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REVIEW ARTICLE

Obstetrics

The effect of weight loss interventions for obesity on fertility and pregnancy outcomes: A systematic review and meta-analysis

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Abstract

Background: Weight loss could improve fertility, perhaps by reducing insulin resistance.

Objectives: To assess the effect of weight loss interventions on fertility in women with obesity not recruited because of known infertility.

Search Strategy: Three databases during 1966–2020, trial registry.

Selection Criteria: Randomized controlled trials (RCTs) with a follow-up of 1 year or more, with a mean cohort BMI of 30 kg/m^2 or above.

Data Collection and Analysis: A systematic review and meta-analysis was conducted. The primary outcome was pregnancy. The secondary outcome was weight change.

Main Results: A total of 27 RCTs (5938 women) were included. Weight loss interventions showed no statistically significant increase in pregnancies compared to control interventions (24 trials, 97 women with pregnancy; risk ratio [RR] 1.43, 95% confidence interval [CI] 0.91–2.23); weight change (mean difference [MD] −2.36 kg, 21 trials, 95% CI −3.17 to −1.55). Compared with low-fat diets, very-low-carbohydrate diets showed no statistically significant effect on women with pregnancy (three trials, 14 women with pregnancy; RR 1.37, 95% CI 0.49–3.84) or weight change (MD −0.32 kg, 95% CI −3.84 to 3.21).

Conclusions: Diet-based weight loss interventions for women with obesity not recruited because of infertility were effective at producing long-term weight loss. The effects on fertility were not statistically significant, but few trials provided data. Weight loss trials should routinely collect fertility outcomes.

Systematic review registration: PROSPERO CRD42017078819.

KEYWORDS
fertility, low-fat diet, obesity, pregnancy, reducing diet, very-low-carbohydrate diet, weight loss

1 | INTRODUCTION

The prevalence of obesity among women of reproductive age is rising globally, with around 20% of women estimated to be obese by 2025.[1] Many leading societies of reproductive medicine promote weight loss as a means of improving fertility in women who are overweight or obese,[2] with a recent publication from the International Federation of Gynecology and Obstetrics (FIGO) recommending greater emphasis on the risks of obesity and the promotion of weight loss in the preconception period.[3] Weight loss interventions are a cost-effective way of managing obesity at a national level.[4] However, the FIGO Committee have identified a lack of translation of preconception guidelines into clinical and public health practice. Randomized controlled trials (RCTs) supporting weight loss as a means to increase pregnancies are limited to a few trials in women with known infertility.[5] It is believed that there are currently no RCTs that specifically examine the effect of weight loss for obesity on fertility for women more generally.

Long-term RCTs of weight loss interventions for adults with obesity were systematically reviewed to examine their effects on fertility as measured by women with new pregnancies. In addition, very-low-carbohydrate diets were compared to low-fat diet interventions, since low-carbohydrate diets may decrease insulin resistance, which has been suggested to improve fertility.[6]

2 | MATERIALS AND METHODS

The study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews of interventions.[7] We used a pre-specified protocol, registered with PROSPERO (No. CRD42017078819).

The included trial cohorts had a mean body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) of 30 or higher, and all participants were aged 18 years and older. Trials undertaken in cohorts of immediately pre- or postnatal women, or in women with known fertility issues, or conditions known to influence fertility, such as polycystic ovarian syndrome, were excluded. Thus, trials of weight loss interventions undertaken exclusively in cohorts of women undergoing fertility treatment or recruited with conditions known to affect fertility, and thus with fertility as a main outcome, were not included in this systematic review. The aim of the present review was to identify drop-outs or losses to follow-up due to pregnancies in weight loss trials in the general population with obesity. Such trials have not been included in previous systematic reviews.

RCTs with a follow-up duration of 1 year or more were included, with interventions focused clearly on weight loss. The main analysis of the present review was of any trials with a weight-reducing diet component or dietary advice, with or without advice for increasing physical activity and/or provision of a physical activity program, on women with new pregnancies, when compared with controls.

The secondary analysis included RCTs that compared a low-fat diet-based intervention (≤30% daily calorie intake from fat) compared with a low-carbohydrate diet (<40 g/day).

The primary outcome was women with pregnancy. Although pregnancy data were sought as outcomes in trials in the searches and trial register, these were only identified as drop-outs or losses to follow-up as indicated in the texts of trials and/or participant flow diagrams. Live birth data were also sought, but none were found. Denominators were adjusted for the number of women randomized in the trials. The authors of 33 RCTs were contacted to clarify data or to request unpublished outcome data, for example, where the trial reported participant drop-out due to pregnancy and the intervention group from which these drop-outs occurred was not given. The secondary outcome was weight change at final follow-up.

Studies were identified by searching the full texts of trial reports in our database of all long-term (≥1 year) RCTs of weight loss interventions for adults with obesity used in our previous systematic reviews and health technology assessments. The study database was derived from previous search strategies compiled from Medline, Embase, and the Cochrane Central Register of Controlled Trials, from 1966 to August 2017.[4,8] Additional studies were identified through review of the references of the retrieved articles. An updated search was undertaken for the years 2017 to 2020. No language exclusions were applied. The search strategy used for Medline and Embase is provided in Appendx S1.

Information collected from the studies included study location, inclusion criteria, intervention descriptions, attrition rate, and length of follow-up. The demographic data of participants were collected, including age, ethnicity, and baseline BMI. A copy of the data extraction form has been included in Appendix S1.

Data were imported into Review Manager version 5.4.1 (The Cochrane Collaboration) for quantitative analysis. In the three cluster RCTs,[9–11] adjustments were made for interclass correlation coefficients.[12] Not all trials provided data that could be used for the meta-analyses on weight change.

A random effects meta-analysis was used for pregnancy outcome data, expressed as risk ratios (RRs) and 95% confidence intervals (CIs), using all female participants randomized for denominators. Mean differences (MD) and 95% CI were estimated for continuous outcomes, giving preference to intention-to-treat data and data taking account of drop-outs. Heterogeneity was assessed between studies using the I^2 test,[12] where substantial heterogeneity was assessed as 50% or more. Since pregnancy outcome data were few, a Bayesian logistic regression model (with non-informative priors) was used with WinBUGS 1.4.319 to assess whether results from the meta-analyses would differ. A funnel plot and Egger's test[13] were used to assess for small study bias in the primary outcome women with pregnancy for interventions versus control, for which we had the largest number of trials. Subgroup analyses were undertaken for weight loss interventions versus control by type of intervention and BMI (≥35 vs. <35). It was planned to look at the effect of age (≥30 years <30 years), but only one trial had a mean age for all participants aged under 30 years at baseline, so this was not undertaken.

The influence of attrition bias (low risk vs. unclear/high risk) was also examined for weight loss interventions versus control and women with pregnancy. Subgroup analyses for attrition bias and type of intervention were post hoc.

3 | RESULTS

Details of the selection process for the 27 included RCTs are summarized in Figure S1. Of the 33 study authors contacted, five provided further information and were included in the review.

Full details of the included studies and interventions can be found in Table S1. Sixteen studies were undertaken in the United States,[9,14–28] two in the UK,[10,29] two in Canada,[11,30] and one each in Australia,[31] Sweden,[32] and Qatar.[33] One RCT was conducted across centers in Germany, the UK, and Australia.[34] Enrolment ranged from 30 participants[32] to 919 participants.[11] Attrition ranged from 2.3%[10] to 53.4%.[31]

The mean age of study groups ranged from 29.4 years[26] to 52.5 years.[10] The mean baseline BMI was 35 or more in nine trials,[9,14–16,18,20,23,26,28] and the highest mean BMI was 39.2.[18] Seven trials recruited participants with obesity-related co-morbidities; three included participants with type 2 diabetes or pre-diabetes,[10,17,33] one trial recruited those with two or more components of the metabolic syndrome,[28] one or more risk factor for coronary heart disease,[23] or one or more risk factor for obesity-related disease.[15,34] One trial was undertaken in a cohort of patients with a diagnosis of serious mental illness.[16]

All trials of weight loss interventions compared to minimal intervention or control had a reducing-diet component, and 12 trials described a diet low in fat with seven providing a specified limit of 30% or less total energy.[16,21,22,26–28,33] Nine trials provided participants with specific calorie intake goals, either a calorie deficit of 500 kcal/day[24,27,31,32] or a limit of 1200–1800 kcal/day to achieve a deficit based on weight at baseline.[20–22,28] The intervention by Taheri et al.[33] was a very low-calorie diet, with participants receiving Cambridge Weight Plan meal replacement products to achieve a daily calorie intake of 800–820 kcal/day. Three trials provided participants with access to commercial weight loss programs (Weightwatchers and Jenny Craig).[21,22,34]

Interventions in all but one trial[11] described promoting physical activity and typically described physical activity goals of more than 150 minutes/week or a daily count of more than 10 000 steps. Three trials included a supervised exercise component in their intervention.[9,16,33] The reducing-diet component was delivered by regular in-person or telephone educational sessions with a trained interventionist in most trials. In six trials, the interventions were primarily digital-based, delivered remotely through a personalized website,[29] smartphone application,[26,31] or through text and multimedia messages.[17,19,24] Where described, the coaching content of educational sessions focused on common behavior change techniques such as goal-setting, identifying barriers to change,[11] and self-monitoring.[20,27,33] Coaching styles, where described, included motivational interviewing[18,25,30] and behavioral counseling,[34] using conceptual frameworks including social cognitive theory,[18,19,24,26,30,31] behavioral self-management,[28] the stages-of-change model,[16] and the transtheoretical model of behavior change.[20,23,26]

Details of the three RCTs comparing low-fat and very-low-carbohydrate diet interventions are included in Table S1. Two trials were undertaken in the United States[35,36] and one in Israel.[37] The mean age of the study groups ranged from 45.5 years[36] to 56 years.[37] The mean baseline BMI was above 35 in two trials,[35,36] and the highest mean BMI was 36.1.[36] One trial recruited participants with type 2 diabetes.[37]

In all three trials, participants in the low-fat diet intervention were instructed to restrict fat intake to less than 30% of daily energy intake. Two trials included a calorie intake goal of 1200–1800 kcal/day based on gender in the low-fat diet intervention.[36,37] The very-low-carbohydrate diet interventions varied. Bazzano et al.[35] maintained a daily carbohydrate limit of 40 g throughout the 12-month intervention period, and participants in both groups received one meal replacement product per day to supplement their assigned diet. In the trials by Foster et al.[36] and Goldstein et al.[37] participants underwent an induction period with a daily carbohydrate limit of 20–25 g. This was increased to 40 g/day after 6 weeks,[36] or by 5 g/day until the desired weight was achieved.[37] In all trials, participants received regular in-person nutrition counseling with a dietician. Bazzano et al.[35] instructed participants at baseline to maintain their level of physical activity throughout the study, whereas Foster et al.[36] included advice regarding physical activity in their interventions.

The risk of bias assessment for the 27 RCTs is included in Table S2. The trials were of variable quality and, as expected, all trials were judged to be at high risk of performance bias. Of the 27 RCTs, 10 were judged to be at low risk of bias in four or more domains. Two trials were judged to have a low risk of bias in just one domain[22,27] and one trial was unclear or had a high risk of bias in all domains.[32] Five trials[16,21,22,24,27] were judged to be at high risk of other biases due to sponsorships and/or company funding. In total, 15 trials had a high or unclear risk for incomplete outcome data due to high numbers of drop-outs and/or imbalances in the final numbers.

The present meta-analysis of 24 RCTs including 5549 women showed a non-significant increase in women with pregnancies associated with weight loss interventions (n = 24 trials, 97 events, RR 1.43, 95% CI 0.91–2.23, I^2 = 0%) (Figure 1), with pregnancy rates of 68/3182 (2.1%) versus 29/2367 (1.2%). A visual inspection of the funnel plot did not suggest small study bias, and Egger's test was not statistically significant (P = 0.907) (Figure S2).

A meta-analysis of 21 RCTs for which reliable weight data were available showed that weight loss interventions led to significant weight change, with a MD of −2.36 kg compared to control groups at the final follow-up (n = 21 trials, MD −2.36 kg, 95% CI −3.17 to −1.55) (Figure 2).

There was substantial heterogeneity in weight lost (I^2 = 77%). The greatest weight loss difference was seen in the trial by Taheri et al.[33] (MD −8.00 kg, 95% CI −10.51 to −5.49), whose intervention

Study or Subgroup	Weight loss Events	Weight loss Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bacon 2002	1	39	0	39	2.0%	3.00 [0.13, 71.46]
Bennett 2018	0	120	1	119	1.9%	0.33 [0.01, 8.03]
Berry 2014	8	119	3	104	11.7%	2.33 [0.63, 8.56]
Bhopal 2014	0	46	2	47	2.2%	0.20 [0.01, 4.14]
Daumit 2013	1	74	1	72	2.6%	0.97 [0.06, 15.26]
Duncan 2020	1	57	0	25	2.0%	1.34 [0.06, 31.92]
Fischer 2016	3	55	2	64	6.4%	1.75 [0.30, 10.07]
Fitzgibbon 2010	2	107	1	106	3.5%	1.98 [0.18, 21.52]
Godino 2019	1	150	2	78	3.5%	0.26 [0.02, 2.82]
Jebb 2011	8	330	0	338	2.4%	17.41 [1.01, 300.44]
Jenkins 2017	4	361	5	405	11.6%	0.90 [0.24, 3.32]
McConnon 2007	2	85	2	85	5.3%	1.00 [0.14, 6.94]
Ost 1976	0	15	1	15	2.0%	0.33 [0.01, 7.58]
Perri 2014	4	341	1	138	4.2%	1.62 [0.18, 14.35]
Rock 2007	1	35	0	35	2.0%	3.00 [0.13, 71.22]
Rock 2010	10	333	0	113	2.5%	7.17 [0.42, 121.35]
Rosas 2015	1	127	1	32	2.6%	0.25 [0.02, 3.92]
Ross 2010	4	175	2	169	7.0%	1.93 [0.36, 10.41]
Shapiro 2012	3	54	0	57	2.3%	7.38 [0.39, 139.65]
Steinberg 2014	3	97	3	97	8.0%	1.00 [0.21, 4.83]
Svetkey 2015	8	169	2	85	8.5%	2.01 [0.44, 9.27]
Taheri 2020	1	21	0	19	2.0%	2.73 [0.12, 63.19]
Trepanowski 2017	1	59	0	27	2.0%	1.40 [0.06, 33.30]
Wadden 2011	1	213	0	98	1.9%	1.39 [0.06, 33.77]
Total (95% CI)		**3182**		**2367**	**100.0%**	**1.43 [0.91, 2.23]**
Total events	68		29			

Heterogeneity: Tau² = 0.00; Chi² = 14.97, df = 23 (P = 0.90); I² = 0%
Test for overall effect: Z = 1.57 (P = 0.12)

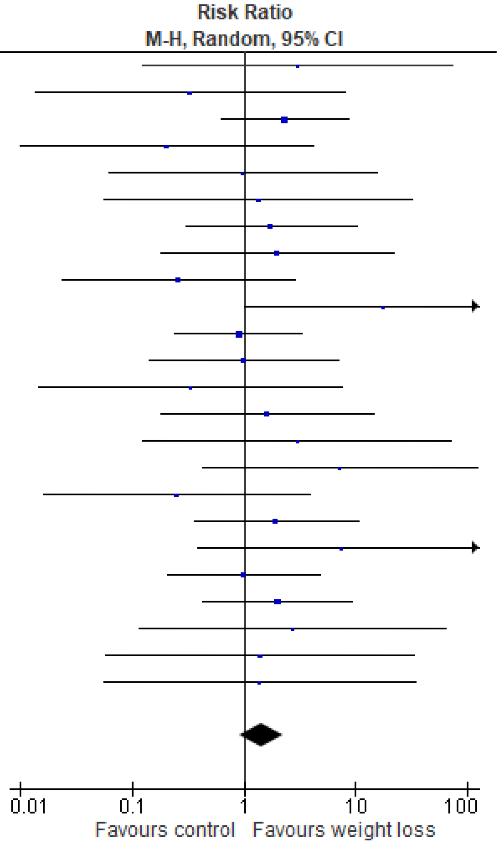

FIGURE 1 Forest plot. Women with pregnancies associated with diet-based weight loss interventions versus control. CI, confidence interval.

involved a 12-week very-low-calorie total diet replacement phase (800–820 kcal/day) with a physical activity program to attend followed by a hypocaloric diet for 9 months. Similarly, the trials by Rock et al.[21,22] in which participants were randomized to a commercial weight loss program and received meal replacement products to supplement a hypocaloric diet with physical activity advice, reported MDs of −5.90 kg and −4.80 kg compared to control groups.

Figures S3 and S4 explore the influence of the types of intervention, that is, whether there was an exercise program to attend or just advice, and the stringency of the prescribed calorie content. Figure S3 showed no statistically significant differences for subgroups and women with pregnancy, whereas Figure S4 suggests that interventions with very low-calorie diets or meal provision, and supervised exercise, could enhance long-term weight loss. Figures S5 and S6 show no statistically significant difference in the response for women with pregnancy or weight change by initial mean BMI at baseline, although the baseline BMI reflects entire trial cohorts.

Figure S7 explores the effect of attrition bias (low risk vs. unclear/high risk) for women with pregnancy from weight loss interventions versus control. The risk ratio for women with pregnancy is 1.10 (95% CI 0.55–2.20) for 10 low-risk trials, compared to 1.71 (95% CI 0.91–2.23) for 14 unclear or high-risk trials, but the statistical testing for subgroup differences was not significant ($P = 0.54$).

The results of the meta-analysis of an association between low-carbohydrate diet-based weight loss interventions and women with pregnancy ($n = 3$ trials, 14 events, RR 1.37, 95% CI 0.49–3.84) was not statistically significant with low heterogeneity ($I^2 = 0\%$) (Figure 3).

For the secondary outcome of weight change at follow-up, the present meta-analysis shows that participants randomized to a low-carbohydrate diet intervention lost marginally more weight than those randomized to a low-fat diet (MD for weight change −0.32 kg, 95% CI −3.84 to 3.21), but there was marked heterogeneity ($I^2 = 82\%$) (Figure 4). The trial by Bazzano et al.[35] reported significantly greater weight change in the very-low-carbohydrate intervention group compared to the low-fat group, with a MD of −3.50 kg (95% CI −5.62 to −1.38).

Results from the Bayesian analyses for pregnancy outcomes did not differ from those presented here.

4 | DISCUSSION

It was discovered that weight loss interventions with a reducing-diet component were associated with increased pregnancies in women with obesity (RR 1.43, 95% CI 0.91–2.23). However, this was not statistically significant despite significant long-term weight loss. Trials of weight loss interventions in groups of women actively trying to become pregnant or undergoing fertility treatments, such as IVF, were not included in the present analysis since these have been covered by other systematic reviews, and the outcome measures of all

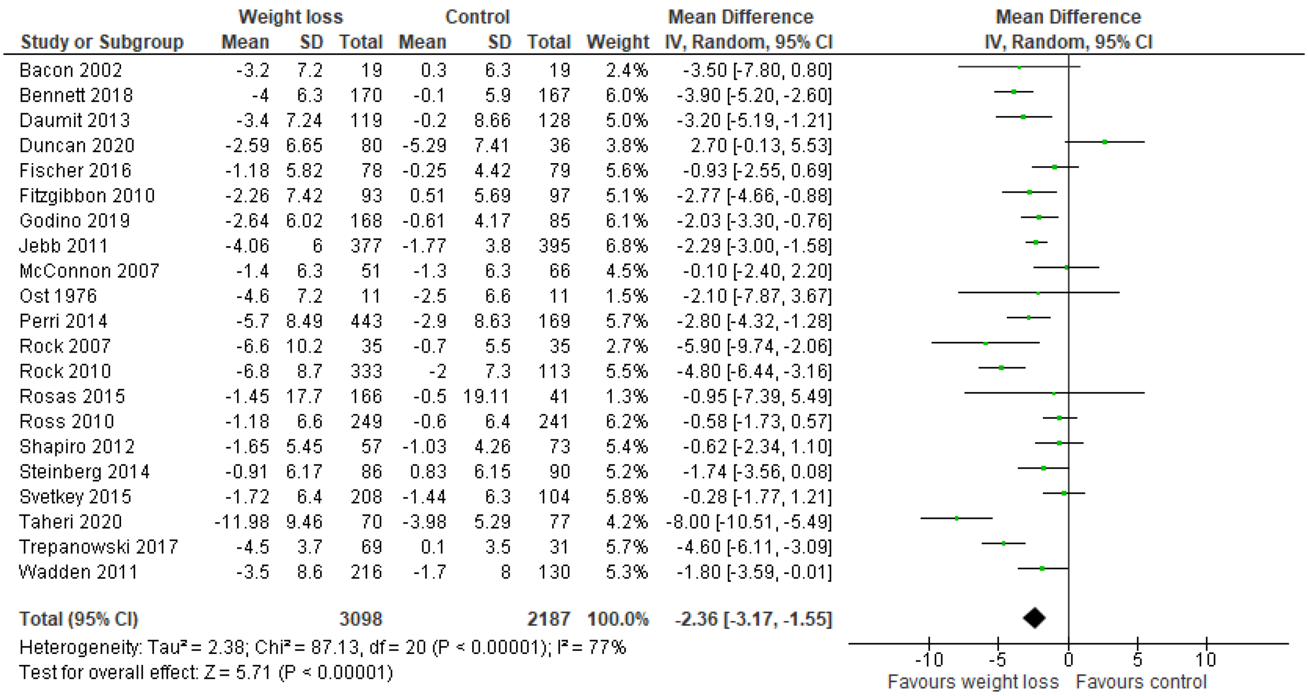

FIGURE 2 Forest plot. Intervention versus control: change in weight (kg). CI, confidence interval; SD, standard deviation.

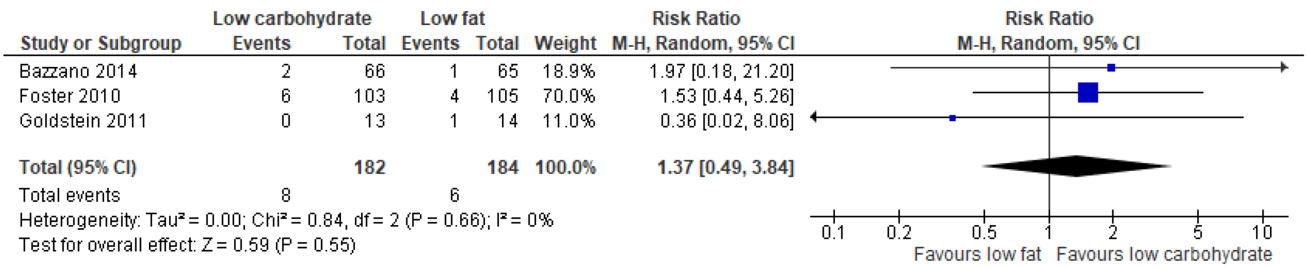

FIGURE 3 Forest plot. Women with pregnancies associated with very-low-carbohydrate versus low-fat diet interventions. CI, confidence interval.

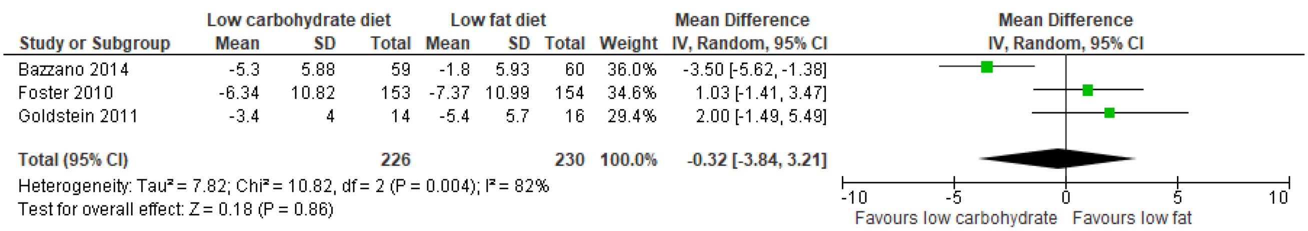

FIGURE 4 Forest plot. Very-low-carbohydrate diet versus low-fat diet interventions: weight change (kg). CI, confidence interval; SD, standard deviation.

included trials were primarily related to weight change and cardiovascular health.

Most dietary interventions used were based on caloric restriction. The highest fertility rate of 6.7% (8/119) was in the intervention by Berry et al.[9] which consisted of weekly in-person educational sessions on nutrition and exercise with no specified calorie limit. Similarly, the intervention group in the trial by Svetkey et al.[26] had a fertility rate of 4.7% (8/169) and received coaching on a moderately hypocaloric diet from a dietitian or through a smartphone application. Two trials that utilized smartphone or text-message based interventions, Shapiro et al.[24] and Fischer et al.[17] also had high fertility rates of 5.5% (3/54) and 5.4% (3/55), respectively. Participants in the most restrictive intervention, a very-low-calorie diet of 800–820 kcal/day with an exercise program in the trial by Taheri et al.[33] had a fertility rate of 4.7% (1/21). Two of the interventions based on commercial weight loss programs,[21,34] were strongly associated with an increased fertility rate and had a risk ratio of 17.41, and 7.17 respectively. However, the third[22] was less significant, with a risk ratio of 3 compared to control. However, all three had extremely wide confidence intervals.

The meta-analysis of three RCTs did not show an association between very-low-carbohydrate diets and fertility, compared to low-fat diets. McGrice and Porter[6] undertook a systematic review of lower-carbohydrate diets (<45% total energy obtained from carbohydrates) compared to control groups and found that a lower carbohydrate diet may increase the fertility rate in women with fertility concerns. However, the evidence was not based on RCTs of very-low-carbohydrate diets (<40 g/day) versus low-fat diets.

The meta-analysis of data from 21 RCTs has shown that weight loss interventions are effective, with a MD of −2.4 kg compared to control groups. The mean weight loss achieved at follow-up ranged from −2.6 kg in the trial by Duncan et al.[31] who utilized a smartphone app-based intervention and a 500 kcal/day deficit diet, to −12 kg in the trial of a very-low calorie (800–820 kcal/day) diet by Taheri et al.[33] The three trials in which intervention group participants achieved a weight loss less than 1.4 kg at follow-up[17,25,30] gave no specified calorie limit and provided participants with dietary advice. These findings suggest that a stricter degree of restriction may be more effective in achieving substantial weight loss. One trial[31] reported greater weight loss in their control group, who received no intervention. However, both the intervention and control groups in that trial had significant reductions in weight from baseline.

The most significant weight loss compared to control groups was seen in trials that provided the intervention groups with pre-packaged food items,[21,22,33] with a MD of −8 kg, −5.9 kg, and −4.8 kg. This supports findings from a systematic review by Astbury et al.[38] who reported that weight loss programs incorporating meal replacements led to greater weight loss at 12 months than comparator programs.

It was discovered that very-low-carbohydrate diets were only slightly more effective for weight loss than low-fat diets (MD −0.32 kg, 95% CI −3.84 to −3.21, $I^2 = 82\%$). The trial by Bazzano et al.[35] contributed significantly to the results and was the only trial in which the MD in weight loss favored the low-carbohydrate group. The very-low-carbohydrate intervention in the trial by Bazzano et al.[35] was the least restrictive, with no specified calorie limit. Interestingly, this trial also supplied participants with meal replacement products to achieve the prescribed diet. That trial also showed significantly lower attrition.

The attrition rate varied across the 24 included RCTs of diet-based weight loss versus control interventions, ranging in intervention groups from 1.2%[10] to 53.8%.[31] No class of intervention was shown to be superior in retaining participants. However, high attrition rates were seen in those that were primarily digital-based. A systematic review by Beleigoli et al.[39] found that digital-based weight loss interventions were superior to control for short-term (<6 months), but not long-term, weight loss, and attrition at follow-up was high.

The present review has several strengths. The lack of studies undertaken in this area necessitated a novel approach to finding pregnancy outcome data, and by extracting pregnancy-related losses to follow-up, it was possible to address the gap in the current evidence base. Another strength was contact with the authors, allowing for the gain of unreported information or clarification of that which was unclear, and the inclusion of five additional RCTs.

The present study also has some limitations. The trials included in the review were not primarily designed to examine the effect of weight loss on fertility. This meant that beyond drop-outs due to pregnancy, the trials had no extractable data on live births and miscarriage. In addition, the time point in studies at which these drop-outs due to pregnancies occurred and the weight loss achieved by the time of drop-out were not reported. Although the majority of studies excluded women who were pregnant or planning a pregnancy at recruitment, the assessment of this was not detailed in the reports. It is therefore possible that participants who dropped out due to pregnancy had become pregnant before randomization. Additional pregnancies occurring towards the end of the follow-up period of the study may also have gone unreported. Three cluster-randomized trials were included in the present review, for which it was not possible to extract reliable weight-change data for the secondary outcome and thus were omitted from the meta-analysis for weight. Trials identified from the search strategy that had a follow-up of less than 12 months and in which the mean cohort BMI was below 30 were excluded. Therefore several trials with pregnancy-related drop-outs that were too short or undertaken in an overweight cohort were not evaluated. Finally, as some studies included both male and female participants and did not report weight outcomes by sex, both both sexes were included for the secondary outcome of weight change.

To evaluate the effect of obesity on fertility more conclusively, trials of weight loss interventions should report pregnancy outcomes and drop-out data in detail. Future research to examine modes of delivery, the optimal duration and intensity of interventions, and body weight targets for optimum fertility should be examined.

AUTHOR CONTRIBUTIONS

BRB and AA designed the study. BRB, CO, AA, ADA, DR, and LW undertook the literature search. Four authors independently confirmed the study eligibility (BRB, AA, CO, and ADA). BRB and CO extracted data, which were checked by AA, and any disparities were resolved by discussion. The authors of articles were contacted in the case of missing data by BRB. Quality assessment was independently undertaken by two authors (AA and BRB) using the Cochrane risk of bias tool version 1, and any disagreement was resolved by discussion. JH undertook the Bayesian data analysis. BRB wrote the first draft. All authors provided comments on drafts.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available in article supplementary material.

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REFERENCES

1. Poston L, Caleyachetty R, Cnattingius S, et al. Preconceptional and maternal obesity: epidemiology and health consequences. *Lancet Diabetes Endocrinol*. 2016;4(12):1025-1036.
2. Kominiarek M, Chauhan S. Obesity before, during, and after pregnancy: a review and comparison of five national guidelines. *Am J Perinatol*. 2016;33(5):433-441.
3. Jacob C, Killeen S, McAuliffe F, et al. Prevention of noncommunicable diseases by interventions in the preconception period: a FIGO position paper for action by healthcare practitioners. *Int J Gynecol Obstet*. 2020;151:6-15.
4. Avenell A, Robertson C, Skea Z, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. *Health Technol Assess*. 2018;22(68):1-246.
5. Hunter E, Avenell A, Maheshwari A, Stadler G, Best D. The effectiveness of weight-loss lifestyle interventions for improving fertility in women and men with overweight or obesity and infertility: a systematic review update of evidence from randomized controlled trials. *Obes Rev*. 2021;22(12):e13325.
6. McGrice M, Porter J. The effect of low carbohydrate diets on fertility hormones and outcomes in overweight and obese women: a systematic review. *Nutrients*. 2017;9(3):204.
7. Moher D, Liberati A, Tetzlaff J, Altman DG, for the PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA stateme. *BMJ*. 2009;339:b253.
8. Avenell A, Broom J, Brown T, et al. Systematic review of the longterm effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess*. 2004;8:1-182.
9. Berry D, Schwartz T, McMurray R, et al. The family partners for health study: a cluster randomized controlled trial for child and parent weight management. *Nutr Diabetes*. 2014;4(1):10.
10. Bhopal R, Douglas A, Wallia S, et al. Effect of a lifestyle intervention on weight change in south Asian individuals in the UK at high risk of type 2 diabetes: a family-cluster randomised controlled trial. *Lancet Diabetes Endocrinol*. 2014;2(3):218-227.
11. Jenkins D, Boucher B, Ashbury F, et al. Effect of current dietary recommendations on weight loss and cardiovascular risk factors. *J Am Cardiol*. 2017;69(9):1103-1112.
12. Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Cochrane; 2021; (Version 6.2, Available from www.training.cochrane.org/handbook).
13. Egger M, Davey-Smith G, Phillips A. Meta-analysis: principles and procedures. *BMJ*. 1997;315:1533-1537.
14. Bacon L, Keim N, Van Loan M, et al. Evaluating a 'non-diet' wellness intervention for improvement of metabolic fitness, psychological well-being and eating and activity behaviors. *Int J Obes Relat Metab Disord*. 2002;26(6):854-865.
15. Bennett G, Steinberg D, Askew D, et al. Effectiveness of an app and provider counseling for obesity treatment in primary care. *Am J Prev Med*. 2018;55(6):777-786.
16. Daumit G, Dickerson F, Wang N, et al. A behavioral weight-loss intervention in persons with serious mental illness. *N Engl J Med*. 2013;368(17):1594-1602.
17. Fischer H, Fischer I, Pereira R, et al. Text message support for weight loss in patients with prediabetes: a randomized clinical trial. *Diabetes Care*. 2016;39:1364-1370.
18. Fitzgibbon M, Stolley M, Schiffer L, et al. Obesity reduction black intervention trial (ORBIT): 18-month results. *Obesity*. 2010;18(13):2317-2325.
19. Godino J, Merchant G, Norman G, et al. Using social and mobile tools for weight loss in overweight and obese young adults (project SMART): a 2 year, parallel-group, randomised, controlled trial. *Lancet Diabetes Endocrinol*. 2016;4(9):747-755.
20. Perri M, Limacher M, Castel-Roberts M, et al. Comparative effectiveness of three doses of weight-loss counseling: two-year findings from the rural LITE trial. *Obesity*. 2014;22(11):2293-2300.
21. Rock C, Flatt S, Sherwood N, et al. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA*. 2010;304(16):1803-1810.
22. Rock C, Pakiz B, Flatt S, et al. Randomized trial of a multifaceted commercial weight loss program. *Obesity*. 2007;15(4):939-949.
23. Rosas L, Thiyagarajan S, Goldstein B, et al. The effectiveness of two community-based weight loss strategies among obese, low-income US Latinos. *J Acad Nutr Diet*. 2015;115(4):537-550.
24. Shapiro J, Koro T, Doran N, et al. Text4Diet: a randomized controlled study using text messaging for weight loss behaviors. *Prev Med*. 2012;55(5):412-417.
25. Steinberg D, Christy J, Batch B, et al. Preventing weight gain improves sleep quality among black women: results from a RCT. *Ann Behav Med*. 2017;51(4):555-566.
26. Svetkey L, Batch B, Lin P, et al. Cell phone intervention for you (CITY): a randomized, controlled trial of behavioral weight loss interventions for young adults using mobile technology. *Obesity*. 2015;23(11):2133-2141.
27. Trepanowski J, Kroeger C, Barnosky A, et al. Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults: a randomized clinical trial. *JAMA Intern Med*. 2017;177(7):930-938.
28. Wadden T, Volger S, Sarwer D, et al. A two-year randomized trial of obesity treatment in primary care practice. *N Engl J Med*. 2011;365(21):1969-1979.
29. McConnon A, Kirk S, Cockcroft J, et al. The internet for weight control in an obese sample: results of a randomised controlled trial. *BMC Health Serv Res*. 2007;7:206.
30. Ross R, Lam M, Blair S, et al. Trial of prevention and reduction of obesity through active living in clinical settings: a randomized controlled trial. *Arch Intern Med*. 2012;172(5):414-424.
31. Duncan M, Fenton S, Brown W, et al. Efficacy of a multi-component m-health weight-loss intervention in overweight and obese adults: a randomised controlled trial. *Int J Environ Res Public Health*. 2020;17(17):6200.
32. Öst L, Götestam K. Behavioral and pharmacological treatments for obesity: an experimental comparison. *Addict Behav*. 1976;1(4):331-338.
33. Taheri S, Zaghloul H, Chagoury O, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2020;8(6):477-489.
34. Jebb S, Ahern A, Olson A, et al. Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial. *Lancet*. 2011;378(9801):1485-1492.

35. Bazzano L, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med*. 2014;161(5):309-318.
36. Foster G, Wyatt H, Hill J, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med*. 2010;153(3):147-157.
37. Goldstein T, Kark J, Berry E, et al. The effect of a low carbohydrate energy-unrestricted diet on weight loss in obese type 2 diabetes patients – a randomized controlled trial. *Espen Eur E J Clin Nutr Metab*. 2011;6(4):e178-e186.
38. Astbury N, Piernas C, Hartmann-Boyce J, et al. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obes Rev*. 2019;20:569-587.
39. Beleigoli A, Andrade A, Cançado A, et al. Web-based digital health interventions for weight loss and lifestyle habit changes in overweight and obese adults: systematic review and meta-analysis. *J Med Internet Res*. 2019;21(1):298.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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