# RESEARCH



# Reconsideration of lowering gestational weight gain guidelines in pregnant women diagnosed with gestational diabetes: evidence from a Belgian study

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# Abstract

**Background** The suitability of the United States National Academy of Medicine guidelines for gestational weight gain in women with gestational diabetes remains uncertain, raising global concerns. This study aimed to evaluate the association of gestational weight gain with pregnancy and birth outcomes and to determine optimal ranges for gestational weight gain per pre-pregnancy body mass index category in women with gestational diabetes.

**Methods** An epidemiological analysis between 2009–2018 analyzed a large Belgian cohort of singleton pregnancies with gestational diabetes and gestational age 38–40 weeks. Multivariate logistic regression assessed associations between gestational weight gain and relevant pregnancy and birth outcomes, with and without adjustment for confounding variables, including maternal age, origin, education, mode of conception, parity, gestational age at delivery, social deprivation, and year of delivery. Potential optimal weight gain ranges were calculated by minimizing the combined risk of small- and large-for-gestational-age infants (SGA, LGA).

**Results** A total of 13,060 women with gestational diabetes were included. Compared to recommended weight gain, gestational weight gain above guidelines occurred in 26.9% and was associated with an increased risk of gestational hypertension (aOR 1.41, 95% CI 1.20–1.66, p < 0.001), emergency caesarean section (aOR 1.45, 95% CI 1.25–1.69, p < 0.001), LGA infants (aOR 1.84, 95% CI 1.63–2.08, p < 0.001), and macrosomia (aOR 1.78, 95% CI 1.55–2.04, p < 0.001). Weight gain less than recommended (40.2%) was associated with a decreased risk of gestational hypertension (aOR 0.81, 95% CI 0.69–0.96, p = 0.015), LGA infants (aOR 0.58, 95% CI 0.50–0.66, p < 0.001), and macrosomia (aOR 0.57, 95% CI 0.49–0.65, p < 0.001), but at the expense of an increased risk of SGA infants (aOR 1.68, 95% CI 1.45–1.96, p < 0.001) and low birth weight (aOR 2.28, 95% CI 1.57–3.32, p < 0.001). Based on current analysis, the optimal ranges for gestational weight gain would be 9 to 14 kg for women with a normal weight, 1 to 9 kg for women with overweight, and -7 to 1 kg for women with obesity.

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Twitter summary: Optimal gestational weight gain for single pregnancies with gestational

diabetes is likely to be lower than current recommendations.

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**Conclusions** This Belgian study suggests that optimal gestational weight gain for singleton at-term pregnancies complicated by gestational diabetes should be lower than current recommendations, highlighting the need to reevaluate gestational weight gain guidelines in this context.

**Keywords** Gestational diabetes mellitus, Gestational weight gain, National Academy of Medicine guidelines, Pregnancy, Recommendations

# Background

Adequate gestational weight gain (GWG) is essential for maternal and fetal health. In 2009, the United States Institute of Medicine [now known as the National Academy of Medicine (NAM)] published revised guidelines for GWG that are based on pre-pregnancy body mass index (BMI) for women with underweight, normal weight, overweight, and obesity [1]. GWG outside those recommendations confers a higher risk of adverse maternal and neonatal outcomes [1, 2]. In a recent metaanalysis in more than 1,000,000 pregnant women, 47% (n=621,004) exceeded the recommended GWG, which was associated with an increased risk of pregnancyinduced hypertension, large-for-gestational-age (LGA) infants, macrosomia (birth weight  $\geq$  4000 g), caesarean delivery, and postpartum weight retention [3]. An epidemiological analysis of more than 300,000 Belgian pregnant women found that better outcomes are predicted for GWG lower than recommended by the NAM in women with class II (BMI 35–39.9 kg/m<sup>2</sup>) and III (BMI  $\geq$  40 kg/  $m^2$ ) obesity [4]. On the other hand, there is also evidence that GWG below NAM recommendations increases the risk of small-for-gestational-age (SGA) infants and preterm birth [3].

The NAM guidelines do not provide specific recommendations for GWG in pregnancies that are complicated by gestational diabetes (GDM), and the evidence on the relationship between GWG outside NAM recommendations and pregnancy outcomes in women with GDM is inconsistent. Several studies have suggested that GWG below recommendations in pregnancies with GDM increases the risk of SGA, while excessive GWG is associated with a higher risk of LGA [5-8]. Recent Belgian research demonstrated that GWG below NAM recommendations occurs frequently in women with GDM, without increased risk for SGA and preterm delivery, and with a better postpartum metabolic profile in the mother, while excessive GWG was associated with increased risk for neonatal hypoglycaemia and worse postpartum metabolic profile in the mother [9]. However, ranges for optimal GWG per pre-pregnancy BMI category could not be determined, given the small number of events for outcomes such as LGA and SGA. Larger studies on GWG in pregnancies with GDM are required globally to determine optimal GWG in relation to relevant pregnancy outcomes. In this Belgian population-based study, we aimed therefore to evaluate the association of GWG as below/within/above NAM recommendations with pregnancy and birth outcomes, and to determine optimal GWG ranges per BMI category in women with GDM. This stratification was selected because the NAM guidelines offer GWG recommendations specifically tailored to the different BMI classifications [1].

## Methods

# Subjects and databases

The Study Centre of Perinatal Epidemiology records maternal, gestational, and neonatal data from all deliveries of all maternity units in the Northern region of Belgium (with about 6.6 million inhabitants, accounting for 60% of the Belgian population, with about 60,000 deliveries per year) [10]. These data are gathered centrally and examined through an error detection program to check for accuracy and completeness. Data collected include maternal and gestational age (completed weeks) at delivery, maternal height and weight before pregnancy, maternal weight just before delivery, parity, gestational hypertension, diabetes (type 1, type 2 or GDM) during pregnancy, mode of delivery, birth weight, congenital anomalies and perinatal mortality. Subsequently, the follow-up of children is coordinated by 'Kind en Gezin' until school age (±2.5 years). 'Kind en Gezin' collects data from anthropometric measurements, socio-economic factors, and developmental milestones of both the child and their family [11]. Through the integration of the 'Study Centre of Perinatal Epidemiology' and 'Kind en Gezin' databases, longitudinal tracking of mothers and their children can be obtained. The databases were merged by a Trusted Third Party, selected by 'Kind en Gezin'. The Trusted Third Party used maternal date of birth, maternal zip-code, and birth date and gender of the child to link the two databases.

We conducted an epidemiological analysis on the data of the merged 'Study Centre of Perinatal Epidemiology' / 'Kind en Gezin' database, focusing on women with GDM between 2009 and 2018 [12]. As the NAM guidelines [1] are based on at term pregnancies, women with preterm delivery (<37 weeks of gestation) were excluded.

In the database, diabetes in pregnancy was classified as one category, including both women with GDM and women with pregestational diabetes (type 1 or type 2 diabetes). It was therefore not possible to separately analyse women with GDM and women with pregestational diabetes. To limit bias by also including women with pregestational diabetes (expected to be max. 10% of the total cohort [13]), only women who delivered between 38–40 weeks of pregnancy were included for this analysis, as such excluding most women with pregestational diabetes as they are generally induced  $\leq$  38 weeks of pregnancy [14, 15]. Previous research from a large Belgian cohort, has demonstrated that 7.5% of all women with GDM delivered preterm [16]. By excluding preterm deliveries, we can therefore expect that only a limited group of women with GDM will also be excluded, while this allows to exclude the majority of women with pregestational diabetes. Realistic ranges for maternal height (1.35–1.95 m), pre-pregnancy weight (35-170 kg), maternal weight at delivery (40-185 kg), and GWG (-45 to+60 kg) were established for inclusion in the analysis.

In 2018, 4.9% (n = 3,080) of all deliveries (n = 62,812) was complicated by GDM or diabetes in pregnancy [17]. Up to 2018, the diagnosis of GDM was generally based on a 100 g oral glucose tolerance test with the Carpenter & Coustan criteria, which in general identify more severe cases of GDM compared to the 2013 WHO criteria [18]. Some centers used the 2013 WHO criteria for the diagnosis of GDM already from 2014 onwards, although these criteria were recommended by the Flemish guidelines only from 2019 onwards for the diagnosis of GDM [19]. If GDM was diagnosed, women were treated in line with the American Diabetes Association (ADA) guidelines, with glucose targets fasting < 5.3 mmol/l, 1 h < 7.8 mmol/l and 2 h < 6.7 mmol/l [18]. If lifestyle alone was insufficient to achieve glycaemic targets, treatment with insulin was initiated, as this is the standard of care for women with GDM in Belgium [20].

The merged database used for current analyses was developed for other research initially [12] and this explains why women without data on breastfeeding were excluded (626 women out of the 569,914 women).

#### **Baseline and outcome measures**

Maternal age, height and pre-pregnancy weight, mode of conception (spontaneous, in vitro fertilization or intracytoplasmic sperm injection, or assisted reproductive therapy with only hormonal treatment including Clomiphene, Letrozole and IUI), parity, gestational hypertension ( $\geq$  140/90 mmHg in pregnancy), induction of labor, mode of delivery, gender of the child, and birth weight were obtained from the 'Study Centre of Perinatal Epidemiology' database. Pre-pregnancy weight and height

were self-reported during pregnancy. Maternal weight at birth was measured in the delivery room or the weight of the last prenatal visit was used if not available. LGA and SGA (respectively birth weight > 90th and < 10th percentile according to standardized Flemish birth charts [21]) were calculated based on the child's birth weight, gender, gestational age, and parity. The pre-pregnancy BMI was stratified into underweight (BMI <  $18.5 \text{ kg/m}^2$ ), normal weight (BMI 18.5–24.9 kg/m<sup>2</sup>), overweight (BMI 25–29.9 kg/m<sup>2</sup>), and obesity (BMI $\geq$ 30 kg/m<sup>2</sup>). GWG was calculated as the difference between pre-pregnancy weight and weight at delivery room or at the last prenatal visit, and was stratified into three categories according to the NAM guidelines based on the pre-pregnancy BMI: within, below, and above recommendations [1]. Socioeconomic and lifestyle data including social deprivation, maternal education and origin [based on birth country or region of the mother, divided into three categories: Europe, Africa and other], and breastfeeding data were obtained from the 'Kind en Gezin' database and were collected during home visits by a nurse or during visits at the 'Kind en Gezin' consultation office by a medical doctor or nurse. Maternal outcomes of interest included rates of gestational hypertension and emergency caesarean section. Neonatal parameters of interest included SGA, LGA, low birth weight (LBW) (<2500 g), and macrosomia (birth weight  $\geq$  4000 g).

#### Statistical analysis

Descriptive statistics were presented as frequencies and percentages for categorical variables and means with standard deviations for continuous variables. The Chisquare test was used for comparing groups on categorical variables, and the Kruskal–Wallis test was used for comparing groups on continuous variables.

Logistic regression models were used to assess the impact of GWG on the outcomes, with results presented as odds ratios (OR) with 95% confidence intervals (CI). ORs were reported with and without adjustment for confounding variables, including maternal age, origin, education, mode of conception, parity, gestational age at delivery, social deprivation, and year of delivery. The year of delivery was included due to the associations with both the rate of adverse pregnancy outcomes and maternal BMI at delivery [4]. Adjusted ORs (aORs) could not be determined for women with underweight given the small number of outcomes in this group. *P*-values < 0.05 were considered statistically significant.

The predicted probability on an adverse outcome for each possible value of gestational weight change was calculated for multiparous women, with the following characteristics, reflecting the average in our patient population: maternal age of 30 years from European origin,

with a secondary education degree and no social deprivation, spontaneous conception, gestational age of 39 weeks and delivery in 2018. The year of delivery was chosen as the most recent available and secondary education was selected as less than half of the women had a higher education. The predicted probabilities were visualized in graphs, stratified per BMI category, aligning with the NAM guidelines, which provide recommendations based on BMI categories. Additionally when pre-pregnancy BMI is not stratified but instead included as an explanatory variable in the logistic regression model, along with the interaction term between GWG and pre-pregnancy BMI, statistical significance is observed for several key outcomes: LGA (p = 0.04), LBW (p = 0.08), and macrosomia (p = 0.008). This further supports the use of stratified analysis to accurately capture the relationship between GWG and pregnancy outcomes. As SGA/LGA are the most common complications with the strongest link with long-term metabolic outcome, the optimal GWG was considered to be the point where the curves of SGA and LGA intersect (as at some point the decrease in LGA risk is associated with increased risk for SGA), as previously described in several other studies who determined estimated optimal GWG [4, 22, 23]. Optimal ranges for GWG were estimated for each BMI category as the window at which the sum of predictive probabilities for LGA and SGA increased no more than 0.5% from the intersection, as reported in previous research [22, 23]. The maximum increase of 0.5% was set to avoid the creation of excessively large GWG ranges [24]. It was not possible to analyse optimal GWG thresholds for women who were underweight and separately for the different classes of obesity [class I (BMI 30-34.9 kg/m<sup>2</sup>), class II (BMI  $35-39.9 \text{ kg/m}^2$ ) and class III (BMI  $\ge 40 \text{ kg/m}^2$ )] due to the small numbers of outcomes in these subgroups. Statistical analyses were performed with SAS software (Version 9.4) by Lieveke Ameye.

#### Results

# Pre-pregnancy BMI and gestational weight gain in the Belgian population

Data of 569,914 singleton deliveries were collected in the merged 'Study Centre of Perinatal Epidemiology' / 'Kind en Gezin' database. After applying the selection criteria and excluding missing values for all relevant variables of interest, a total of 13,060 cases with GDM were withheld for the analysis (Additional file 1: Fig. S1).

Based on the pre-pregnancy BMI, 2.4% (313) of all women with GDM in our cohort were underweight, 42.1% (5492) had a normal weight, 29.6% (3865) were overweight and 26.0% (3390) were living with obesity (16.2% class I, 6.9% class II, and 2.8% class III). Of all women included in the analysis, 32.8% (4290) gained

weight during pregnancy within the NAM recommendations, whereas 40.2% (5253) gained less and 26.9% (3517) gained more weight than recommended. Gaining weight above the NAM recommendations was highest in the population with overweight (37.5%) and obesity (36.5%), and lowest in the population with underweight (6.4%). Women with GWG above NAM guidelines were slightly younger, lower educated, more often from an ethnic minority, less often multiparous, had a higher pre-pregnancy BMI, and less often breastfed compared to women with GWG within guidelines (Table 1). GWG below guidelines occurred in 63.6% of all women with underweight, in 53.9% of those with normal weight, in 27.0% of those with overweight, and in 30.9% of those with obesity. Women with GWG below guidelines were more often White, higher educated and had a lower prepregnancy BMI compared to women with GWG within guidelines (Table 1). Maternal and neonatal characteristics for GWG below, within, and above guidelines for each pre-pregnancy BMI category separately are presented in the Additional file: Table S1.

# Association of gestational weight gain with adverse pregnancy outcomes

Women with GDM in our cohort with excessive GWG demonstrated a higher percentage of gestational hypertension [11.8% (416) vs. 8.1% (346), aOR 1.41, 95% CI (1.20-1.66), p < 0.001 and emergency caesarean section [15.0% (527) vs. 9.7% (414), aOR 1.45, 95% CI (1.25-1.69), p < 0.001 compared to women with GWG within NAM recommendations (Additional file 1: Table S2). This trend was particularly noticeable among individuals with a higher BMI. For instance, among women with excessive GWG and a normal BMI, gestational hypertension was reported in 7.9% versus 17.2% in women with obesity and excessive GWG (Table 2). For emergency caesarean section, the prevalence rose from 5.0% in underweight women to 18.7% in those with obesity and excessive GWG (Table 2). In the total cohort, women with excessive GWG had significantly higher odds of delivering LGA infants, with rates of 26.2% (920) vs. 15.6% (669), yielding an adjusted odds ratio of 1.84, (95% CI (1.63–2.08), *p* < 0.001). Likewise, the incidence of macrosomia was greater among this group at 19.0% (667) vs. 11.7% (502), yielding an adjusted odds ratio of 1.78 ( 95% CI (1.55–2.04), p < 0.001) when compared to those with GWG within the recommended range (Additional file 1: Table S2). Prevalences increased with increasing BMI, from 10.0% in women with underweight to 31.2% in those living with obesity who gained weight above recommendations for LGA and from 10.0% to 23.1% for macrosomia (Table 2). On the other hand, excessive GWG corresponded to lower odds of SGA [4.8% (169)

# Table 1 Maternal and neonatal characteristics for different categories of gestational weight gain

	below guidelines ( <i>n</i> = 5253 40.2%)	within guidelines ( <i>n</i> = 4290, 32.8%)	above guidelines ( <i>n</i> = 3517 26.9%)	<i>p</i> -value below vs. within	<i>p</i> -value above vs. within
Mean age (SD)	31.7 (4.9)	31.6 (4.9)	31.0 (5.1)	0.575	< 0.001
Origin, % (n)					
Europe	75.1 (3918)	74.2 (3155)	72.2 (2515)	0.003	0.031
Africa	15.9 (829)	14.8 (629)	17.0 (592)		
Other	9.0 (469)	11.0 (467)	10.8 (377)		
Education, % (n)					
No degree or primary education	7.6 (377)	7.6 (303)	7.6 (247)	< 0.001	< 0.001
Lower secondary or special education	10.2 (505)	12.1 (482)	14.1 (460)		
Higher secondary education	29.3 (1445)	33.6 (1341)	40.6 (1321)		
Higher education	52.8 (2604)	46.7 (1864)	37.7 (1227)		
Living in deprivation, % (n)	14.6 (765)	16.0 (681)	17.6 (616)	0.072	0.052
Multiparity, % (n)	60.3 (3168)	59.0 (2533)	56.2 (1977)	0.210	0.012
Pre-pregnancy BMI (kg/m <sup>2</sup> ), mean (SD)	25.8 (6.0)	26.9 (5.8)	28.4 (5.3)	< 0.001	< 0.001
Pre-pregnancy BMI category, % (n)					
Underweight	3.8 (199)	2.2 (94)	0.6 (20)	< 0.001	< 0.001
Normal weight	56.3 (2960)	40.1 (1721)	23.1 (811)		
Overweight	19.9 (1045)	31.9 (1370)	41.2 (1450)		
Obese I	10.9 (573)	16.3 (700)	24.0 (843)		
Obese II	6.1 (318)	6.6 (283)	8.6 (301)		
Obese III	3.0 (158)	2.8 (122)	2.6 (92)		
Conception, % (n)	, , , , , , , , , , , , , , , , , , ,	. ,			
Spontaneous	90.6 (4658)	91.9 (3849)	92.0 (3141)	0.075	0.989
Hormonal	3.6 (187)	2.8 (117)	2.9 (98)		
IVF	3.0 (154)	2.9 (122)	2.8 (96)		
ICSI	2.8 (143)	2.4 (100)	2.3 (80)		
Gestational hypertension, % (n)	6.1 (322)	8.1 (346)	11.8 (416)	< 0.001	< 0.001
Gestational age at delivery (weeks), mean (SD)	38.8 (0.8)	38.8 (0.8)	38.8 (0.8)	0.568	0.011
Induction of labor, % (n)	36.0 (1893)	39.9 (1711)	42.8 (1506)	< 0.001	0.009
Method of delivery, % (n)					
Spontaneous	69.9 (3673)	63.5 (2726)	56.4 (1985)	< 0.001	< 0.001
Vacuum extraction	8.6 (454)	10.0 (430)	9.3 (327)		
Forceps	0.4 (21)	0.4 (16)	0.4 (14)		
Vaginal breech	0.1 (5)	0.0 (1)	0.1 (2)		
Planned cesarean section	13.2 (692)	16.4 (703)	18.8 (662)		
Emergency cesarean section	7.8 (408)	9.7 (414)	15.0 (527)		
Male gender baby, % (n)	49.4 (2595)	52.8 (2263)	52.6 (1849)	0.001	0.876
Birth weight (g), mean (SD)	3339.0 (433.7)	3457.0 (450.8)	3590.9 (493.7)	< 0.001	< 0.001
LBW (<2500 g), % (n)	2.0 (106)	1.1 (47)	0.7 (26)	< 0.001	< 0.001
Macrosomia (≥4000 g), % (n)	6.9 (363)	11.7 (502)	19.0 (667)	< 0.001	< 0.001
- SGA, % (n)	11.3 (596)	7.4 (317)	4.8 (169)	< 0.001	< 0.001
LGA, % (n)	9.4 (495)	15.6 (669)	26.2 (920)	< 0.001	< 0.001
Breastfeeding, % (n)					
Exclusively at 6 months	9.0 (473)	8.9 (382)	8.2 (287)	0.102	0.031
Exclusively at 12 weeks, but < 6 months	22.3 (1167)	20.5 (877)	18.5 (649)		
Exclusively at 6 days, but < 12 weeks	34.2 (1796)	34.2 (1464)	34.1 (1199)		
Not breastfeeding at 6 days	34.5 (1808)	36.5 (1563)	39.2 (1376)		

Categorical variables are presented as frequencies % (n); continuous variables are presented as mean (SD). Differences are considered significant at p-value < 0.05. NAM recommendations were used for the definition of GWG below, within and above guidelines (for underweight women < 12.5 kg, between 12.5 and 18 kg and more than 18 kg, for normal weight women < 11.5 kg, between 11.5 and 16 kg and more than 16 kg, for overweight women < 7 kg, between 7 and 11.5 kg and more than 11.5 kg, for obese women in < 5 kg, between 5 and 9 kg and more than 9 kg, respectively)

Abbreviations: BMI Body Mass Index, IVF in vitro fertilization, ICSI intracytoplasmic sperm injection, LBW low birth weight; SGA: small-for-gestational-age, LGA large-for-gestational-age, NAM National Academy of Medicine

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	GWG as recommended (reference)	GWG less thar	recommended				GWG more tha	n recommended			
	% (n/N)	(N/N)	Crude OR (95% CI)	<i>p</i> -value	aOR (95% CI)	<i>p</i> -value	% (n/N)	Crude OR (95% CI)	<i>p</i> -value	aOR (95% Cl)	<i>p</i> -value
Underweight ( $n = 313$ )											
Gestational hypertension	8.5 (8/94)	4.02 (8/199)	0.45 (0.16–1.24)	0.122			15 (3/20)	1.90 (0.46–7.89)	0.379	ı	
Emergency c-section	4.3 (4/94)	6.0 (12/199)	1.44 (0.45–4.60)	0.535	I	I	5.0 (1/20)	1.18 (0.13–11.19)	0.883	ı	I
SGA	8.5 (8/94)	19.6 (39/199)	2.62 (1.17–5.86)	0.019	1		5.0 (1/20)	0.57 (0.07–4.80)	0.602	ı	ı
rga	9.6 (9/94)	4.0 (8/199)	0.40 (0.15–1.06)	0.065	ı	1	10.0 (2/20)	1.05 (0.21–5.27)	0.953	ı	ı
LBW (< 2500 g)	2.1 (2/94)	4.5 (9/199)	2.18 (0.46–10.29)	0.325		ı	0.0 (0/20)	0.00 (0.00-1)	0.972	ı	ı
Macrosomia (≥ 4000 g)	9.6 (9/94)	1.5 (3/199)	0.14 (0.04–0.55)	0.004	ı	ı	10.0 (2/20)	1.05 (0.21–5.27)	0.953	I	I
Normal weight ( <i>n</i> = 5492)											
Gestational hypertension	6.2 (107/1721)	4.7 (140/2960)	0.75 (0.58–0.97)	0.029	0.78 (0.59–1.02)	0.070	7.9 (64/811)	1.29 (0.94–1.78)	0.118	1.33 (0.95–1.87)	0.102
Emergency c-section	9.5 (164/1721)	6.4 (188/2960)	0.64 (0.52–0.80)	< 0.001	0.64 (0.51–0.81)	< 0.001	11.7 (95/811)	1.26 (0.96–1.65)	0.091	1.18 (0.88–1.58)	0.261
SGA	7.1 (122/1721)	11.4 (337/2960)	1.68 (1.36–2.09)	< 0.001	1.76 (1.40–2.21)	< 0.001	3.6 29/811	0.49 (0.32–0.74)	0.001	0.44 (0.28–0.69)	< 0.001
LGA	14.7 (253/1721)	7.9 (235/2960)	0.50 (0.41–0.60)	< 0.001	0.49 (0.40–0.59)	< 0.001	23.9 (194/811)	1.82 (1.48–2.25)	< 0.001	1.84 (1.47–2.30)	< 0.001
LBW (< 2500 g)	0.8 (14/1721)	2.0 (60/2960)	2.52 (1.41–4.53)	0.002	3.85 (1.95–7.62)	< 0.001	0.5 (4/811)	0.60 (0.20–1.84)	0.376	0.36 (0.08–1.68)	0.196
Macrosomia (≥4000 g)	10.2 (175/1721)	5.5 (162/2960)	0.51 (0.41–0.64)	< 0.001	0.48 (0.38–0.60)	< 0.001	16.6 (135/811)	1.76 (1.39–2.25)	< 0.001	1.96 (1.51–2.55)	< 0.001
Overweight ( <i>n</i> = 3865)											
Gestational hypertension	6.5 (89/1370)	5.2 (54/1045)	0.78 (0.55–1.11)	0.171	0.80 (0.55–1.16)	0.240	9.4 (137/1450)	1.50 (1.14–1.98)	0.004	1.55 (1.15–2.08)	0.004
Emergency c-section	9.1 (125/1370)	8.0 (84/1045)	0.87 (0.65–1.16)	0.347	0.94 (0.68–1.28)	0.679	13.8 (200/1450)	1.59 (1.26–2.02)	< 0.001	1.53 (1.18–1.99)	0.001
SGA	9.4 (129/1370)	11.4 (119/1045)	1.24 (0.95–1.61)	0.114	1.31 (0.99–1.73)	0.056	5.4 (79/1450)	0.55 (0.41–0.74)	< 0.001	0.56 (0.41–0.76)	< 0.001
LGA	13.6 (187/1370)	9.9 (103/1045)	0.69 (0.54–0.89)	0.005	0.66 (0.50–0.87)	0.003	23.3 (338/1450)	1.92 (1.58–2.34)	< 0.001	1.96 (1.58–2.42)	< 0.001
LBW (< 2500 g)	1.8 (24/1370)	2.0 (21/1045)	1.15 (0.64–2.08)	0.643	1.26 (0.67–2.34)	0.473	0.8 (11/1450)	0.43 (0.21–0.88)	0.021	0.45 (0.21–0.94)	0.033

	GWG as recommended (reference)	GWG less tha	in recommended				GWG more th	an recommended			
	% (N/N)	% (N/N)	Crude OR (95% CI)	<i>p</i> -value	aOR (95% Cl)	<i>p</i> -value	% (N/N)	Crude OR (95% CI)	<i>p</i> -value	aOR (95% Cl)	<i>p</i> -value
Macrosomia (≥ 4000 g)	10.8 (148/1370)	7.8 (81/1045)	0.69 (0.52–0.92)	0.012	0.66 (0.48–0.90)	0.008	16.9 (245/1450)	1.68 (1.35–2.09)	< 0.001	1.84 (1.45–2.34)	< 0.001
Obese ( $n = 3390$ )											
Gestational hypertension	12.9 (142/1105)	11.4 (120/1049)	0.88 (0.68–1.14)	0.317	0.87 (0.66–1.14)	0.302	17.2 (212/1236)	1.40 (1.12–1.77)	0.004	1.39 (1.09–1.78)	0.008
Emergency c-section	11.0 (121/1105)	11.8 (124/1049)	1.09 (0.84–1.42)	0.525	1.17 (0.88–1.56)	0.287	18.7 (231/1236)	1.87 (1.47–2.37)	< 0.001	1.72 (1.33–2.23)	< 0.001
SGA	5.2 (58/1105)	9.6 (101/1049)	1.92 (1.38–2.69)	< 0.001	1.89 (1.33–2.69)	< 0.001	4.9 (60/1236)	0.92 (0.64–1.33)	0.663	0.85 (0.57–1.26)	0.407
ГGА	19.9 (220/1105)	14.2 (149/1049)	0.67 (0.53–0.84)	0.001	0.70 (0.55–0.88)	0.003	31.2 (386/1236)	1.83 (1.51–2.21)	< 0.001	1.89 (1.54–2.32)	< 0.001
LBW (< 2500 g)	0.6 (7/1105)	1.5 (16/1049)	2.43 (1.00–5.93)	0.051	2.37 (0.95–5.91)	0.065	0.9 (11/1236)	1.41 (0.54–3.65)	0.480	1.16 (0.43–3.15)	0.775
Macrosomia (≥ 4000 g)	15.4 (170/1105)	11.2 (117/1049)	0.69 (0.54–0.89)	0.004	0.71 (0.54–0.92)	0.010	23.1 (285/1236)	1.65 (1.34–2.03)	< 0.001	1.77 (1.41–2.22)	< 0.001
The results were presented with conception, parity, gestational. between 12.5 and 18 kg and m women < 5 kg, between 5 and 5 and obesity (BMI $\ge$ 30 kg/m <sup>2</sup> )	n crude and adjusted o age, social deprivation, ore than 18 kg, for norr kg and more than 9 k	dds ratios with 9 , and year of deliv mal weight wom g, respectively). T	5% confidence intervals (' very. NAM guidelines were en < 11.5 kg, between 11.5 'he pre-pregnancy BMI wa	vithin' group used for the and 16 kg ar s stratified in	as reference gr definition of g nd more than 1 to underweigh	oup). Multiv estational we 6 kg, for over t (BMI < 18.5	ariate analyses we eight gain below, v weight women < kg/m <sup>2</sup> ), normal w	ere adjusted for maternal a <u>c</u> within, and above guideline 7 kg, between 7 and 11.5 kg eight (BMI 18.5–24.9 kg/m <sup>2</sup>	ge, origin, ed es (for under g and more t <sup>2</sup> ), overweigh	ucation, mode weight women than 11.5 kg, foi it (BMI 25–29.9	of < 12.5 kg, ` obese kg/m <sup>2</sup> ),

Abbreviations: GWG gestational weight gain, a OR adjusted odds ratio, CI confidence interval, SGA small-for-gestational-age, LGA large-for-gestational-age, LBW low birth weight, NAM National Academy of Medicine

Table 2 (continued)

vs. 7.4% (317), aOR 0.61, 95% CI (0.50–0.75), p < 0.001] (Additional file 1: Table S2). However, when considering the risk in the BMI categories separately, the impact of excessive GWG on SGA was no longer significant among women with obesity (Table 2).

In the total cohort of women with GDM, GWG less than recommended was associated with a lower occurrence of gestational hypertension [6.1% (322) vs. 8.1% (346), aOR 0.81, 95% CI (0.69-0.96), p=0.015], LGA [9.4% (495) vs. 15.6% (669), aOR 0.58, 95% CI (0.50-0.66), *p* < 0.001], macrosomia [6.9% (363) vs. 11.7% (502), aOR 0.57, 95% CI (0.49-0.66), p<0.001], as well as a trend toward a decreased risk of emergence caesarean section [7.8% (408) vs. 9.7% (414), aOR 0.86, 95% CI (0.74–1.01), p = 0.060], compared to GWG as recommended by the NAM. However this was at the expense of an increased risk of SGA infants [11.3% (596) vs. 7.4% (317), aOR 1.68, 95% CI (1.45-1.96), p<0.001] and infants with LBW [2.0% (106) vs. 1.1% (47), aOR 2.28, 95% CI (1.57–3.32), p < 0.001] (Additional file 1: Table S2). When considering the outcomes per BMI category separately, no significant association was found between higher BMI classes and the adjusted risk of emergency caesarean section (Table 2). Inadequate GWG was also associated with an increased risk of LBW in normal-weight women, although this association was not significant in women with higher BMI classes. The risk for SGA infants remained significantly increased in women with obesity who had GWG below the recommended guidelines. In contrast, a trend towards a reduced risk of SGA was observed in women with overweight who also had GWG below these recommendations (Table 2).

### Prediction model for optimal gestational weight gain

In the prediction model, using data from all eligible women, GWG was implemented as a continuous variable and the predicted probability of a selection of adverse outcomes was calculated for any given value of GWG. The predicted probabilities were calculated for a multiparous White woman of 30 years, with a secondary education degree and no social deprivation, with spontaneous conception, gestational age of 39 weeks at delivery in 2018. Subsequently, the predicted probabilities were plotted for normal, overweight and obesity pre-pregnancy BMI categories separately in Fig. 1. Optimal GWG for these women with GDM, at the intersection of the SGA and LGA curves, corresponded with a weight gain of 11 kg in women with a normal BMI, 6.5 kg in women with overweight, and -1.5 kg in women with obesity. Correspondingly, the window for optimal GWG, estimated as the range with the sum of predictive probabilities increasing no more than 0.5% from the optimal GWG point, was 9 to 14 kg for normal weight women, 1 to 9 kg for women with overweight, and -7 to 1 kg for those living with obesity (Table 3). Sensitivity analyses on pregnancy outcomes based on NAM guidelines compared to the newly proposed GWG thresholds based on current analyses, show in general lower adverse pregnancy outcomes with the lower GWG recommendations (Additional file 1: Table S3).

# Discussion

To date, there are no specific recommendations for GWG available for women with GDM. The findings of this large Belgian population-based study suggest that optimal GWG for single at term pregnancies with GDM should be lower than current recommendations by NAM, as the estimated optimal GWG ranges in our analysis are lower than the NAM targets, i.e. 9 to 14 kg for women with a normal weight, 1 to 9 kg for women with overweight, and -7 to 1 kg for those living with obesity. Excessive GWG has been demonstrated to be an additive risk factor for adverse pregnancy outcomes both in women with GDM and in women with pregestational diabetes [25, 26]. Using lower targets for GWG in women with GDM, might therefore lead to improved pregnancy outcomes. However, as these data are based on a observational study from a mostly Caucasian Belgian population, a large randomized controlled trial (RCT) is needed to confirm that treatment of women with GDM according to these lower GWG targets, will effectively reduce the risk for adverse pregnancy outcomes. Moreover, well designed cohort studies are needed to validate these recommendations in diverse multi-ethnic populations. Additionally, the WHO is currently revising global GWG guidelines to address key gaps, highlighting the importance to have more evidence on specific GWG recommendations for women with GDM. Before potentially recommending weight loss in women with GDM and obesity, more data from large cohort studies and/or RCT's on the safety of weight loss in pregnancy in this population is needed.

Our results are in contrast with the epidemiological analysis of 330,000 Belgian pregnant women without diabetes or GDM, that found that the calculated most optimal GWG corresponded well with current NAM guidelines for the underweight, normal weight and overweight BMI categories, but that better outcomes were predicted for GWG less than recommended by the NAM only in women with class II and III obesity [4]. Few studies attempted to optimize NAM targets for women with diabetes or GDM [23, 26–29]. In Denmark, findings from a RCT in 360 women living with obesity without diabetes and national Danish guidelines for healthy normal weight women have led to the development of the Copenhagen guidelines for GWG in women with diabetes, with a recommended GWG of 10 to 15 kg for women with a BMI



Fig. 1 Predicted probabilities of selected adverse outcomes in relation to GWG for the different BMI categories. (A Normal; B Overweight; C Obese). Abbreviations: BMI: body mass index; GWG: gestational weight gain, CS: caesarean section, SGA: small-for-gestational-age, LGA: large-for-gestational-age, LBW: low birth weight. The predicted probabilities were calculated for a multiparous White woman of 30 years, with a secondary education degree and no social deprivation, with spontaneous conception, gestational age of 39 weeks at delivery in 2018

Pre-pregnancy BMI category	Total GWG (kg) for single pregnancies according to NAM guidelines	Total GWG (kg) proposed for single pregnancies with GDM
Underweight (BMI < 18.5 kg/m <sup>2</sup> )	12.5 – 18.0	_
Normal ( BMI 18.5–24.9 kg/m <sup>2</sup> )	11.5 – 16.0	9.0 - 14.0
Overweight (BMI 25–29.9 kg/m <sup>2</sup> )	7.0 – 11.5	1.0 – 9.0
Obese (BMI $\ge$ 30 kg/m <sup>2</sup> )	5.0 – 9.0	-7.0 - 1.0

Table 3 NAM recommendations for GWG versus proposed GWG recommendations for women with gestational diabetes

Abbreviations: NAM National Academy of Medicine, GWG gestational weight gain, BMI Body Mass Index

between 18.5–25 kg/m<sup>2</sup>, 5 to 8 kg for women with overweight, and 0 to 5 kg for women with obesity [26, 30]. Two retrospective cohort studies in women with GDM created new GWG ranges by subtracting 1-2 kg from the NAM recommendations but showed inconsistent results. While one study among 3095 Australian women with GDM concluded that modification of NAM criteria, including more restrictive targets (i.e., setting lower limit for GWG), did not lead to a significant decrease in adverse outcomes, another study in 1,200 Chinese women with GDM demonstrated that adhering to more stringent GWG targets (i.e., more tightly controlled) was associated with a decreased risk of LGA and macrosomia [27, 28]. A more recent prospective cohort study in 3013 Chinese women with GDM estimated potential optimal GWG ranges by minimizing the joint risk of LGA and SGA, and showed that optimal GWG was lower than NAM targets and decreased the risk of LGA and macrosomia, without increasing the risk of SGA or preterm birth. However, this study could not determine GDMspecific GWG targets for women with underweight and obesity, given the small number of participants in these groups. Another recent Chinese epidemiologic analysis in over 12,000 women with GDM confirmed that more stringent GWG ranges in all BMI categories were more protective for adverse outcomes [31]. However, since GWG is influenced by ethnicity and body composition, the GWG targets that are proposed in these Chinese studies cannot be generalized to women from other ethnicities such as the predominantly Caucasian population in our study [32].

In our cohort, only 32.8% gained weight within NAM recommendations, whereas 40.2% gained less and 26.9% gained more weight than recommended. In the general pregnant population, excessive GWG is generally more common, since women without GDM often do not receive lifestyle counselling to limit GWG. The latest report of the 'Study Centre of Perinatal Epidemiology' from 2022 indicated that respectively 31.0% and 33.7% of all pregnant women gained weight below and above NAM targets [33]. A recent meta-analysis of more than 88,000 women found that almost half of

all pregnant women gained more weight than recommended [3]. Our study found that a higher percentage of women with GDM had GWG below the recommendations. This observation aligns with a retrospective study of 56,616 pregnant women, demonstrating that people with GDM had a considerably higher incidence of insufficient GWG and a reduced proportion of excessive GWG compared to people with normal glucose tolerance [34]. This is most likely due to the fact that women with GDM need to implement lifestyle measures, including physical activity and dietary adjustments, which leads to reduced GWG [18, 26].

Excessive GWG was independently associated in our study with an increased risk of adverse maternal and neonatal outcomes, including gestational hypertension, emergency caesarean section, LGA and macrosomia. This is in line with a recent study, which demonstrated that women with (pre)gestational diabetes and excessive GWG were at increased risk for caesarean delivery, preeclampsia, LGA, and macrosomia [8]. Two large meta-analyses confirmed that GWG above NAM guide-lines is associated with an increased risk of pregnancy-induced hypertension, caesarean section, LGA and macrosomia in healthy pregnancies as well as in pregnancies complicated by GDM [3, 35].

Consistent with the findings described for the general Belgian pregnant population, we established that adverse pregnancy outcomes are much more prevalent among individuals with excessive GWG in higher BMI categories compared to those with excessive GWG in lower BMI categories [4]. Maternal obesity is a considerable public health concern, as the incidence of obesity in women of childbearing age has increased substantially in the past decades [36]. In a recent Belgian populationbased study of more than 330,000 pregnant women, about one third were living with overweight or obesity [4], and maternal obesity increased from 10.3% in 2009 to 11.4% in 2014. In the most recent report of the 'Study Centre of Perinatal Epidemiology' report of 2022, these figures further increased, with 26.4% of women living with overweight and 15.8% with obesity [33]. In our cohort, pre-pregnancy overweight (29.6%) or obesity

(26.0%) was present in more than half of all women with GDM. Maternal obesity and GDM are the most common, often coinciding, metabolic complications during pregnancy and are both independently associated with adverse pregnancy outcomes [37]. In addition, maternal obesity not only increases the risk of adverse pregnancy outcomes, but also has an impact on the metabolic health of the offspring [38, 39]. While dietary interventions during pregnancy have been shown to improve maternal dietary behaviors and have a modest effect on GWG, there is no evidence of an effect on early childhood obesity or persistent effects on maternal weight after birth [40]. Early interventions prior to conception should therefore be developed to support women with obesity of childbearing age with weight management strategies, not only to promote maternal and fetal health during pregnancy, but also to reduce the intergenerational burden of maternal obesity [41].

Even though excessive GWG should be avoided in women with GDM because of the established negative consequences for mother and child, it is also important to consider the risks of not gaining enough weight during pregnancy. While this study has shown that GWG less than recommended was associated with a lower likelihood of gestational hypertension, LGA and macrosomia, this was at the expense of an increased risk of SGA and LBW across all BMI categories. Previous research in 8,322 deliveries complicated by (pre)gestational diabetes confirmed these results [8]. However, other research found that lower GWG than recommended by NAM did not increase the risk of SGA [23, 35]. The estimated optimal GWG range in our study is based on the intersection between LGA and SGA and therefore, by definition, confers the lowest possible risk of SGA while taking into account the lowest possible risk of LGA as well.

This study has several important strengths. Our findings are derived from an extensive amount of high-quality population-based data, reflecting the real pregnant population with GDM in Belgium. To avoid bias by including women with pregestational diabetes and women with preterm deliveries, we only included women with at term deliveries between 38-40 weeks of pregnancy. As sociodemographic characteristics could impact BMI, GWG, and their influence on adverse pregnancy outcomes, we corrected for confounding factors such as maternal age, parity, social deprivation and origin in the multivariate analysis, thereby investigating the independent effect of GWG on perinatal outcomes. Moreover, we applied an established statistical approach to estimate optimal GWG ranges, based on the lowest intersection between LGA and SGA for the different pre-pregnancy BMI categories, instead of using more subjective methods such as subtracting a self-selected amount of weight of the existing NAM guidelines [23, 24]. Our research has some limitations. First, because pre-pregnancy weight was self-reported, underestimation of maternal pre-pregnancy weight may have occurred and could have influenced the calculation of pre-pregnancy BMI and GWG. However, while misclassification could influence prevalence estimates of pre-pregnancy weight and GWG adequacy, evidence shows that reporting errors do not seem to seriously bias observed associations between pregnancy-related weight and birth outcomes [42]. Second, we could not perform multivariate analysis and explore potential optimal GWG ranges for women with underweight because of their limited sample size. For the same reason, we could not provide specific recommendations for the separate classes of obesity, as was done in the previous population-based study in women without (pre)gestational diabetes [4]. Another limitation is that the database did not include information on glycaemic control or diabetes treatment. Without these data, it is difficult to assess whether variations in GWG are potentially confounded by differences in glycaemic control and/or diabetes treatment, which can have an impact on pregnancy outcomes, such as the risk of macrosomia or LGA infants [43, 44]. Moreover, diabetes in pregnancy in our database included both women with GDM and women with pregestational diabetes. It was therefore not possible to separately analyse women with GDM and women with pregestational diabetes. However, by excluding women with deliveries  $\leq$  38 weeks of pregnancy, we can anticipate that the vast majority of women with pregestational diabetes are excluded from current analysis [14, 15]. However, women with GDM delivering at 37 weeks were therefore also excluded. Additionally, 626 women out of 569,914 were excluded due to missing breastfeeding data, which accounts for only 0.11% of the overall sample. This exclusion is therefore unlikely to significantly impact the overall findings. Another limitation of our study is that maternal weight at birth was either measured in the delivery room or, if unavailable, from the last prenatal visit. We were unable to provide the exact percentage of women for whom delivery room weight was used, and this variability may influence the results. By excluding preterm deliveries, also women with GDM might have been excluded. However, this would be a limited number, as previous research in our Belgian population has demonstrated that only 7.5% of women with GDM delivered preterm [16]. While the predicted probabilities derived from our models can be calculated for any combination of explanatory variables (e.g., GWG, maternal age, parity, social deprivation), their applicability to other settings remains uncertain. External validation in different populations is necessary to determine the generalizability of these models to other countries or

settings. Furthermore, the classification of fetal growth in the 'Study Centre of Perinatal Epidemiology' database relied on the Flemish birth charts, which do not consider ethnicity. Consequently, our findings are primarily applicable to the Belgian population (including mostly a Caucasian population) and may not accurately reflect other ethnic groups. This distinction should be taken into account when interpreting our results.

#### Conclusions

In conclusion, we showed that in our Belgian cohort, GWG above NAM guidelines was associated with an increased risk of adverse pregnancy outcomes in women with GDM, and that this risk was more pronounced within higher pre-pregnancy BMI categories. In addition, our findings suggest that optimal gestational weight gain for single at-term pregnancies with GDM should be lower than current recommendations. While these findings highlight an important association, our results are based on observational data and may not be generalizable to other ethnic groups. Further research is essential, as data from RCTs and large cohort studies in diverse populations are needed to validate these recommendations before considering adjustments to clinical guidelines.

#### Abbreviations

BMI Body mass index CS Caesarean section GDM Gestational diabetes GWG Gestational weight gain LBW Low birth weight LGA Large-for-gestational-age NAM National Academy of Medicine RCT Randomized controlled trial SGA Small-for-gestational-age

# **Supplementary Information**

The online version contains supplementary material available at https://doi. org/10.1186/s12916-025-03992-5.

Additional file 1: Fig S1. Flow chart. Tables S1-3. Table S1–Maternal and neonatal characteristics by GWG and BMI. Table S2. Adjusted odds of perinatal outcomes by GWG. Table S3. Sensitivity analyses: NAM recommendations vs. study proposal

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#### Authors' contributions

KB and CM1 designed the study project, together with LA who coordinated and executed the statistical analysis. KB, IG and CM1 wrote the first draft of the manuscript. CM1, IG and LA contributed to figure and table creating. KB, CM1, IG, LA, BVdS, RD, AB and CM2 contributed to the study design, including data collection, data interpretation, and manuscript revision. CM1 and KB are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. KB, CM1, IG, LA, BVdS, RD, AB and CM2 had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors read and approved the final version of the manuscript.

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#### Data availability

Selected anonymous data collected in the study and additional documents can be made available to others not involved in the study upon reasonable request to the corresponding author.

#### Declarations

#### Ethics approval and consent to participate

As this study was based on database research of data collected as part of routine care for quality control, no ethics approval was needed.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

KB reports research funding and receipt of study devices from Medtronic for the investigator-initiated CRISTAL study, receipt of study devices from Dexcom, received study medication of Novo Nordisk for the investigator-initiated SERENA study, received consulting fees from Astrazeneca and Lilly, and served on the speaker bureau for Novo Nordisk, AstraZeneca and Mundipharma. RD reports receiving consulting fees from Metagenics, Procter & Gamble Company and Janssen Pharmaceutics and served on the speaker bureau for Metagenics, Procter & Gamble Company and Janssen Pharmaceutics. AB reports research support for analyzing epidemiological data (2023-2024) from Novo Nordisk. CM2 serves or has served on the advisory panel for Novo Nordisk, Sanofi, Eli Lilly and Company, Novartis, Boehringer Ingelheim, Roche, Medtronic, Imcyse, Insulet, Biomea Fusion and Vertex. Financial compensation for these activities has been received by KU Leuven; KU Leuven has received research support for CM2 from Medtronic, Imcyse, Novo Nordisk, Sanofi and ActoBio Therapeutics; CM2 serves or has served on the speakers bureau for Novo Nordisk, Sanofi, Eli Lilly and Company, Medtronic and Boehringer Ingelheim. Financial compensation for these activities has been received by KU Leuven. CM2 is president of EASD. All external support of EASD is to be found on www.easd.org. All disclosures are unrelated to the present work.

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