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Original Research Article

Gestational weight gain according to the Brazilian charts and its association with maternal and infant adverse outcomes

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ABSTRACT

Background: The lack of gestational weight gain (GWG) recommendations for low- and middle-income countries is a significant concern.

Objectives: To identify the ranges on the Brazilian GWG charts associated with lowest risks of selected adverse maternal and infant outcomes.

Methods: Data from 3 large Brazilian datasets were used. Pregnant individuals aged ≥ 18 , without hypertensive disorders or gestational diabetes were included. Total GWG was standardized to gestational age-specific z-scores according to Brazilian GWG charts. A composite infant outcome was defined as the occurrence of any of small-for-gestational age (SGA), large-for-gestational age (LGA), or preterm birth. In a separate sample, postpartum weight retention (PPWR) was measured at 6 and/or 12 mo postpartum. Multiple logistic and Poisson regressions were performed with GWG z-scores as the exposure and individual and composite outcomes. GWG ranges associated with the lowest risk of the composite infant outcome were identified using noninferiority margins.

Results: For the neonatal outcomes, 9500 individuals were included in the sample. For PPWR, 2602 and 7859 individuals were included at 6 and 12 mo postpartum, respectively. Overall, 7.5% of the neonates were SGA, 17.6% LGA, and 10.5% were preterm. Higher GWG z-scores were positively associated with LGA birth, whereas lower z-scores were positively associated with SGA births. The risk of the selected adverse neonatal outcomes were lowest (within 10% of lowest observed risk) when individuals with underweight, normal weight, overweight, or obesity gained between 8.8–12.6; 8.7–12.4; 7.0–8.9; and 5.0–7.2 kg, respectively. These gains correspond to probabilities of PPWR ≥ 5 kg at 12 mo of 30% for individuals with under and normal weight, and $<20\%$ for overweight and obesity.

Conclusions: This study provided evidence to inform new GWG recommendations in Brazil.

Keywords: gestation, gestational weight gain, pregnancy, primary health care, reference values, weight gain

Introduction

Gestational weight gain (GWG) is an important indicator to be monitored during pregnancy because of its association with adverse maternal and child health outcomes [1, 2]. Several systematic reviews and meta-analyses show that GWG is associated with the occurrence of small- and large for gestational age birth (SGA and LGA, respectively), preterm birth (PTB), cesarean delivery, and excess postpartum weight

retention (PPWR) [1, 2]. In 2009, the US Institute of Medicine (IOM) published GWG guidelines, which recommend a weight gain of 12.5–18 kg for individuals who start their pregnancy as underweight, 11.5–16 kg for normal weight, 7–11.5 kg for overweight, and 5–9 kg for obesity [3]. These recommendations are the most commonly-used guidelines globally [4].

The IOM guidelines were developed specifically for North American pregnant individuals based on evidence from high-income

Abbreviations: AGA, Adequate for gestational age; BB, Birth in Brazil; BMCNC, Brazilian Maternal and Child Nutrition Consortium; BMI, Body mass index; GWG, gestational weight gain; IOM, Institute of Medicine; LGA, large for gestational age; PPWR, postpartum weight retention; PTB, preterm birth; RR, Rate ratios; SGA, small for gestational age; SISVAN, Brazilian Food and Nutrition Surveillance System.

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countries [3]. The lack of GWG recommendations designed for low- and middle-income countries, such as Brazil, is a significant concern. Weight gain trajectories among Brazilian pregnant individuals are different from North Americans [5], making it plausible that recommended ranges for Brazilian individuals also differ from those identified by the IOM.

Several recent attempts to propose new GWG ranges for other populations have been made [6–8]. However, those initiatives were mainly for high-income or Asian countries, did not consider the relative seriousness of different outcomes related to pregnancy weight gain, or were established without taking into account important adverse maternal outcomes related to weight gain, such as excess PPWR.

In 2021, GWG charts for Brazilian pregnant individuals were published using data from the Brazilian Maternal and Child Nutrition Consortium (BMCNC) [9]. These charts described the patterns of weight gain among apparently healthy individuals, but cutoffs for GWG monitoring or optimal weight gain ranges for public health pregnancy weight gain recommendations were not defined. Adopting these curves in the public health care services across the country requires the definition of recommended GWG ranges. Thus, this study aimed to evaluate the association between GWG classified according to the new Brazilian charts and the occurrence of maternal and infant adverse outcomes to inform the identification of recommended GWG ranges based on these outcomes.

Methods

Study design and sample

This study was conducted using data from the following 3 sources: the BMCNC, the Birth in Brazil (BB) study, and administrative data from the Brazilian Food and Nutrition Surveillance System (SISVAN). The first 2 cohorts were used to obtain information on shorter-term neonatal outcomes, whereas the latter cohort was used to obtain information on the longer-term maternal outcome of excess PPWR.

The BMCNC dataset includes 21 studies conducted in Brazil since 1990. The process of creating the harmonized dataset used in the analyses (e.g., standardization of variables, identification of outliers, heterogeneity assessment) has previously been described in detail [10]. The current analyses were based on a dataset with 17,344 participants aged 18–45 years old, in singleton pregnancies that did not result in abortions or stillbirth, and with no prepregnancy diabetes, hypertension, or infectious or cardiovascular diseases.

BB was a nationwide study conducted in 2011–2012 in all Brazilian states, with a representative sample. Details about data collection are available in Leal et al. [11]. For this analysis, we used a subsample comprising 15,115 participants with data collected from the pregnancy booklet. We also excluded individuals with implausible gestational ages and those who did not meet the inclusion criteria mentioned previously (i.e., who were adolescents, were pregnant with multiple fetuses, had prepregnancy diabetes, hypertension, or other diseases before pregnancy, or whose pregnancy ended with an abortion or stillbirth).

In both datasets, we excluded individuals with complications during pregnancy (hypertensive disorders, diabetes, or other diseases that could affect weight gain during pregnancy, such as HIV, syphilis, other infectious, cardiovascular, or thyroid diseases, whenever these conditions were registered); those with weight or weight gain measurements flagged as outliers [10], and those who did not have data available for the calculation of prepregnancy body mass index (BMI [in kg/m²]), namely self-reported weight or height. We also excluded measurements

taken before 10 and after 40 wks of gestation because this is the interval available in the Brazilian GWG charts for classification. Finally, we excluded participants whose last weight measurement was taken more than 14 days before delivery. We compared the distribution of key variables in the combined dataset before and after excluding participants without a last measurement of weight within this 14-day window before delivery. This aimed to evaluate the plausibility of assuming that the remaining individuals with total GWG were similar to those without this measurement.

The third data source used was the SISVAN, an administrative system from the Brazilian Ministry of Health. The system collects anthropometric and sociodemographic data in all the human lifecycle phases. For pregnant individuals, the data are collected by health care professionals who work in primary care settings, during routine prenatal care and following a standardized protocol [12]. We obtained the data collected from 2008 to 2020. The procedures used to clean the SISVAN data are described elsewhere [13]. The SISVAN data does not include information on the date of delivery. For this reason, we calculated the estimated delivery date by adding 40 wks to the last menstrual period date. Next, the cleaned data from pregnant individuals with a visit in the third pregnancy trimester ($n = 346,312$) were linked to the data from all individuals followed in the system, and those with available weight measurement at ≥ 36 wks of pregnancy and between 5–7 and 11–13 mo after the estimated delivery date were selected. In the event that an individual had more than 1 measurement during pregnancy, the measurement closest to 40 wks was selected. If the individual had more than 1 measurement in the postpartum period, the measurements closest to 6 or 12 mo were used. We also compared the distribution of the key variables among the individuals in the SISVAN dataset during pregnancy or postpartum with those selected for this study.

Main variables

The main exposure variable of this study was total GWG, calculated as the difference between the weight measured in the last prenatal visit that occurred within 14 days before delivery and self-reported prepregnancy weight. Total GWG was then converted into gestational age- and prepregnancy BMI-specific z -scores and percentiles from Brazilian charts for pregnancy weight gain [9].

Birth weight was converted into sex- and gestational age-specific percentiles using the INTERGROWTH-21st charts [14] and categorized as SGA (<10th percentile), LGA (>90th percentile), and adequate for gestational age (AGA, ≥ 10 th and ≤ 90 th percentile). PTB was defined as a delivery <37 wks of gestation [15].

Gestational age during pregnancy and at birth was standardized in the studies participating in the BMCNC and in BB study and calculated according to the date estimated by ultrasound when performed before 24 wks of gestation. If ultrasound data were not available or if the ultrasound measurement was conducted after 24 wks, the date of the last menstrual period was used [10].

We also created a composite variable (referred to hereafter as “equally-weighted” outcome) defined as the occurrence of any of the above outcomes: SGA, LGA, or PTB. Participants who delivered either SGA, LGA, or preterm neonates received a code 1 and the others, 0. However, because public health experts and families view some of these events as being more serious than others (e.g., a PTB is viewed as more serious an adverse event than an LGA birth) and the most common outcome in the sample (LGA) would play the largest role in the results, we also conducted an analysis in which the components of the composite were weighted according to their severity (16). The

weights used to create this severity-weighted composite outcome were obtained from a Delphi panel of patients and experts from the USA [17]. The panel was conducted to establish the seriousness of several maternal and child health outcomes that have consistently been associated with GWG. We used the median score of the final rating of each outcome as weights: 30 points for LGA, 40 for SGA, and 80 for PTB.

PPWR at 6 and 12 mo was calculated as the difference between the weight measured, respectively, at 5–7 or 11–13 mo postpartum and self-reported prepregnancy weight. PPWR was then classified as ≥ 5 or < 5 kg [18], and ≥ 10 or < 10 kg.

Although low-birth weight (birth weight < 2500 g) was not included in our primary analysis because it was not identified as a key outcome for studies of diet and lifestyle in a recent WHO Delphi consensus panel [19], we estimated the relationship between GWG and low birth weight for readers who might be interested in understanding how GWG according to the Brazilian charts is associated with the probabilities of this outcome.

Covariates

Based on the literature review and on the available variables in the BMCNC and BB datasets, we adjusted the models of the neonatal outcomes for the following confounders: maternal age (years), smoking during pregnancy (collected in different manners in the studies of the BMCNC and in BB and reclassified as yes or no), and prepregnancy BMI (in kg/m^2). The later was calculated as the division of self-reported weight, in kilograms, and measured height, in meters squared, and, when categorized, the WHO cutoffs were considered (underweight: < 18.5 kg/m^2 ; normal weight: ≥ 18.5 and < 25.0 kg/m^2 ; overweight: ≥ 25.0 and < 30.0 kg/m^2 ; and obesity: ≥ 30.0 kg/m^2) [20]. We conducted a sensitivity analysis by limiting our cohort to studies in the BMCNC for which more detailed information on confounding factors were collected, including gravidity (first or not first pregnancy), marital status (lives or does not live with partner), education (classified in 4 categories: 0–4, 5–8, 9–11, and ≥ 12 schooling years), and consumption of alcohol during pregnancy (also collected in different manners in the studies comprising the BMCNC and reclassified as yes or no).

For PPWR, the set of adjustment variables was limited to those available in the SISVAN. We adjusted the models by maternal age (years), participation in the conditional cash transfer “Bolsa Família” (yes or no), and prepregnancy BMI as a continuous variable.

Ethics

The Research Ethics Committee of the Federal University of Rio de Janeiro Maternity Teaching Hospital approved this study (protocol: 85914318.2.0000.5275). In addition, all incorporated studies were individually approved by their institutional research ethics committees. Informed consent was obtained from the participants of each study, which was conducted following the principles of the Declaration of Helsinki. The data from the SISVAN were deidentified and analyzed in a secure environment with access restricted to the analysts of the project.

Statistical analyses

We described the frequency of each adverse outcome (SGA, LGA, PTB, and PPWR) according to total GWG across the BMI categories and used chi-square tests to compare those proportions.

We used regression analyses to estimate the association between total GWG z-scores calculated from the Brazilian charts and the selected outcomes, separately and combined. The regression analyses

were stratified by prepregnancy BMI (< 25 ; ≥ 25 and < 30 ; and ≥ 30 kg/m^2). We combined participants classified as under and normal weight in the models because of the small sample size in the underweight category and the fact that the Brazilian charts for those 2 prepregnancy BMI categories are similar [9]. To account for the nonlinear relationship between GWG z-scores and the outcomes, we modeled the z-scores as restricted cubic splines [21]. For the individual outcomes (SGA, LGA, PTB, and PPWR), we used restricted cubic splines with 3 knots, based on the default locations in the software. Crude and adjusted models were run using logistic regression models. Thereafter, we extracted the predicted probabilities for each model, with the adjustment variables centered at the population averages. The predicted probabilities of each outcome were then plotted according to the GWG z-scores.

For the severity-weighted neonatal composite outcome, we created a variable weighting each outcome differently, according to the results of the aforementioned Delphi panel. We further divided the scores by 10 to obtain rounded values that would represent a count for the Poisson models. For both equally- and severity-weighted neonatal outcomes, we considered 5 knots for GWG z-scores for participants classified as under and normal weight and 3 knots for overweight and obesity. The number of knots was decided based on Akaike Information Criteria, Bayesian Information Criteria, and on the available sample size, and the location was based on the default determined by the software. The models were also adjusted with Poisson with robust variance regressions, and the same set of confounders was used. For the severity-weighted outcome, we used bootstrapping to estimate 95% CIs with 200 replications [16].

To define GWG ranges associated with the lowest risk of the equally- and severity-weighted neonatal outcome, we used an approach based on the principles of noninferiority margins [22, 23]. This is a pragmatic approach to identify an optimal GWG range associated to the lowest risk for the development of adverse maternal and infant outcomes. We identified GWG z-scores corresponding to noninferiority margins of 5%, 10%, 15%, and 20% (i.e., increased risks for the composite outcomes of 5%, 10%, 15%, or 20% or greater would not be considered acceptable). For each fitted Poisson regression model, we extracted the marginal predicted risks across the z-scores continuum (from -3 to $+3$ in 0.1 intervals), and subsequently, identified the z-score value where the risk of the outcome was lower. This nadir value was used as reference in the calculation of rate ratios (RR) and respective 95% CIs. This way, it was possible to compare the risk of GWG z-scores above or below this referent z-score [22]. Then, we identified the z-scores values where the upper limit of the 95% CIs exceeded the predefined margins of 5%, 10%, 15%, and 20% ($\text{RR} = 1.05, 1.10, 1.15$, and 1.20). These comparisons were plotted, the margins identified, and it was possible to determine the optimal GWG z-score ranges (and consequently, the values in kilograms) for each of those margins for the neonatal outcomes combined.

For individuals with overweight and obesity, it was not possible to identify a reference value in which the risk of the outcome was lower because the risk curve for these categories were not U-shaped. Therefore, we decided to use the z-score corresponding to the lower limits of the IOM ranges (7 kg, ~ -0.9 z-score for overweight, and 5 kg, 0 z-score for obesity). These values were defined considering that the IOM guidelines are the GWG recommendations currently used in Brazil and that there are several systematic reviews and metaanalyses showing that the risk of adverse outcomes is higher below those thresholds [1, 2, 24, 25].

For PPWR, we adopted a different approach because it was only available in a different dataset. After determining the marginal predicted probabilities with the adjustment variables centered in the population average for each 0.1 z-score in the continuum between -3 and $+3$, we identified the probabilities in the upper limit of the z-scores corresponding to the 5%, 10%, 15%, and 20% margins of the severity-weighted neonatal outcome. In this way, we determined the probability of PPWR of individuals gaining in the upper limit of the optimal ranges defined for the neonate.

The analyses were conducted in R (versions 3.6 and 4.0) and STATA (version 15). The classification of GWG in the Brazilian charts was performed using a function in R for the extraction of z-scores in generalized additive models for location, scale, and shape.

Results

The final dataset of the BMCNC included 5278 individuals (Supplemental Figure 1A), and 4222 were available in the BB dataset (Supplemental Figure 1B). The combination of those datasets resulted in a sample of 9500 pregnant individuals. In the SISVAN, 2602 individuals were included in the 6-month and 7859 in the 12-month period (Supplemental Figure 1C).

The comparison between the 9500 participants with total GWG available for the analyses revealed that they were similar to the initial 18,006 participants with any GWG data when the BMCNC and the BB datasets were combined. The distribution of key variables, such as maternal age and prepregnancy BMI classification, were very similar in the 2 datasets (Supplemental Table 1). For the SISVAN data, the distribution of those key variables was also similar in all the compared datasets. The distribution of the data according to the region of the country was also consistent in the smaller dataset used in the analyses (Supplemental Table 2).

The prevalence of SGA and LGA birth varied by prepregnancy BMI. The highest prevalence of SGA birth was observed among individuals with underweight (13.1%), whereas the lowest among those with overweight (5.4%) and obesity (5.3%). High prevalence of LGA

was observed for all participants, and especially among those with overweight (22.3%) and obesity (23.2%). The prevalence of PTB did not vary by BMI (Table 1).

For PPWR, approximately one-third of the individuals from the SISVAN retained ≥ 5 kg at 6 (33.2%) and 12 mo (31.4%) postpartum and $\sim 11\%$ had values ≥ 10 kg in the same intervals. Statistically significant differences between prepregnancy BMI categories were observed only for PPWR ≥ 5 kg at 6 and 12 mo and for PPWR ≥ 10 kg at 6 mo only (Table 1).

For all BMI categories, the probability of LGA increased with increasing GWG, whereas the probability of SGA decreased. The association between GWG and PTB was almost linear for participants with overweight. For those with under- or normal weight and obesity, probabilities were stable at lower weight gain values, and only started to increase above weight gain z-scores of 0 (i.e., 50th percentile) (Figure 1). The same pattern for individuals with under- or normal weight was observed for the 3 outcomes when the analyses were limited to normal weight (Supplemental Figure 2). The relationship between GWG and LBW is very similar to the relationship between GWG and SGA, for all BMI categories (Supplemental Figures 3 and 4).

For individuals with under- or normal weight, risks of the equally-weighted composite neonatal outcome followed a U-shaped curve, with the lowest risks at a weight gain z-score of -0.6 . Patterns were unchanged after weighting the composite outcome for the severity of the component events. RRs, which quantified the increase in risk of the severity-weighted outcome at various weight gain z-score values compared with the weight gain value associated with lowest risk (z-score of -0.6), are shown in Figure 2. Compared with this nadir, individuals with a GWG z-score of 0 (50th percentile) had a 4% increase in the risk of the weighted composite outcome (RR: 1.04; 95% CI: 0.92, 1.18).

The CIs associated with these RRs were used to determine the weight gain values at which risks are not meaningfully increased compared with the weight gain value associated with lowest risk. For example, the first z-score values in which the increase in the risk is no more than 10% above this nadir was identified as the value in which the upper limit of the CI does not exceed 1.10 (10% increase in the risk).

TABLE 1
Distribution of the selected adverse outcomes according to prepregnancy body mass index

Outcomes	All pregnant individuals n (%)	Underweight (<18.5 kg/m ²) n (%)	Normal weight (≥ 18.5 and <25.0 kg/m ²) n (%)	Overweight (≥ 25.0 and <30.0 kg/m ²) n (%)	Obesity (≥ 30.0 kg/m ²) n (%)	P value ²
Neonatal						
Small for gestational age	590 (7.5)	75 (13.1)	390 (7.8)	92 (5.4)	33 (5.3)	<0.001
Large for gestational age	1561 (17.6)	65 (11.6)	859 (15.7)	460 (22.3)	177 (23.2)	<0.001
Preterm birth (<37 wks)	995 (10.5)	78 (12.2)	632 (10.7)	205 (9.5)	80 (10.0)	0.182
Maternal ¹						
PPWR ≥ 5 kg at 6 mo	863 (33.2)	45 (39.1)	503 (35.8)	212 (30.4)	103 (26.8)	0.001
PPWR ≥ 10 kg at 6 mo	290 (11.2)	22 (19.1)	157 (11.2)	73 (10.5)	38 (9.9)	0.039
PPWR ≥ 5 kg at 12 mo	2465 (31.4)	150 (31.3)	1,301 (31.6)	654 (29.8)	360 (31.6)	0.025
PPWR ≥ 10 kg at 12 mo	886 (11.3)	59 (14.7)	466 (11.3)	233 (10.6)	128 (11.2)	0.130

PPWR, Postpartum weight retention.

¹ Weight retention at 6 and 12 (± 1) mo postpartum were considered.

² P value for the Chi-squared test.

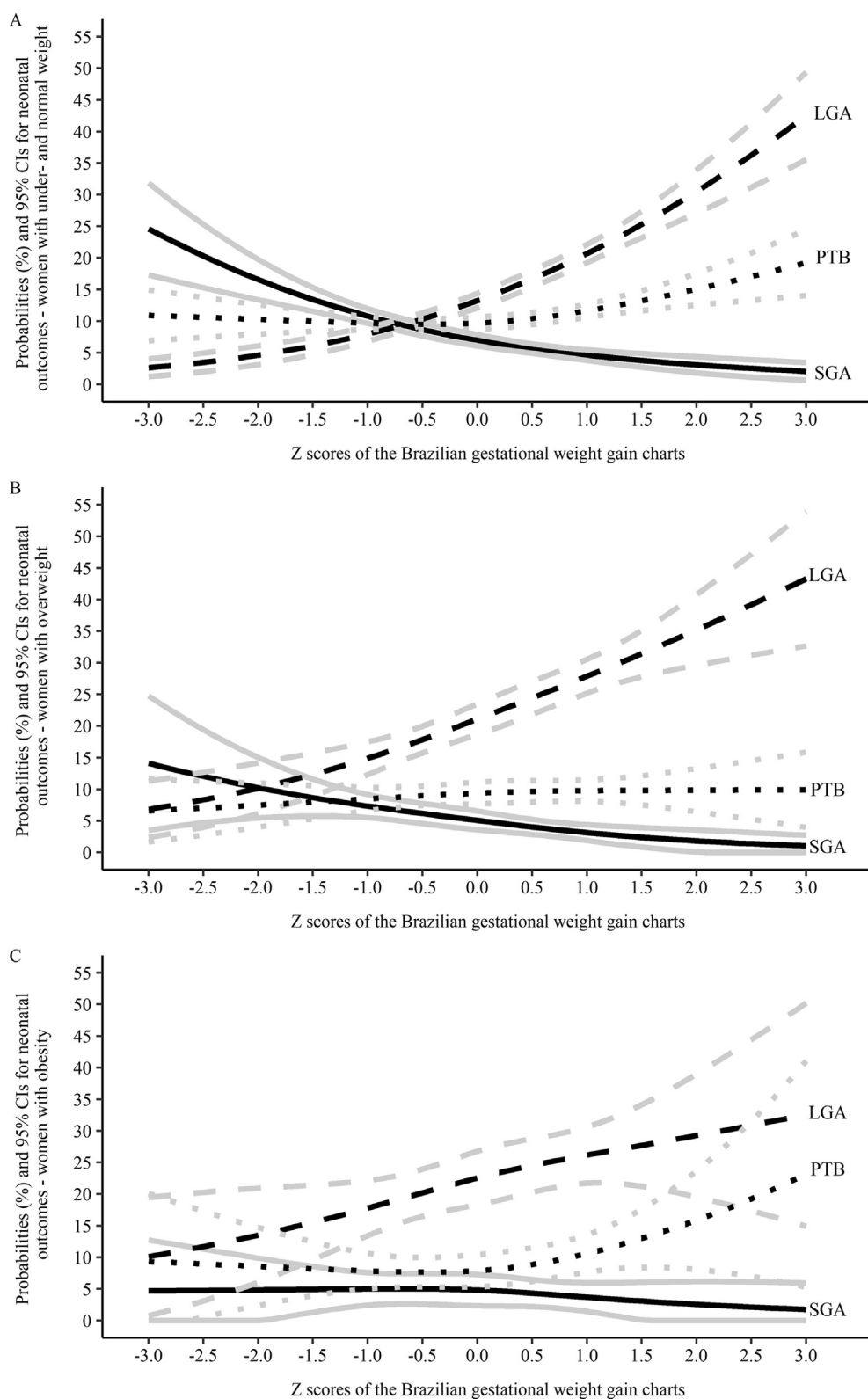


FIGURE 1. Adjusted predicted probabilities and 95% CIs for adverse neonatal outcomes according to the z-scores of the Brazilian GWG charts: (A) prepregnancy under- and normal weight ($n = 6537$ individuals); (B) prepregnancy overweight ($n = 2163$ individuals); (C) prepregnancy obesity ($n = 800$ individuals). Note: Probabilities were extracted from logistic regression models, with the adjustment variables (maternal age, education, smoking habit, and continuous prepregnancy BMI) centered at the population averages. There may be a small variation in the sample size in the adjusted models because of missing data in the adjustment variables. LGA, large for gestational age; PTB, pre-term birth; SGA, small for gestational age.

These occurred at GWG z-scores of -1.1 (RR: 1.04; 95% CI: 0.99, 1.10) and -0.3 (RR: 1.01; 95% CI 0.94, 1.08) (Figure 2, Table 2). Similarly, if a 20% increase in risk above this nadir is considered as the maximum acceptable increase in the risk of those outcomes, the optimal ranges for GWG at 40 wks would fall between the -1.5 and 0 z-score, which correspond to 6.7 and 14.0 kg for the equally weighted

outcome, and between -1.4 and 0 z-score (7.2–14.1 kg) for the severity-weighted outcome. In both cases, the upper limit of the ranges (margins of 20%) fell exactly in the 50th percentile of the GWG curves. The values of the ranges considering other magnitude of increase in the risk (5%, 10%, and 15%) are also virtually identical for both the equally- and severity-weighted outcomes (Figure 2, Supplemental

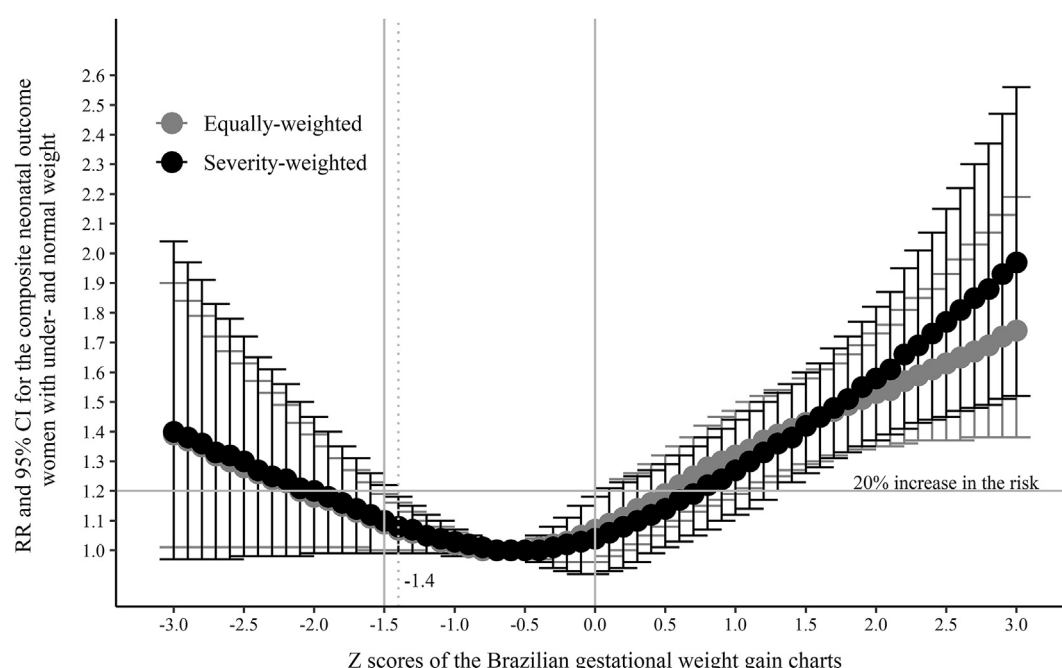


FIGURE 2. Adjusted relative risk and noninferiority margins (20%) for the occurrence of the composite equally- (gray) and severity- (black) weighted outcome according to the z-scores of the Brazilian GWG charts in 6537 individuals with prepregnancy under- and normal weight. Straight gray vertical lines refer to the ranges considering 20% of noninferiority margins for the equally-weighted outcome; dotted gray vertical lines refer to the ranges considering 20% of noninferiority margins for the severity-weighted outcome (-1.4 is the exact z-score corresponding to the lower limit). Straight gray horizontal line refers to the RR of 1.2 (20% increase in the risk). Note: Outcomes included in the composite: small- and large for gestational age, and preterm birth (<37 wks). Risks were extracted based on Poisson with robust variance models, adjusted for maternal age, education, smoking habit, and continuous prepregnancy BMI. There may be a small variation in the sample size in the adjusted models because of missing data in the adjustment variables. RR, rate ratios.

Table 3). The same pattern was observed (similar risk curves and GWG ranges) when only participants with normal weight were considered (Supplemental Figure 5, Supplemental Table 4).

For individuals with overweight, considering the z-score of -0.9 (corresponding to ~ 7 kg from the 2009 IOM lower limit) as the point where the risk of the 3 outcomes is lower for both equally- and severity-weighted outcome, a 10% increase in the risks for those outcomes would represent a range between -0.9 and -0.6 z-scores (~ 7.0 – 8.9 kg) (Figure 3, Supplemental Table 5). For a 20% increase, the optimal GWG range would be between -0.9 and -0.2 z-scores (7.0 – 11.1 kg) for the equally weighted, and -0.9 and -0.3 z-scores (7.0 – 10.5 kg) for the severity-weighted outcome.

The optimal GWG ranges for the equally- and severity-weighted outcomes for individuals with obesity, with a nadir of -0.6 z-score (~ 5 kg from the 2009 IOM lower limit) and a 20% increase in the risk for those outcomes, are also identical: -0.6 to 0 z-score (5.0 – 8.9 kg). Again, for the equally- and severity-weighted outcomes, the upper limit of the ranges fell exactly on the 50th percentile of the curves (Figure 4, Supplemental Table 6). The values for the risks (point estimates) in all BMI categories were very similar when the models were adjusted for a larger set of covariates (data not shown).

For weight retention at 6 and 12 mo, we observed that higher GWG was linked with higher probabilities for PPWR ≥ 5 and ≥ 10 kg, for all BMI categories. For both intervals (6 and 12 mo), the increase in the probability of PPWR ≥ 10 kg began above the 50th percentile of all charts, whereas the increase in the probability of PPWR ≥ 5 kg was almost linear throughout the continuum of GWG z-scores (Figure 5A, B, and C; Supplemental Figures 6–8).

For individuals with under or normal weight, gaining 14 kg by the 40th wk of pregnancy represented a probability of 38% and 33% of PPWR ≥ 5 kg at 6 and 12 mo, respectively. For PPWR ≥ 10 kg, the probabilities were close to 10% on both intervals (9% at 6 and 10% at 12 mo). For those with overweight, gaining 10.5 kg represented a probability of 24% and 28% of PPWR ≥ 5 at 6 and 12 mo, respectively, and 7%–8% of PPWR ≥ 10 kg in the same intervals. For those with obesity, GWG of 8.9 kg at 40 wks was associated with a probability of PPWR ≥ 5 kg at 6 mo of 26%, with an increase at 12 mo (33.5%). The same increase was observed for the probability of PPWR ≥ 10 kg, with values of 6% at 6 and 8.7% at 12 mo (Table 2). If the probability of PPWR ≥ 5 kg at 6 mo is fixed at 20%, the upper limit of GWG at 40 wks for individuals with under- or normal weight would be ~ 8 kg. For those with overweight, 9 kg, and for obesity, also 8 kg. If the probability of PPWR ≥ 5 kg at 12 mo is considered, the limits are similar for under- or normal weight (7.8 and 7.7 kg) and lower for overweight (7 kg) and for obesity (4.0 kg) (Supplemental Tables 7–10).

Discussion

In the current study, we were able to identify GWG ranges based on newly published Brazilian charts associated with the lowest risks of SGA, LGA, and PTB, and excess PPWR, using 3 large datasets from Brazil. If an increase of no more than 10% in the risks for the equally- or severity-weighted neonatal outcome is considered acceptable, the ranges would be approximately: 8.3–12.6 kg for underweight; 8.2–12.4 kg for normal weight; 7.0–8.9 kg for overweight; and 5.0–7.2 kg for

TABLE 2

Gestational weight gain z-scores, percentiles, and kilograms (kg) at 40 gestational wks for the ranges associated with lower acceptable risks of the severity-weighted outcome and respective probabilities of weight retention ≥ 5 and ≥ 10 kg at 6 and 12 mo postpartum

BMI category (kg/m ²)	Noninferiority margins	GWG z-scores	GWG percentiles	GWG in kg (exact values)	Probability of PPWR in the upper limit of the ranges			
					6 mo postpartum		12 mo postpartum	
					PPWR ≥ 5 kg	PPWR ≥ 10 kg	PPWR ≥ 5 kg	PPWR ≥ 10 kg
Under- and normal weight (< 25.0)	5%	−0.9 to −0.4	18.4 to 34.5	Underweight Normal weight	9.7–12.2 9.6–11.9	30.6 6.4	27.9 7.6	
	10%	−1.1 to −0.3	13.6–38.2	Underweight Normal weight	8.8–12.6 8.7–12.4	32.4 6.9	29.2 8.1	
	15%	−1.3 to −0.1	9.7–46.0	Underweight Normal weight	7.8–13.6 7.7–13.4	36.2 8.1	31.9 9.3	
	20%	−1.4 to 0.0	8.1–50.0	Underweight Normal weight	7.2–14.1 7.2–13.8	38.3 8.9	33.4 10.0	
Overweight (≥ 25.0 and <30.0) ¹	5%	−0.9 to −0.8	18.4–21.2	7.0–7.8	17.4	4.8	20.3	5.7
	10%	−0.9 to −0.6	18.4–27.4	7.0–8.9	19.6	5.5	23.0	6.6
	15%	−0.9 to −0.5	18.4–30.8	7.0–9.5	20.9	5.9	24.4	7.0
	20%	−0.9 to −0.3	18.4–38.2	7.0–10.5	24.1	7.0	27.5	8.0
Obesity (≥ 30.0) ¹	5%	−0.6 to −0.5	27.4–30.8	5.0–5.9	14.3	2.4	25.2	5.6
	10%	−0.6 to −0.3	27.4–38.2	5.0–7.2	18.3	3.5	28.5	6.6
	15%	−0.6 to −0.2	27.4–42.1	5.0–7.8	20.6	4.2	30.2	7.2
	20%	−0.6 to 0.0	27.4–50.0	5.0–8.9	25.6	6.0	33.5	8.7

BMI, Body mass index; GWG, Gestational weight gain; PPWR, Postpartum weight retention.

¹ For individuals with overweight and obesity, the lower limit and nadir was defined based on the IOM 2009 ranges (7 and 5 kg, respectively).

obesity. In our case, using equally and severity-weighted outcomes resulted in very similar ranges for all the BMI categories. The upper limits of those ranges would entail probabilities of weight retention ≥ 5 kg between 18 and 32% at 6 and 23 and 30% at 12 mo postpartum.

The upper limits of the optimal ranges for the equally- and severity-weighted neonatal outcomes defined in this study were lower than the recommendations currently in place in Brazil (the 2009 IOM guidelines), for under-, normal, and overweight individuals, even when an increase in risk of up to 20% is considered (14.1 in this study compared with 18 kg in the IOM for underweight; 13.8 compared with 16 kg for normal weight; and 10.5 compared with 11.5 kg for overweight). For obesity, accepting the same amount of increase in risk would result in a range of 5–8.9 kg, which is very close to the 9-kg IOM upper limit for this BMI category [3].

The lower values for the upper limits of the ranges observed in this study can be partially explained by the high prevalence of LGA birth observed in the sample (~18%). The increase in the prevalence of LGA with a decrease in SGA has been observed in Brazil in the last 10 years. Falcão et al. [26] analyzed 5,521,517 live births in Brazil between 2012 and 2015 and observed a prevalence of SGA of 7.8%, and LGA of 17.1%, which align with the values observed in this study. The higher prevalence of LGA, when compared with the other outcomes, shifts the nadir of risk to systematically lower values, and, consequently, the upper limit of the optimal ranges. Although LGA is the outcome rated with the lowest weight in the Delphi panel (30 points compared with 40

for SGA and 80 for PTB), excessive growth has been associated with long-term adverse outcomes for the children, such as obesity [27, 28]. Thus, reducing the upper limits of the ranges for GWG recommendations in all BMI categories is necessary to reduce the risks of LGA in Brazil.

The GWG ranges suggested by our findings for under-, normal, and overweight are also different from those proposed by the Lifecycle project, especially for individuals with overweight (2.0 to < 16.0 in the Lifecycle compared with 7.0–10.5 kg in Brazil, with 20% margins) [6]. The ranges for all the BMI categories also differ from those proposed for Chinese individuals [7]. However, it is important to highlight that the ranges proposed by both studies did not consider weights for the incorporated outcomes and were defined based on a different statistical analysis [6, 7].

Three recent studies aimed to define optimal GWG ranges [6–8], but the lack of longer-term adverse maternal outcomes is a critical shortcoming. The 2009 IOM guidelines were the only ones to date to derive recommendations that take the risks of adverse maternal outcomes, including PPWR, into account [3]. In our study, although using a different dataset (the BMCNC and BB for neonatal outcomes and the SISVAN for PPWR) we were able to determine the probabilities of weight retention at 6 and 12 mo postpartum. It is noteworthy that an increase of no more than 20% in the risk of the neonatal outcomes would be associated with a high absolute probability (>20%) for PPWR at 6 and 12 mo for all BMI categories. Moreover, most of the available studies in this area do not include

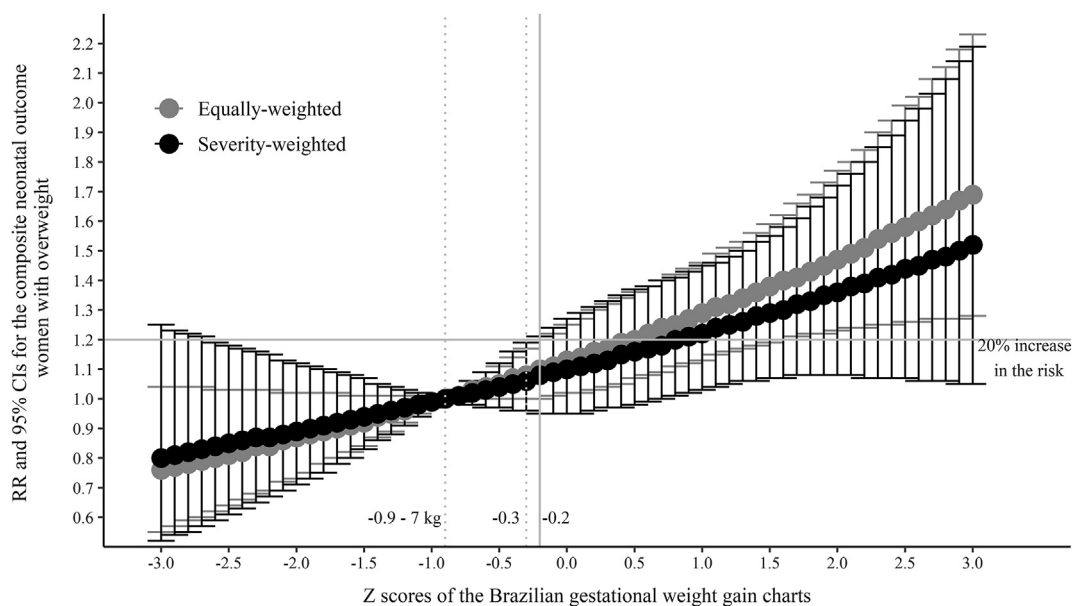


FIGURE 3. Adjusted relative risk and noninferiority margins (20%) for the occurrence of the composite equally- (gray) and severity- (black) weighted outcome according to the z-scores of the Brazilian GWG charts in 2163 individuals with prepregnancy overweight. Straight gray vertical line refers to the upper limit of the range considering 20% of noninferiority margins for the equally-weighted outcome (-0.2 z-score); dotted gray vertical line at -0.3 z-score refers to the ranges considering 20% of noninferiority margins for the severity-weighted outcome. The lower limit of the ranges (gray dotted vertical line at -0.9 z-score) was defined based on the IOM 2009 ranges (7 kg). Straight gray horizontal line refers to the RR of 1.2 (20% increase in the risk). Note: Outcomes included in the composite: small- and large for gestational age, and preterm birth (<37 wks). Risks were extracted based on Poisson with robust variance models, adjusted for maternal age, education, smoking habit, and continuous prepregnancy BMI. There may be a small variation in the sample size in the adjusted models because of missing data in the adjustment variables. RR, rate ratios.

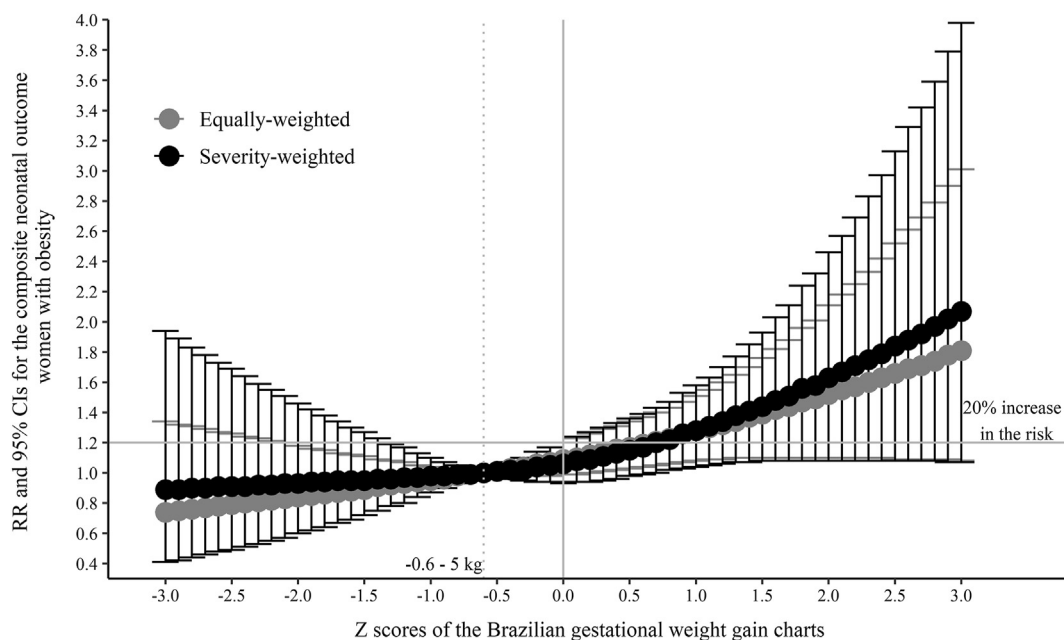


FIGURE 4. Adjusted relative risk and noninferiority margins (20%) for the occurrence of the composite equally- (gray) and severity- (black) weighted outcome according to the z-scores of the Brazilian GWG charts in 800 individuals with prepregnancy obesity. Straight gray vertical line refers to the upper limit of the range considering 20% of noninferiority margins for both equally- and severity-weighted outcome (0 z-score); dotted gray line refers to the lower limit of the range defined based on the IOM 2009 range (5 kg, -0.6 z-score). Straight gray horizontal line refers to the RR of 1.2 (20% increase in the risk). Note: Outcomes included in the composite: small- and large for gestational age, and preterm birth (<37 wks). Risks were extracted based on Poisson with robust variance models, adjusted for maternal age, education, smoking habit, and continuous prepregnancy BMI. There may be a small variation in the sample size in the adjusted models because of missing data in the adjustment variables. RR, rate ratios.

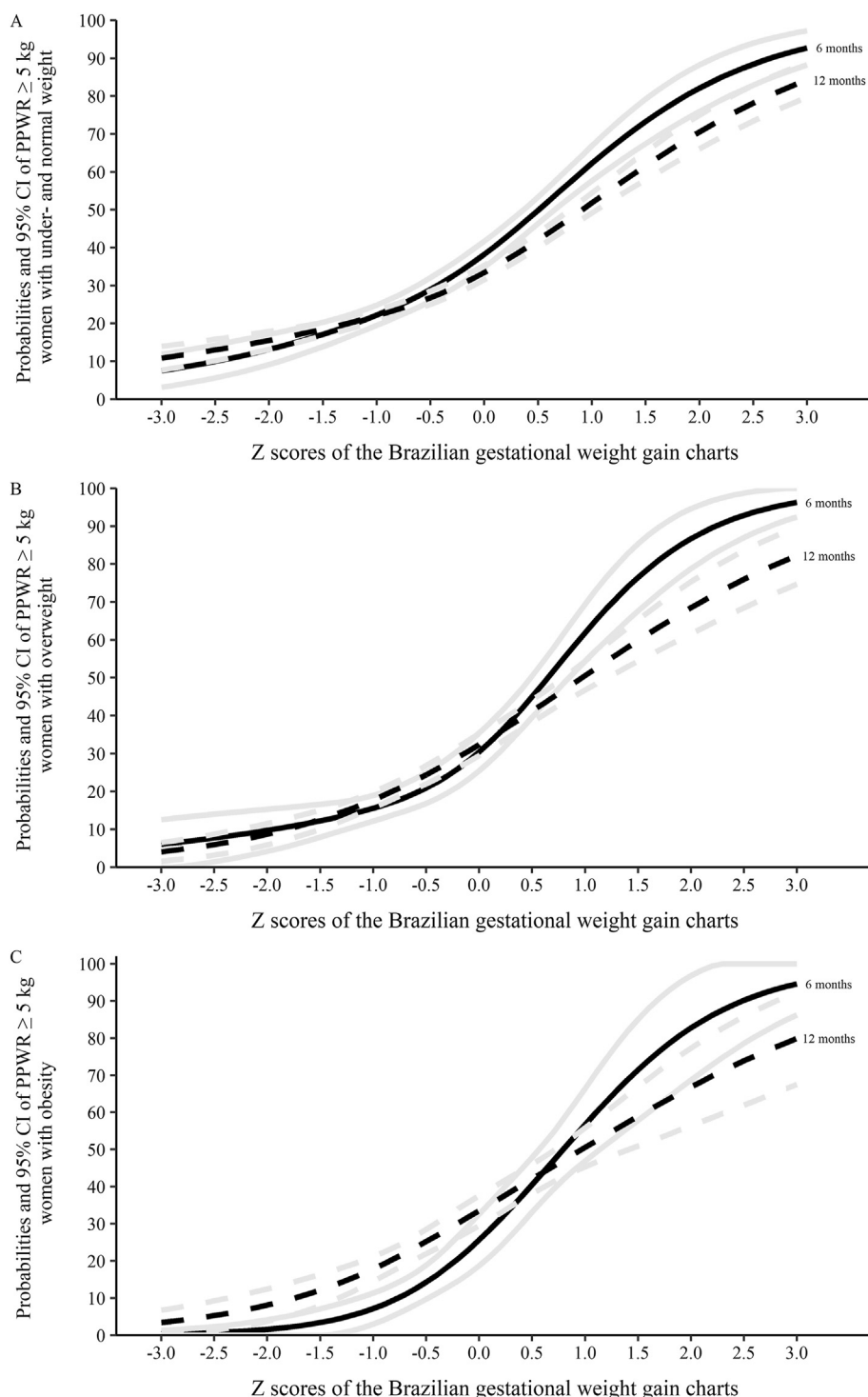


FIGURE 5. Adjusted predicted probabilities and 95% CIs for the occurrence of weight retention ≥ 5 kg at 6 ($n = 2602$ individuals) and 12 ($n = 7859$ individuals) mo postpartum according to the z-scores of the Brazilian GWG charts: (A) prepregnancy under- and normal weight; (B) prepregnancy overweight; (C) prepregnancy obesity. Note: Probabilities were extracted from logistic models, with the adjustment variables (maternal age, participation in a conditional cash transfer program—“Bolsa Familia”, and continuous prepregnancy BMI) centered at the population averages. There may be a small variation in the sample size in the adjusted models because of missing data in the adjustment variables. PPWR, postpartum weight retention.

a broader set of infant and maternal outcomes that would allow for a more robust definition of the optimal GWG ranges.

Identifying where the cut-points for recommended weight gain should fall along the GWG continuum is a challenge for policymakers. By using the adaptation of the noninferiority margins approach, we were able to define a set of optimal ranges considering different amounts of increase in the risk for the combined neonatal outcome. The final decision regarding the recommended ranges involves a discussion with experts, stakeholders, and patients in Brazil, to better understand what they consider as an acceptable increase in the risks for neonatal

and maternal outcomes. Nonetheless, even though the nadir is the point where the risk for the outcomes is the lowest, the absolute risk of adverse outcomes may not necessarily be low in those points. Thus, even if an increase of no more than 20% in the risk is deemed acceptable, the absolute risks associated with this threshold could be unacceptably high. For instance, the probability of LGA at the nadir for overweight (-0.9 z-score) is 15.5%. If a no more than 20% increase in the risk of the neonatal outcomes is accepted, at the upper limit of the optimal range (-0.3 z-score), the probability of LGA would be 21%. Therefore, it may be important to consider lower increases in the risks

from the nadir (5% or 10% rather than 20%), particularly for individuals with overweight and obesity, who already depart from a higher risk of those outcomes [29].

The risk curve for the neonatal outcomes for individuals with overweight and obesity was not U-shaped, and, therefore, required us to alter our analytic approach for these 2 categories. The rationale to use the IOM lower limits (7 and 5 kg) simultaneously as nadir and lower limits for the ranges based on the literature considered that those values would not represent an increase in the risk for other outcomes. A recent meta-analysis on the impact on GWG recommendations on adverse outcomes for individuals with obesity showed that those who gained <5 kg, when compared with those who gained within the IOM guidelines, did not have a significant increase in SGA rates, with lower rates of LGA, preeclampsia, and cesarean delivery [30]. We did not have the necessary data to propose a reduction in the lower limits of the ranges for those BMI categories. The decision to use the IOM values as the lower limits for our ranges needs to be revisited when stronger evidence becomes available, especially if more outcomes are incorporated in the analyses.

To our knowledge, this is the first initiative from a middle-income country to inform GWG optimal ranges that accounts for the consequences of deviations on GWG for maternal health in addition to the consequences for the newborn. Our use of different weights when combining the neonatal outcomes, the inclusion of an important and longer-term maternal outcome (PPWR), and the use of a pragmatic methodology to define the optimal ranges are important strengths.

However, some limitations are worth considering. First, we lacked data on important outcomes, such as neonatal mortality and maternal morbidity during pregnancy, as well as a dataset that included all the necessary outcomes. The lack of outcomes could help explain the similar results observed for the equally- or the severity-weighted composite indexes. However, considering that most of the unavailable outcomes (especially hypertensive disorders and gestational diabetes) are related to weight gain above the IOM upper limits [31, 32] and that our optimal ranges are below those limits, we may expect that the ranges identified in this study would represent a reduction in the risks of those outcomes as well.

There are also several limitations in the SISVAN dataset. One is the fact that these are administrative data collected in the routine of public health care services, thus they lack standardization in the data collection. Another limitation is the absence of the delivery date and information about twin pregnancies. Although we considered an interval between 6 [5–7] and 12 [11–13] mo postpartum, not knowing the exact date to properly identify the period is a major limitation. However, when we compared the values for PPWR observed in this study with those observed in smaller studies conducted in Brazil [33, 34], the similarity of the distributions reinforced the possibility of using the SISVAN data, despite this limitation. The third shortcoming is the substantial reduction in the sample size available in the SISVAN in the postpartum period. This reduction in the sample size highlights the importance of the continuous monitoring of maternal weight in the postpartum period—not just among the beneficiaries of the conditional cash transfer program (>70% of the dataset). Enhancing the quality of administrative data in Brazil is a fundamental step, especially to evaluate the impact of adopting new ranges on the selected outcomes and on others in the future.

Finally, the lack of information on how gestational age was obtained in several studies composing the BMCNC dataset and the use of the LMP date to calculate gestational age in the SISVAN without

confirmation through an ultrasound are limitations worth mentioning. However, in the largest cohort composing the dataset used in the analysis of neonatal outcomes (the BB study—44.4% of the dataset), 75.1% of the gestational age measurements were calculated using ultrasound data (data not shown).

In conclusion, this study provides the initial evidence to inform the adoption of new GWG recommendations in Brazil. We identified optimal ranges with upper limits lower than those currently in place. Discussing the appropriate trade-off between maternal and infant risks with experts, stakeholders, and patients is the next necessary step to define the final recommendations to be adopted in Brazil. In addition, for the ranges to be used in other locations, external validation is needed and should consider the local epidemiologic conditions, and the best available maternal and infant outcomes.

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Conflict of interest

KMR is a member of the Journal's Editorial Board. All other authors report no conflicts of interest.

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Appendix B

Consortium information

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Data Availability

The BMCNC is managed by the team of researchers from the Nutritional Epidemiology Observatory, Federal University of Rio de Janeiro. Datasets are not yet available for public use, but requests can be made to the coordinator of the project (gilberto.kac@gmail.com) and the consortium group is consulted regarding data sharing for specific studies. Details regarding access to the data can be obtained through the consortium data repository: https://dataverse.nutricao.ufjf.br/dataverse/conmai_openaccess. The Birth in Brazil dataset is not available for public use, but requests can be made to the project coordinators (duca@ensp.fiocruz.br; barrosdc61@gmail.com). The SISVAN dataset is available upon request to the Brazilian Ministry of Health, following specific Brazilian laws. The codes used for the analyses are also available upon request (thaisrangelnut@gmail.com).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajcnut.2022.11.021>.

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