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Gestational weight gain and childhood body mass index across three generations: Results from the 1993 Pelotas (Brazil) Birth Cohort

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Summary

Background: Gestational weight gain (GWG) has been associated with the accumulation of body fat in offspring, but little is known about the intergenerational relationship.

Objective: To assess the effect of GWG in grandmothers and mothers on the child's body mass index (BMI).

Methods: This is a sub-study nested in the 1993 Pelotas (Brazil) Birth Cohort at 22 years follow-up visit. We calculated the BMI-for-age *z*-score (BAZ) and evaluated overweight (>2 SD in ≤5 years of age and >1 SD for >5 years of age for BAZ). Grandmothers' and mothers' GWG were calculated as the difference between weight in the beginning of pregnancy and the last recorded weight before delivery. We standardized the GWG by adjusting for pre-gestational BMI. We also categorized GWG as adequate, excessive, or insufficient, in accordance with the Institute of Medicine (2009). Linear and logistic regressions stratified by child's age (≤2 years; 2.01-5 years; >5 years) were used. Structural equations were modelled to calculate the total, indirect, and direct effects of grandmothers' and mothers' GWG on children's BAZ.

Results: Nine hundred and forty-six out of 1113 children evaluated were 5 years of age or under. There was an indirect effect (through maternal birthweight, maternal pre-gestational BMI, maternal GWG, and child birthweight) of grandmother GWG on grandchild BAZ, from 2.01 to 5 years of age [β = 0.12 $_{95\%}$CI: 0.04-0.20 (P < 0.01)]. Maternal GWG directly increased the child's BAZ at >5 years of age [β = 0.34 $_{95\%}$CI: 0.15-0.53 (P < 0.001)].

Conclusions: GWG's effect on BMI does seem to be transmitted across three generations. Managing this will require health education during the gestational period for women and their families.

KEYWORDS
childhood, gain, gestational weight, intergenerational effect, obesity, offspring

1 | INTRODUCTION

Childhood overweight is among the most relevant public health problems worldwide,[1] and is also related to overweight in adulthood. Globally, in 2017, high body mass index (BMI) was associated with 2.4 million deaths and 70.7 million disability-adjusted life years (DALYs) in females, and 2.3 million deaths and 77.0 million DALYs in males.[2] In Brazil, approximately one-third of school-aged children are affected by overweight.[3]

Body fat accumulation has a multifactorial aetiology that includes, but is not limited to, diet, metabolic disorders, an obesogenic environment, poor socio-economic conditions, genetic susceptibility, and prenatal exposure to maternal obesity.[4,5] In children, the accumulation of body fat is related to an increased risk of cardiovascular disease, high blood pressure, dyslipidaemia, and insulin resistance, which may affect optimal child development and quality of life.[5,6]

Observational studies have linked gestational weight gain (GWG) during pregnancy to children's BMI,[7-10] suggesting that body fat accumulation is not only affected by immediate circumstances, but can be programmed by intrauterine exposures. A meta-analysis from 162 129 mothers and their children showed that approximately 11% to 19% of overweight in children may be attributable to excessive GWG.[8] A population-based study in Southern Brazil found that the higher the GWG in mothers, the higher the body fat mass at 6 years of age.[9] Other studies have suggested that the association of higher maternal GWG and offspring obesity persists into adolescence[10] and adulthood.[11]

GWG reflects the expansion and growth of fluids and tissues from the foetus, placenta, and uterus.[12] Research suggests that foetal over-nutrition during pregnancy is an important contributor to metabolic dysregulation later in life.[13] The foetal over-nutrition hypothesis claims that increased foetal exposure to nutrients (particularly glucose, lipids, and amino acids) may lead to persistent adaptations in the structure and function of adipose tissue (increased expression of adipogenesis, lipogenesis, and adipokine genes) and to the regulation of appetite and energy metabolism, leading to greater susceptibility to obesity at later ages.[13-15] However, it is unclear whether intrauterine programming continues in a third generation nor if it occurs directly via epigenetic information from the gametes or indirectly via intrauterine exposures in generation two.[15-17] A Scottish study with 1457 grandmother-mother-grandchild triads concluded that grandmother birthweight was associated with grandchild birthweight, independently of maternal birthweight.[18]

There is a paucity of studies assessing intergenerational health effects in the literature, since long-term follow-ups from participants are required. To date, we have found no studies that evaluated the effect of GWG on nutritional status in childhood in three generations. In Pelotas, Brazil, there is a birth cohort study with data from three generations.[19] Thus, this study aims to investigate the effect of grandmothers GWG and mothers GWG on the BMI for age (BMI/age) of the children, who are children of 1993 Pelotas Birth Cohort participants.

2 | METHODS

2.1 | Population

The 1993 Pelotas Birth Cohort is a population-based longitudinal study carried out in the city of Pelotas and has assessed the participants' children in its last follow-up at 22 years of age.[19,20] Pelotas is a medium-size municipality in Southern Brazil with approximately 340 000 inhabitants (2018 Brazilian population census).

2.2 | 1993 Pelotas (Brazil) Birth Cohort

The 1993 Birth Cohort enrolled all live born babies between January 1 and December 31 of 1993 from mothers who lived in the urban area of Pelotas or in the neighbourhood of *Jardim América* (part of the municipality of Capão do Leão). Among the 5265 births occurring in that year, 5249 agreed to take part in the longitudinal study.

Previous publications[21,22] provide detailed information on the cohort follow-up visits. At ages 1, 3, 6, 12, and 48 months, subsamples were evaluated. At ages 11, 15, 18, and 22 years old, all cohort members were sought to be assessed. The 22-year follow-up visit started in August 2015 and lasted for 9 months. All located members were invited to attend the cohort clinic and participate in the follow-up visit; 3810 were evaluated, 175 (3.5%) refused to participate, and 1071 (21.7%) were considered losses. The follow-up rate was 76.3%, including those who completed the interviews and those known to have died (N = 193).[20]

2.3 | The second generation of the 1993 Pelotas (Brazil) Birth Cohort

During the contact to update 1993 Birth Cohort participants registration for the new follow-up visit at 22 years of age, we asked the participants if they had any children. In the event of an affirmative answer, we also invite their children to be assessed. This is the study of the Second Generation of the 1993 Birth Cohort—93Cohort-II.[19] A total of 1650 offspring were identified, of whom 21 died before follow-up, 44 could not attend the study site, and 373 were not evaluated because the father had no contact with the child, the participant did not reside in the city, did not participate in the 22-year follow-up, or did not respond to invitations via telephone (non-verbal refusal). A total of 1212 were evaluated in 93Cohort-II (response rate was 73.4%, including deaths).[19]

Our study used data from children participating in the 93Cohort-II Study, whom we called generation 3 (G3). The participants of the 1993 Pelotas Birth Cohort were called mothers or generation 2 (G2) and their mothers were called grandmothers or generation 1 (G1).

2.4 | Dependent variable

We calculated the G3 BMI in *z*-scores based on sex and the child's age (BAZ) according to World Health Organization standards.[23,24] *Z*-score values above +5 or below -5 were considered outliers and excluded from the association analysis (n = 10 children). We also evaluated child overweight status: >2 SD in ≤5 years of age and >1 SD for >5 years of age for BAZ.[23,24]

G3 up to 2 years of age were weighed on their mother's lap, while once they reached 5 years of age they were weighed alone, wearing light clothes and without shoes using a scale (Tanita, precision 100 g). G3 older than 5 years were weighed on the scale coupled to the BODPOD®. The length of G3 up to 2 years of age was measured using a Harpenden Infantometer (precision 1 mm) and the height of G3 over 2 years was checked using a fixed stadiometer with 1 mm precision.

2.5 | Independent variables

GWG in G1 and G2 was calculated as the difference between weight at the beginning of pregnancy and the last weight just before delivery.

G1 weight at the beginning of pregnancy was extracted during hospital interview from the antenatal card or through self-report (if the information was not available on the card) through the question: "*How much did you weigh right before you got pregnant or at your first prenatal visit?*" in the perinatal follow-up of 1993 Pelotas Birth Cohort Study within 24 hours after childbirth. Regarding G1 weight at the end of the pregnancy, this was measured by verification of hospital admission records by a trained team of interviewers. Women were weighed while wearing light clothes and no shoes using the Filizola scale (precision 100 g), calibrated weekly by the research team using standard weights.

G2 weight at the beginning and at the end of pregnancy was recalled by women at the 1993 Birth Cohort 22-years follow-up, through the questions: "*What was your weight at the beginning of <CHILD 1>'s pregnancy?*" and "*What was your weight at the end of <CHILD 1>'s pregnancy?*"

Studies have found good agreement between measured and maternal recall pre-pregnancy weight information.[25,26] Additional exploratory analyses (in 1993 Birth Cohort databases) were conducted to estimate the agreement between G2 body weight measured at 15, 18 and 22 years of age follow-up visits as compared to G2 recalled pre-pregnancy weight. G3 age was considered to select the follow-up closest to the period before G2 pregnancy: <3 years of age (G2 follow-up at 22 years), 3 to 5 years (G2 follow-up at 18 years), and ≥6 years (G2 follow-up at 22 years). Concordance correlation coefficients were moderate to high (CCC = 0.79, CCC = 0.79, and CCC = 0.59, respectively).

Standardized values of G1 and G2 GWG were calculated considering adjustment for pre-gestational BMI (GWGz). The G1 and G2 GWG were also categorized according to the Institute of Medicine (IOM) guidelines[12] as adequate, excessive, or insufficient, depending on their pre-gestational BMI. Adequate GWG was defined as 12.5 to 18.0 kg in underweight women (<18.5 kg/m^2); 11.5 to 16.0 kg in adequate BMI women (18.5-24.9 kg/m^2); 7.0 to 11.5 kg in overweight women (25.0-29.9 kg/m^2); and 5.0 to 9.0 kg in women with obesity (≥30 kg/m^2). Women below the lower limit were classified as insufficient GWG and those above the upper limit of this range were classified as excessive GWG.[12]

2.6 | Confounder variables

As confounder variables, we consider G1 and G2 ages (full years at childbirth), schooling (full years of formal education), G1 family income (quintiles), G2 asset index (based on a principal component analysis of the ownership of goods and assets,[27] then divided into quintiles), G1 number of antenatal care visits (discrete number), G1 and G2 smoking during pregnancy (no/yes), and pre-gestational BMI. Pre-gestational BMI was calculated through the standard formula—[weight/(height in metres)^2]—and later classified into four categories as described above.

G1 pre-gestational BMI was calculated using early pregnancy weight (obtained by recall, as described above) and height (measured at the hospital upon admission for delivery by hospital staff during the perinatal visit of 1993 Pelotas Birth Cohort Study; the research team retrieved this information from maternity records). G2 pre-gestational BMI was similarly calculated using recalled early pregnancy, and height was measured by a trained team at this moment.

2.7 | Statistical analysis

Proportions and 95% confidence intervals ($_{95\%}$CI) for categorical variables and means and respective standard deviations (±SD) for continuous characteristics were calculated. Pearson chi-square and Fisher's exact test were used to evaluate the relationship between G1 and G2 GWG IOM recommendation categories and covariates.

The analyses were stratified by G3 age (≤2 years; 2.01-5 years; >5 years) due to the existence of statistical interaction between G3 overweight status and G1 GWG with G3's age categories (testparm *P* value <0.0001).

Mediation analyses were conducted to test G1 GWG and G2 GWG total, direct and indirect effects on G3 BMI. Coefficients were generated by structural equation models used to estimate a system of linear equations to test the fit of a hypothesized "causal" model.[28] This statistical is available in the STATA software using the command "*sem*." The total effect is defined as the sum of the direct and indirect effects. The direct effect tested existence of a relationship between G1 GWG or G2 GWG and G3 BAZ, and the indirect effect considered the effect via G2 and/or G3 anthropometric variables. A theoretical model of the possible relationship between variables in G1, G2, and G3 with G3 BMI is shown in Figure 1. The included continuous variables were: G2 birthweight (kg), G2 pre-gestational BMI (kg/m^2), G2 GWG (kg), and G3 birthweight (kg).

To verify the associations between G1 and G2 GWG IOM recommendation categories and G3 overweight status, crude and adjusted

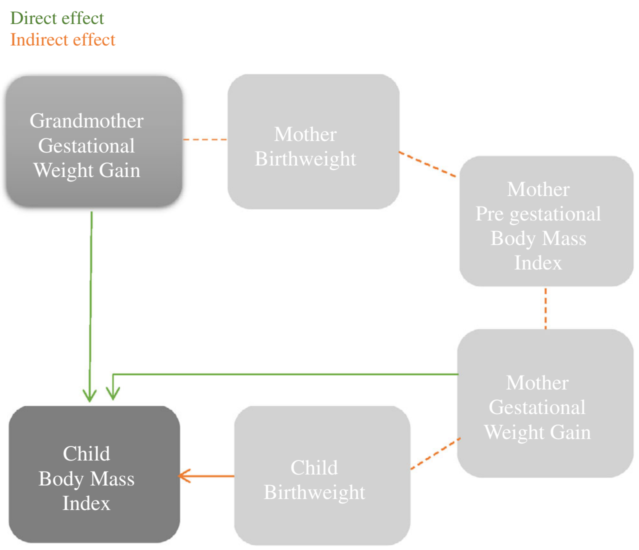

FIGURE 1 Theoretical model for association between grandmother (G1) and maternal (G2) gestational weight gain and grandchild (G3) BMI. 1993 Pelotas (Brazil) Birth Cohort

odds ratios (OR) were calculated through multivariate logistic regression models. Crude and adjusted linear regression models were used to describe the relationship between G1 and G2 GWG continuous and categorical variables and G3 BAZ. Results were considered statistically significant with *P* values <0.05.

All analyses were carried out using Stata version 16.0 (StataCorp, College Station, Texas).

3 | RESULTS

Of the 1212 children included in 93Cohort-II study, a total of 1113 with complete anthropometric data were evaluated; 52.8% were boys, approximately 85% were 5 years of age or under, and one-fifth of them received breastfeeding until the time of the interview (Table 1). Among G3 participants not evaluated in the present study (n = 99), the majority had >5 years of age (39.4%; n = 39).

The proportion of G2 who had children before 20 years of age was higher than the corresponding proportion of grandmothers (G1) (46.0% vs 22.6%). In G2, the proportion of women with 12 or more years of schooling increased by 6.5 times compared to G1 (0.9% in G1 to 5.9% in G2), the proportion of smoking during pregnancy decreased by half (44.9% in G1 vs 20.6% in G2), and the rate of pre-pregnancy obesity more than doubled (5.1% in G1 vs 12.8% in G2)—Table 1.

Characteristics for each generation related to the G1 GWG recommendation categories are also presented in Table 1. Excessive GWG in G1 was higher at 30 years of age or older (27.7%), among those who did not smoke during pregnancy (23.0% vs 16.7%), and among women with pre-gestational obesity (36.4%). Insufficient GWG in G1 was higher among younger women (<20 years—50.6%), in those who smoked during pregnancy (48.6%), and those with underweight pre-gestational BMI (55.6%). Approximately 40% of the daughters of G1 with excessive GWG had an intermediate level of education (5-11 years) and almost half were classified as overweight/obesity (47.0%). G1 with insufficient GWG had daughters less educated (55.0%) and most had low pre-pregnancy weight (61.2%). All the G3 characteristics were similar among the categories of recommendation of the G1 GWG.

Mean G1 GWG, adjusted for pre-gestational BMI, was 10.98 kg (SD ± 1.23), while for G2 it was 13.09 kg (SD ± 2.15) (data not presented in tables). The proportion of GWG according to IOM recommendations in G1 is also presented in Table 1; almost half showed insufficient GWG (44.6%), while for G2 this was shown by one-third of women. Excessive GWG was 20.0% for G1 and 35.3% for G2. Evaluating changes from G1 to G2, almost 16% of G2 women with insufficient GWG were daughters of G1 women with insufficient GWG (data not presented in tables).

Figure 2 shows the relationship between G3 BAZ by age categories according to G1 (a) and G2 (b) GWG standardized in z scores. G1 GWG was not related to G3 BAZ, despite a higher slope in children aged more than 5 years old (β = 0.19; $_{95\%}$CI: −0.01-0.40). For each increase in G2 GWG *z* score, the older (>5 years of age) G3 BAZ increased in 0.28 *z* scores ($_{95\%}$CI: 0.11-0.45). This did not apply to G3 in other age groups (≤2 years of age: β = 0.06, $_{95\%}$CI: −0.10-0.23; and 2.01 to 5 years of age: β = 0.13, $_{95\%}$CI: −0.002-0.26).

Table 2 shows the total, direct, and indirect effects of G1, G2, and G3 anthropometric variables on the G3 BAZ, by age categories. The total effects observed were mainly due to direct effects of GWG on G3 BAZ, except to G1 GWG and G3 BAZ. Among G3 aged ≤2 years, only G3's birthweights (β = 0.301, $_{95\%}$CI: 0.066-0.536) were related to their BAZ. For G3 aged 2.01 to 5 years, the G2 pre-pregnancy BMI (β = 0.079, $_{95\%}$CI: 0.047-0.112) and the G2 GWG (β = 0.171, $_{95\%}$CI: 0.031-0.311) were positively related to G3 BAZ, mainly due to the direct effect. In G3 aged 2.01 to 5 years, an indirect effect of G1 GWG on G3 BAZ (β = 0.115, $_{95\%}$CI: 0.035-0.195) was also observed. Among the older G3, G3 birthweight (β = 0.522, $_{95\%}$CI: 0.037-1.006), G2 pre-gestational BMI (β = 0.071, $_{95\%}$CI: 0.027-0.114), and G2 GWG (β = 0.351, $_{95\%}$CI: 0.162-0.541) were related to G3 BAZ.

The results of total, direct, and indirect effects for all interrelations are shown in the supporting information.

Table 3 shows the crude and adjusted relation between GWG recommendation categories and G3 overweight status. Overweight prevalence in our study was 13.9% ($_{95\%}$CI: 12.0;16.0), being higher in older G3 (36% at >5 years of age). G1 GWG not was related with G3 classified with overweight. However, excessive G2 GWG increased by 15-fold the chance of G3 between 2.01 and 5 years of age being classified as overweight and by approximately fivefold in G3 > 5 years of age, compared to G3 whose mothers were classified as adequate GWG.

4 | DISCUSSION

Our results showed that GWG has an indirect effect through the G1 (going through G2 birthweight, G2 pre-gestational BMI, G2 GWG, and

TABLE 1 Characteristics of three generations of 1993 Pelotas (Brazil) Birth Cohort, RS, Brazil

Characteristics	A Child sample (G3) (n = 1113) *N* (%)	B Grandmother (G1) gestational weight gain according to Institute of Medicine (2009) classification *N* (%)[a] Adequate 368 (35.2%)	Excess 211 (20.2%)	Insufficient 466 (44.6%)	*P* value[b]
Child (G3)					
Gender					0.113
Male	588 (52.8)	211 (37.8)	103 (18.3)	243 (43.2)	
Female	525 (47.2)	157 (32.2)	108 (22.1)	223 (45.7)	
Age (years)					0.074
2 or less	469 (42.1)	160 (36.5)	96 (21.9)	183 (41.7)	
2.01 to 5	465 (41.8)	155 (35.6)	90 (20.6)	191 (43.8)	
5.01 or more	179 (16.1)	53 (31.2)	25 (14.7)	92 (54.1)	
Birthweight (g)					0.163
<2500	124 (12.3)	36 (31.0)	20 (17.2)	60 (51.7)	
2500 or more	883 (87.7)	311 (37.3)	169 (20.3)	353 (42.4)	
Breastfeeding duration					0.929
<6 months	511 (52.6)	174 (36.7)	90 (18.9)	210 (44.3)	
6 months or more	210 (21.6)	68 (33.8)	42 (20.9)	91 (45.3)	
Yet	250 (25.8)	81 (34.8)	49 (21.1)	103 (44.2)	
Mother (G2)					
Age (years)					0.224
<20	512 (46.0)	163 (33.8)	90 (18.7)	228 (47.4)	
20 to 23	601 (54.0)	205 (36.4)	121 (21.5)	238 (42.2)	
Schooling (years)					0.036
0 to 4	54 (4.9)	10 (25.0)	8 (20.0)	22 (55.0)	
5 to 8	600 (54.0)	176 (31.5)	114 (20.4)	269 (48.1)	
9 to 11	393 (35.3)	154 (40.5)	78 (20.5)	148 (39.0)	
12 or more	65 (5.9)	28 (43.1)	11 (16.9)	26 (40.0)	
Smoking during pregnancy					0.665
No	873 (79.4)	297 (35.8)	170 (20.5)	362 (43.7)	
Yes	227 (20.6)	70 (34.3)	38 (18.6)	96 (47.1)	
Pre-pregnancy BMI					0.001
Underweight	74 (10.4)	21 (31.4)	5 (7.5)	41 (61.2)	
Normal	383 (53.9)	132 (36.7)	62 (17.2)	166 (46.1)	
Overweight	163 (22.9)	51 (32.9)	39 (25.2)	65 (41.9)	
Obese	91 (12.8)	42 (48.3)	19 (21.8)	26 (29.9)	
Gestational Weight Gain[c]					0.089
IOM classification					
Adequate	218 (31.1)	70 (36.8)	32 (16.8)	88 (46.3)	
Excess	238 (34.0)	81 (34.8)	57 (24.5)	95 (40.8)	
Insufficient	244 (34.9)	95 (40.4)	35 (14.9)	105 (44.7)	
Grandmother (G1)					
Age (years)					0.003
<20	252 (22.6)	75 (31.9)	41 (17.5)	119 (50.6)	
20 to 29	607 (54.5)	224 (39.0)	105 (18.3)	246 (42.8)	
30 or more	254 (22.8)	69 (29.4)	65 (27.7)	101 (43.0)	

(Continues)

TABLE 1 (Continued)

Characteristics	A Child sample (G3) (n = 1113) N (%)	B Grandmother (G1) gestational weight gain according to Institute of Medicine (2009) classification N (%)[a] Adequate 368 (35.2%)	Excess 211 (20.2%)	Insufficient 466 (44.6%)	P value[b]
Schooling (years)					0.047[d]
0 to 4	500 (45.1)	142 (31.5)	93 (20.6)	216 (47.9)	
5 to 8	519 (46.8)	184 (36.7)	98 (19.5)	220 (43.8)	
9 to 11	80 (7.2)	35 (44.3)	17 (21.5)	27 (34.2)	
12 or more	10 (0.9)	7 (70.0)	0 (0.0)	3 (30.0)	
Smoking during pregnancy					0.017
No	613 (55.1)	206 (35.6)	133 (23.0)	239 (41.4)	
Yes	500 (44.9)	162 (34.7)	78 (16.7)	227 (48.6)	
Pre-pregnancy BMI					<0.001
Underweight	109 (10.2)	35 (32.4)	13 (12.0)	60 (55.6)	
Normal	719 (67.0)	259 (37.2)	114 (16.4)	324 (46.5)	
Overweight	190 (17.7)	59 (31.9)	64 (34.6)	62 (33.5)	
Obese	55 (5.1)	15 (27.3)	20 (36.4)	20 (36.4)	

Notes: 99 children had no BMI/age information, and 39.4% (n = 39) had >5 years of age ($P < 0.05$). Column **A**, the proportions are read in column; Column **B**, the proportions are read in row.
[a]Of the total 1113 in G3, 1045 had G1 gestational weight gain information.
[b]Pearson chi-square.
[c]Of the total 1113 in G3, 700 had G2 gestational weight gain information.
[d]Fisher's exact test.

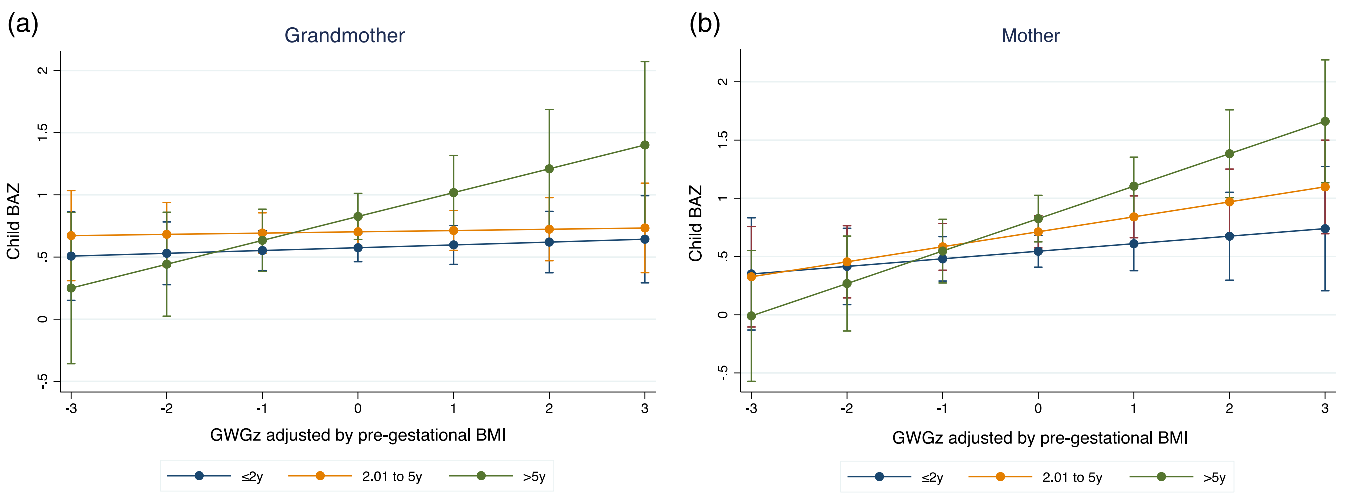

FIGURE 2 Child BMI *z* score by age categories according to gestational weight gain *z* score for G1 (a) and G2 (b)

G3 birthweight) and a direct effect through the G2 on the G3 BMI. In addition, excessive G2 GWG increased the chance of the G3 being overweight after 2 years of age.

The mechanisms related to the association between GWG and BMI in future generations are not fully understood, but it is known that they are underlying by gene-environment interactions.[13,15] It has been postulated that body fat accumulation may affect offspring predisposition to epigenetic modifications, which can alter the phenotype over time.[13,29] However, we did not find a direct association between G1 GWG and the nutritional status of the G3, which leads us to believe that there is no biological effect (if any, it is small) that cannot be modified over the generations. On the other hand, we identified an indirect relationship that included anthropometric variables of the G2 birthweight, G2 pre-gestational nutritional status, G2 GWG,

TABLE 2 Path analysis of the total, indirect, and direct effects of grandmother's, mother's, and child's anthropometric variables on child BAZ by age categories

	Total effect					Indirect effect					Direct effect				
	Coef.	SE	*P*	95%CI		Coef.	SE	*P* [f]	95%CI		Coef.	SE	*P* [f]	95%CI	
≤2 years															
GWG G1[a]	0.025	0.068	0.711	−0.108	0.159	0.011	0.026	0.665	−0.039	0.061	0.014	0.071	0.842	−0.125	0.153
Birthweight G2[b]	0.187	0.135	0.166	−0.078	0.451	0.038	0.028	0.174	−0.017	0.092	0.149	0.134	0.266	−0.113	0.412
BMI G2[c]	0.007	0.012	0.577	−0.017	0.030	−0.003	0.002	0.200	−0.007	0.001	0.009	0.012	0.426	−0.014	0.032
GWG G2[d]	0.055	0.078	0.485	−0.099	0.208	0.017	0.014	0.223	−0.010	0.043	0.038	0.078	0.624	−0.114	0.190
Birthweight G3[e]	**0.301**	**0.120**	**0.012**	**0.066**	**0.536**	–	–	–	–	–	**0. 301**	**0.120**	**0.012**	**0.066**	**0.536**
2.01 to 5 years															
GWG G1[a]	0.055	0.081	0.501	−0.105	0.214	**0.115**	**0.041**	**0.005**	**0.035**	**0.195**	−0.060	0.082	0.461	−0.220	0.100
Birthweight G2[b]	0.152	0.179	0.397	−0.199	0.503	0.004	0.070	0.952	−0.133	0.142	0.147	0.171	0.389	−0.188	0.483
BMI G2[c]	**0.079**	**0.017**	**<0.001**	**0.047**	**0.112**	0.007	0.004	0.084	−0.001	0.014	**0.073**	**0.017**	**<0.001**	**0.040**	**0.105**
GWG G2[d]	**0.171**	**0.071**	**0.017**	**0.031**	**0.311**	0.028	0.018	0.125	−0.008	0.064	**0.143**	0.073	0.051	0.001	0.286
Birthweight G3[e]	0.203	0.120	0.091	−0.032	0.439	–	–	–	–	–	0.203	0.120	0.091	−0.032	0.439
>5 years															
GWG G1[a]	0.187	0.129	0.149	−0.067	0.440	0.100	0.071	0.156	−0.038	0.239	0.086	0.121	0.476	−0.151	0.323
Birthweight G2[b]	**0.522**	**0.247**	**0.035**	**0.037**	**1.006**	0.160	0.115	0.163	−0.065	0.385	0.361	0.229	0.114	−0.087	0.810
BMI G2[c]	**0.071**	**0.022**	**0.001**	**0.027**	**0.114**	0.003	0.008	0.707	−0.012	0.018	**0.068**	**0.021**	**0.001**	**0.026**	**0.109**
GWG G2[d]	**0.351**	**0.097**	**<0.001**	**0.162**	**0.541**	0.011	0.015	0.438	−0.017	0.040	**0.340**	**0.097**	**<0.001**	**0.150**	**0.530**
Birthweight G3[e]	0.187	0.198	0.346	−0.202	0.576	–	–	–	–	–	0.187	0.198	0.346	−0.202	0.576

Note: 1993 Pelotas (Brazil) Birth Cohort.
[a]Grandmother's adjustment variables: age, schooling, family income, antenatal consultations number, smoke during pregnancy, pre-gestational body mass index.
[b]Grandmother's adjustment variables: a + gestational weight gain adjusted by pre-gestational body mass index.
[c]Adjustment variables: b + mother birthweight, mother age, mother schooling, mother assets index.
[d]Adjustment variables: c + mother smoke during pregnancy, mother pre-gestational body mass index.
[e]Adjustment variables: d + mother gestational weight gain adjusted by pre-gestational body mass index.
[f]Wald test.
Bold vaules indicates statistically significant.

TABLE 3 Relationship between grandmother's and mother's gestational weight gain and child's overweight

	Child overweight[a] OR ($_{95\%}$CI)											
	≤2 years n = 36 (7.7%)				2.01 to 5 years n = 54 (11.7%)				>5 years n = 63 (36.0%)			
Gestational weight gain	**Crude**	**P^d**	**Adjusted**	**P^d**	**Crude**	**P^d**	**Adjusted**	**P^d**	**Crude**	**P^d**	**Adjusted**	**P^d**
Grandmother[b]	(n = 438)		(n = 425)		(n = 431)		(n = 421)		(n = 167)		(n = 163)	
IOM recommendation												
Adequate	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Excess	1.31 (0.47;3.67)	0.604	1.22 (0.43;3.46)	0.704	1.14 (0.52;2.47)	0.746	1.15 (0.52;2.56)	0.733	0.55 (0.19;1.57)	0.291	0.55 (0.18;1.65)	0.287
Insufficient	1.82 (0.79;4.17)	0.158	1.97 (0.84;4.63)	0.119	0.84 (0.43;1.63)	0.599	0.89 (0.43;1.81)	0.739	0.71 (0.35;1.41)	0.324	0.69 (0.33;1.41)	0.305
Mother [c]	(n = 290)		(n = 269)		(n = 275)		(n = 248)		(n = 130)		(n = 121)	
IOM recommendation												
Adequate	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Excess	0.34 (0.09;1.27)	0.108	0.28 (0.07;1.19)	0.084	**5.60 (1.61;19.5)**	**0.005**	**15.6 (1.94;126.1)**	**0.010**	**3.47 (1.37;8.75)**	**0.008**	**4.61 (1.46;14.6)**	**0.009**
Insufficient	0.70 (0.28;1.77)	0.452	0.59 (0.20;1.73)	0.340	2.37 (0.61;9.27)	0.215	2.10 (0.51;8.61)	0.300	2.00 (0.75;5.34)	0.167	1.54 (0.49;4.86)	0.461

Note: 1993 Pelotas (Brazil) Birth Cohort.

[a]Defined according to WHO 2006 and WHO 2007: >2 SD for children ≤5 years and >1 SD for children >5 years of age.

[b]Adjustment variables: grandmother age, grandmother schooling, grandmother family income, antenatal consultations number, grandmother smoke during pregnancy, grandmother pre-gestational body mass index.

[c]Adjustment variables: a + mother age, mother schooling, mother family income, mother smoke during pregnancy, mother pre-gestational body mass index.

[d]Pearson chi-square test.

Bold vaules indicates statistically significant.

and G3 birthweight. However, this finding was only for just one age range, which should be interpreted with caution.

All of the factors involved in the G3 body fat accumulation pathway presented in this study are modifiable through adopting healthy lifestyle habits such as an adequate diet and consistent physical activity.[1,5] It is estimated that 21.7% to 41.7% of childhood overweight/obesity prevalence could be attributed to maternal overweight and obesity together.[5] In addition, evidence suggests that maternal obesity has also persistent long-term health effects in offspring.[8,15] In the same sense, the case of grandmother GWG does not only affect pregnancy outcomes but may also have persistent effects on offspring and grandchildren BMI.[16-18] We showed that the G2 GWG increased the chances of G3 over 2 years of age being overweight, as the literature has already shown.[8,11] A meta-analysis from 37 pregnancy and birth cohorts, including 162 129 mothers and their children from Europe, North America, and Australia, showed that excessive GWG was directly associated with a higher risk of childhood overweight/obesity in early, mid, and late childhood [OR = 1.39 ($_{95\%}$CI: 1.30-1.49); OR = 1.55 ($_{95\%}$CI: 1.49-1.60), and OR = 1.72 ($_{95\%}$CI: 1.56-1.91), respectively], when compared to adequate GWG.[8]

We also found that G1 GWG was related to G2 birthweight, which has a direct influence on G3 BMI. Similarly, a study using data from the Aberdeen Maternity and Neonatal Databank evaluated 1457 grandmother-mother-grandchild triads identified the perpetuation of birthweight in three generations.[18] Birthweight is frequently used as a surrogate marker of the intrauterine environment.[12] Previous epidemiological studies have shown that both low and high birthweight are linked to increased risk of body fat accumulation, cardiovascular disease, and type 2 diabetes in later life.[14,15] It is known that other characteristics, such as gestational diabetes, may be related to the birthweight and/or BMI of offspring.[29] The present work did not present statistical models adjusted for gestational diabetes because of low prevalence levels [G1: 2.5% ($_{95\%}$CI: 1.7-3.7) and G2: 3.8% ($_{95\%}$CI: 2.7-5.4)] were not compatible in the model.

Our work showed that the G2 GWG increased the chance of the G3 being overweight over 2 years of age, as the literature has already demonstrated.[8,11] One possible explanation for these associations is that children who have experienced maternal excessive GWG are at increased risk of obesity due to developmental programming in utero as well as exposure to the same obesogenic environment and lifestyle from the mother, such as high-caloric food intake and low physical activity.[15] Children over 2 years of age have already incorporated familiar habits and behaviours that may influence their nutritional status.[30]

Gestation is certainly an important period for foetal growth, development, and physiological changes in mothers and offspring.[12] It is a window of opportunity for interventions in maternal lifestyles to sustain a healthy weight during pregnancy, as women are known to become more motivated to adopt healthy behaviours when they believe that their baby may benefit.[31] It is also fundamental to mention the importance of quality prenatal care in the support of pregnant women and her families. Intervention strategies should mainly include adherence to a healthy diet and physical activity. Despite this, our study found that the proportion of excessive GWG worsened between the G1 and G2 generations, increasing by 67%.

Inadequate weight gain during pregnancy (either insufficient or excessive) is related to unsatisfactory reproductive outcomes for both the pregnant woman and the foetus.[7,12] Insufficient GWG is associated with intrauterine growth retardation, prematurity, and low birthweight.[7,12] On the other hand, excessive weight gain during pregnancy predisposes women to pre- and postpartum problems such as gestational diabetes, preeclampsia, hypertensive pregnancy, haemorrhage, and postpartum weight retention.[29] Besides, the children of mothers who gain more weight during pregnancy have a higher risk of becoming overweight in early childhood and other life stages.[10,11,15,29] In our study, women of low education, as well as those with underweight or overweight, had the highest percentages of inadequate GWG. These are potentially modifiable with targeted interventions to reach those who are the most vulnerable.

The main limitation of this study relates to participants' recall about G1 and G2 weight at the beginning of pregnancy. Recalled anthropometric measurements are widely used in epidemiological research due to high agreement with measured information.[25,26,32] Data from the North Carolina Early Pregnancy Study were used as the gold standard to evaluate the accuracy of pre-pregnancy weight, providing information reported after almost 30 years from 109 women, and showed that about 90% of women recalled their pre-pregnancy weight correctly.[25] However, research in Latin American showed that women underestimate their weight by, on average, 2.0 ± 5.0 kg.[32] In the same vein, a Brazilian study that used data from face-to-face interviews and prenatal cards (gold standard) in 17 093 women verified an underestimation of 1.51 kg (SD = 3.44) and 0.79 kg/m^2 (SD = 1.72) of pre-gestational weight and body mass index, respectively.[26] Before carrying out our work, we estimated the quality of information recalled by G2 by comparing the pre-pregnancy weight recall with data collected during the cohort follow-ups. We have seen that although the recall period is long in some cases (16.1% of children over 5 years), we found moderate-to-high concordance correlation coefficients—described in Section 2. For G3, the recall error is possibly lower than that of G2 due to the shorter recall period. In G1, weight at the end of pregnancy was measured, but G2 also recalled weight at the end of pregnancy, increasing the likelihood of misclassification. An underestimation of pre-gestational weight could affect the calculation of pre-gestational BMI, as well as the estimation of G1 and G2 GWG, consequently reducing the magnitude of the association with BMI in three generations.

It is worth mentioning that about 60% of the G2 had one child and 31.6% had two, being that in four cases G2 answered about the GWG for both twin children.

Our analysis had several strengths. First, it is one of the only cohorts worldwide to have most of the anthropometric and sociodemographic data from grandmothers collected mostly directly and prospectively. Furthermore, we were able to assess the effects of a wide range of confounding variables.

5 | CONCLUSIONS AND RECOMMENDATIONS

Gestational weight gain was shown to have an effect on child BMI across three generations, indirectly through the grandmother and directly through the mother. Gestational weight is a modifiable factor among a range of other factors that influence offspring weight. For this reason, effective strategies for prevention and treatment must include health education for pregnant women and their families that support appropriate gestational weight gain and healthy pre-pregnancy weight, especially in vulnerable groups such as women with less education and inadequate pre-gestational weight. Preventing childhood overweight is a public health challenge; given the condition's significant impact on the development of morbidities, risk factors such as inadequate gestational weight gain must receive special attention in order to avoid being perpetuated from generation to generation.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Bruna C. Schneider and Helen Gonçalves conceived and designed the study. Bruna C. Schneider and Fernando C. Wehrmeister analysed and interpreted the data. Bruna C. Schneider drafted the manuscript. Helen Gonçalves, Fernando C. Wehrmeister, and Ana M. B. Menezes critically revised the manuscript. All authors approved the final version of the manuscript for submission.

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