracy of the diagnosis and treatment information was confirmed for a selection of cases by hand-searching each record individually. Where women had several eligible pregnancies during the period of data collection, only the first eligible pregnancy was included.

Maternal weight and height were measured at antenatal booking in the community. Pre-pregnancy BMI was based upon measured weight at antenatal booking (8–12 weeks). In the small percentage (~ 2%) of cases where no booking weight was recorded, self-reported pre-pregnancy weight was used. Following a diagnosis of GDM, women were weighed fortnightly at the diabetes in pregnancy clinic using the same set of scales, which are

regularly calibrated (Seca, Birmingham, UK). Maternal weights recorded within < 1 week of our defined 28- and 36-week time-points were included in the analysis.

<H2>Detection of GDM

During the time of data collection, all pregnant women were invited for screening using random plasma glucose (typically 12–16 weeks' gestation) at antenatal booking. Women with a random plasma glucose > 7.0 mmol/l or a previous diagnosis of GDM were offered a 75-g oral glucose tolerance test (OGTT) within 1 week of booking. All women without known GDM/pre-existing diabetes were screened at 24–28 weeks with a 50-g glucose challenge test: women with a glucose challenge test result > 7.7 mmol/l were then referred for a 75-g OGTT [17,18]. Additional OGTTs were performed in later pregnancy on an ad hoc basis where indicated clinically. Women with known pre-existing diabetes were excluded. The diagnostic criteria for GDM were based upon the criteria of the International Association of the Diabetes in Pregnancy Study Groups (IADPSG) with a slightly higher fasting threshold (75-g OGTT 0 h $\geq$ 5.3 mmol/l; 1 h $\geq$ 10.0 mmol/l; 2 h $\geq$ 8.5 mmol/l). On average, 15% of our antenatal population have an OGTT and the overall prevalence of GDM is ~ 5%[19]

Following diagnosis, women with GDM were seen every 2–4 weeks at a multidisciplinary clinic (joint obstetrics, diabetes specialist nurse, physician, dietician and midwife), encouraged to monitor their blood glucose levels at least four times daily (fasting and 1-h post breakfast, lunch and dinner). As per the standard care pathway in our institution, women with a new diagnosis of GDM received individual dietary advice and were advised to follow a low glycaemic index diet and avoid excessive weight gain for the remainder of pregnancy.

Women with hyperglycaemia despite dietary modification received metformin or insulin treatment according to the guidelines of the National Institute for Health and Care Excellence (NICE) [20]. The decision to start metformin rather than insulin was based upon patient choice following advice from their physician. Women who did not achieve the NICE glycaemic control targets with metformin alone were advised to start insulin. Many of these women continued to take metformin, if it had shown some efficacy and was not associated with side effects. All treatments being received at 36 weeks' gestation were recorded and used in the analysis. All women diagnosed with GDM were offered a post-partum OGTT at 6–8 weeks following delivery.

<H2>Laboratory analysis

For the OGTT, venous blood was collected using fluoride–oxalate tubes and analysed using a hexokinase method (Dimension RXL MAX Clinical Chemistry System, Siemens Healthcare Diagnostics, Deerfield, IL, USA) in our accredited laboratory (Clinical Pathology Accreditation, UK).

<H2>Definitions

Total gestational weight gain was defined as weight change in kilograms between pre-pregnancy/booking weight and weight at 36 weeks (0–36 weeks). Early gestational weight gain was defined as weight gain between the pre-pregnancy/booking weight and 28 weeks (0–28 weeks). Late gestational weight gain occurred between 28 and 36 weeks. Infants born before 36 weeks were not included in the analysis of total or late gestational weight gain.

LGA and small for gestational age (SGA) were defined as birthweight > 90th and < 10th percentile for gestational age respectively. These outcomes were defined using population-specific *z*-scores with adjustment for estimated gestational age at birth and for the sex of the baby.

Post-partum glucose tolerance was measured using a 75-g OGTT at 6–8 weeks following delivery.

<H2>Statistical analysis

Data were collected for demographic information, maternal weight, glucose screening results and pregnancy outcomes. Participant characteristics are presented as *n* (%) for categorical data and mean (IQR) for continuous data. We did not impute missing data.

Where possible, data were analysed as continuous variables to avoid categorization of quantitative data. Gestational weight gain was assessed using both the Institute of Medicine (IOM) guidelines and as a percentage gain from baseline or pre-pregnancy weight [22].

Associations between antenatal characteristics, pregnancy outcomes and gestational weight gain were assessed using multivariate logistic regression and results are presented as odds ratios (95% confidence intervals). Findings were considered statistically significant at an alpha level of 0.05. Statistical analysis was performed using STATA® (version 12.0; StataCorp, College Station, TX, USA) or the R statistical software package version 2.14.1.

Possible confounders were identified for all outcomes based on the literature and by assessment of other variables. For each measurement, the strongest two to four independent confounders were included as an adjustment, provided they were potentially on the causative pathway.

Some 546 pregnancies were identified which met the inclusion criteria; 417 pregnancies had information available on pre-pregnancy weight or booking weight. Data on weight at 28 and 36 weeks were available for 159 and 456 pregnancies, respectively. Total gestational weight gain, early gestational weight gain and late gestational weight gain could be calculated in 376, 129 and 144 pregnancies, respectively (Fig. 1). Assessment of missing data shows that data were missing at random. Some 120 individuals had data available for calculation of total, early and late gestational weight gain.

Odds ratios were adjusted for pre-pregnancy BMI and antenatal glucose concentrations. Models relating to fetal growth (LGA and SGA) were also adjusted for parity, which was independently associated with fetal growth outcomes. Further adjustments, for example, for maternal age, did not substantially affect these analyses. Models relating to delivery mode (vaginal delivery, Caesarean section and instrumental delivery) were also adjusted for birthweight *z*-score which takes account of gestational age at birth and infant gender.

<H1>Results

Baseline characteristics of the study population are shown in Table 1. Not all women had data available for each time point (Fig. 1). Mean maternal weights at 0, 28 and 36 weeks were 76.8 (62.0–88.9) kg, 88.9 (72.1–102.6) kg and 89.6 (72.8–101.8) kg, respectively. Total

gestational weight gain was negatively associated with pre-pregnancy BMI (beta coefficient −0.79; CI −0.89 to −0.68, $P < 0.001$) and positively associated with infant birthweight *z*-score (adjusted for sex and gestation, beta coefficient 0.02; CI 0.01 to 0.04, $P < 0.001$).

<H2>Effect of gestational weight gain upon pregnancy outcomes

The effect of total gestational weight gain, early gestational weight gain and late gestational weight gain (expressed as a percentage change from pre-pregnancy weight) on pregnancy outcomes and treatment requirements are shown in Table 2. Total gestational weight gain was strongly associated with fetal growth, both positively with LGA ($P < 0.001$) and negatively with SGA ($P < 0.05$). Increased total gestational weight gain increased the likelihood of Caesarean delivery ($P < 0.01$) and reduced the likelihood of spontaneous vertex (vaginal) delivery (SVD) ($P < 0.001$). Although early gestational weight gain is considered important for the development of GDM, it was not associated with any of the studied pregnancy outcomes. Late gestational weight gain was associated with increased odds of LGA ($P < 0.05$) and instrumental delivery ($P < 0.01$). Women with higher degrees of late gestational weight gain had higher postnatal glucose concentrations ($P < 0.05$ for both fasting and 2-h OGTT glucose concentrations). However, the absolute difference in fasting concentrations was relatively small (0.1 mmol/l). The difference was more marked with postnatal 2-h OGTT glucose concentrations, of 5.4 mmol/l (97 mg/dl) for women in the first tertile of late gestational weight gain ($n = 47$) and 6.1 mmol/l (110 mg/dl) for women in the third tertile (n=50).

<H2>The effects of treatment

The use of metformin and insulin were considered potential confounders in the assessment of outcomes such as LGA, SGA and delivery modality. Although metformin was related to gestational weight gain, its effects were entirely removed by adjustment for pre-pregnancy BMI, suggesting that in this study, metformin tended to be used for women with a higher pre-pregnancy BMI (who tend to have lower amounts of gestational weight gain overall). Growth and delivery outcomes were adjusted for pre-pregnancy BMI and further adjustment for metformin use did not alter the effects.

The use of insulin (as a categorical variable) was not associated with total, early or late gestational weight gain, and adjustment for insulin use did not affect growth or delivery outcomes. Total insulin dose was related to late GWG but defining a causal relationship here is not straightforward. Undoubtedly, insulin can make women gain weight, but increased weight gain may increase blood glucose and increase treatment requirements. Furthermore, this relationship was skewed by outliers among our data. We therefore adjusted for antenatal glucose concentrations (measurement at time 0 in the diagnostic OGTT) rather than for insulin dosage. Late gestational weight gain was associated with requiring higher total daily doses of insulin ($P < 0.05$), affecting both short-acting (novorapid; $P < 0.05$) and long-acting (insulatard; $P < 0.001$) insulin doses. Insulin-requiring women in the first tertile of late gestational weight gain ($n = 25$) required on average 18 units of insulin per day at 36 weeks, whereas those in the third tertile ($n = 25$) required 41 units.

<H2>Classification of gestational weight gain

Gestational weight gain was categorized in two ways: percentage gestational weight gain from pre-pregnancy weight and adherence to the IOM guidelines [22] (Tables 3 and 4a). Pregnancy outcomes categorized according to percentage gestational weight gain were assessed over three subgroups (< 5%, 5–15% and > 15% of pre-pregnancy weight gained) (Table 3). Compared with women who gained 5–15% body weight, women with < 5% gestational weight gain had a lower likelihood of delivery by Caesarean section ($P < 0.01$), increased likelihood of SVD ($P < 0.01$) and no significant change in the rate of LGA (5%) or SGA (10%). Compared with women who gained 5–15% body weight, women who gained > 15% body weight had a lower likelihood of SVD ($P < 0.05$) and a higher likelihood of delivery by Caesarean section ($P < 0.05$) with an increased risk of LGA ($P < 0.05$).

Women were reclassified according to whether they had gained under, according to, or above the IOM recommendations for pregnancy weight gain, specific to their pre-pregnancy/booking BMI category (Table 4a). Of the 375 women included in this analysis, 29.6% gained weight within recommended limits, whereas 44.5% and 25.9% gained below or above the recommended limits respectively. For women who gained below the IOM recommendations, there was an almost sevenfold increase in the risk of SGA ($P < 0.01$), resulting in an SGA rate of 11% (LGA rate 6%). In comparison, women who gained weight within IOM recommended targets had 2% SGA and 11% LGA and those with excessive gestational weight gain above the IOM recommendations had 7% SGA and 18% LGA. Women who gained weight above recommended limits had an increased likelihood of delivery by Caesarean section ($P < 0.05$) and a decreased likelihood of SVD ($P < 0.05$) compared with those who gained weight within recommended limits.

The IOM recommendations also suggest that all women should gain at least 5 kg during pregnancy (Table 4b). Further analysis was performed to identify if GWG < 5 kg is associated with an excess of adverse outcomes in this cohort of women with established GDM. Gestational weight gain < 5 kg was associated with a lower likelihood of delivery by Caesarean section ($P < 0.05$) and a higher chance of SVD ($P < 0.05$). There was a lower likelihood of LGA ($P < 0.01$), but also a trend towards an increased likelihood of SGA ($P = 0.07$) resulting in an SGA rate of 9% and an LGA rate of 4%. When birthweight was analysed as a continuous variable, there was a significant association between GWG < 5 kg and lower birthweight ($P < 0.01$). There was no association between gestational weight gain < 5 kg and the need for insulin treatment for GDM or postnatal fasting glucose.

<H1>Discussion

This study demonstrates that gestational weight gain has significant associations with fetal growth, delivery modality and insulin requirements during pregnancy. Late gestational weight gain (after 28 weeks) is also associated with post-partum glucose concentrations. These findings suggest that control of gestational weight gain should be a priority following a diagnosis of GDM, for optimizing maternal and fetal outcomes, and that 28 weeks' gestation is not too late to offer lifestyle advice or intervention.

Our findings are consistent with other reports demonstrating that total gestational weight gain in women with GDM is associated with LGA [8, 23]. However, in clinical practice, many women already have excessive gestational weight gain at the time of GDM diagnosis, raising the concern that the appropriate window for intervention to control weight gain has passed.

This study suggests that intervening to control gestational weight gain even after GDM diagnosis could improve outcomes resulting in reduced LGA rates, reduced maternal insulin doses, decreased Caesarean sections, and improved maternal post-partum glucose tolerance. In fact, per kilogram of weight gained, late gestational weight gain appeared to have a larger effect upon rates of LGA, compared with total gestational weight gain. Control of gestational weight gain in the context of GDM has the potential to improve women's health in both the long and the short term. However, clinical behaviour change is notoriously difficult to achieve and trials of diet and exercise interventions to limit gestational weight gain in women at risk of GDM have achieved modest benefits overall [23–26]. One recent study by Hodson and colleagues [16] demonstrated that limiting gestational weight gain using a low-calorie diet in GDM is feasible and acceptable to women when good support from the multidisciplinary healthcare team is provided.

This retrospective observational study used clinical data from a single large tertiary referral centre to identify associations between gestational weight gain and pregnancy outcomes in women with GDM. The use of a single centre provides consistency in the screening and identification of women with GDM and in the advice and treatment given to women after diagnosis. Throughout the study, the protocols for initiation of GDM treatment, dose titration and delivery planning were delivered by a single clinical team, which minimizes unintentional variation within the cohort. Although not all women had data available for weight at all time-points, analysis suggests that weights are missing at random among the GDM population. The sample size and the well characterized nature of our cohort are sufficient to draw useful conclusions, but of course do not replace the need for robust prospective studies in this field.

Rates of LGA were low overall in this study (10.4%), with relatively low levels of gestational weight gain following diagnosis of GDM. The reasons for this are unclear but may be a result of advice to avoid excessive weight gain during the last trimester of pregnancy given to women in our centre following GDM diagnosis. As described previously [27], our population is predominantly white (89%) with relatively low levels of ethnic diversity (5% Asian, < 2% Black), which may limit the applicability of our findings to other populations. However, gestational weight gain has previously been shown to be related to pregnancy outcomes in many different ethnic groups [28].

Excessive gestational weight gain is currently defined for healthy, non-diabetic women using the IOM guidelines (2009) based upon a woman's pre-pregnancy BMI [29]. However, many pregnant women exceed these targets and have excessive weight gain, particularly in the context of GDM. There are currently no specific thresholds to guide weight management in GDM. The guideline from NICE regarding women with diabetes in pregnancy highlights the importance of pre-pregnancy and post-partum weight control but does not mention gestational weight gain [20]. The American Diabetes Association supports 'weight management' as part of standard medical care for women with GDM, referring to the IOM 2009 guidelines [29,30]. Our results suggest that calculating appropriate gestational weight gain based on a percentage of pre-pregnancy BMI might help to identify more women at risk of adverse outcomes than absolute weight gain standards. However, further work is needed to identify which targets are most appropriate for women with GDM, who are already at higher risk of pregnancy complications compared with women with normal glucose tolerance during pregnancy.

Although the association between maternal weight and pregnancy outcomes is well established, it remains unclear exactly how excessive gestational weight gain might affect the fetus. One possibility is that excessive gestational weight gain causes a deterioration in maternal glycaemia which promotes fetal growth and predisposes to more medical interventions around delivery. The current study supports this hypothesis as treatment requirement were higher in women with higher gestational weight gain. However, it is also possible that excessive gestational weight gain reflects a maternal diet rich in calorie-dense foods, such as sugar and fat, which in turn promotes excessive fetal growth.

The current study suggests that a kilogram of weight gained in the latter part of pregnancy has a larger effect upon fetal growth than weight gain earlier in pregnancy. This may be because the fetal growth rate is highest in late pregnancy, and a factor such as weight gain which accelerates that growth might have an exponential effect, particularly if it is associated with higher glycaemia and higher insulin doses. Conversely, it may be that weight gained after the diagnosis of GDM has more metabolic influence, while women earlier in pregnancy have less metabolic consequences of weight gain prior to developing GDM.

Although LGA remains a particular concern in offspring of women with GDM, inadequate gestational weight gain also carries the risk of poor fetal growth. SGA rates are generally low in infants born to mothers with GDM, which makes this issue particularly difficult to study in depth. SGA has been associated with both inadequate and excessive maternal weight in previous work [31,32]. In this study, SGA rates were significantly increased in women with gestational weight gain below the IOM thresholds but also non-significantly increased in women with excessive gestational weight gain (Table 4a). This suggests that women who

attain an appropriate level of gestational weight gain may reduce the risk of both LGA and SGA to their infants. Further work is needed to clarify the relationship between SGA and weight changes in pregnancy and how this might vary in women with GDM. Our work suggests that controlling, but not severely restricting, gestational weight gain after GDM diagnosis is likely to be optimal in terms of fetal growth.

<H1>Conclusion

Our study suggests that control of gestational weight gain in women with GDM should be a priority to improve outcomes in terms of normalizing fetal growth and maximizing the chances of uncomplicated delivery. Furthermore, our results suggest that 28 weeks is not too late for women to benefit from limiting further gestational weight gain. In this study, women who maintained a stable weight after GDM diagnosis at 28 weeks had the best pregnancy outcomes for both mother and child. These findings suggest an urgent need to explore optimal methods of supporting weight control in women with GDM.

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Competing interests

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Author contributions

CLM identified the study question, designed the study, analysed and interpreted the data, wrote and revised the manuscript. CEMA designed the study, analysed and interpreted the data, wrote and revised the manuscript. HRM contributed to data analysis, reviewed and revised the manuscript and contributed to the discussion. LH contributed to data collection, data collation and reviewed and revised the final manuscript. All authors gave approval of the final version of the manuscript prior to publication.

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FIGURE 1 Use of antenatal data at booking, 28 and 36 weeks in order to assess total, early and late gestational weight gain. GWG, gestational weight gain; wk, week.

Table 1. Baseline characteristics of the study population

		Gestational weight gain		
Outcomes		Total (0–36 weeks) *n* = 376	Early (0–28 weeks) *n* = 129	Late (28–36 weeks) *n* = 144
Total weight gain, kg		9.1 (5.1–13.1); median 8.9	7.7 (4.0–11.2); median 7.8	7.7 (4.0–11.2); median 7.8
Total weight gain, % of pre-pregnancy weight		13.3 (6.4–19.4); median 13.3	10.8 (4.7–16.7); median 9.4	10.8 (4.7–16.7); median 9.4
Maternal BMI at booking, kg/m^2		28.8 (23.4–32.7)	30.9 (24.01–36.4)	30.6 (23.7–36.2)
Maternal age, years		34.0 (30.7 – 37.8)	34.3 (30.84 – 38.1)	34.0 (30.2 – 38.2)
Estimated gestational age at GDM diagnosis, weeks		28.1 (27.9–30.1); median 28.9	24.5 (19.6–28.0); median 27.4	24.7 (19.9–28.0); median 27.4
Parity	0	164 (43.6)	46 (36.6)	51 (35.4)
	1	131 (34.8)	42 (32.6)	47 (32.6)
	≥2	75 (19.9)	38 (29.5)	43 (29.9)
	Unknown	6 (1.6)	2 (1.6)	3 (2.1)
Mode of delivery	Vaginal delivery (inc VBAC)	167 (44.4)	57 (44.2)	66 (45.8)
	Instrumental delivery	57 (15.2)	18 (14.0)	19 (13.2)
	Caesarean delivery	152 (40.4)	54 (41.9)	58 (40.3)
	Unknown	0 (0)	0 (0)	1 (0.7)
Birthweight , g		3256 (2975–3535)	3151 (2880–3390)	3215 (2944–3475)
Gestational age at delivery, weeks		38.6 (38.1–39.1)	38.2 (37.9–38.9)	38.4 (38.0–38.9)
Large for gestational age		39 (10.4)	9 (7.0)	13 (9.2)
Small for gestational age		28 (7.6)	10 (8.2)	10 (7.04)
Fasting glucose at diagnosis, mmol/l		4.9 (4.3–5.3)	5.0 (4.4–5.5)	5.0 (4.4–5.4)
Fasting glucose post-partum, mmol/l		4.7 (4.4–5.0)	4.8 (4.3–5.1)	4.8 (4.3–5.1)
Treatment	Dietary management only	176 (46.8)	46 (35.7)	54 (37.5)
	Metformin only at 36 weeks	48 (12.8)	17 (13.2)	19 (13.2)
	Insulin only at 36 weeks	108 (28.8)	39 (30.2)	40 (27.8)
	Metformin and insulin at 36 weeks	44 (11.7)	27 (20.9)	31 (21.5)

Values are given as mean ± IQR or *n* (%). VBAC, vaginal birth after Caesarean.

Table 2. The effect of total gestational weight gain, early gestational weight gain and late gestational weight gain on pregnancy outcomes and treatment requirements in women with GDM

Outcomes	Gestational weight gain Total (0–36 weeks) *n* = 376	Early (0–28 weeks) *n* = 129	Late (28–36 weeks) *n* = 144
Categorical variables (logistic regression)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Large for gestational age	1.08 (1.03 to 1.12)***	1.05 (0.94 to 1.16)	1.17 (1.01 to 1.37)*
Small for gestational age	0.93 (0.87 to 0.99)*	0.89 (0.79 to 1.01)	1.03 (0.88 to 1.20)
Vaginal delivery (including VBAC)	0.94 (0.91 to 0.97)***†	0.97 (0.91 to 1.03)†	0.97 (0.87 to 1.08)†
Caesarean delivery	1.05 (1.02 to 1.08)** †	1.06 (1.00 to 1.12)†	0.91 (0.80 to 1.02)†
Instrumental delivery	1.01 (0.97 to 1.05)†	0.95 (0.88 to 1.03)†	1.26 (1.03 to 1.55)**†
Dietary management only at 36 weeks	1.00 (0.97 to 1.03)	1.00 (0.94 to 1.07)	1.03 (0.91 to 1.15)
On Metformin at 36 weeks	0.98 (0.95 to 1.02)	0.98 (0.93 to 1.04)	0.95 (0.85 to 1.06)
On Insulin at 36 weeks	1.01 (0.98 to 1.05)	1.02 (0.96 to 1.09)	1.01 (0.90 to 1.13)
Continuous variables (linear regression)	Beta coefficient (95% CI)	Beta coefficient (95% CI)	Beta coefficient (95% CI)
Birthweight z score	0.02 (0.01 to 0.04)***	0.02 (−0.01 to 0.04)	0.04 (< 0.01 to 0.08)
Post-partum fasting glucose	< 0.01 (−0.01 to < 0.01)	−0.01 (−0.02 to 0.01)	0.03 (< 0.01 to 0.07)*
Post-partum 2-h OGTT glucose	0.01 (−0.01 to 0.03)‡	−0.02 (−0.07 to 0.04)‡	0.12 (< 0.01 to 0.22)*‡
Total daily insulin dose (36 weeks)	0.52 (0.01 to 1.03)*	1.20 (−0.19 to 2.60)	4.37 (1.92 to 6.82)***
Total insulatard dose (36 weeks)	0.13 (−0.08 to 0.34)	0.21 (−0.25 to 0.67)	1.42 (0.62 to 2.21)***
Total novorapid dose (36 weeks)	0.38 (−0.17 to 0.92)	0.81 (−0.63 to 2.25)	3.03 (0.07 to 6.00)*

*$P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Odds ratio (95% CI) for categorical outcomes and beta coefficient (95% CI) for linear outcomes. Gestational weight gain categories were analysed as per cent change from pre-pregnancy/baseline weight and odds ratios/beta coefficients have been adjusted for antenatal fasting glucose (OGTT T0), parity and pre-pregnancy BMI, except where otherwise indicated (see below).

†Delivery mode analyses adjusted for antenatal fasting glucose (OGTT T0), pre-pregnancy BMI, parity and birthweight z score.

‡Post-partum 2-h OGTT glucose concentration adjusted for antenatal 2-h OGTT glucose, pre-pregnancy BMI and parity.

OGTT, oral glucose tolerance test; VBAC, vaginal birth after Caesarean.

Table 3. Outcomes for women with total gestational weight gain (n = 376) in categories, expressed as OR (95% CI).

	Gestational weight gain < 5% (n = 74)	5–15% (n = 152)	> 15% (n = 150)
Categorical variables (logistic regression)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Large for gestational age	0.30 (0.07 to 1.20)	1.00 (Referent)	2.83 (1.23 to 6.53)*
Small for gestational age	2.43 (0.81 to 7.32)	1.00 (Referent)	0.55 (0.20 to 1.53)
Vaginal delivery (including VBAC)	2.86 (1.47 to 5.57)**†	1.00 (Referent)	0.58 (0.34 to 1.00)* †
Caesarean delivery	0.36 (0.18 to 0.74)**†	1.00 (Referent)	1.73 (1.02 to 2.92)* †
Instrumental delivery (forceps or ventouse)	0.84 (0.29 to 2.44)†	1.00 (Referent)	0.98 (0.47 to 2.04)†
Dietary management only at 36 weeks	1.05 (0.52 to 2.14)	1.00 (Referent)	1.23 (0.71 to 2.14)
On metformin at 36 weeks	1.38 (0.70 to 2.70)	1.00 (Referent)	0.93 (0.50 to 1.72)
On insulin at 36 weeks	0.66 (0.32 to 1.37)	1.00 (Referent)	0.92 (0.51 to 1.65)
Continuous variables (linear regression)	Beta coefficient (95% CI)	Beta coefficient (95% CI)	Beta coefficient (95% CI)
Birthweight z score	−0.12 (−0.40 to 0.15)	0.00 (Referent)	0.44 (0.22 to 0.67)***
Post-partum fasting glucose	−0.05 (−0.22 to 0.11)	0.00 (Referent)	−0.13 (−0.26 to −0.01)*
Post-partum 2-hour OGTT glucose	−0.30 (−0.82 to 0.21)‡	0.00 (Referent)	−0.03 (−0.43 to 0.36)‡
Total daily insulin dose (36w)	−6.25 (−16.51 to 4.02)	0.00 (Referent)	9.71 (1.05 to 18.37)*
Total insulatard dose (36w)	0.39 (−3.95 to 4.72)	0.00 (Referent)	2.83 (−0.82 to 6.49)
Total novorapid dose (36w)	−6.40 (−17.30 to 4.50)	0.00 (Referent)	6.52 −1.53 to 14.58)

*P < 0.05, **P < 0.01, ***P < 0.001.

Models have all been adjusted for pre-pregnancy BMI, parity and antenatal fasting glucose except where otherwise indicated (see below). Models for modes of delivery have also been adjusted for birthweight z score, which takes account of gestational age and sex of the baby. All models adjusted for antenatal fasting glucose (OGTT T0), pre-pregnancy BMI and parity, unless otherwise indicated.

†Delivery mode analyses adjusted for antenatal fasting glucose (OGTT T0), pre-pregnancy BMI, parity and birthweight z score.

‡Post-partum 2-h OGTT glucose concentration adjusted for antenatal 2-h OGTT glucose, pre-pregnancy BMI and parity.

VBAC, vaginal birth after Caesarean.

Table 4. Assessment of the validity of IOM recommendations for gestational weight gain in women with by GDM and the minimum recommended gestational weight gain of 5 kg (n = 375; n = 1 missing height and therefore BMI)

(a) Assessing the validity of the IOM recommendations

	Gained below IOM recommendations (n = 167)	Gained according to IOM recommendations (n = 111)	Gained above IOM recommendations (n = 97)
Categorical variables (logistic regression)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Large for gestational age	0.43 (0.17 to 1.08)	1.00 (Referent)	1.57 (0.69 to 3.57)
Small for gestational age	6.85 (1.54 to 30.47)*	1.00 (Referent)	4.14 (0.81 to 21.29)
Vaginal delivery (including VBAC)	1.06 (0.63 to 1.79)†	1.00 (Referent)	0.46 (0.25 to 0.86)*†
Caesarean delivery	0.76 (0.45 to 1.29)†	1.00 (Referent)	1.87 (1.05 to 3.34)*†
Instrumental delivery	1.63 (0.75 to 3.52)†	1.00 (Referent)	1.20 (0.48 to 2.98)†
Dietary management only at 36 weeks	1.41 (0.80 to 2.46)	1.00 (Referent)	1.11 (0.58 to 2.12)
On Metformin at 36 weeks	0.77 (0.43 to 1.38)	1.00 (Referent)	0.63 (0.32 to 1.24)
On Insulin at 36 weeks	0.85 (0.47 to 1.55)	1.00 (Referent)	1.54 (0.81 to 2.96)
Continuous variables (linear regression)	Beta coefficient (95% CI)	Beta coefficient (95% CI)	Beta coefficient (95% CI)
Birthweight (g)	−0.28 (−0.51 to −0.05)*	0.00 (Referent)	0.06 (−0.02 to 0.32)
Postnatal fasting glucose	0.03 (−0.09 to 0.16)	0.00 (Referent)	< 0.01 (−0.15 to 0.15)
Post-partum 2-h OGTT glucose	0.05 (−0.34 to 0.44)‡	0.00 (Referent)	0.19 (−0.26 to 0.63)‡
Total daily insulin dose (36w)	−1.50 (−10.68 to 7.67)	0.00 (Referent)	9.08 (−0.36 to 18.51)
Total insulatard dose (36w)	2.30 (−1.50 to 6.10)	0.00 (Referent)	5.05 (1.15 to 8.96)*
Total novorapid dose (36w)	−3.23 (−11.83 to 5.37)	0.00 (Referent)	6.34 (−2.54 to 15.23)

(b) Assessing the validity of the recommended 5kg minimum weight gain, regardless of pre-pregnancy BMI

	Gained < 5 kg (n = 91)	All other women (n = 285)
Categorical variables (logistic regression)	Odds ratios (95% CI)	Odds ratios (95% CI)
Large for gestational age	0.18 (0.05 to 0.64)**	1.00 (Referent)
Small for gestational age	2.27 (0.86 to 6.00)	1.00 (Referent)
Vaginal delivery (including VBAC)	1.94 (1.11 to 3.38)*†	1.00 (Referent)
Caesarean delivery	0.53 (0.30 to 0.95)*†	1.00 (Referent)
Instrumental delivery	1.00 (0.42 to 2.39)†	1.00 (Referent)
Dietary management only at 36 weeks	1.18 (0.64 to 2.17)	1.00 (Referent)
On metformin at 36 weeks	1.31 (0.72 to 2.38)	1.00 (Referent)
On insulin at 36 weeks	0.63 (0.33 to 1.19)	1.00 (Referent)
Continuous variables (linear regression)	Beta coefficient (95% CI)	Beta coefficient (95% CI)

Birthweight z score	−0.34 (−0.58 to −0.10)**	0.00 (Referent)
Post-partum fasting glucose	0.10 (−0.04 to 0.23)	0.00 (Referent)
Post-partum 2-h OGTT glucose	−0.07 (−0.50 to 0.36)‡	0.00 (Referent)
Total daily insulin dose (36 weeks)	−8.09 (−17.26 to 1.08)	0.00 (Referent)
Total insulatard dose (36 weeks)	−0.48 (−4.32 to 3.35)	0.00 (Referent)
Total novorapid dose (36 weeks)	−6.34 (−15.91 to 3.22)	0.00 (Referent)

*$P < 0.05$, **$P <$ 0.01, ***$P < 0.001$.

Outcomes were expressed as OR (95% CI). The Institute of Medicine (IOM) recommendations state that normal weight, overweight and obese women are advised to gain 11.4–15.9 kg, 6.8–11.4 kg and 5.0–9.1 kg respectively [29]. Models have all been adjusted for pre-pregnancy BMI, antenatal fasting glucose and parity except where otherwise indicated (see below).

All models adjusted for antenatal fasting glucose (OGTT T0), pre-pregnancy BMI and parity, unless otherwise indicated

†Adjusted for antenatal fasting glucose (OGTT T0), pre-pregnancy BMI and birthweight *z* score

‡Adjusted for antenatal 120-min glucose (OGTT T120) and pre-pregnancy BMI.

VBAC, vaginal birth after Caesarean