Effectiveness of a normative nutrition intervention in Chilean pregnant women on maternal and neonatal outcomes: the CHiMINCs study

Maria Luisa Garmendia,[1] *Camila Corvalan,*[1] *Marcela Araya,*[2] *Paola Casanello,*[3,4] *Juan Pedro Kusanovic,*[3,5] *and Ricardo Uauy*[1,4]

[1]Institute of Nutrition and Food Technology (INTA), University of Chile, Santiago, Chile; [2]Department of Women and Newborn Health Promotion, Faculty of Medicine, University of Chile, Santiago, Chile; [3]Department of Obstetrics and Gynecology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; [4]Department of Pediatrics, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; and [5]Center for Research and Innovation in Maternal-Fetal Medicine (CIMAF), Department of Obstetrics and Gynecology, Sótero del Río Hospital, Santiago, Chile

ABSTRACT

Background: Some nutritional interventions have shown their efficacy in reducing gestational weight gain (GWG); however, their applicability in routine care is limited.

Objective: We assessed the effectiveness of a low-intensity and high-coverage nutritional intervention on maternal and offspring outcomes; the intervention enhanced existing nutritional health care standards and practices at the primary health care level in Chile.

Methods: This study was a cluster-randomized controlled trial of 12 primary health care centers (PHCCs) from Santiago, Chile. PHCCs were randomly allocated to either nutritional intervention [intervention group (IG), $n = 5$] or routine care [control group (CG), $n = 7$]. A total of 4631 pregnant women were recruited (IG, $n = 2565$; and CG, $n = 2066$). Primary outcomes were adequate GWG and glycemic control in mothers and birth weight, birth length, macrosomia, and large for gestational age in neonates. The intervention consisted of 4 key actions: training of health care professionals on nutritional recommendations, counseling of pregnant women on diet and physical activity recommendations, offering a physical activity program implemented in the participating PHCCs, and adequate referral to dietitians. Women randomly assigned to the CG received routine antenatal care.

Results: At baseline, the mean age was 26.1 y; 45% of women were primipara and 24% were obese. No differences were found in the percentage of women achieving adequate GWG (IG: 30.3%, compared with CG: 31.3%; OR: 0.94; 95% CI: 0.81, 1.09), but women in the IG had lower GWG than those in the CG (11.3 compared with 11.9 kg; mean difference: −0.63 kg; 95% CI: −1.19, −0.08). Effects of the intervention were significantly higher in women with obesity at the begining of pregnancy (mean difference: −1.24 kg; 95% CI: −2.18, −0.30; P for interaction < 0.05). No differences were found between groups regarding maternal glycemic control or neonatal outcomes.

Conclusions: Our findings demonstrate that a low-intensity, high-coverage intervention delivered through the Chilean public health care system under standard operating conditions reduces GWG and has the potential for successful scale-up. This trial was registered at clinicaltrials.gov as NCT01916603. *Am J Clin Nutr* 2020;112:991–1001.

Keywords: pregnancy, obesity, gestational weight gain, birth weight, clinical trial, Chile

Introduction

Pregestational obesity and gestational weight gain (GWG) above the recommended amount predict a future risk of obesity and associated metabolic conditions for both the mother and the offspring (1–3). These conditions are related to adverse pregnancy [gestational diabetes mellitus (GDM) and preeclampsia], obstetric (cesarean delivery), neonatal (macrosomia or neonates large for gestational age), and long-term (obesity and noncommunicable diseases in the offspring) outcomes (4, 5). In addition, obesity is a self-perpetuating disorder; daughters of obese women are more vulnerable to becoming obese and are more likely to have offspring that share this vulnerability (6). Obesity in pregnancy also has economic consequences. Among pregnant women, those who are obese and their children have

Funded by the Chilean National Fund for Scientific and Technological Development, FONDECYT no. 1130277.

Role of the funding source: The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Supplemental Tables 1–9 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

Address correspondence to MLG (e-mail: mgarmendia@inta.uchile.cl).

Abbreviations used: CG, control group; CHiMINCs, Chilean Maternal and Infant Nutrition Cohort Study; GDM, gestational diabetes mellitus; GWG, gestational weight gain; IG, intervention group; IOM, Institute of Medicine; OGTT, oral-glucose-tolerance test; PA, physical activity; PHCC, primary health care center.

Received January 31, 2020. Accepted for publication June 15, 2020.

First published online July 21, 2020; doi: https://doi.org/10.1093/ajcn/nqaa185.

higher health care utilization and costs than do women who are normal weight and their offspring (7, 8).

In 2009, the Institute of Medicine (IOM) of the United States published revised GWG guidelines based on prepregnancy BMI (in kg/m^2) categories (9). These guidelines recommend the following GWG categories based on prepregnancy BMI: underweight (BMI: <18.5 kg/m^2; range: 12.5–18.0 kg), normal weight (BMI: ≥18.5–24.9 kg/m^2; 11.5–16.0 kg), overweight (BMI: 25.0–29.9 kg/m^2; 7.0–11.5 kg), and obese (BMI: ≥30.0 kg/m^2; 5.0–9.0 kg).

Some studies of nutritional interventions during pregnancy have demonstrated their efficacy in reducing GWG (10, 11). These studies are usually designed as high-intensity interventions with small sample sizes, thus limiting their applicability in routine care (11, 12). Further research is needed to confirm the effectiveness of high-coverage interventions on maternal and offspring outcomes and to assess the feasibility and ability of health care systems to deliver these interventions (11, 13, 14).

The Chilean Maternal and Infant Nutrition Cohort Study (CHiMINCs) is a cluster-randomized controlled trial aimed at assessing the effectiveness of a low-intensity and high-coverage nutritional intervention by enhancing existing nutritional health care standards and practices at the primary health care level. This intervention aimed to improve adequate GWG and maternal glycemic control as well as adequate weight, length, and BMI growth during the first year of life. Here, we report results regarding maternal and neonatal outcomes (birth weight, gestational age, and fetal growth) and also consider potential adverse effects.

Subjects and Methods

Study design and setting

The CHiMINCs study is a cluster randomized controlled trial conducted in 12 primary health care centers (PHCCs) from 2 of the largest urban counties of the Southeast Health Area of Santiago, Chile [La Florida (n = 5) and Puente Alto (n = 7)]. In Chile, pregnant women seek services from PHCCs at the first signs of pregnancy and, on average, they receive 5 (maximum 7) midwife assessments prior to delivery (at <14 wk and at 20, 25, 30, 34, 37, and 40 wk of pregnancy) (15). The intervention was delivered through the national health care system under standard operating conditions. The cluster units were randomly allocated to: *1*) enhanced implementation of nutritional health care standards [intervention group (IG)], or *2*) routine care [control group (CG)]. Details of the study protocol have been published elsewhere (16).

Recruitment and randomization

PHCCs that had coverage of more than 400 new pregnancies per year were invited to participate in the study as part of a collaborative agreement between the Institute of Nutrition and Food Technology and the Southeast Health Area and La Florida and Puente Alto counties. Twelve PHCCs fulfilled the inclusion criteria (from a total of 17 PHCCs), and all of them agreed to participate. PHCCs were randomly allocated to either the nutritional intervention (n = 5) or routine care (n = 7). Randomization was performed prior to the recruitment of participants. At the first prenatal visit, midwives invited pregnant women to participate in the study. If they agreed, they were then contacted by the study staff installed in each of the PHHCs, informed consent was obtained, and baseline information was collected. All pregnant women who attended these PHCCs between January 2014 and April 2015 who fulfilled enrollment criteria were invited to participate by the PHCC midwives.

Participants

The inclusion criteria for pregnant women were as follows: <15 wk of gestation, between 16 and 40 y of age, residence within catchment areas of selected PHCCs, and no plans to move for the following 2 y. Women were excluded if they had high-risk pregnancies indicated by any of the following guidelines of the Chilean Ministry of Health: prior history of abortion (>2), children with low birth weight (<2500 g), prematurity or perinatal death, current multiple gestation, uterine scar, chronic diseases (17), or currently underweight (BMI <18.5 kg/m^2). We contacted 5585 pregnant women, but we further excluded 954 pregnant women when enrollment criteria were rechecked, 448 in whom we could not obtain pregestational BMI, 110 who were underweight, 188 aged <16 or >40 y, 60 with multiple pregnancy, and 148 with diagnoses of high-risk pregnancy. The final total sample was 4631 pregnant women (2565 in the IG and 2066 in the CG).

Intervention

The CHiMINCs intervention was designed to support the implementation of evidence-based and up-to-date guidelines in primary health care (**Supplemental Table 1**). The intervention consisted of 4 key actions: *1*) training of health care professionals on nutritional recommendations; *2*) counseling of pregnant women on diet and physical activity (PA) recommendations; *3*) offer of a PA program implemented in the participating PHCC; and *4*) adequate referral to PHCC dietitians. Specific details on the intervention have been provided elsewhere (16). Briefly, the intervention was based on IOM 2009 GWG recommendations (9) and on dietary and PA recommendations from the American College of Obstetricians and Gynecologists and the United Kingdom National Health Service (18, 19); the intervention also aimed to improve the communication skills of PHCC professionals. In each of the PHCC visits, midwives provided to women on a 1-by-1 basis specific recommendations for the allowed GWG for the next visit assisted using a computer chart developed based on IOM 2009 recommendations. The midwives also provided healthy nutrition and PA messages. Messages included the following: benefits of breastfeeding, avoidance of the consumption of sugar-sweetened beverages, restriction of bread consumption to 2 pieces per day, replacement of fatty meat with lean meat and fish; and eating a variety of vegetables and fruits each day instead of foods rich in fat and calories. At each visit, pregnant women were also invited to attend 1-h PA classes. Sessions were delivered at each PHCC supervised by PA trainers 3 times per week, and they included exercises to achieve moderate intensity PA. Finally, midwives should refer pregnant women to dietitians according to defined criteria based on noncompliance

with the IOM recommendations (9): gaining >3 kg in the first trimester, independently of their baseline nutritional status; and gaining >3 kg/mo for women with normal weight, 2 kg for overweight women and 1.5 kg for obese women during the second and third trimesters.

Routine care

Women who received prenatal care from PHCCs and were randomly assigned to CG received routine antenatal care and nutritional counseling according to national guidelines (17). The classification of nutritional status in pregnant women is evaluated through the Atalah's chart based on BMI increases according to gestational age (20). Chilean guidelines include GWG recommendations based on nutritional status, but no further advice was given at each prenatal appointment to achieve adequate GWG. Dietary recommendations, including the extra consumption of 350 calories/d during the second and third trimesters, respectively (17).

Main outcome measures

The primary outcomes in mothers were as follows. Adequate GWG, defined as the proportion of women with a GWG within the IOM 2009 recommendations. GWG was defined as the weight at delivery (38.5 ± 1.9 wk) or the weight at the last visit prior to delivery in the PHCC (36.4 ± 5.9 wk) minus the pregestational weight self-reported by the pregnant woman at the first visit to the PHCC (correlation between pregestational weight and measured weight at the first antenatal visit = 0.99). GWG was classified as below, within or above the 2009 IOM guidelines according to each prepregnancy BMI category (9).

Adequacy of glycemic control was routinely assessed at 24–28 wk of pregnancy following a 1-step procedure with a 75-g oral-glucose-tolerance test (OGTT); GDM was defined according to the Chilean Ministry of Health Guidelines as having a fasting plasma glucose (FPG) concentration >100 mg/dL or 2-h values of >140 mg/dL in the OGTT at 24–28 wk of pregnancy (17, 21, 22).

Primary outcomes in offspring were adequate birth weight and birth length, macrosomia, and large for gestational age in neonates. Appropriate birth weight for gestational age was defined according to Alarcón-Pittaluga curves (between the 10th and 90th percentiles) (23). Infant macrosomia was defined as birth weight >4000 g, and infant born large for gestational age as a birth weight ≥90th percentile according to Alarcón-Pittaluga curves (23).

Secondary outcomes were divided into *1*) implementation outcomes (number of trained midwives and dietitians per PHCC, compliance with protocol by health personnel, perceptions of the intervention, etc.) and *2*) participant compliance outcomes (referral to dietitian's clinic, attendance at PA sessions, etc.).

We also considered potential adverse events, including premature birth (<37 wk), infants with low birth weight (birth weight <2500 g), infant born small for gestational age [birth weight ≤10th percentile for gestational age according to Alarcón-Pittaluga curves (23)], and low score at 1 min and at 5 min on the Apgar score test (score below 7) (24).

Data collection

Given the effectiveness approach of the study, we based our data collection on pre-existing records. From the electronic clinical records available at the PHCCs, we obtained data on sociodemographic, obstetric, and lifestyle characteristics, pregestational BMI and height at the first prenatal appointment (80% at <10 wk of pregnancy), weight at each visit, and maternal health status during pregnancy, including glucose metabolism assessments, GDM diagnosis, other diagnosis (e.g., hypertension or preeclampsia), and health care indicators (referral to dietitian or to secondary care). Sociodemographic, obstetric, morbidity, and lifestyle data were validated against questionnaires conducted by the study team at recruitment.

Delivery information, including maternal weight at delivery, duration of the pregnancy (based on ultrasound at 11–13 + 6 wk), mode of delivery (cesarean section, vaginal, or forceps), birth weight, and length of the offspring, were obtained from maternity records of the largest hospital of the southeastern area of Santiago (Dr Sotero del Rio Hospital) and complemented the data from the electronic records of PHCCs. This was possible because in Chile there is a universal identifier, the Rol Unico Tributario (RUT), that allows data to be linked from different sources.

We also collected information to assess the degree of implementation of the intervention. Online surveys to all the professionals ($n = 67$) of the PHCCs in the intervention group (3 rounds) and phone surveys to a random sample of the pregnant women ($n = 20.9\%$ of the estimated sample size) were conducted. Surveys were designed to collect information on the delivery of recommendations or surveys, reasons for a lack of compliance with the intervention, referral to a dietitian, or effectiveness of the intervention. PA trainers recorded participant attendance to PA classes.

Statistical analyses

We performed the statistical analysis on an intention-to-treat basis. Baseline characteristics between groups were compared using *t*-tests (for continuous variables) or chi-square tests (for categorical variables). Analysis was performed taking into account the cluster design (PHCCs). To test the effects of the intervention on continuous responses, such as GWG, glucose concentration, or birth weight, we used a multilevel mixed-effects linear regression model (xtmixed module in STATA software). The effects of intervention were estimated as β coefficients (mean differences) and 95% CIs. For binary responses, such as the above recommendations for GWG, GDM, or macrosomia, we used the multilevel mixed-effects logistic regression models (xtmelogit module in STATA software). The effects of the intervention were estimated as ORs and 95% CIs. Models were adjusted by baseline data. Models for GWG or GWG according to recommendations as outcomes were adjusted by pregestational BMI, maternal age at recruitment, gestational age at delivery, primipara status, and other variables that were significantly different between the groups at baseline. Models in which maternal glycemic control was the outcome were adjusted by pregestational BMI, maternal age at recruitment, gestational age, primipara status, secondary care referral, and other variables that were significantly different between the groups at baseline. Models for neonatal outcomes were adjusted by pregestational BMI, maternal age, gestational

age at delivery, primipara status, and other variables that were significantly different between the groups at baseline. We also tested for the interaction effects between pregestational BMI and the intervention on GWG, and stratum-specific treatment effects were estimated. Models did not include imputation techniques for missing values.

Sensitivity analyses were also perfomed in subgroups of participants if the total sample excluded those who were diagnosed with GDM and in the subsample of women in whom GWG was defined as the weight at delivery minus the pregestational weight (including and excluding diagnosis of GDM).

All tests performed were 2 sided, with $P < 0.05$ considered statistically significant. All analyses were conducted using Stata version 13.0.

Sample size.

The original calculation of sample size was estimated based on the hypothesized effect sizes using existing data and the likely rates of study dropout (20%). Assuming that 50% of Chilean women currently meet IOM GWG recommendations (25), a 2-tailed α of 0.05, 80% power, and an intraclass correlation coefficient of 0.008% (26) (based on the cluster design of the study), we needed to recruit 200 women in each PHCC ($n = 1200$ per arm to obtain a final sample size of 960 per arm) to detect a 20% difference in the achievement of IOM 2009-GWG recommendations between groups (IG compared with CG). During the follow-up of the first study participants, we realized that some study outcomes that were collected from electronic records of the PHCCs were underreported (such as blood glucose concentration). To achieve the desired power because of the logistical impossibility of increasing the number of clusters, we decided to increase the cluster size to evaluate the effect of the intervention on all primary outcomes, although the number needed per arm under individual randomization in some outcomes could be exceeded (27).

Ethical approval

The protocol for this study was approved by the Ethics Committees of the Institute of Nutrition and Food Technology of University of Chile (approval certificate number 18, July 25, 2012), the Catholic University of Chile (approval certificate number 12-238, August 7, 2012), and the Southeast Health Service (approval certificate August 9, 2012). All participants provided written informed consent. This trial was registered at clinicaltrials.gov as NCT01916603.

Results

General characteristics at recruitment

The total sample ($n = 4631$, IG = 2565, and CG = 2066) was included in the intention-to-treat analyses. Prepregnancy weight was obtained in the total sample (by questionnaire at baseline). GWG during pregnancy was available in 4563 (98.5%) women without differences between groups (IG = 2528 and CG = 2035). Laboratory results for fasting glucose concentration from the OGTT could be extracted from clinical records in a subsample of 1769 participants (38%, IG = 1019 and CG = 750) and 2-h glucose concentration in 1667 participants (36%, IG = 966 and CG = 701). However, a determination with respect to GDM was stated in 72.6% of the medical records ($n = 3363$ women), with significant differences between groups (IG = 1968, 76.7% and CG = 1395, 67.5%; $P < 0.05$). Delivery data were extracted in 82.7% of the sample (17.3% of loss to follow-up: 0.4% due to abortion, 0.3% transferred to another health center, and 16.7% in whom the reason could not be determined). From medical records, maternal weight at delivery was obtained in a subsample of 2981 women (64.4%) (IG = 1670 and CG = 1311). Birth weight was assessed in 3763 infants (81.3%); 2111 newborns of mothers were allocated to the IG, and 1652 of mothers were allocated to the CG.

Table 1 outlines the baseline sociodemographic and clinical characteristics of the women study participants. The average age of the cohort was 26.1 ± 5.9 y, and the average gestational age at admission was 10.6 ± 42 wk. Forty-five percent of women were primipara, and the average BMI was 26.8 ± 5.1 kg/m^2, with 34% of women being overweight and 24% obese.

Degree of implementation

The degree of implementation of the intervention was variable. In phone surveys to pregnant women, 96% of the participants declared having been informed about their GWG, and 61% reported that midwives reminded them how much they should gain by the following check-up (**Supplemental Table 2**). Seventy-eight percent of the women remembered receiving any of the nutritional messages. Fifty-seven percent of the total trained professionals of the IG answered the online surveys. On average, 100% declared that they communicated with pregnant women about their current weight and 86% reported that they communicated how much weight they should gain until the next appointment to comply with the recommendations (**Supplemental Table 3**).

Attendance at the physical activity sessions was very low (>10% of the participants).

The average number of appointments with midwives was similar in both groups (6.3 in the IG and 6.3 in the CG, $P > 0.05$), but more women were referred to dietitians in the IG (35% in the IG compared with 20% in the CG, $P < 0.05$). A higher proportion of women allocated to the IG had a secondary care referral during pregnancy for health reasons (25.9% compared with 23.2%, $P < 0.05$); among them, the most frequent diagnoses were GDM (31.1%), obesity (11.9%), urinary tract infection (15.4%), and anemia (8.6%) (data not shown).

Gestational weight gain

Table 2 shows the results of the intervention on GWG both as a co ntinuous outcome and categorized according to IOM 2009 recommendations. First, we calculated differences between groups using the *t*-test or chi square test. Then, crude and adjusted regression models (mean differences or OR and 95% CI) were performed because of differences in some variables between groups at baseline. Women in the IG had significantly lower GWG (mean 11.3 kg) than did those in the CG (mean 11.9 kg) (adjusted mean difference: 0.63 kg; 95% CI: −1.19, −0.08). Pregestational BMI showed a significant interaction with the effect of the intervention on GWG ($P < 0.05$), resulting in a higher difference between groups in women with obesity (adjusted mean difference: −1.24 kg; 95% CI: −2.18, −0.30) (Table 2).

TABLE 1 Baseline characteristics of the study population[1]

	Intervention group ($n = 2565$)	Control group ($n = 2066$)	P value[2]
Age, y	26.3 ± 6.0	25.8 ± 5.7	0.003
Adolescent (16–20 y), *n* (%)	392 (15.3)	350 (17.1)	0.105
Education, *n* (%)			0.051
≤8 y	336 (13.7)	323 (15.9)	
9–12 y	1562 (63.6)	1295 (63.5)	
>12 y	559 (22.8)	420 (20.6)	
Civil status, *n* (%)			<0.001
Single	1139 (45.7)	1078 (54.1)	
Married/living with partner	1320 (53.0)	888 (44.6)	
Divorced/widow	32 (1.3)	27 (1.4)	
Working, *n* (%)	1091 (45.2)	790 (41.8)	0.025
Number of people per household	3.6 ± 1.8	3.4 ± 1.7	<0.001
Gestational age at recruitment, wk	11.0 ± 4.2	10.1 ± 4.1	<0.001
Primipara, *n* (%)	925 (44.8)	763 (45.5)	0.657
Number of children	0.7 ± 1.0	0.7 ± 1.0	0.627
Pregestational weight, kg	67.5 ± 13.8	67.2 ± 13.9	0.532
Height, cm	158.3 ± 5.7	158.1 ± 5.8	0.231
Pregestational BMI, kg/m^2	26.8 ± 5.1	26.9 ± 5.1	0.793
Pregestational BMI categories, *n* (%)			0.964
Normal (18.5–24.9 kg/m^2)	1078 (42.0)	874 (42.3)	
Overweight (25.0–29.9 kg/m^2)	875 (34.1)	697 (33.7)	
Obese (≥30.0 kg/m^2)	612 (23.9)	495 (24.0)	

[1]Values are means ± SDs unless otherwise indicated.
[2]Differences between groups were compared using a *t*-test (for continuous variables) or chi-square test (for categorical variables).

No differences were found between participants assigned to the intervention compared to women assigned to routine care in the proportion of adequate GWG (IG 30.3% compared with CG 31.3%; adjusted OR: 0.94; 95% CI: 0.81, 1.09). Pregestational BMI showed a significant interaction with the effect of the intervention on adequate GWG ($P < 0.05$), resulting in a lower proportion of adequate GWG in the IG in women with normal BMI (adjusted OR: 0.73; 95% CI: 0.54, 0.97). We also found a smaller but not significant proportion of women who exceeded the IOM recommendations (36.6% compared with 39.2%; adjusted OR: 0.96; 95% CI: 0.77, 1.19) and showed a significant interaction by nutritional status (adjusted OR for obesity: 0.75; 95% CI: 0.52, 1.08) (Table 2).

In the subsample of women in which we could obtain weight at delivery, women of the PHCCs allocated to the IG gained significantly less than women allocated to the CG gained, but this difference was nonsignificant after adjustments were made for covariables (adjusted mean difference: −0.39 kg; 95% CI: −0.94, 0.15). We observed a significant interaction between pregestational nutritional status and the intervention on GWG ($P < 0.10$); however, no significant differences were found by subgroups of pregestational BMI (e.g., for obesity, adjusted mean difference: −0.94 kg; 95% CI: −2.13, 0.26). No differences were found between groups in the proportion of women who achieved an adequate GWG but who also showed differences by pregestational nutritional status (P for interaction = 0.025) (**Supplemental Table 4**). Women with a normal pregestational BMI showed a lower percentage of adequate GWG (OR: 0.66; 95% CI: 0.49, 0.89).

Maternal glycemic control

At 24–28 wk of pregnancy, the fasting glucose concentration at the OGTT was slightly higher in the IG than in the CG, but the difference was not statistically significant (adjusted mean difference: 1.31 mg/dL; 95% CI: −0.16, 2.78). At 2 h, a higher glucose concentration was observed in the IG than in the CG, which was not statistically significant in the adjusted models ($P > 0.05$). The incidence of GDM was higher in the IG than in the CG (16% in the IG compared with 13% in the CG; $P < 0.05$); however, this difference was not statistically significant in the adjusted model (adjusted OR: 1.22; 95% CI: 0.86, 1.74) (**Table 3**).

In the subsample of women in whom we were able to obtain weight at delivery, GDM was higher in the IG than in the CG (IG 17% compared with CG 13%, but this difference was not observed in adjusted models (adjusted OR: 1.38; 95% CI: 0.92, 2.07) (**Supplemental Table 5**).

As sensitivity analyses, we repeated models excluding women with a diagnosis of GDM in both the total sample and in the subsample of women in whom weight at delivery could be obtained (**Supplemental Tables 6–9**); the direction of the effects was consistent across models but showed lower precision in some estimates due to a smaller sample size in subgroups.

Neonatal outcomes

Twenty percent of women allocated to the IG had a cesarean section compared to 23% in the CG, without significant differences between groups. **Table 4** shows the study results in neonatal outcomes; there were no significant differences between

TABLE 2 Maternal GWG by treatment group[1]

				Treatment effect[3] [mean difference (95% CI)]		Treatment effect [OR (95% CI)]	
	Intervention group	Control group	*P* value[2]	Crude	Adjusted	Crude	Adjusted
GWG, kg	11.3 ± 6.7	11.9 ± 6.7	0.003	−0.82 (−1.53, −0.11)	−0.63 (−1.19, −0.08)		
Pregestational normal weight ($n = 1919$)	12.9 ± 6.3	13.2 ± 6.0	0.196	−0.57 (−1.43, 0.29)	−0.07 (−0.66, 0.52)		
Pregestational overweight ($n = 1554$)	11.1 ± 6.7	11.7 ± 6.8	0.086	−0.78 (−1.78, 0.22)	−0.67 (−1.42, 0.09)		
Pregestational obesity ($n = 1090$)	8.6 ± 6.6	9.7 ± 7.1	0.014	−1.03 (−1.84, −0.21)	−1.24 (−2.18, −0.30)		
GWG within IOM recommendations, *n* (%)	767 (30.3)	637 (31.3)	0.484			0.97 (0.89, 1.06)	0.94 (0.81, 1.09)
Pregestational normal weight ($n = 636$)	336 (31.7)	300 (34.9)	0.135			0.87 (0.61, 1.25)	0.73 (0.54, 0.97)
Pregestational overweight ($n = 466$)	262 (30.3)	204 (29.7)	0.797			1.03 (0.83, 1.28)	1.21 (0.93, 1.57)
Pregestational obesity ($n = 302$)	169 (28.1)	133 (27.3)	0.764			1.04 (0.80, 1.36)	1.08 (0.78, 1.50)
GWG >IOM recommendations, *n* (%)	925 (36.6)	798 (39.2)	0.598			0.96 (0.84, 1.11)	0.96 (0.77, 1.19)
Pregestational normal weight ($n = 505$)	273 (25.8)	232 (27.0)	0.679			1.05 (0.83, 1.33)	1.32 (0.96, 1.82)
Pregestational overweight ($n = 729$)	396 (45.7)	333 (48.4)	0.519			0.97 (0.89, 1.06)	0.74 (0.49, 1.13)
Pregestational obesity ($n = 489$)	256 (42.5)	233 (47.8)	0.323			0.86 (0.65, 1.15)	0.75 (0.52, 1.08)
GWG <IOM recommendations, *n* (%)	836 (33.1)	600 (29.5)	0.054			1.16 (1.00, 1.34)	1.21 (1.01, 1.44)
Pregestational normal weight ($n = 778$)	451 (42.6)	327 (38.1)	0.053			1.26 (0.96, 1.64)	1.41 (1.04, 1.91)
Pregestational overweight ($n = 359$)	208 (24.0)	151 (22.0)	0.622			1.07 (0.81, 1.42)	0.93 (0.66, 1.32)
Pregestational obesity ($n = 299$)	177 (29.4)	122 (25.0)	0.422			1.14 (0.83, 1.58)	1.18 (0.78, 1.76)

[1]Values are means ± SDs unless otherwise indicated. GWG, gestational weight gain, defined as weight at delivery or the last weight measured at the primary health care level—pregestational weigh; IOM, Institute of Medicine.

[2]Based on *t*-test for GWG or chi-square test for GWG categorized according IOM 2009 recommendations.

[3]Based on multilevel mixed-effects linear regression model for GWG as continuous variable (treatment effect estimated by β coefficients and 95% CI) and on multilevel mixed-effects logistic regression models for GWG categorized according IOM 2009 recommendations as binary variable (treatment effect estimated by OR and 95% CI). Adjusted for the baseline data: pregestational BMI, maternal age, gestational age, primipara status, education, civil status, working status and number of people per household. *P*-interaction between intervention and pregestational BMI on GWG = 0.023. *P*-interaction between intervention and pregestational BMI on GWG within IOM 2009 recommendations = 0.017. *P*-interaction between intervention and pregestational BMI on GWG above IOM 2009 recommendations = 0.004. *P*-interaction between intervention and pregestational BMI on GWG below IOM 2009 recommendations = 0.326.

TABLE 3 Maternal glycemic control by treatment group[1]

				Treatment effect[3] [mean difference (95% CI)]		Treatment effect [OR (95% CI)]	
	Intervention group	Control group	*P* value[2]	Crude	Adjusted	Crude	Adjusted
Fasting glucose concentration at 24–28 wk, mg/dL	87.2 ± 11.3	85.5 ± 11.1	0.002	2.93 (−0.61, 6.49)	1.31 (−0.16, 2.78)		
Pregestational normal weight ($n = 740$)	85.6 ± 11.8	82.9 ± 8.9	<0.001	2.73 (1.18, 4.27)	2.65 (0.25, 5.06)		
Pregestational overweight ($n = 593$)	87.0 ± 10.7	86.1 ± 8.9	0.277	0.91 (−0.73, 2.55)	0.44 (−1.92, 2.80)		
Pregestational obesity ($n = 436$)	90.1 ± 10.7	89.3 ± 15.2	0.518	0.80 (−1.62, 3.23)	0.93 (−2.00, 3.84)		
Glucose concentration at 24–28 wk, 2 h after 75 g of glucose, mg/dL	115.9 ± 27.4	112.7 ± 25.4	0.014	3.25 (0.66, 5.83)	2.94 (−1.02, 6.90)		
Pregestational normal weight ($n = 678$)	111.5 ± 26.3	105.6 ± 22.6	0.002	5.89 (2.13, 9.65)	5.05 (−0.09, 10.19)		
Pregestational overweight ($n = 569$)	116.3 ± 27.9	116.7 ± 24.5	0.869	− 0.37 (−4.81, 4.06)	− 3.35 (−9.28, 2.59)		
Pregestational obesity ($n = 420$)	122.5 ± 27.2	119.2 ± 28.2	0.235	4.05 (−2.47 to 10.58)	6.42 (−0.52 to 13.36)		
Gestational diabetes mellitus, *n* (%)	316 (16.1)	179 (12.8)	0.009			1.31 (1.03, 1.67)	1.22 (0.86, 1.74)
Pregestational normal weight ($n = 1390$)	76 (9.5)	34 (5.8)	0.011			1.65 (1.12, 2.44)	2.00 (0.91, 4.41)
Pregestational overweight ($n = 1155$)	68 (17.4)	68 (14.3)	0.159			1.22 (0.92, 1.60)	0.87 (0.50, 1.53)
Pregestational obesity ($n = 818$)	121 (24.7)	76 (23.1)	0.590			1.07 (0.83, 1.37)	1.23 (0.68, 2.23)

[1]Values are means ± SDs unless otherwise indicated.

[2]Based on *t*-test for glucose concentration or chi-square test for gestational diabetes mellitus.

[3]Based on multilevel mixed-effects linear regression model for glucose concentration as continuous variables (treatment effect estimated by β coefficients and 95% CI) and on multilevel mixed-effects logistic regression models for gestational diabetes mellitus as binary variable (treatment effect estimated by OR and 95% CI). Adjusted by baseline data: pregestational BMI, maternal age, gestational age, primipara status, education, civil status, working status and number of people per household, glucose concentration at baseline and secondary care referral. *P*-interaction between intervention and pregestational BMI on fasting glucose concentration in the oral glucose tolerance test at 24–28 wk = 0.122. *P*-interaction between intervention and pregestational BMI on glucose concentration 2 h after 75 of glucose in the oral glucose tolerance test at 24–28 wk = 0.932. *P*-interaction between intervention and pregestational BMI on gestational diabetes mellitus incidence = 0.321.

TABLE 4 Neonatal outcomes by treatment group[1]

	Intervention group ($n = 2111$)	Control group ($n = 1652$)	*P* value[3]	Treatment effect[4] [mean difference (95% CI)]		Treatment effect [OR (95% CI)]	
				Crude	Adjusted	Crude	Adjusted
Birth weight, g	3333.2 ± 124.7	3359.8 ± 131.5	0.143	− 0.03 (−0.07, 0.01)	− 0.02 (−0.06, 0.02)		
Length at birth, cm	49.1 ± 0.06	49.2 ± 0.07	0.206	− 0.24 (−0.55, 0.07)	− 0.10 (−0.50, 0.30)		
Appropriate for gestational age,[2] *n* (%)	1333 (77.6)	1,052 (78.6)	0.537			0.95 (0.80, 1.13)	0.97 (0.75, 1.14)
Macrosomia, *n* (%)	196 (9.3)	139 (8.4)	0.352			1.18 (0.88, 1.58)	1.16 (0.84, 1.62)
Large for gestational age,[2] *n* (%)	237 (13.5)	171 (12.4)	0.340			1.10 (0.89, 1.36)	1.01 (0.78, 1.31)

[1] Values are means ± SDs unless otherwise indicated.
[2] Appropriate for gestational age and large for gestational age were estimated in 2080 babies of the intervention group and in 1633 of the control group.
[3] Based on *t*-test for birth weight and length at birth or chi-square test for macrosomia and large for gestational age.
[4] Based on multilevel mixed-effects linear regression model for birth weight and length at birth as continuous variables (treatment effect estimated by β coefficients and 95% CI) and on multilevel mixed-effects logistic regression models for macrosomia and large for gestational age as binary variables (treatment effect estimated by OR and 95% CI). Adjusted by baseline data: pregestational BMI, maternal age, gestational age at delivery, primipara status, education, civil status, working status and number of people per household (models for birth weight, length at birth and macrosomia) or by pregestational BMI, maternal age, primipara status, education, civil status, working status and number of people per household (models for large for gestational age). *P*-interaction between intervention and pregestational BMI on birth weight = 0.871. *P*-interaction between intervention and pregestational BMI on length at birth = 0.719. *P*-interaction between intervention and pregestational BMI on appropriate for gestational age = 0.388. *P*-interaction between intervention and pregestational BMI on macrosomia = 0.835. *P*-interaction between intervention and pregestational BMI on large for gestational age = 0.565.

the 2 treatment groups ($P > 0.05$; e.g., for appropriate for gestational age; adjusted OR: 0.97; 95% CI: 0.75, 1.14).

Adverse events

The intervention did not have any detectable adverse effects on outcomes related to deficient fetal growth (incidence of preterm birth, low birth weight, and small for gestational age or Apgar scores) ($P > 0.05$) (**Table 5**).

Discussion

Our results show that a low-intensity, but high-coverage intervention delivered through primary health care centers was not effective in improving adequate GWG. Other trials have already suggested that nutritional interventions are effective in reducing GWG but not enough to show differences in the proportion of women who gain weight within recommendations (25, 28–30). However, the intervention was effective in decreasing GWG. GWG was 630 g lower in the intervention group than in the control group, once adjustments were made for covariables. This trial adds to the evidence that nutritional interventions in diet and/or PA are effective in reducing GWG, even when delivered under the standard operating conditions of primary health care. The effect size of our intervention is slightly lower than those found in other nutritional interventions (25, 31–34), which can be explained by the low intensity of our intervention. However, we found that the intervention had a higher impact in the group of obese women; in this subgroup, women allocated to the IG gained 1.2 kg less than did those allocated to the CG. This interaction by nutritional status was also observed in the meta-analysis of Thangaratinam et al. (10), showing a higher reduction in GWG in the subgroup of obese and overweight pregnant women (mean difference: −2.1 kg, *P* for interaction = 0.05), but the treatment effect of our study was higher than that reached by Poston et al. (34) in an intervention in a large sample of obese pregnant women (−0.55 kg). The observed reduction in GWG in obese pregnant women is relevant because it corresponds to 14–25% of the GWG recommendations in this subgroup (5–9 kg). We believe these results may indicate that nutritional counseling may be more effective in the population groups that need it the most.

The impact of this lower GWG on health in the short and long term is not clear. A higher GWG may contribute to greater postpartum weight retention, which could lead women to face the next pregnancy in worse condition, contributing to the obesity epidemic to a higher degree (35, 36).

Although the intervention did not show a higher incidence of adverse events, participants with pregestational normal weight allocated to the IG comprised a significantly lower percentage of women with a GWG within recommendations. This finding may be partially explained by the facts that Chilean recommendations are stricter than the IOM recommendations (10–13 kg) (20) or that normal weight women in Chile are much more weight concious than their counterparts. Taken together, we believe these findings support another argument for targeting the current intervention to overweight and obese women, which would also contribute to better allocation of resources.

Moreover, we found that the intervention did not improve maternal glycemic control. We found that participants in the IG

TABLE 5 Adverse effects by treatment group[1]

	Intervention group ($n = 2111$)	Control group ($n = 1652$)	P value[2]	Treatment effect [OR (95% CI)][3]	
				Crude	Adjusted
Preterm birth (<37 wk), *n* (%)	161 (9.4)	96 (7.2)	0.030	1.34 (1.03, 1.74)	1.57 (0.74, 3.23)
Low birth weight, *n* (%)	127 (6.0)	78 (4.7)	0.082	1.27 (0.97, 1.68)	1.23 (0.86, 1.77)
Small for gestational age, *n* (%)	153 (8.9)	121 (9.0)	0.904	1.29 (0.97, 1.72)	1.31 (0.71, 2.41)
Apgar 1 score <7, *n* (%)	140 (6.8)	116 (7.2)	0.620	0.88 (0.60, 1.30)	0.77 (0.35, 1.72)
Apgar 5 score <7, *n* (%)	73 (3.6)	67 (4.2)	0.328	0.78 (0.45, 1.36)	0.94 (0.32, 2.78)

[1]Preterm birth and small for gestational age were estimated in 2080 babies of the intervention group and in 1633 of the control group. Apgar scores were estimated in 2057 babies of the intervention group and in 1605 of the control group.

[2]Based on chi-square test.

[3]Based on multilevel mixed-effects logistic regression models (treatment effect estimated by OR and 95% CI). Adjusted by baseline data: pregestational BMI, maternal age, gestational age at delivery, primipara status, education, civil status, working status and number of people per household (models for low birth weight and Apgar 1 and Apgar 5 scores) or by pregestational BMI, maternal age, primipara status, education, civil status, working status and number of people per household (models for preterm birth and small for gestational age). *P*-interaction between intervention and pregestational BMI on preterm birth = 0.515. *P*-interaction between intervention and pregestational BMI on low birth weight = 0.807. *P*-interaction between intervention and pregestational BMI on small for gestational age = 0.792. *P*-interaction between intervention and pregestational BMI on Apgar 1 score <7 = 0.675. *P*-interaction between intervention and pregestational BMI on Apgar 5 score <7 = 0.755.

had a higher incidence of GDM than those in the CG, although this result was not significant in the adjusted models. Although several nutritional interventions during pregnancy have also shown a null effect on GDM (25, 30, 31, 37, 38), a recent review of the effects of diet and exercise interventions to prevent GDM, which included 23 randomized controlled trials, demonstrated a risk reduction of 1% (average RR: 0.85; 95% CI: 0.71, 1.01). However, these investigators concluded that the evidence is too limited to be put into practice and that more studies are needed (39).

Additionally, we did not find any differences between the groups in outcomes related to birth. The overall incidences of small for gestational age (SGA) and large for gestational age (LGA) according to national standards were 9% and 13%, respectively (5% and 18% according to Intergrowth-21 standards, respectively; κ statistic = 0.73), which were very similar to those presented in other national reports (40). This lack of impact on neonatal outcomes is also observed in most lifestyle interventions (9), even though the "Gesund leben in der Schwangerschaft"/Healthy living in pregnancy (GeliS) trial found a small decrease in birth weight and length with the antenatal intervention even in the absence of an effect on GWG or GDM (37). Some authors have suggested that the maternal metabolic condition programs early placenta function and gene expression in the first trimester of pregnancy when interventions have not yet started, emphasizing that nutritional intervention should focus on reducing maternal obesity before conception (41, 42).

Among the components of this intervention was a PA program, specifically designed for pregnant women and supervised by trained instructors. This program was the unique component of the intervention not delivered through the primary health care system, which currently does not offer any physical activity program aimed at pregnant women. However, adherence to PA class attendance was very low. On average, 1 out of every 10 pregnant women in the centers attended at least 1 PA class. Our adherence was lower than that reported in other studies, which may be due to the lower intensity of our study. The levels of sedentarism in nonpregnant Chilean women of childbearing age reach 90% (43), and the failure of this intervention shows that, against our hypothesis, pregnancy does not seem like a good time to make changes in PA. The participants who were consulted in the telephone surveys stated the following as the main reasons for their low attendance: their low availability of time and their lack of developing a habit to perform PA. Given this poor adherence, the results of the intervention could be attributed to the component of monitoring of weight gain and nutritional counseling delivered by the health care system. Thangaratinam et al. (10) reported that dietary interventions are more effective in reducing GWG than are those based on PA only or those with combined dietary and exercise interventions. A European randomized trial also observed that the group randomly assigned to a healthy eating intervention was more effective in reducing GWG than was the group allocated to PA, but the authors argue that the GWG in the physical activity group could reflect an increase in muscle mass but not in fat (44).

A relevant finding of our study is the high prevalence of pregestational excess weight observed in the participants; 1 out of every 3 pregnant women was overweight, and 1 out of 4 was obese. These figures are slightly higher than those reported in the National Health Survey at the national level for women of childbearing age (43). Evidence regarding the effects on maternal and child health is more consistent with respect to pregestational obesity than to GWG above the recommended amount (45). Therefore, this high prevalence of excess weight emphasizes the importance of implementing individual and structural strategies aimed at women having a normal nutritional status before becoming pregnant.

This study is not exempt from limitations. First, all of the information related to the study outcomes was extracted from electronic clinical records routinely collected at health centers. This could produce an underestimation of the effects of the intervention. Additionally, due to the real-world setting of this study, we could not obtain all the information related to outcomes in the participants because it was not always recorded in their medical records. The percentage of missing values was particularly high for the results of glucose concentration, which were only obtained in 37% of the participants although

a diagnosis of GDM was stated in 73% of the medical records. Similar to most studies of pregnancy, pregestational weight was self-reported, and could have been underestimated by women, especially in overweight and obese participants. However, the abovementioned underestimation should be similar in both arms of randomization. In addition, PHCC professionals and participants in the IG were not blinded to the intervention, because they received training (professionals) and nutritional messages and PA classes (participants). Another limitation could be the small number of clusters involved in the trial, which could lead to an inflated type I error rate; however, this design was preferred over an individual-based design because of logistic feasibility and the avoidance of potential contamination between the 2 treatment groups (46).

Among the strengths, we highlight the large sample size of the study and its randomized controlled design. In addition, the primary health care setting increases its chances of generalization.

Our findings demonstrate that a low-intensity high-coverage intervention delivered through the national health care system under standard operating conditions reduces GWG, particularly in obese women, although it was insufficient to improve adequate GWG. These results highlight the potential of this intervention to be scaled up without the inclusion of many additional resources and therefore be considered part of the national strategy for preventing GWG among obese pregnant women. More studies are needed to evaluate the impact of this lower GWG at the population level on postpartum weight retention and on the short- and long-term health of mothers and their offspring.

The Chilean Maternal Nutrition Cohort Study (CHiMINCs, trial registration NCT01916603) was funded by the Chilean National Fund for Scientific and Technological Development, FONDECYT#1130277. The Ministry of Health of Chile, the South East Health Service, and the La Florida and Puente Alto counties have provided kind support for the implementation of the study. We thank all the participants in this study for generously helping us in this research.

The authors' responsibilities were as follows—MLG, CC, RU, PC, MA, JPK: planned and designed the research; MLG, CC, RU, MA: participated in data collection and data analysis; MLG, CC, RU: performed the literature research and figures; and all authors: participated in data interpretation and writing the final manuscript for submission, and read and approved the final manuscript. The authors report no conflicts of interest.

References

1. Poston L. Gestational weight gain: influences on the long-term health of the child. Curr Opin Clin Nutr Metab Care 2012;15(3):252–7.
2. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. Rev Obstet Gynecol 2008;1(4):170–8.
3. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics 2005;115(3):e290–6.
4. O'Reilly JR, Reynolds RM. The risk of maternal obesity to the long-term health of the offspring. Clin Endocrinol 2013;78(1):9–16.
5. Nelson SM, Matthews P, Poston L. Maternal metabolism and obesity: modifiable determinants of pregnancy outcome. Hum Reprod Update 2010;16(3):255–75.
6. Hanson MA, Bardsley A, De-Regil LM, Moore SE, Oken E, Poston L, Ma RC, McAuliffe FM, Maleta K, Purandare CN, et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". Int J Gynaecol Obstet 2015;131(Suppl 4):S213–53.
7. Morgan KL, Rahman MA, Macey S, Atkinson MD, Hill RA, Khanom A, Paranjothy S, Husain MJ, Brophy ST. Obesity in pregnancy: a retrospective prevalence-based study on health service utilisation and costs on the NHS. BMJ Open 2014;4(2):e003983.
8. Morgan KL, Rahman MA, Hill RA, Khanom A, Lyons RA, Brophy ST. Obesity in pregnancy: infant health service utilisation and costs on the NHS. BMJ Open 2015;5(11):e008357.
9. Institute of Medicine, National Research Council (US). Weight gain during pregnancy: reexamining the guidelines. Washington, DC: National Academies Press; 2009.
10. Thangaratinam S, Rogozinska E, Jolly K, Glinkowski S, Roseboom T, Tomlinson JW, Kunz R, Mol BW, Coomarasamy A, Khan KS. Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. BMJ 2012;344:e2088.
11. Ronnberg AK, Nilsson K. Interventions during pregnancy to reduce excessive gestational weight gain: a systematic review assessing current clinical evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system. BJOG 2010;117(11):1327–34.
12. Poston L, Chappell LC. How should women be advised on weight management in pregnancy? BMJ 2012;344:e2774.
13. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P. Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis. BMC Med 2012;10:47.
14. Tanentsapf I, Heitmann BL, Adegboye AR. Systematic review of clinical trials on dietary interventions to prevent excessive weight gain during pregnancy among normal weight, overweight and obese women. BMC Pregnancy Childbirth 2011;11:81.
15. Government of Chile, Ministry of Health. Manual de atención personalizada en el proceso reproductivo. Santiago: 2008.
16. Garmendia ML, Corvalan C, Araya M, Casanello P, Kusanovic JP, Uauy R. Effectiveness of a normative nutrition intervention (diet, physical activity and breastfeeding) on maternal nutrition and offspring growth: the Chilean maternal and infant nutrition cohort study (CHiMINCs). BMC Pregnancy Childbirth 2015;15:175.
17. Government of Chile Ministry of Health. Guía perinatal. Santiago, Chile: Ministry of Health; 2015.
18. The American College of Obstetricians and Gynecologists [Internet]. Available from: https://www.acog.org/Patients/FAQs/Exercise-During-Pregnancy (accessed 06-08 2019).
19. UK National Health Service [Internet]. Available from: https://www.nhs.uk/conditions/pregnancy-and-baby/healthy-pregnancy-diet/ (accessed 06-08-2019).
20. Atalah E, Castillo LC, Castro SR, Aldea PA. [Proposal of a new standard for the nutritional assessment of pregnant women]. Rev Med Chil 1998;125:1429–36.
21. Government of Chile, Ministry of Health. Guía perinatal. Santiago: 2015.
22. Asociación Latinoamericana de Diabetes (ALAD). Consenso Latinoamericano de Diabetes y Embarazo. 2008.
23. Milad AM, Novoa PJM, Fabres BJ, Samamé MMM, Aspillaga MC. Recomendación sobre Curvas de Crecimiento Intrauterino. Revista chilena de pediatría 2010;81:264–74.
24. Apgar V. A proposal for a new method of evaluation of the newborn infant. Curr Res Anesth Analg 2015;120(5):1056–9.
25. Asbee SM, Jenkins TR, Butler JR, White J, Elliot M, Rutledge A. Preventing excessive weight gain during pregnancy through dietary and lifestyle counseling: a randomized controlled trial. Obstet Gynecol 2009;113(2 Pt 1):305–12.
26. Stevens J, Taber DR, Murray DM, Ward DS. Advances and controversies in the design of obesity prevention trials. Obesity (Silver Spring) 2007;15(9):2163–70.
27. Hemming K, Eldridge S, Forbes G, Weijer C, Taljaard M. How to design efficient cluster randomised trials. BMJ 2017;358:j3064.
28. Althuizen E, van der Wijden C, van Mechelen W, Seidell J, van Poppel M. The effect of a counselling intervention on weight changes during and after pregnancy: a randomised trial. BJOG 2013;120(1):92–9.
29. Kinnunen TI, Pasanen M, Aittasalo M, Fogelholm M, Hilakivi-Clarke L, Weiderpass E, Luoto R. Preventing excessive weight gain during pregnancy—a controlled trial in primary health care. Eur J Clin Nutr 2007;61:884.

30. Thornton YS, Smarkola C, Kopacz SM, Ishoof SB. Perinatal outcomes in nutritionally monitored obese pregnant women: a randomized clinical trial. J Natl Med Assoc 2009;101(6):569–77.
31. Ronnberg AK, Ostlund I, Fadl H, Gottvall T, Nilsson K. Intervention during pregnancy to reduce excessive gestational weight gain—a randomised controlled trial. BJOG: Int J Obstet Gy 2015;122(4):537–44.
32. Claesson IM, Brynhildsen J, Cedergren M, Jeppsson A, Sydsjo A, Josefsson A. Weight gain restriction during pregnancy is safe for both the mother and neonate. Acta Obstet Gynecol Scand 2009;88(10):1158–62.
33. Wolff S, Legarth J, Vangsgaard K, Toubro S, Astrup A. A randomized trial of the effects of dietary counseling on gestational weight gain and glucose metabolism in obese pregnant women. Int J Obes 2008;32(3):495–501.
34. Poston L, Bell R, Croker H, Flynn AC, Godfrey KM, Goff L, Hayes L, Khazaezadeh N, Nelson SM, Oteng-Ntim E, et al. Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol 2015;3(10):767–77.
35. Ma D, Szeto IM, Yu K, Ning Y, Li W, Wang J, Zheng Y, Zhang Y, Wang P. Association between gestational weight gain according to prepregnancy body mass index and short postpartum weight retention in postpartum women. Clin Nutr 2015;34(2):291–5.
36. Amorim AR, Rössner S, Neovius M, Lourenço PM, Linné Y. Does excess pregnancy weight gain constitute a major risk for increasing long-term BMI? Obesity 2007;15(5):1278–86.
37. Kunath J, Gunther J, Rauh K, Hoffmann J, Stecher L, Rosenfeld E, Kick L, Ulm K, Hauner H. Effects of a lifestyle intervention during pregnancy to prevent excessive gestational weight gain in routine care—the cluster-randomised GeliS trial. BMC Med 2019;17(1):5.
38. Bain E, Crane M, Tieu J, Han S, Crowther CA, Middleton P. Diet and exercise interventions for preventing gestational diabetes mellitus. Cochrane Database Syst Rev 2015(4):CD010443. doi: 10.1002/14651858.CD010443.pub2.
39. Shepherd E, Gomersall JC, Tieu J, Han S, Crowther CA, Middleton P. Combined diet and exercise interventions for preventing gestational diabetes mellitus. Cochrane Database Syst Rev 2017;11:CD010443.
40. Garmendia ML, Matus O, Mondschein S, Kusanovic JP. Gestational weight gain recommendations for Chilean women: a mathematical optimization approach. Public Health 2018;163:80–6.
41. Catalano P, deMouzon SH. Maternal obesity and metabolic risk to the offspring: why lifestyle interventions may have not achieved the desired outcomes. Int J Obes 2015;39(4):642–9.
42. Ma RCW, Schmidt MI, Tam WH, McIntyre HD, Catalano PM. Clinical management of pregnancy in the obese mother: before conception, during pregnancy, and post partum. Lancet Diabetes Endocrinol 2016;4(12):1037–49.
43. Government of Chile, Ministry of Health. Encuesta Nacional de Salud 2009-2010. Santiago; 2010.
44. Simmons D, Jelsma JG, Galjaard S, Devlieger R, van Assche A, Jans G, Corcoy R, Adelantado JM, Dunne F, Desoye G, et al. Results from a European multicenter randomized trial of physical activity and/or healthy eating to reduce the risk of gestational diabetes mellitus: The DALI Lifestyle Pilot. Dia Care 2015;38(9):1650–6.
45. Moll U, Olsson H, Landin-Olsson M. Impact of pregestational weight and weight gain during pregnancy on long-term risk for diseases. PLoS One 2017;12(1):e0168543.
46. Kahan BC, Forbes G, Ali Y, Jairath V, Bremner S, Harhay MO, Hooper R, Wright N, Eldridge SM, Leyrat C. Increased risk of type I errors in cluster randomised trials with small or medium numbers of clusters: a review, reanalysis, and simulation study. Trials 2016;17(1):438.