Original Article

Combined dietary-exercise intervention for gestational weight gain and birthweight: a meta-analysis

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Background and Objectives: Excessive gestational weight gain has been associated with higher risk for large for gestational age newborns. This systematic review and meta-analysis aims to assess whether an intensive diet and exercise intervention has an effect in reducing gestational weight gain and large for gestational age newborns. **Methods and Study Design:** The search was conducted on PubMed and Cochrane database. Through PRISMA flow diagram, clinical trials which met the inclusion criteria were selected. Risk of bias, sensitivity analysis, and quality of evidence assessment were conducted using adequate statistical tests, and the quality of evidence was performed by GRADE method. A random-effect model was used to estimate the statistical significance of the meta-analysis. **Results:** Ten clinical trials met the inclusion criteria. Using the random-effect model and a sensitivity analysis, it was found that an intensive patient-centered intervention reduced gestational weight gain when compared with standard prenatal care (Z=6.21 (p<0.00001); Tau²=0.00; Chi²=3.90, df=4 (p=0.42); I²=0%), and the quality of evidence was moderate. An intensive diet and exercise intervention decreased the number of large for gestational age newborns (Z=2.20 (p=0.03); Tau²=0.14; Chi²=7.84, df=4 (p=0.10); I²=49%), and the quality of evidence using the GRADE approach was moderate. **Conclusion:** The present review and meta-analysis indicates that an intensive diet and exercise intervention reduced gestational weight gain and large for gestational age newborns.

Key Words: gestational weight gain, RCT, diet and exercise interventions, large for gestational age, birthweight

INTRODUCTION

Maternal overweight and obesity, as well as excessive gestational weight gain (GWG), have been associated with higher risk for large for gestational age newborns (LGA),[1–3] postpartum weight retention,[4,5] caesarean delivery,[1,6] gestational diabetes,[7,8] preeclampsia,[1,5,6] and fetal and infant death.[8] A recent systematic review conducted in six studies showed a consistent association of excessive GWG and the development of offspring adiposity or other metabolic diseases early in life, during adolescence, or adulthood.[9] The mechanisms through which exposures in utero affect the metabolic outcomes of the offspring are not completely understood; however, evidence from epidemiological studies and animal models indicate that maternal undernutrition,[10,11] overnutrition, [10,11] and hormone imbalance[12] are critical factors in the process known as "intrauterine programming".[13] The anabolic hormone insulin is particularly relevant in this process, and is directly linked to maternal blood glucose levels;[10] other important hormones include growth hormone, insulin-like growth factors, catecholamines, thyroid hormones, and placental hormones.[12] During the postpartum period, the adipocyte derived hormones, interleukin-6 (IL-6),[14] adiponectin,[15] and leptin[15,16] are involved in satiety, insulin signalling, and adipogenesis;[15,16] additionally, they play a major role in "developmental programming".[16] Thus, prenatal maternal weight and GWG could interfere irreversibly in the development of organs involved in the control of food intake and metabolism, and may also influence the prevalence and severity of obesity and other metabolic diseases in future generations.

Target GWG for reducing poor maternal and infant outcomes has long been debated. In 2009, the Institute of Medicine (IOM) published revised recommendations using BMI cutpoints from the World Health Organization (eg, overweight=25.0-29.9 kg/m^2 instead of 26.0-29.9 kg/m^2), and added specific recommendations for women with BMI >30 kg/m^2, previously lacking from the 1990 guidelines.[17] Current IOM GWG recommendations for underweight mothers (BMI <18.5 kg/m^2), is 13-18 kg; for normal weight (BMI >18.5-24.9 kg/m^2), 11-16 kg; for overweight (BMI 25.0-29.9 kg/m^2), 7-11 kg; and for obese (BMI >30 kg/m^2), 5-9 kg.[17] Nevertheless, these new recommendations have given rise to controversial reactions from some experts who believe that the weight gain goals are too challenging, especially for overweight

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and obese women.[18]

Using the IOM guidelines for monitoring gestating women, the American College of Obstetricians and Gynecologists recommends determining a woman's BMI and discussing appropriate weight gain, diet, and exercise at the initial visit and periodically throughout the pregnancy.[18] Nevertheless, in the USA a study conducted by Langford et al reported that only 21% of pregnant women achieved the 2009 IOM recommendations.[6] Consequently, in the past few years several studies have been conducted to improve GWG outcomes to meet IOM criteria; a great number of randomized clinical trials (RCT) that compare standard prenatal care and a diet and exercise modification intervention have been developed. According to the current position of the Academy of Nutrition and Dietetics, intervention type and intensity seem to affect the efficacy of the programs; effective programs tended to last six weeks or longer, focus on improving both dietary intake and physical activity (PA) intensity, and actively engage women through routine monitoring of weight gain and/or food intake and PA intensity. Yet, this type of intensive diet and exercise intervention (IDEI) has not been isolated in any of the previous systematic reviews and meta-analysis. Therefore, the aim of this review was to analyse RCT using the 2009 IOM criteria for GWG and the 2016 Academy of Nutrition and Dietetics recommendations; furthermore, a meta-analysis was performed to assess the effect of the IDEI on GWG and LGA; we also compared those results with previous non-IDEI systematic reviews.

MATERIALS AND METHODS

Literature search strategy

We carried out a comprehensive search using PUBMED database with the following mesh terms: infant health, maternal health, overweight, birth weight, obesity, pregnancy, prenatal care, and randomized controlled trial. The reference lists of the retrieved studies were restricted by date (January 2008 to January 2016) and searched manually. In addition, the COCHRANE library was searched for systematic reviews and its reference list was also searched manually using the same restrictions as PUBMED. Our primary outcomes were: (a) large for gestational age newborns (defined as >90th percentile or >4000 g) and (b) gestational weight gain (GWG).

Selection criteria

Studies under consideration were evaluated independently for appropriateness of inclusion and methodological quality without consideration of their results by four authors (AJC, MB, PM, and ML), according to the PRISMA guidelines for systematic reviews of randomized trials. All published randomized controlled trials in which pregnant women received an IDEI (diet and exercise) and lasted more than 6 weeks/interventions were considered for inclusion. Excessive GWG was defined according to prevailing IOM guidelines. To ensure the quality of the systematic review, trials were excluded if they were: non-randomized, quasi-randomized controlled trials, those which lacked any of the outcomes evaluated, or if they were pilot studies.

Data extraction and quality assessment

Using Microsoft Excel®, we designed a spreadsheet to collect study data (Table 1). Thereafter, two review authors (PM, ML) independently extracted data from included studies and performed a risk of bias analysis for every study. The risk of bias analysis considered the generation of the randomization sequence (computer-generated sequence judged as low risk), allocation concealment (with central telephone randomization, website protected, unrelated study staff, or sealed opaque envelopes judged as low risk), blinding of outcome assessors (judged as low risk when present), statistical power (with >80% judged as low risk), retention rate (with <20% attrition judged as low risk), and intention to treat analysis (judged as low risk when present). Once the primary outcomes and the risk analysis of all studies were obtained, a discussion of the results was conducted; discrepancies were corrected using the original articles for reference. Data were entered into the Review Manager Software (RevMan 5.3.5) and SPSS v 21 (macro for Meta-regression by David B. Wilson) by both review authors (PM, ML). Results were independently evaluated for accuracy by two more authors (MB, AJ). To evaluate the quality of evidence, we used the GRADE approach for systematic reviews; two review authors independently evaluated each outcome for risk of bias, inconsistency, imprecision, indirectness, and publication bias. Results were later compared and reviewed by two additional authors (MB, AJ) and evidence was rated from high to very low.

Statistical analysis

The meta-analysis was performed using Revman 5.3.5 for our two primary outcomes: (a) LGA and (b) GWG. For the overall estimation of LGA infants' OR and 95% CI outcome, dichotomous data was used in an inverse variance statistical method. The combined risk estimates were calculated using the random-effect model. Results were graphed using a forest plot with a scale of 30.0. To obtain the second outcome (GWG), data was inputted to obtain standard mean difference using continuous data in an inverse variance statistical method and random effect model; a scale of 2.00 was used in a forest plot graphic. Differences with $p<0.05$ were considered significant. In each meta-analysis outcome, statistical heterogeneity was calculated using Tau², I² and Chi²; we regarded results as having substantial heterogeneity if there was an I² >25% with either a Tau² >zero, or a low p value (less than 0.10) in the Chi² test. Finally, sensitivity analyses were carried out to explore the effect of trial quality by excluding studies with risk of bias concerns. A meta-regression was performed to identify the factors that contribute to heterogeneity, isolating the factors BMI, percent of obese population, weeks of gestation at the beginning of the intervention, intervention duration, socioeconomic status among the studies, race, and age.

RESULTS

Literature search

As shown in Figure 1, 137 full text articles were obtained by searching PUBMED database, and 30 additional full text articles were identified through the 2015 Cochrane

Table 1. Characteristics of randomized controlled trials with ILI on GWG and LGA included in the systematic review

Author	Population criteria	N	Intervention	Initial BMI	Difference between groups; final BMI or GWG (Kg)	LGA or macrosomia	Quality risk of bias
Poston et al,[19] 2015 United Kingdom	Women >16 years with a BMI >30 kg/m² and a singleton pregnancy between 15-18.6 weeks of gestation. Individuals were excluded if they had underlying disorders, or if they were currently being prescribed metformin.	Total: 1555 SPC: 772 ILI: 783	SPC: Routine antenatal appointments at their trial center. ILI: Within 1 week of randomization, women attended an individual interview with a health trainer, and eight further health trainer-led group or individual sessions once a week for 8 weeks. They were also provided with a handbook, a DVD with recommendations and a pedometer.	SPC BMI: 36.3 (4.6) ILI BMI: 36.3 (5.0)	SPC GWG: 7.76 (4.6) ILI GWG: 7.19 (4.6) Mean difference 95% CI: -0.55 (-1.08 to -0.02), p=0.041*	SPC LGA: 8% ILI LGA: 9% OR (95% CI): 1.15 (0.83 to 1.59), p=0.40 IG >4000 g OR (95% CI): 0.99 (0.77–1.27), p=0.93	Randomization and intention to treat analysis Blinding not possible Allocation concealment unknown SP: 80% Maternal ReR: 82.3% Neonatal ReR: 97.8%
Dodd et al,[20] 2014 Australia	Women with BMI >25kg/m² and singleton pregnancy at 10-20 weeks gestation were eligible. Exclusion criteria: Women with type 1 or 2 diabetes diagnosed before pregnancy.	Total: 2212 SPC 1104 ILI: 1108	SPC: Local hospital guidelines. ILI: Combination of individualized dietary, physical activity and behavioral strategies at 2 and 28 weeks after randomization. Reinforcement by trained research assistants via telephone call at 22, 24, and 32 weeks of gestation and a face-to-face visit at 36 weeks of gestation.	SPC: BMI 31.1 (27.6-35.8) ILI: BMI 31.0 (28.0-35.9)	SPC GWG: 9.44 (5.77) ILI GWG: 9.39 (5.74) (95% CI): -0.04 (-0.55 to 0.48), p=0.89 SPC weekly WG: 0.45 ILI weekly WG: 0.45 (95% CI): 0.00 (-0.03 to 0.03), p=0.99	SPC LGA: 21% ILI LGA: 19% OR (95% CI): 0.90 (0.77-1.07), p=0.24 ILI > 4000 g, OR (95% CI): 0.82 (0.68-0.99), p=0.04*	Randomization, allocation concealment and blinding of outcome assessors SP: 80%, with 15% attrition ReR: 71.5% Intention to treat analysis
Vesco et al,[21] 2014 USA	English speaking women with BMI ≥30 kg/m², aged 18 years or older, up to 21 weeks gestation. Women were excluded if they required specialized nutritional care (for example, a history of bariatric surgery), or had plans to leave the area during the expected follow up period (through 1 year postpartum).	Total: 118 SPC: 60 ILI: 58	SPC: Received a one-time advice session from the study dietitian. ILI: Followed a DASH dietary pattern and ACOG physical recommendations (30min moderate PA per day), with individual sessions at 1st and 2nd week post randomization, followed by weekly group sessions (with a mean of 7.4 patients/session.)	SPC BMI: 36.8±4.7 ILI BMI: 36.7±5.2	SPC GWG (34 wks): 8.4±4.7 ILI GWG (34 wks): 5.0±4.1 Mean difference 95% CI: -3.4 (-5.1 to -1.8), p≤0.001* SCG weekly GWG: 0.44±0.2 IG weekly GWG: 0.3±0.2 Mean difference (95% CI): -0.2 (-0.3 to -0.1), p≤0.001*	SPC LGA: 26% ILI LGA: 9% Relative risk OR (95% CI): 0.28 (0.09-0.84), p=0.02* SPC>4000g: 22% ILI >4000g: 11% OR(95% CI): 0.42 (0.14-1.18), p=0.09*	Randomization and blinding Allocation concealment unknown. SP: 80%, alpha .05 ReR: 95% Intention to treat analysis

ILI: intensive lifestyle intervention; GWG: gestational weight gain; LGA: large for gestational age; N: number of population; BMI: body mass index; CI: confidence interval; LIE: low intensity exercise; MIE: moderate intensity exercise; OR: odds ratio; ReR: retention rate; SP: statistical power; SPC: Standard Prenatal Care; SD: standard deviation; WG: weight gain; DASH: dietary approaches to stop hypertension; ACOG: The American college of obstetricians and gynecologist; PA: physical activity; SOGC: The society of obstetricians and gynecologists of Canada; CAISM: Centro de atencao integral a saude da mulher; FCM: Food Choice Map; HR: heart rate; LI: low intensity; MI: moderate intensity. *Statistically significant. †p value was calculated using REVMAN 5.3.5.

Table 1. Characteristics of randomized controlled trials with ILI on GWG and LGA included in the systematic review (cont.)

Author	Population criteria	N	Intervention	Initial BMI	Difference between groups; final BMI or GWG (Kg)	LGA or macrosomia	Quality risk of bias
Hui,[22] 2011 Canada	No diabetic pregnant women (<26 weeks of pregnancy) living in Winnipeg. Applicants were excluded by physicians if they had medical or obstetric contraindications to exercise during pregnancy	Total: 224 SPC: 112 ILI: 112	SPC: Received standard prenatal care recommended by the SOGC. ILI: Exercise regimen, 3-5 times/week (including a weekly exercise session and multiple home sessions) of mild-to-moderate exercise for 30–45 min/session. Dietary interviews and counseling were provided twice to each participant by registered dietitians, the first at enrollment and the second 2 months after enrolment.	SPC BMI: 25.7±5.1 ILI BMI: 24.9±5.4	SPC GWG: 15.2±5.9 ILI GWG: 14.1±6.0 p=0.28	SPC: 17.0 % ILI: 11.8 % p=0.41	Computer generated randomization and allocation concealment Blinding of statisticians SP: 80%, 86/Group (alpha=0.05) ReR: 84.8% Intention to treat analysis not done.
Nascimento, [24] 2011 Brazil	Women with pre-gestational BMI categorized as overweight or obese, age ±18 years, and gestational age between 14 and 24 weeks. Exclusion criteria were multiple gestations, exercising regularly and conditions that contraindicate exercise.	Total: 82 SPC: 42 ILI: 40	SPC: Followed routine prenatal care advice. ILI: Exercise was performed by the women under the guidance of a trained physical therapist in weekly classes. The protocol consisted of light-intensity to moderate-intensity exercises. In addition, counseling on home exercise (to be performed five times a week) was given. Received standardized nutritional counseling from the Service of Nutrition and Dietetics (CAISM).	SPC BMI: 36.4±6.9 ILI BMI: 34.8±6.6 p=0.26	Final BMI ILI: 38.6±6.2 Final BMI SPC: 41.4±6.6 p=0.004* IG WG: 10.3±5.0 CG WG: 11.5±7.4 p=0.54	SPC: 24.2 % ILI: 24.2 % p=0.91†	Computer generated randomization, with allocation concealment SP: 70%, significance level 5% Intention to treat analysis ReR: 97%
Hui et al,[23] 2014 Canada	Less than 20 weeks of pregnancy, no existing diabetes during pregnancy. Exclusion criteria: existence of medical or obstetric contraindication for exercise during pregnancy.	Total: 113 CG: 56 IG: 67	SPC: Received standard prenatal care as by the SOGC. ILI: Received instructed exercise program in community based weekly classes 3-5 times a week. Consisted in mild-to-moderate aerobic exercise, stretching and strength exercise for 30-40 min/time. Alternatively, followed the exercise DVD instruction at home. Received one-on-one private dietary consultation at baseline and at two months after.	BMI<24.9: SPC: 22.6±1.9 ILI: 21.6±2.2 BMI >25: SPC: 29.7±1.3 ILI: 29.5±5.1	BMI <24.9: SPC: 16.23±4.38 ILI: 12.9±3.72 p=0.03* BMI >25: SPC: 14.39±7.05 ILI: 15.21±7.5 p=0.26	BMI <24.9: SPC: 11% ILI: 7% p=0.902 BMI >25: SPC: 3% ILI: 15% p=0.13	Study staff was not blinded. The statistical analysis was performed by a third party. Intention to treat analysis not needed. ReR: 100%
Sagedal et al,[27] 2016 Norway	Nulliparous women with a singleton pregnancy at ≤20 wks of gestation, pre-pregnancy BMI ≥19 kg/m^2. Exclusion criteria were pre-existing diabetes, disabilities, continued substance abuse, or planned relocation outside of the study area before delivery	Total: 606 SPC: 303 ILI: 303	SPC: Received routine prenatal care in accordance with Norwegian standards ILI: Dietary counseling was performed by telephone, with an initial consultation and then a follow-up 4–6 weeks later, each of approximately 20 minutes. The physical activity component consisted of access to twice-weekly exercise classes at a local gym facility.	SPC BMI: 23.5±3.7 ILI BMI: 23.8±4.1	SPC GWG: 15.8±5.7 ILI GWG: 14.4±6.2 95% CI (-2.4, -0.3) p=0.009*	LGA SPC: 3.7% LGA ILI: 2.4% 95% CI (0.24, 1.64) p=0.351	Computer-generated randomization with allocation concealment. Research assessors were blinded. SP: 80% ReR: 91.1% Intention to treat analysis

ILI: intensive lifestyle intervention; GWG: gestational weight gain; LGA: large for gestational age; N: number of population; BMI: body mass index; CI: confidence interval; LIE: low intensity exercise; MIE: moderate intensity exercise; OR: odds ratio; ReR: retention rate; SP: statistical power; SPC: Standard Prenatal Care; SD: standard deviation; WG: weight gain; DASH: dietary approaches to stop hypertension; ACOG: The American college of obstetricians and gynecologist; PA: physical activity; SOGC: The society of obstetricians and gynecologists of Canada; CAISM: Centro de atencao integral a saude da mulher; FCM: Food Choice Map; HR: heart rate; LI: low intensity; MI: moderate intensity. *Statistically significant. †p value was calculated using REVMAN 5.3.5.

Table 1. Characteristics of randomized controlled trials with ILI on GWG and LGA included in the systematic review (cont.)

Author	Population criteria	N	Intervention	Initial BMI	Difference between groups; final BMI or GWG (Kg)	LGA or macrosomia	Quality risk of bias
Althuizen,[25] 2012 Netherlands	Women were eligible for participation when they were: expecting their first child, able to read, write and speak Dutch, in the first 14 weeks of gestation.	Total: 246 SPC: 123 ILI: 123	SPC: Received routine prenatal care. ILI: The intervention program consists of 5 individual counselling modules together with a general information brochure. Women attended these counselling sessions over a period of 30 weeks. The counselling sessions aimed to balance optimize energy intake and physical activity	SPC BMI: 23.5±3.8 ILI BMI: 24.0±4.2	SPC GWG: 11.6±4.1 ILI GWG: 11.1±3.2 95% CI (1.10 to 1.00)	Macrosomia SPC: 14% ILI: 19% 95% CI (0.76–3.41)	Computer generated randomization with allocation concealment. SP: 80 % ReR: 89% Intention to treat analysis. Blinding unknown
Ruiz et al,[26] 2013 Spain	Women with singleton and uncomplicated gestation, not at high risk of preterm delivery, those who were sedentary (not exercising for >20 minutes on >3 days a week) and not participating in any other trial. Women with any obstetric contraindication to exercise were not eligible to participate in the study.	Total: 962 SPC: 481 ILI: 481	SPC: Received general nutrition and physical activity counseling from health care professionals. ILI: The women in this group received all aspects of standard care plus a structured, supervised, light- to moderate-intensity 50- to 55-minute exercise intervention program 3 days a week from week 9 to weeks 38 to 39.	SPC BMI: 23.7±0.9 ILI BMI: 23.5±4.2 p=0.35	SPC GWG: 13.2±4.3 ILI GWG: 11.9±3.8 95% CI (0.534 to 1.545) $p \leq 0.001^{*}$	Macrosomia SPC: 5.0% ILI: 2.1% 95% CI (0.165-0.751) p=0.007*	Computer generated randomization with allocation concealment Blinding not mentioned SP: > 90%, alpha.05 in a group of 393 participants. Intention to treat analysis ReR: 85.6%
Ruchat et al,[30] 2012 Canada	Normal-weight pregnant woman between 16 and 20 weeks gestation, and should not have participated in any structured exercise program during pregnancy. Exclusion criteria: maternal age <18 yrs. or >40 yrs., smoking, multiple pregnancy, presence of chronic disease, or other contraindication to exercise.	Total: 94 SPC: 45 ILI: 49	SPC: received routine prenatal care. ILI: Walked at their calculated target HR zone of 70% heart rate reserve three to four times per week (participants wore a HR monitor to ensure they were exercising within the predetermined target HR). The participants were expected to complete an additional two to three exercise sessions by their own. Each participant followed a modified gestational diabetes meal plan to control nutritional intake.	SPC BMI: 22.4±1.9 ILI BMI: MIE: 21.7±1.9 LIE: 22.1±1.7	SPC GWG: 18.3±5.3 ILI MIE GWG: 14.9±3.8, p=0.003* ILI LIE GWG: 15.3±2.9, p=0.01*	Macrosomia SPC: 6.6% ILI MIE: 11.5% ILI LIE: 8.7%	Randomized block procedure Allocation concealment and blinding not mentioned Per-protocol analysis SP not mentioned ReR: 67%

ILI: intensive lifestyle intervention; GWG: gestational weight gain; LGA: large for gestational age; N: number of population; BMI: body mass index; CI: confidence interval; LIE: low intensity exercise; MIE: moderate intensity exersice; OR: odds ratio; ReR: retention rate; SP: statistical power; SPC: Standard Prenatal Care;SD: standard deviation; WG: weight gain; DASH: dietary approaches to stop hypertension; ACOG: The American college of obstetricians and gynecologist; PA: physical activity; SOGC: The society of obstetricians and gynecologists of Canada; CAISM: Centro de atencao integral a saude da mulher; FCM: Food Choice Map; HR: heart rate; LI: low intensity; MI: moderate intensity.*Statistically significant. †p value was calculated using REVMAN 5.3.5.

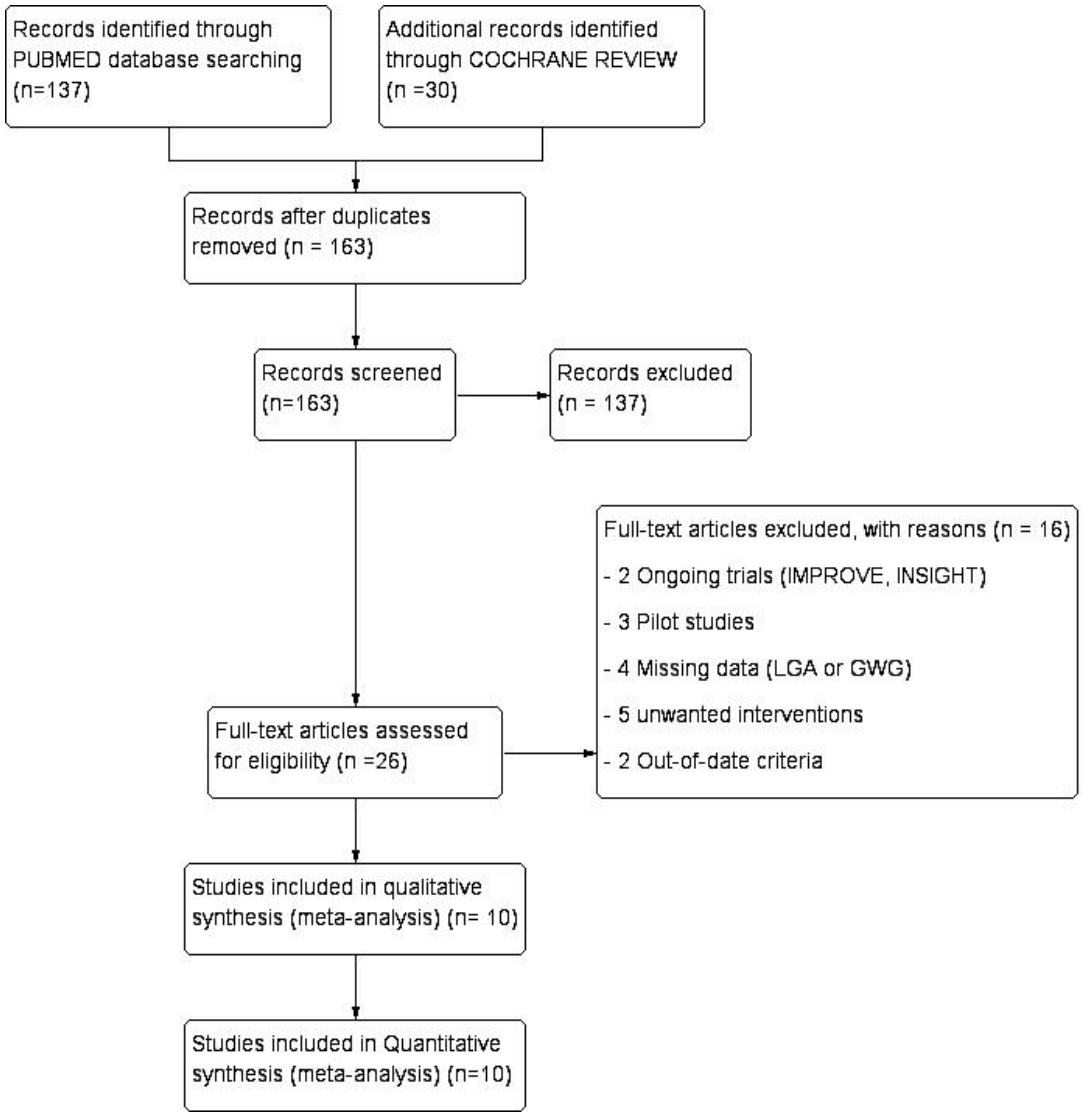

Figure 1. Systematic review flow diagram.

review. After excluding 4 duplicates, 163 records were identified for title and abstract revision. Of the 163 articles screened, 137 were excluded because they weren't randomized controlled trials, leaving 26 articles for full text revision. Of those, two were excluded because they were ongoing trials (IMPROVE, INSIGHT); three were pilot studies; five had unwanted interventions (not IDEI); two used previous IOM criteria; and four potential studies had missing data (GWG or LGA). To deal with missing data we contacted the authors through Researchgate, but there was no response. Therefore, at the end of the selection process, ten studies met the inclusion criteria and were included in the systematic review and meta-analysis. The characteristics of the studies are shown in Table 1.

Systematic review: risk of bias

The generation of the randomization sequence using computer software was clearly stated for nine[19–27] of the ten trials, and all were judged as having a low risk of bias. Of the ten studies, allocation concealment was adequate in nine by means of opaque envelopes,[24] conducted by staff without involvement in the study,[20,22,23,28] using a password protected website,[19] and through computed randomized assignment;[21,25-27] any of these methods were adequate for low risk of bias. Blinding of participants and caregivers was not possible given the nature of the study, and the overall effect of this deficiency was considered as an unclear risk. The blinding of outcome assessors was achieved by four studies,[20-23] and the rest were classified as high risk. A greater than 80% retention rate was achieved in eight studies,[19,21-27] and eight studies used intention to treat analysis in their outcomes;[19-21,23-27] in both cases the studies lacking these conditions were classified as high risk or unclear. Due to the above mentioned analysis it was concluded that the quality of evidence resulting from this review was moderate.

Meta-analysis: participants

The total number of participants involved in the meta-analysis was 6164 pregnant women, and the number of participants in each study ranged from 82[24] to 2212.[20] Most studies were conducted in high-income countries, including Australia,[20] Canada,[22,23] United Kingdom,[19] United States,[21] Norway,[27] The Netherlands,[25] Germany,[28] Spain,[26] and Brazil, a leading economy in the developing world.[24] All studies reported age and initial body mass index (BMI) at baseline and these were similar between study and control groups. Socioeconomic status and/or

level of education was reported in eight[19-21,23-27] out of the ten studies, most of which included a population with a predominantly low- or middle-income socioeconomic status.[19,22,23,25,26,29] Race distribution was reported in seven studies, with comparable allocation in the groups. The overall population had the following distribution: White (73.4%), Asian (3.71%), Indian (0.83%), Canadian Aboriginal (1.22%), Black (9.63%), other (4.19%), and unknown (6.99%). Smoking history was reported in four of the included studies,[19-21,27] with similar distribution between groups. Most studies recruited women with less than 21 weeks of gestation (80.0%); one study enrolled women before 14 weeks of gestation,[26] and one before 5 weeks of gestation.[25] All included studies used the BMI cutpoints from the 2009 IOM guidelines. Five of the included studies were conducted in women from all BMI cutpoints,[22,23,25-27] two studies were conducted in overweight and obese women,[20,24]two studies recruited strictly obese women,[19,21] and one recruited strictly normal BMI women.[30]

Interventions

The diet and exercise interventions included in this review followed the recommendations established by the United Kingdom Royal College of Obstetricians and Gynecologists,[19,20] American College of Obstetricians and Gynecologists,[21,24,26]American Centers for Disease Control and Prevention,[25]American College of Sports Medicine,[30] Society of Obstetricians and Gynecologists of Canada,[28,29] Health Canada,[22] Canadian Medical Association Institute,[23] Dutch Nutrition Center,[25] and the Australian Department of Health.[20] The interventions were designed using four main components: (1) shaping behaviour by providing knowledge of a healthy diet and recommended physical activity; (2) setting behavioral goals based on the baseline situation (BMI, diet, physical activity) and the individual preferences of the women; (3) prompting self-monitoring of behaviour by recording diet and physical activity in a log book, software, or other means; and (4) providing constant assessment of participants and intervention reinforcement. All intervention programs had six or more encounters with participants, lasted six weeks or longer, focused on improving both dietary intake and PA intensity, and actively engaged women through routine monitoring of weight gain and/or food intake and PA.[19-27,30] In addition to the individualized sessions, the intervention included weekly group supervised meetings in five clinical trials,[19,21-24] which were not necessarily led by health-care professionals. The group meetings were designed to monitor and provide social reinforcement throughout the pregnancy by discussing potential barriers, solving problems, and providing feedback to participants.

Outcomes

Using an inverse variance statistical method with random effect model, it was found that an IDEI involving diet and exercise during pregnancy had a statistically significant reduced amount of GWG when compared with standard prenatal care (Z=3.15 (p=0.002);Tau²=0.03; Chi²=38.2, df=9 (p<0.0001); I²=76%)(Figure 2). The heterogeneity of the results was reduced after studies with interventions up to 34 weeks of gestational age[21] (Z=2.72 (p=0.007); Tau²=0.02; Chi²=27.5, df=8 (p=0.0006); I²=71%), studies measuring GWG at 36 weeks of gestation,[20,24,25] and those without registered GWG at 36 weeks were excluded[19] (Z=6.21 (p<0.00001); Tau²=0.00; Chi²=3.90, df=4 (p=0.42); I²=0%). After conducting Meta-regression including the ten studies, no statistically significant value was found for any of the variables studied. Using the GRADE approach it was found that the quality of evidence was moderate.

Using an inverse variance statistical method with random effect model, we found that an IDEI involving diet modification and exercise during pregnancy decreased the number of LGA newborns when compared with standard prenatal care; however, the results were not statistically significant (Z=1.30 (p=0.19); Tau²=0.06; Chi²=14.7, df=9 (p=0.10); I²=39%). A further sensitivity analysis (Figure 3), including studies in which the introduction of intervention began closest to conception and ended at or near delivery, was conducted. Studies in which the length of intervention did not include women with less than 16 weeks of gestation and/or continued towards the delivery date were excluded; thus, only interventions lasting at least 20 weeks of pregnancy were included.[20,21,26,27,30] The analysis included 3880 pregnant women, with a statistically significant reduction in the number of LGA events compared with standard prenatal care (Z=2.20(p=0.03); Tau²=0.14; Chi²=7.84, df=4 (p=0.10); I²=49%). The heterogeneity was further reduced when only interventions that continued toward delivery were included (Z=3.31 (p=0.0009); Tau²=0.00; Chi²=1.27, df=3 (p=0.74); I²=0%).[21,26,27,30] Using the GRADE approach it was found that the quality of the evidence was moderate.

DISCUSSION

This review shows that an IDEI during pregnancy reduces GWG with a level of evidence from moderate to high. All studies included were RCT conducted across different nations, mostly developed countries. The risk of bias evaluation was low to moderate risk in most studies, and the interventions were all based on accepted guidelines from different national organizations. The magnitude of total effect involving GWG was moderately heterogeneous due to many factors, including the initiation period of the intervention, different types of participants according to BMI status, socioeconomic status, parity, timing and periodicity of the measurements, etc. In addition, the results of the meta-analysis and sensitivity analysis indicate that IDEI during pregnancy reduced GWG. The direction of treatment effect favouring IDEI to reduce GWG was consistent throughout the trials, except for Althuizen et al.[25] However, a sensitivity analysis was conducted to isolate these factors resulting in low heterogeneity of results.

Multiple studies conducted in animal models have shown a strong association between metabolic disturbance exposure in utero and subsequent offspring development of obesity and metabolic disorders, even with adequate birthweight infants.[11] In a recent systematic review,[31] a strong association between healthcare cost and BMI (p<0.001) was observed. Among children born to obese mothers (RR: 1.72, 95% CI 1.71 to 1.73), the cost

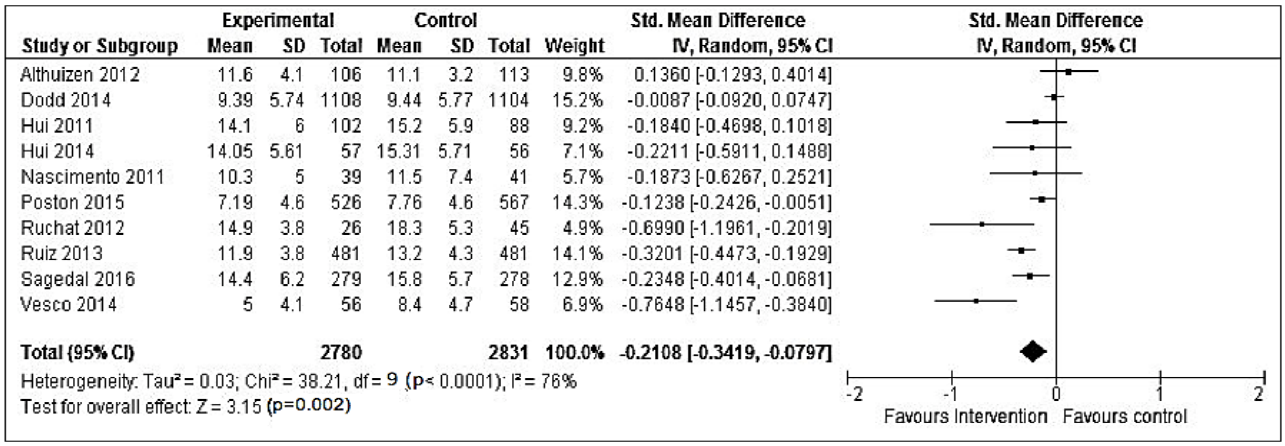

Figure 2. Forest plot of mean gestational weight gain comparison. Squares indicate the study-specific effect size (ES) derived from comparison between IDEI and standard prenatal care (size of square reflects the study's statistical weight); horizontal lines indicate 95% confidence interval; diamond indicates the summary effect size estimate with its corresponding 95% confidence interval.

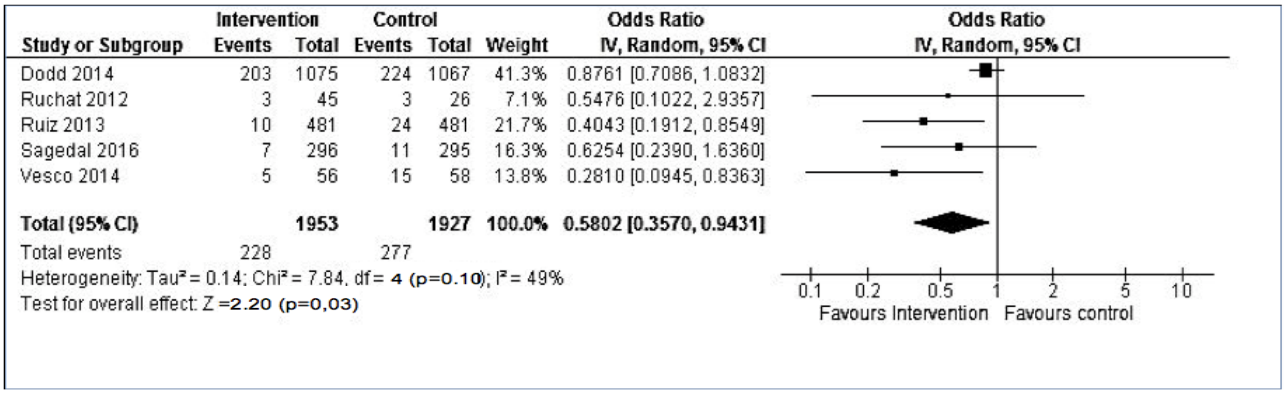

Figure 3. Forest plot of OR for large for gestational age newborns. Squares indicate the study-specific effect size (ES) derived from comparison between IDEI and standard prenatal care (size of square reflects the study's statistical weight); horizontal lines indicate 95% confidence interval; diamond indicates the summary effect size estimate with its corresponding 95% confidence interval.

of care was 72% higher, compared with infants born to healthy weight mothers.[31] Therefore, the reduction of GWG might result in lower incidence of the components of the metabolic syndrome among their offspring.[5-7,12]

In addition, among the studies included in this review, fewer LGA newborns were seen, but no statistical significance was observed. Nevertheless, the sensitivity analysis carried out showed a statistically significant variation in the number of events between control and intervention groups. This finding is inconsistent with previous meta-analysis and systematic reviews from Cochrane[24] and Dodd et al,[23] which might be due to the inclusion in the former reviews of non-IDEI studies with heterogeneous length of interventions, as well as studies with different GWG criteria.

Among the limitations of this review is the setting in which most studies were conducted. The majority of studies include mostly white, low or middle-income women from developed countries. Hispanics were not included in any of the clinical trials, although one study from Spain[32] and one from Brazil[24] was included. However, IDEI during pregnancy is seldom conducted in developed countries.[32] Further and more homogeneous studies are warranted in different sanitary systems, different settings of developing countries, and in populations with different levels of education, SES, and lacking or with limited universal health care.

The strength of this study is that only studies meeting the 2009 IOM recommendations were analysed, thus making it more homogeneous; in addition, a Meta regression was conducted in an attempt to isolate the factors that make the studies more heterogeneous.

Conclusion

In conclusion, this review from RCT, compared with the IOM 2009 recommendations, provides evidence that supports the use of IDEI as an approach to reduce excessive GWG and LGA infants. This indicates that IDEI might be a helpful strategy to prevent future obesity and other components of metabolic syndrome in newborns.

AUTHOR DISCLOSURES

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